Musculoskeletal Infection Society

32ND Annual Open Scientific Meeting

MUSCULOSKELETAL INFECTION SOCIETY

August 5-6, 2022

PITTSBURGH, PENNSYLVANIA

IN PERSON AND VIRTUAL MEETING

Please join us!

33rd Annual Open Scientific Meeting

of the

Musculoskeletal Infection Society

MUSCULOSKELETAL INFECTION SOCIETY

SALT LAKE CITY
UTAH

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for updates

Objectives

At the conclusion of this educational activity, participants will:

- Understand the utility of articulating spacers, antibiotic loaded cement, and intraosseous vancomycin in the management of musculoskeletal infections;

- 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 physicians including orthopaedic surgeons, infectious disease specialists 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 this Other activity, MSIS 31st Annual Open Scientific Virtual Meeting, for a maximum of ***10.5 AMA PRA Category 1 Credits™***. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Course Director and Musculoskeletal Infection Society President

Brian A. Klatt, 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

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MUSCULOSKELETAL INFECTION SOCIETY

32nd Annual Open Scientific Meeting
August 5-6, 2022
Pittsburgh, PA

AGENDA

Virtual =All times noted are EASTERN DAYLIGHT TIME

Friday, August 5, 2022
Grand Station 1-2

7:00am	Registration Opens
7:00-8:00am *Grand Station 3-5*	Breakfast **Visit Exhibitors and e-Posters**
7:50-7:59am	Welcome, Disclosures Brian A. Klatt, MD
Session I	**DIAGNOSTICS** Moderators: Drs. Alberto Carli and Julie Reznicek
8:00-8:06am	Synovial Fluid Microorganism Antigen Testing Demonstrates Good Nationwide Performance ***Carl Deirmengian**, Brett Levine, Alex McLaren, Alvin Ong, Pearl Paranjape*
8:07-8:13am	Utility of Synovial Biomarkers in the Diagnosis of Acute PJI ***Saad Tarabichi**, Graham Goh, Colin Baker, Matthew Sherman, Diana Fernández-Rodriguez, Javad Parvizi*
8:14-8:20am	Far from perfect: Synovial fluid next-generation sequencing (NGS) in diagnosing periprosthetic joint infection *Tejbir Pannu, **Jesus M Villa**, Preston Grieco, Jorge Manrique, Aldo Riesgo, Alison Klika*

8:21-8:27am	The Utility of Next Generation Sequencing in Revision TJA ***Colin Baker**, Karan Goswami, Saad Tarabichi, Graham Goh, Javad Parvizi*
8:28-8:36am	Discussion
8:37-8:43am	A New Tool for C. acnes Detection: Antigen Immunoassay *Krista Toler, Pearl Paranjape, Alex McLaren, **Carl Deirmengian***
8:44-8:50am	The Impact of Specimen Transport Time on Synovial Fluid Culture is Minimal *Krista Toler, Van Thai-Paquette, **Alex McLaren**, Carl Deirmengian*
8:51-8:57am	Diagnosing prosthetic joint infection in total hip arthroplasty: a comparison of fluoroscopic- and ultrasound-guided hip aspiration ***Emily Boes**, Michael Archibeck, John Wheelwright, Brenna Blackburn, Masaru Teramoto, Daniel Cushman*
8:58-9:06am	Discussion
SYMPOSIUM #1	**Critical Role of FDG-PET in the Management of MSK infections**
9:07-9:27am	Abass Alavi, MD Professor, Department of Radiology Pearlman School of Medicine, University of Pennsylvania
9:28-9:38am	Discussion
Session II	**BASIC SCIENCE – 1** Moderators: Drs. Kenneth Urish and Laura Certain
9:39-9:45am	Arthroplasty Surgery Alters the Local Immune Composition of the Knee Joint ***Kyle Cichos**, Vidya Sagar Hanumanthu, Chander Raman, Elie S Ghanem*
9:46-9:52am	Characterizing the Local Immune Environment in a Murine Model of Periprosthetic Joint Infection (PJI) ***Christopher Hamad**, Joseph K Kendal, Zeinab Mamouei, Nicholas Peterson, Alan Li, Jeremiah Taylor, Abdulrahman Almalouhi, Parsa Asachi, Micheal Yeaman, Nicholas Bernthal*
9:53-9:59am	Prospective ex vivo activity of PLG0206, an engineered antibacterial peptide, on chronic periprosthetic joint infection total knee arthroplasty components: the Knee Explant Analysis (KnEA) Study *Dana Parker, Kimberly Brothers, Jonathan Mandell, John Koch, Despina Dobbins, Jonathan Steckbeck, David Huang, **Kenneth Urish***

10:00-10:06am Development of a PJI microJoint Bioreactor for the study of Bacteriophage Activity
***Beth Knapick**, Dana Parker, Kimberly Brothers, Peter Alexander, James Doub, Kenneth Urish*

10:07-10:13am An Engineered Antimicrobial Peptide, PLG0206, Reduces Biofilm Mass and Increases Survival in a Rabbit Model of Staphylococcus aureus Periprosthetic Joint Infection
***Kimberly Brothers**, Jonathan Mandell, Masashi Taguchi, Dana Parker, Peter Alexander, Despina Dobbins, David Huang, Nicholas Pachuda, Kenneth Urish*

10:14-10:24am Discussion

10:25-10:39am Break
Visit Exhibitors and ePosters

SYMPOSIUM #2 **Antibiotics and Diagnostics 201 – taking your knowledge to the next level**
Moderator: Dr. Laura Certain

10:40-11:00am Peri-operative Antibiotic Choices
Sandra Nelson, MD
Massachusetts General Hospital

11:01-11:21am Infection Diagnostics
Robin Patel, MD
Mayo Clinic

11:22-11:42am Oral Antibiotics for Bone and Joint Infections
Nicolas Cortes-Penfield, MD
University of Nebraska Medical Center

11:43-11:53am Discussion

Session III **REIMPLANTATION**
Moderators: Drs. Antonia Chen and Meredith Schade

11:54am-12:00pm The 2018 ICM definition of periprosthetic hip and knee infection is of no value in determining the outcome of reimplantation in two-stage revision
Tejbir S Pannu, Jesus M Villa, Nicolas Piuzzi, Aldo M Riesgo,
***Carlos Higuera-Rueda,** Alison Klika*

12:01-12:07pm	Utility of Diagnostic Tests Prior to Reimplantation in Patients Undergoing Two-Stage Revision Total Joint Arthroplasty: A Systematic Review and Meta-Analysis ***Irfan Khan**, Brandon Boyd, Antonia Chen, Nicholas Cortes-Penfield, Thomas Myers, Timothy Brown, Gina Suh, Gerald McGwin, Elie Ghanem, Yale Fillingham*
12:08-12:14pm	Utility of Synovial Biomarkers in Predicting Failure following Reimplantation ***Saad Tarabichi**, Graham Goh, Irfan Khan, Colin Baker, Javad Parvizi*
12:15-12:21pm	Diagnostic Utility and Thresholds for Commonly Obtained Serum and Synovial Markers prior to Reimplantation in Periprosthetic Joint Infection ***Abhijit Seetharam**, Julian Dilley, R. Michael Meneghini, Michael Kheir*
12:22-12:28pm	Is Joint Aspiration Needed before Reimplantation? ***Emanuele Chisari**, Leanne Ludwick, Taylor D'Amore, Jenna Mandel, Brendan Gleason, Javad Parvizi*
12:29-12:39pm	Discussion
12:40-1:14pm *Grand Station 3-5*	Lunch "Box Lunch" **Visit Exhibitors and e-Posters**
SYMPOSIUM #3	**Musculoskeletal Infection** **Literature review of economic impact and advocacy issues**
1:15-1:30pm	Brian A Klatt, MD Assistant Professor, Department of Orthopaedic Surgery University of Pittsburgh
Session IV	**OUTCOMES AND ECONOMICS OF MUSCULOSKELETAL INFECTION** Moderators: Drs. Jessica Seidelman and Michael O'Malley
1:31-1:37pm	Financial Burden of Septic Total Hip Arthroplasty Revisions Compared to Aseptic Ones - Call for New Procedural Coding? *Jesus Villa, Tejbir Pannu, Robert Eysler, Alison Klika, **Carlos Higuera-Rueda***

1:38-1:44pm	Financial Burden of Septic Total Knee Arthroplasty Revisions Compared to Aseptic Ones - Call for New Procedural Coding? ***Jesus Villa**, Tejbir Pannu, Robert Eysler, Alison Klika, Wael Barsoum, Carlos Higuera-Rueda*
1:45-1:51pm	Onoderaâ€™s prognostic nutritional index a valuable measure in predicting complications after TKA ***Alisina Shahi**, Tae Kim, Matthew Brown, Ali Oliashirazi*
1:52-1:58pm	An externally validated algorithm for prediction of in-hospital and ninety-day mortality after spinal epidural abscess ***Akash Shah**, Aditya Karhade, Olivier Groot, Thomas Olson, Joseph Schwab*
1:59-2:05pm	Factors Associated With Periprosthetic Joint Infection in Hip Hemiarthroplasty *Jonathan Bourget-Murray, Isabel Horton, Jared Morris , Antoine Bureau, Simon Garceau, Hesham Abdelbary, George Grammatopoulos, **Nicholas Tubin***
2:06-2:16pm	Discussion
2:17-2:23pm	Cutibacterium acnes Native Vertebral Osteomyelitis: A Case Series ***Matteo Passerini**, Julian Maamari, Don Bambino Geno Tai, Zelalem Temesgen, Aaron Tande, Elie Berbari*
2:24-2:30pm	Incidence of Unexpected Positive Sonication Results in Presumed Aseptic Knee and Hip Revision Arthroplasty ***Alan Wilson**, Stuti Patel, Johannes Plate, Michael O'Malley, Brian Klatt*
2:31-2:37pm	Skin microbiome and effect of decolonization ***Diana Fernández-Rodriguez**, Jeongeun Cho, Emanuele Chisari, Javad Parvizi*
2:38-2:44pm	Streptococcal Periprosthetic Joint Infections: Prognosis and Outcomes ***Colleen Wixted**, Andy Schwartz, Billy Kim, Isabel Prado, Breanna Polascik, Edward Hendershot, Michael Bolognesi, William Jiranek, Jessica Seidelman, Thorsten Seyler*
2:45-2:51pm	A Multicenter Prospective Investigation on Physical and Mental Health After Girdlestone Resection Arthroplasty ***Colleen Wixted**, Breanna Polascik, Niall Cochrane, Sean Ryan, Ran Schwarzkopf, Antonia Chen, Thorsten Seyler*
2:52-3:02pm	Discussion

3:03-3:19pm	Break **Visit Exhibitors and e-Posters**
SYMPOSIUM # 4	**Coding in Musculoskeletal Infection Care for Ortho and ID doctors** Moderators: Drs. Brian Klatt and Angela Hewlett
3:20-4:45pm	Matthew Twetten, MA, MHCDS Karen Zupko & Associates
4:46-5:30pm	Discussion
5:30pm	Adjourn **Visit Exhibitors and e-Posters**
6:00pm	**Join us for the Presidents Reception in the *Reflections Room*** Cocktails and Dinner Buffet Dress: Business Casual

Saturday, August 6, 2022

6:30-8:00am *Grand Station 3-5*	Breakfast **Visit Exhibitors and e-Posters**
7:00-7:45am	MSIS Business Meeting (MSIS Members only)
Session V	**BASIC SCIENCE - 2** Moderators: Drs. Kenneth Urish and Laura Certain
8:00-8:06am	Non-Eluting Zimmer Bactiguard Implant Coating Provides Early Protection Against Infection in a Murine Model of Periprosthetic Joint Infection (PJI) ***Zeinab Mamouei**, Christopher Hamad, Nicholas Peterson, Joseph Kendal, Alan Li, Jeremiah Taylor, Abdulrahman Almalouhi, Aaron Kavanaugh, Fabrizio Billi, Nicholas M Bernthal*
8:07-8:13am	Irrigation and Brush Sonication remove mature staphylococcal biofilm on clinical orthopedic implants: An in-vitro evaluation ***Zachary Coles**, Christina A Chao, Tyler Khilnani, Mathias Bostrom, Alberto Carli*

8:14-8:20am	Combined DAIR and PhotothermAA Gel Decreases Implant Biofilm Burden and Soft Tissue Infection in a Rabbit Model of PJI, A Pilot Study ***Anabelle Visperas**, Nathalie Milbrandt, Pedro Rullan, Yu Hsin Tsai, Zhifei Ye, Dehau Jiang, Nicolas Piuzzi, Alison Klika, Anna Cristina Samia, Carlos Higuera*
8:21-8:27am	Do antiseptic irrigation solutions have different efficacies on different orthopedic surfaces against staphylococcal biofilm? An in-vitro evaluation ***Tyler Khilnani**, Zachary Coles, Christina Chao, Mathias Bostrom, Alberto Carli*
8:28-8:34am	Periprosthetic Joint Infection and the Trojan Horse Theory: Examining the Role of Gut Dysbiosis and Epithelial Integrity ***Emanuele Chisari**, Jeongeun Cho, Marjan Wouthuyzen-Bakker, Javad Parvizi*
8:35-8:45am	Discussion

SYMPOSIUM # 5

8:46-9:40am	**A Survey of the annual meeting of the MSIS** Moderator: Dr. Javad Parvizi
9:41-9:59am	Break **Visit Exhibitors and e-Posters**
Session VI	**CLINICAL MANAGEMENT OF MUSCULOSKELETAL INFECTIONS** Moderators: Drs. Matthew Dietz and Neel Shah
10:00-10:06am	An externally validated algorithm predicts failure of non-operative management for spinal epidural abscess ***Akash Shah**, Aditya Karhade, Olivier Groot, Thomas Olson, Joseph Schwab*
10:07-10:13am	Closed Incision Negative Pressure Therapy Reduces Incidence of Re-Operation for Surgical Site Infection in Spine Surgery ***Anthony Oyekan***
10:14-10:20am	Subspecialty Training Improves Treatment Success Following Debridement, Antibiotics, and Implant Retention in Total Knee Arthroplasty ***Nicholas Tubin**, Jonathan Bourget-Murray, Isabel Horton, Antoine Bureau, Hesham Abdelbary, George Grammatopoulos, Simon Garceau, Jared Morris*

10:21-10:27am Childs-Pugh Class B/C Increases Risk of Early Mortality in HCV Patients Undergoing Elective TJA Regardless of Treatment Status
***Kyle Cichos**, Antonia F Chen, Erik N Hansen, Eric Jordan, Kian Niknam, Gerald McGwin Jr, Elie Ghanem*

10:28-10:38am Discussion

10:39-10:45am Impact of Bacterial Phenotypic Variation with Bacteriophage therapy: A Pilot Study with Prosthetic Joint Infection Isolates
***James Doub**, Ken Urish, Martin Lee*

10:46-10:52am Low Friction Spacers for Two-Stage Exchange Show Decreased Bacterial Colonization Compared to Cement Molds and Static Spacers
***Brandon Couch**, Alan Wilson, Frank Plate, Brian Klatt, Michael O'Malley*

10:53-10:59am Incidence of PJI Following Extensor Mechanism Reconstruction in TKA Patients
***Colin Baker**, Peter Gold, Qudratullah Qadiri, Andrew Hughes, Paul Courtney*

11:00-11:06am What is the relevance of the presence or absence of effusion around a total knee replacement scheduled for aspiration? When should we perform a lavage?
*Bashiar Thejeel, Joseph Nguyen, **Alberto Carli**, Theodore Miller*

11:07-11:17am Discussion

11:18-11:40am **Introduction of Incoming President: Laura Certain, MD PhD**
Brian A Klatt, M.D.
Presentation of Awards
Jon T. Mader Award
Jeanette Wilkins Award
e-Poster Award
Closing Remarks; *Brian A Klatt, MD*

Adjourn

2022 MSIS ePosters

Monitor 1

22-AEP-1035	Risk Factors for Surgical Site Infection after Operative Management of Pilon Fractures *Brandon Boyd, Anthony Wilson, Kyle cichos, Sudarsan Murali, Alexander Mihas, David Patch, Gerald McGwin, Michael Johnson, Clay Spitler, Elie Ghanem*
22-AEP-975	Combining Bacteriophage and Vancomycin is More Efficacious in Treating MRSA Aggregates Formed in Human Synovial Fluid Compared to Using Vancomycin or Bacteriophage Alone *Mariam Taha, Hesham Abdelbary*
22-AEP-921	Serum Glucose Variability Increases the Risk of Complications Following Aseptic Revision Hip and Knee Arthroplasty *Graham S Goh, Ilan Small, Terence L Thomas, Mohammad S Abdelaal, Noam Shohat, Javad Parvizi*
22-AEP-897	Staphylococcus aureus strains Causing Mild, Moderate, and Severe Illness among Children with Acute Hematogenous Osteomyelitis Demonstrate Unique Transcriptional Pathways *Lawson Copley, Lawson A Copley, Laura Filkins, Yared Kidane*
22-AEP-955	Pharmacokinetic Profile of 7-Day Local Irrigation of Vancomycin and Tobramycin for Treatment of Periprosthetic Joint Infection *Kevin Warner, Brian de Beaubien , Bradley Reddick, Kenneth Urish, Bryan Springer*
22-AEP-948	Increased Surgical Site Subcutaneous Fat Thickness Is Associated with Infection after Lumbar Laminectomy with Instrumented Fusion *Anthony A Oyekan, James Rooney, Dominic Ridolfi, Jay Dalton, Aaron Zheng, Stephen R Chen, Melissa Tang, Emmett J Gannon, Joon Y Lee, Jeremy D Shaw*
22-AEP-1023	Sarcopenia Increases the Risk of Mortality but not SSI after Acetabular ORIF *Kyle H Cichos, Gerald McGwin Jr, Elie S Ghanem*
22-AEP-942	Low Dose Aspirin for VTEp Results in Lower PJI Rates *Farideh Najafi, Joseph K Kendal, Nicholas V Peterson, Kerri-Anne Ciesielka, Diana Fernandez-Rodriguez , Camilo Restrepo, Javad Parvizi, Nicholas M Bernthal*

Monitor 2

22-AEP-899	Hemoglobin A1c as a Predictor of Surgical Site Infection in Orthopaedic Trauma Patients *Steven T Greene, Tyler McGee, Taylor Kot, Priyanka Nehete, Eldrin Bhanat, Patrick Bergin*
22-AEP-1034	Re-Infection after 2-Stage Exchange for PJI: Can the Organism be Predicted? *Andrew J Clair, Rory Metcalf, Bryan D Springer, Thomas K Fehring, Susan M Odum, Taylor M Rowe, Jesse E Otero*
22-AEP-902	High Mortality After Revision TKA for PJI is Related to Preoperative Morbidity and the Disease Process but Not Treatment *Nicholas P Drain, Dominique M Bertolini, Austin W Anthony, Muhammad W Feroze, Richard Chao, Sadie E Longo, Neel B Shah, Kenneth L Urish*
22-AEP-911	Hardware removal due to infection after open reduction and internal fixation: trends and predictors. *Alisina Shahi, Ali Oliashirazi*
22-AEP-1042	Mask-wearing practices during COVID-19 do not influence pre-operative S. aureus colonization rates *Cameron G Thomson, Erin S Grawe, Jorge H Figueras, Kimberly A Hasselfeld, Anthony F Guanciale*
22-AEP-941	Closed Suction Drains after Revision for Infected TJA May Not be Necessary *Farideh Najafi, Michael Meghpara, Jonah M Stein, Matthew Sherman, Nicholas V Peterson, Camilo Restrepo, Javad Parvizi*
22-AEP-1018	Pseudomonas Prosthetic Joint Infections: Is there a role for monotherapy? *Billy I Kim, Andrew M Schwartz, Colleen Wixted, Isabel Prado, Breanna Polascik, Edward Hendershot, Michael Bolognesi, William Jiranek, Jessica Seidelman, Thorsten M Seyler*
22-AEP-943	Sterile Back Table in the OR Can Harbor Infective Pathogens *Farideh Najafi, Diana FernÃ¡ndez-RodrÃ-guez , Javad Parvizi*

Monitor 3

22-AEP-905 The Engineered Antimicrobial Peptide, PLG0206, has Potent Biofilm and Planktonic Activity Against Multi-Drug Resistant ESKAPE Organisms
Jonathon B Mandell, Kimberly M Brothers, Dean Shinabarger, Christopher Pillar, Despina Dobbins, Nicholas Pachuda, David B Huang, Jonathan Steckbeck, Kenneth L Urish

22-AEP-903 Sub-Optimal Dosing of Vancomycin Increases Rates of Biofilm Formation and Surgical Infection in an Animal Model
Kimberly M Brothers, Dana M Parker, Masashi Taguchi, Kenneth L Urish

22-AEP-916 Assessment of Staphylococcal Clinical Isolates from Periprosthetic Joint Infections for Potential Bacteriophage Therapy
Brian J De Palma, Sumon Nandi, Waqas Chaudhry, Martin Lee, Aaron J Johnson, James B Doub

22-AEP-908 The Joint Microenvironment Decreases MRSA Resistance to Cefazolin
Charles G Gish, Dana M Parker, kimberly M Brothers, Kenneth L Urish

22-AEP-1030 Intrawound Vancomycin Powder does not Alter Biologic Stability (Osseointegration) in a Murine Model of Joint Arthroplasty
Christopher D Hamad

22-AEP-926 mazEF toxin anti-toxin mediated regulation of Staphylococcus aureus biofilm growth and antibiotic tolerance
Jonathan B Mandell, Charles Gish, Dana Parker, Kimberly Brothers, Kenneth L Urish

22-AEP-937 New Era in Understanding Periprosthetic joint infections: Microbiome, Antigen Trafficking and The Breach in Gut Epithelia Barrier
Emanuele Chisari, Jeongeun Cho, Marjan Wouthuyzen-Bakker , Javad Parvizi

22-AEP-969 Staphylococcal aggregate morphology and protection from antibiotics is dependent on unique mechanisms arising from various postsurgical joint composition and fluid motion
Amelia M Staats , Peter W Burback , Daniel Li, Anne Sullivan , Paul Stoodley

Monitor 4

22-AEP-984 The Majority of Biofilm Studies in Orthopedic Surgery Lack Direct Visualization of Biofilm and Utilize and In Vitro Study Design: Results of a Systematic Review
Daniel A Driscoll, Tyler K Khilnani, Ajay Premkumar, Sita Nirumpama Nishtala, Mathias P Bostrom, Alberto V Carli

22-AEP-1037 The influence of micro structured surface features on the accumulation of bovine synovial fluid induced aggregates of Staphylococcus aureus
Tripti T Gupta, Niraj K Gupta, Khushi Patel, Paul Stoodley

22-AEP-907 Methicillin resistance in Staphylococcus aureus is media dependent
Charles G Gish, Jonathan B Mandell , Kimberly M Brothers, John A Koch, Kenneth L Urish

22-AEP-970 Mitochondrial Response to In Vivo Prosthetic Joint Infection (PJI)
Nour Bouji, Matthew Dietz

22-AEP-952 Histologic mapping of Staphylococcus Aureus infection in an established PJI cemented hemiarthroplasty hip rat model at acute and chronic stages
Hesham Abdelbary

22-AEP-922 Disrupting Biofilms from Titanium with a CHG Antimicrobial Irrigation System
Isabel Laubach, Jessica Sanders, Marnie Peterson, Carolyn Twomey, Tanya Eberle

22-AEP-990 Establishment of a Novel Gram-Negative Prosthetic Joint Infection Rat Model Using Uncemented Hip Hemiarthroplasty
Mazen M Ibrahim, Hesham Abdelbary, Thien F Mah

22-AEP-940 Synovial CRP is a Useful Adjunct for Diagnosis of Periprosthetic Joint Infection
Colin M Baker, Graham S Goh, Saad Tarabichi, Noam Shohat, Javad Parvizi

Monitor 5

22-AEP-920	Culture Results Cannot Always Be Relied on During Revision Total Joint Arthroplasty: A Multicenter Study *Graham S Goh, Saad Tarabichi, Colin M Baker, Luigi Zanna, Mustafa Citak, Javad Parvizi*
22-AEP-961	Absolute Neutrophil Count: a Marker for Diagnosis of Chronic Periprosthetic Joint Infection *Troy D Bornes, Allina A Nocon, Jonathan S Yu, John Rezkalla, Mark P Youssef, David J Mayman, Alberto V Carli, Peter K Sculco*
22-AEP-927	Serum D-Dimer: A Promising Marker to Guide Timing of Reimplantation *Saad Tarabichi, Graham S Goh, Colin M Baker, Karan Goswami, steven Yacovelli, Javad Parvizi*
22-AEP-910	Synovial fluid absolute neutrophil count a promising marker for diagnosing periprosthetic joint infection *Alisina Shahi, Ali Oliashirazi, Tae W Kim, Javad Parvizi*
22-AEP-929	When Do Cultures First Turn Positive in Patients with PJI? *Saad Tarabichi, luigi zanna, Qudratullah qadiri, graham S goh, Mustafa Citak, javad Parvizi*
22-AEP-1002	Do delta changes in synovial WBC count and PMN% anticipate the outcome of reimplantation? *Tejbir S Pannu, Jesus M Villa, Joseph Palmer, Nicolas Piuzzi, Aldo M Riesgo, Carlos A Higuera*
22-AEP-909	Mapping Bacterial Biofilm on Explanted Orthopedic Hardware: An Analysis of 14 Consecutive Cases *Jacob R Brooks, Matthew Pigott, Douglas Chonko, Anne Sullivan, Kelly Moore, Paul Stoodley*

Monitor 6

22-AEP-1038	Does the timing of antibiotic administration affect culture results in resection arthroplasty for PJI? *John Pinski, Rory Metcalf, Jesse E Otero, Susan M Odum, Taylor M Rowe, Thomas K Fehring*
22-AEP-928	Serum D-dimer: An Excellent Screening Test for Periprosthetic Joint Infection *Saad Tarabichi, Graham S Goh, Colin M Baker, Emanuele Chisari, Alisina Shahi, Javad Parvizi*
22-AEP-934	Polymicrobial PJI Failures: Reinfection or Persistence? *Emanuele Chisari, Leanne Ludwick, Nicolas Piuzzi, Craig Della Valle, Carlos Higuera, Javad Parvizi*
22-AEP-971	Diagnosing Prosthetic Joint Infection in patients with Inflammatory Arthritis *Susan M Goodman, Insa Mannstadt, Kathleen Tam, Alina Nocon, Deanna Jannat-Khah, Andy Miller, Peter Sculco, Mark Figgie, Alberto Carli*
22-AEP-1008	Does performance of D-Dimer for diagnosis of periprosthetic joint infection change with the virulence of infecting organism? *Tejbir S Pannu, Jesus M Villa, Denise Jimenez, Aldo M Riesgo, Carlos A Higuera*
22-AEP-978	Defining the Role of Synovial Alpha-Defensin in the Diagnosis of Periprosthetic Joint Infection *Nathanael D Heckmann, Jennifer C Wang, Paul Won, Brian C Chung, Lucas Mayer, Alexander B Christ, Donald B Longjohn, Daniel A Oakes, Jay R Lieberman*
22-AEP-960	Synovial Absolute Neutrophil Count is an Accurate Diagnostic Marker for Prosthetic Joint Infection in Revision Total Joint Arthroplasty *Abhijit Seetharam, Julian E Dilley, R. Michael Meneghini, Michael M Kheir*
22-AEP-898	Synovial Neutrophil-to-Lymphocyte Ratio and ANC are not Superior to PMN% in detecting PJI *Julian E Dilley, Robert M Meneghini, Michael M Kheir, Abhijit Seetharam*

Monitor 7

22-AEP-1028	Similar 90-day surgical site infection rates between robotic-assisted and manual total knee arthroplasty: A large patient cohort *Antonia F Chen, Laura Scholl, Todd Gutowski, Sietske Witvoet, Daniele De Massari*
22-AEP-1025	History of COVID-19 Infection and the Risk of post-operative VTE after Primary Total Joint Arthroplasty *Nick OgrincHannah Szapary , Alexander Farid , David Novikov, Antonia F Chen , Michael Kain*
22-AEP-914	Total Knee Arthroplasty Can Save Lungs *Alisina Shahi, Ali Oliashirazi, Lawrence Miller*
22-AEP-1019	Rotational Muscle Flap Coverage for Soft Tissue Defects After Prosthetic Knee Infections *Billy Kim, Colleen Wixted, Andrew Schwartz, William Jiranek, Sean Ryan, Thorsten Seyler*
22-AEP-1041	Arthroplasty Surgery Impacts the Local Vitamin D Concentration Within the Knee Joint *Kyle Cichos, Andrzej Slominski, Elie Ghanem*
22-AEP-1032	Permanent articulating spacer versus two-stage exchange for chronic PJI: A propensity-score matched study *Elshaday Belay, Colleen Wixted, Billy Kim, Samuel Wellman, Michael Bolognesi, William Jiranek, Thorsten Seyler*
22-AEP-950	Direct anterior approach in primary THA increases the risk of reoperation for superficial infection but not deep prosthetic joint infection compared to posterolateral approach *Brian P Chalmers, Simarjeet Puri, Adam Watkins, Agnes D Cororaton, Andy O Miller, Alberto Carli, Michael Alexiades*
22-AEP-947	Rate of Recurrent Infections and Implant Removal After Initial Debridement in Spine Surgery *Anthony A Oyekan, Dominic Ridolfi, Aaron Zheng, Audrey Chang, Noel Bien Carlos, Ryan Lin, Brandon Couch, Melissa Tang, Joon Y Lee, Jeremy D Shaw*

Monitor 8

22-AEP-974	Surgical Duration Increases the Risk of Infection Following Total Knee Arthroplasty *Jamie Heimroth, Max L Willinger, Nipun Sodhi, Ariel Henig, Alain Sherman, Jonathan R Danoff*
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MUSCULOSKELETAL
INFECTION SOCIETY

2022

ABSTRACTS

897 Staphylococcus aureus strains Causing Mild, Moderate, and Severe Illness among Children with Acute Hematogenous Osteomyelitis Demonstrate Unique Transcriptional Pathways

Authors Lawson A Copley, Laura Filkins, Yared Kidane

Background and Rationale Children with acute hematogenous osteomyelitis (AHO) demonstrate a broad spectrum of illness, ranging from mild to severe. Substantial genomic heterogeneity exists amongst Staphylococcus aureus (SA) isolates of children with AHO. It is uncertain if genomic variation plays a role in the differentiation of clinical phenotypes.

Study Question The purpose of this study is to determine if there are transcriptional differences among SA strains isolated from children with varying illness severity.

Methods Clinical SA isolates from children with AHO having mild (MSSA-29), moderate (MRSA-12), and severe (MRSA-9) illness were grown under controlled conditions through log phase in Mueller Hinton Broth. RNA isolation and sequencing were performed at 6 timepoints. RNA sequencing libraries were prepared and differentially expressed gene (DEG) analysis followed the NASA RNA-Seq consensus pipeline to provide DEGs sorted by adjusted p-value and log fold-change.

Results SA isolates demonstrated distinctive growth curve patterns. MSSA-29 grew faster and with a steeper log-phase than MRSA-12 and MRSA-9. Principal Component Analysis demonstrated unique transcriptional behavior between the strains. Gene Ontology analysis showed significantly differentiated translation, ribosome activity, glycolytic, and biosynthetic processes. Kyoto Encyclopedia of Genes and Genomes enrichment analysis depicted significantly differentiated pathways with over-expressed behaviors of SA infection, bacterial invasion, and ABC transporters of the moderate and severe strains when compared to the mild strain which favored pathways of biosynthesis and metabolism (Fig 1).

Discussion Transcriptional differences potentially underlie clinical phenotype differentiation among children with AHO. This study is limited by in vitro methodology and does not account the impact of host immunologic response or effects of constrained growth conditions in vivo. However, profound differences of growth and transcription, which were observed in this study, are important in that they establish a tendency of bacterial behavior which appears to make trade-offs of growth and metabolism for mild strains and virulence for severe strains.

Conclusion This study demonstrates unique transcriptional pathways of SA strains isolated from children with AHO with mild, moderate and severe phenotypes.

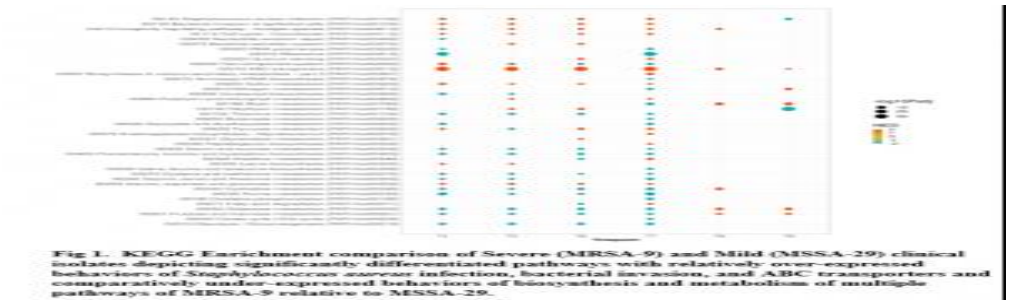


Fig 1. KEGG Enrichment comparison of Severe (MRSA-9) and Mild (MSSA-29) clinical isolates depicting significantly differentiated pathways with relatively over-expressed behaviors of *Staphylococcus aureus* infection, bacterial invasion, and ABC transporters and comparatively under-expressed behaviors of biosynthesis and metabolism of multiple pathways of MRSA-9 relative to MSSA-29.

898 Synovial Neutrophil-to-Lymphocyte Ratio and ANC are not Superior to PMN% in detecting PJI

Authors Julian E Dilley, Robert M Meneghini, Michael M Kheir, Abhijit Seetharam

Background and Rationale Periprosthetic joint infection (PJI) is a devastating complication after total joint arthroplasty (TJA) with a high morbidity, mortality, and cost. Serum and synovial biomarkers are currently used in the diagnosis of PJI. Serum neutrophil-to-lymphocyte (NLR) ratio has shown promise as an inexpensive test in diagnosing infection, but there have been no known reports of synovial NLR or absolute neutrophil count (ANC) in the diagnosis of chronic PJI.

Study Question This studyâ€™s aim was to evaluate the utility of synovial (SF) NLR and absolute neutrophil count (ANC) as a diagnostic tool to predict PJI. We hypothesize that the use of SF NLR and ANC will increase the diagnostic accuracy of PJI when compared with standard criteria and traditional markers of PJI.

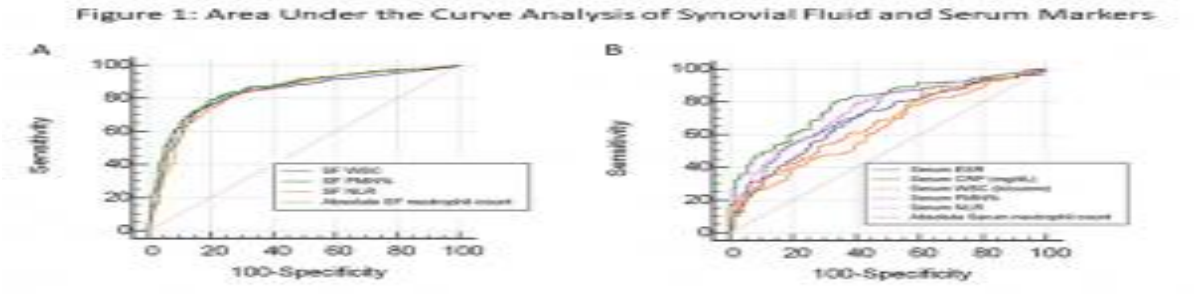
Methods A retrospective review of 730 patients that had a primary total joint arthroplasty and underwent aspiration for chronic PJI or aseptic reasons. SF white blood cell count (WBC), SF polymorphonuclear percentage (PMN%), SF NLR, SF ANC, serum erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP), serum WBC, serum PMN%, serum NLR, and serum ANC had their utility in diagnosing PJI examined by area under the curve analysis (AUC). The Delong test was used to compare AUCs of serum and SF markers.

Results The AUCs for SF WBC, PMN%, NLR, and ANC were 0.835, 0.841, 0.827, and 0.850, respectively. SF ANC was a significantly better diagnostic marker than SF NLR (p=0.027) and SF WBC (p=0.003), but not PMN% (p=0.365) (Fig. 1A). SF NLR was inferior to PMN% (p=0.006), but not different from SF WBC (p=0.510). The AUCs for serum ESR, CRP, WBC, PMN%, NLR, and ANC were 0.695, 0.787, 0.632, 0.724, 0.741, and 0.665, respectively (Fig. 1B). Serum CRP outperformed all other serum markers ($p<0.05$) except for PMN%, and NLR (p=0.051 and p=0.130, respectively). Serum PMN% and NLR were similar to serum ESR (p=0.471 and p=0.237, respectively).

Discussion SF ANC outperformed SF NLR and WBC, but it was similar to PMN%. SF NLR was also found to be inferior to PMN%. However, the lack of superiority to PMN% alone questions the supplemental utility of these tests to the current diagnostic standard.

Conclusion SF ANC and NLR were not superior to the traditional marker, SF PMN%. However, SF ANC had similar performance to PMN% in diagnosing chronic PJI, whereas SF NLR was a poorer diagnostic marker comparatively. As for serum markers, CRP demonstrated the best performance for detecting PJI.

Figure 1: Area Under the Curve Analysis of Synovial Fluid and Serum Markers



899 Hemoglobin A1c as a Predictor of Surgical Site Infection in Orthopaedic Trauma Patients

Authors Steven T Greene, Tyler McGee, Taylor Kot, Priyanka Nehete, Eldrin Bhanat, Patrick Bergin

Background and Rationale Over thirty-four million people in the United States have diabetes mellitus (DM) and use hemoglobin A1c (A1c) to monitor glycemic control. Patients with DM who undergo orthopaedic surgery experience a higher rate of postoperative complications. Prior research involving DM and complications in orthopaedic patients has primarily focused on elective procedures.

Study Question The purpose of this study was to evaluate A1c as a predictor of postoperative surgical site infection (SSI) in orthopaedic trauma patients.

Methods The study aim was addressed via retrospective chart review. Inclusion criteria included patients aged 18 years or older treated surgically for an acute fracture by a fellowship trained orthopaedic trauma surgeon at University of Mississippi Medical Center from July 1, 2012 - December 1, 2020 with a value for A1c available within three months of their surgery. Patients were excluded if they underwent surgery for a diagnosis other than fracture or if they were initially treated for their fracture at an outside hospital. The primary outcome was SSI as defined by â€œFracture related infection: A consensus on definition from an international expert group,â€ by Metsemakers et al. The overall rate of infection for the cohort was calculated. A receiver operating characteristic curve (ROC) was calculated using A1c as a predictor for SSI criteria. SSI in patients with A1c values above and below the cutoff for diagnosis of DM (A1c <6.5) was analyzed using the Pearson Chi-Square Test.

Results 608 patients met criteria for analysis. There were signs of SSI in 18.9% (115/608) of patients. A ROC curve was performed with an area under the curve of 0.530. In patients with normal A1c levels, an infection rate of 17.9% (66/369) was identified. This was similar to the rate of infection in patients meeting criteria for DM (49/239, 20.5%) (p=0.458). In patients with uncontrolled DM (A1c >10), the infection rate was 19.4% (7/36) compared with 18.9% (108/572) in patients with A1c less than 10 (p=1.00).

Discussion Numerous studies have demonstrated higher rates of postoperative complications in patients undergoing elective orthopaedic surgery with elevated A1c values. No statistical significance was identified between the rate of SSI in orthopaedic trauma patients with A1c values above and below the cutoff for diagnosis of DM.

Conclusion A1c did not predict postoperative SSI in this cohort of patients undergoing fracture surgery.

901 Impact of Bacterial Phenotypic Variation with Bacteriophage therapy: A Pilot Study with Prosthetic Joint Infection Isolates

Authors James Doub, Ken Urish, Martin Lee

Background and Rationale Bacteriophage therapy holds promise as a adjuvant in the treatment of prosthetic joint infections. However many aspects of bacteriophage therapy are unknown. Furthermore, given the specificity of bacteriophage attachment receptors, the current paradigm is to use a single arthrocentesis bacterial isolate to then match to a bacteriophage therapeutic thereby extrapolating activity to all bacteria in vivo. Obstinately, the main bacteriophage attachment receptor for Staphylococcus aureus is teichoic acid and this receptor is known to have phenotypic variations in different in vivo environments. Consequently, the aim of this study was to determine if bacteriophage activity is similar across all in vivo prosthetic joint infection environments.

Study Question Do Staphylococcal bacteriophages have the same activity to clinical isolates from different in vivo environments for individual patients.

Methods Patients with prosthetic joint infections who had Staphylococcus aureus cultured from arthrocentesis cultures and at least three deep tissue cultures were analyzed for bacterial growth inhibition with a library of 56 Staphylococcal bacteriophages. Activity of bacteriophages were compared to the different in vivo environments for each patient.

Results Discordant bacteriophage activity was seen across the different in vivo environments. As well bacteriophages with the most robust lytic potential to the arthrocentesis isolates usually did not have activity to all the deep tissues clinical isolates.

Discussion Variations of bacteriophage activity can occur between the different in vivo clinical environments which is likely secondary to different glycosylation patterns of bacteriophage attachment receptors. Specifically for Staphylococcus aureus glycosylation alterations of teichoic acid in different in vivo environments is likely the mechanism for the discordant activity. Consequently, this finding has important ramifications when using bacteriophage therapy for prosthetic joint infections.

Conclusion These findings suggest the need to use numerous isolates to then match to a bacteriophage therapeutic. It also reinforces the need to use bacteriophage therapy with conventional surgical interventions at this nascent stage. Furthermore, if discordant activity is present to the arthrocentesis isolate compared to deep tissue isolates retreatment is needed to have effective reproducible outcomes.

902 High Mortality After Revision TKA for PJI is Related to Preoperative Morbidity and the Disease Process but Not Treatment

Authors Nicholas P Drain, Dominique M Bertolini, Austin W Anthony, Muhammad W Feroze, Richard Chao, Sadie E Longo, Neel B Shah, Kenneth L Urish

Background and Rationale Periprosthetic joint infection (PJI) is associated with high mortality rates, however the etiology is unclear. Studies have shown that comorbidities are not predictive of failure after treatment of PJI. Hip fractures present a similar patient population wherein mortality correlates with functional status. This raises the question of whether high PJI mortality is secondary to similar preoperative morbidity, or whether there is an association with surgical treatment or the PJI disease process.

Study Question Time and cause of death were compared to establish if differences exist between septic and aseptic groups. We then investigated whether differences in mortality rate were associated with preoperative morbidity, surgical treatment, or the PJI disease process.

Methods A retrospective case-control study comparing septic to aseptic groups was completed. Time to death was analyzed with Cox proportional hazards regression and plotted with Kaplan-Meier curves. Change in Charlson comorbidity index (CCMI) over time was assessed using linear mixed model analysis.

Results A total of 222 (184 septic, 38 aseptic) patients were analyzed. The septic group had earlier mortality ($p=0.01$). There was no significant difference for any single cause of death. Preoperative CCMI was higher in the septic group ($p<0.01$). Both septic and aseptic groups had significant increases in CCMI from preoperative to 3 years postoperative ($p<0.01$) and time of death ($p<0.01$) timepoints. The septic group had a higher CCMI 3 years postoperatively ($P<0.01$) and at time of death ($P=0.04$), but not 1 year postoperatively ($p=0.12$).

Discussion The higher preoperative CCMI in the septic group demonstrates an association between preoperative morbidity and mortality. Treatment did not alter morbidity, as there was no significant change in CCMI between preoperative and one year postoperative timepoints. The significant increase in CCMI within both groups between preoperative and both 3 year postoperative and time of death timepoints combined with the higher CCMI in the septic group at these timepoints implies that the pathogenesis of PJI may cause larger increases in morbidity over time.

Conclusion Septic revision TKA is associated with earlier mortality compared to aseptic revision TKA. The earlier mortality associated with PJI is associated with both higher preoperative morbidity and the PJI disease process, but not surgical treatment.

903 Sub-Optimal Dosing of Vancomycin Increases Rates of Biofilm Formation and Surgical Infection in an Animal Model

Authors Kimberly M Brothers, Dana M Parker, Masashi Taguchi, Kenneth L Urish

Background and Rationale Antibiotic stewardship is a cornerstone in prevention of development of antibiotic resistant organisms. This has great public health benefit protecting the availability of effective antibiotics, but less obvious benefit at the individual level. At levels below the minimum inhibitory concentration (MIC), antibiotics have been observed to alter growth rates of many bacteria including Staphylococcus aureus, the primary organism associated with orthopaedic infection. This is a particular concern with orthopaedic infection as bone and joints are less permeable to antibiotics and have a notoriously lower level of bioavailability as compared to other tissue leading to exposure to sub minimal inhibitory concentrations (sub-MIC) of antibiotics. Clinical studies have reported increased rates of surgical infection when vancomycin is used as compared to cefazolin.

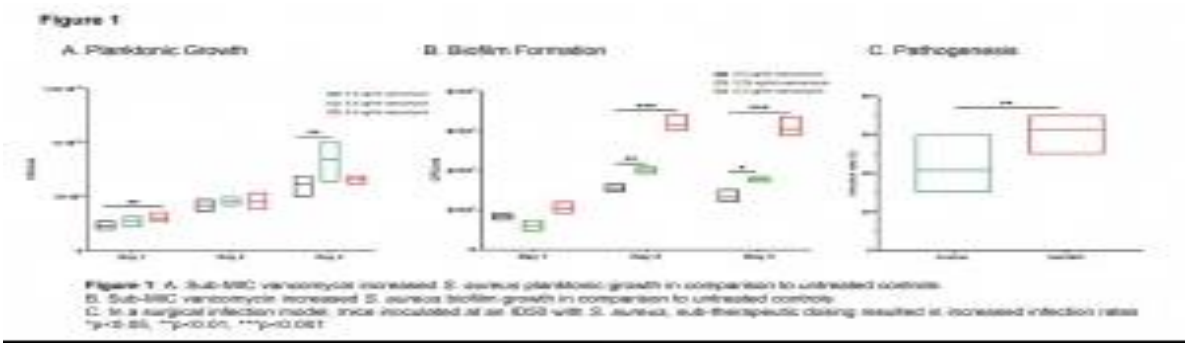
Study Question The focus of this study was to determine the effect of sub-minimal inhibitory concentrations (MIC) of vancomycin on Staphylococcus aureus growth, biofilm formation, and virulence.

Methods S. aureus strains were used for all experiments. Bacteria were grown planktonically and were monitored using spectrophotometry. Quantitative agar culture was used to measure S. aureus biofilm biomass on titanium rods treated with sub-MIC vancomycin. A mouse abscess model was used to confirm phenotypes in vivo.

Results At 1/4 MIC, statistically significant increased rates of planktonic growth were observed in comparison to untreated controls (Fig 1A). Treatment with 1/4 and 1/2 MIC vancomycin resulted in increased biofilm formation by approximately 150% ($p<0.05$) and 244% ($p<0.001$) in comparison to controls by 72 hours (day 3) of growth (Fig 1B). Similar findings were observed in the Newman and SH1000 strain backgrounds. In a mouse abscess model, the biofilm mass (CFU) of the sub-MIC group was significantly greater at 3 days post infection ($p<0.01$). The infection rate was 44.38% (Control) and 62.08% (sub-MIC) at 3 days post infection ($p=0.03$) (Fig 1C).

Discussion Sub-MIC concentrations of vancomycin promoted S. aureus planktonic growth and biofilm formation, phenotypic measures of bacterial virulence. Our results suggest the importance of proper antibiotic selection and dosing.

Conclusion This highlights the importance of proper antibiotic stewardship and dosing of vancomycin for both surgical prophylaxis and treatment of orthopaedic infection.



904 Prospective ex vivo activity of PLG0206, an engineered antibacterial peptide, on chronic periprosthetic joint infection total knee arthroplasty components: the Knee Explant Analysis (KnEA) Study

Authors Dana M Parker, Kimberly M Brothers, Jonathon B Mandell, John A Koch, Despina Dobbins, Jonathan Steckbeck, David B Huang, Kenneth L Urish

Background and Rationale Periprosthetic joint infection (PJI) is one of the more severe complications associated with total knee and hip arthroplasty (TKA, THA). Debridement, antibiotics, and implant retention is an attractive method to manage PJI but fails in approximately 60% of cases. This high failure rate is largely due to the formation of an antibiotic tolerant biofilm. PLG0206 is a broad-spectrum antimicrobial agent against multidrug resistant organisms. Pre-IND models of PJI demonstrate that PLG0206 can rapidly eliminate Staphylococcus aureus biofilms associated with implants.

Study Question The objective of this study is to evaluate the efficacy of PLG0206 in decreasing bacterial burden on infected arthroplasty materials in the setting of periprosthetic joint infection (PJI).

Methods The patientâ€™s infected implant was washed with 50 ml Dulbeccoâ€™s PBS (dPBS) and submerged ex vivo in 1 mg/mL PLG0206 in dPBS for 15 minutes. After treatment, the sample was washed with 50 mL of dPBS and sonicated in dPBS containing 1% Tween 20 for 5 minutes. After sonication, 100 microliters of the implant sonication fluid was serially diluted and plated for colony forming unit (CFU) analysis. The remaining explanted implant from the same patient served as a control and was processed similarly but without exposure to PLG0206.

Results After 15 minutes of treatment with PLG0206, the bacterial burden of both gram-positive and gram-negative bacteria were successfully reduced with more than a 3-log reduction (Table 1). After treatment with PLG0206, 10 of the 18 (56%) infected implants were culture negative. Collectively, infected prosthetics exposed to PLG0206 demonstrated a mean log reduction of 6 (range 2.9-7.70).

Discussion In comparison to untreated samples, 1 mg/ml PLG0206 treatment for 15 minutes successfully reduced the biofilm bacterial burden of both gram-positive and gram-negative bacteria on infected prostheses. The average log reduction was 6, which is considered bactericidal. These findings support the development of PLG0206 as a local irrigation solution of at least a 1 mg/mL concentration in the wound cavity for 15 minutes for patients undergoing treatment of a PJI occurring after TKA or THA.

Conclusion TKA implants from chronic PJI had a 4 log10 reduction in biofilm after treatment with PLG0206, a new broad-spectrum antimicrobial peptide.

Table 1: Culture and CFU log reduction among bacteria identified from periprosthetic knee joints exposed and not exposed to PLG0206

#	Culture	MDR	CFU/mL untreated	CFU/mL treated	Log reduction
1	S. epidermidis	Clindamycin, Erythromycin, Gentamicin, Oxacillin	5.0×10^7	0	7.7
2	S. epidermidis	Clindamycin, Erythromycin, Gentamicin, Oxacillin	5.0×10^7	0	7.7
3	S. aureus (MRSA)	Oxacillin, Erythromycin	5.0×10^7	0	7.7
4	S. hemolyticus	Clindamycin, Gentamicin, Oxacillin, Rifampin, Sulfa/Trimethoprim	7.5×10^2	0	2.9
5	S. aureus (MSSA)	None	5.0×10^7	1.2×10^3	3.6
6	S. capitis	None	5.0×10^7	0	7.7
7	E. coli	Ampicillin, Ampicillin/Sulbactam	5.0×10^7	10	6.7
8	E. coli	Ampicillin, Ampicillin/Sulbactam	5.0×10^7	60	5.9
9	S. epidermidis	None	5.0×10^7	90	5.7
10	Morganella parapluticae	None	5.0×10^7	0	7.7
11	Morganella parapluticae	None	5.0×10^7	0	7.7
12	E. faecalis	None	5.0×10^7	10	6.7
13	S. aureus (MRSA)	Oxacillin	5.0×10^7	0	7.7
14	S. dysgalactiae	None	6.7×10^3	60	4.8
15	S. epidermidis	Penicillin	5.0×10^7	0	7.7
16	S. epidermidis	Oxacillin, Tetracycline, Bactrim (sulfa/trimethoprim)	5.0×10^7	0	7.7
17	S. epidermidis	Oxacillin, Tetracycline, Bactrim (sulfa/trimethoprim)	5.0×10^7	10	6.7

905 The Engineered Antimicrobial Peptide, PLG0206, has Potent Biofilm and Planktonic Activity Against Multi-Drug Resistant ESKAPE Organisms

Authors Jonathon B Mandell, Kimberly M Brothers, Dean Shinabarger, Christopher Pillar, Despina Dobbins, Nicholas Pachuda, David B Huang, Jonathan Steckbeck, Kenneth L Urish

Background and Rationale Periprosthetic joint infection (PJI) is a common and severe complication associated with total knee and hip arthroplasty. PJI can be caused by ESKAPE pathogens which are associated with a high level of multi-drug resistance (MDR). Debridement, antibiotics and implant retention (DAIR) is an attractive method to manage PJI but fails in approximately 60% of cases. The high failure rate is largely due to formation of an antibiotic tolerant biofilm. The broad spectrum engineered peptide PLG0206 has been developed to improve therapeutic index.

Study Question We hypothesized that PLG0206 would have broad spectrum activity against ESKAPE pathogens.

Methods CLSI protocol was used to measure the minimum inhibitory concentration (MIC) against each organism. Implant material was inoculated with 0.5â€‰Ã—â€‰106 CFU/mL. Mature biofilm developed over 48 hours, implants were washed, and then treated with 1 mg/mL PLG0206 for 5, 15, and 30 minutes. Quantitative culture (colony forming unit, CFU) analysis was completed. In a large animal model (New Zealand white rabbit), we completed a DAIR procedure with similar in vitro PLG0206 conditions as compared to an irrigation and debridement alone followed by subcutaneous cefazolin treatment.

Results In the ESKAPE pathogens tested, PLG0206 displayed similar MIC values to that of clinically used antibiotics (Table 1). The three most resistant MDR isolates from each organism were then selected for biofilm culture. Similar activity was observed with MDR ESKAPE biofilms cultured on implant material (Figure 1) with greater than a 3log10 reduction in biofilm. Next, we tested the efficacy of PLG0206 in an acute PJI rabbit model. When a DAIR was completed with the addition of PLG0206 as an irrigation adjuvant, survival was 63% as compared to 0% (100% mortality) in the traditional DAIR control group ($p<0.05$).

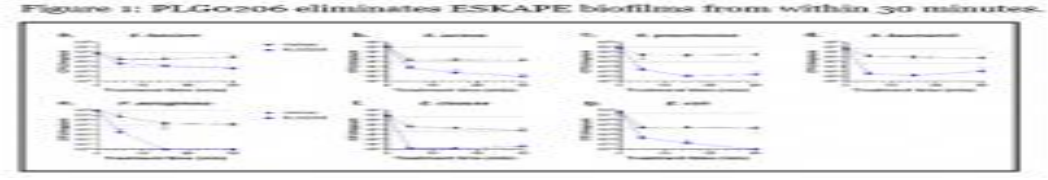
Discussion PLG0206 had broad spectrum activity against ESKAPE pathogens organisms resistant to traditional antibiotics. PLG0206 maintained high activity against ESKAPE biofilms. This in vitro activity was also observed in vivo in our S. aureus acute PJI large animal model.

Conclusion PLG0206 has completed a phase I safety study and has potential to serve as a new class of broad-spectrum antimicrobials with biofilm activity in orthopaedic and other hospital acquired infections

Table 1: PLG0206 displays broad spectrum activity against planktonic ESKAPE pathogens.

Species	N	PLG	LVX	SPX	TGC	LZD	VAN	COL
E. faecalis	2	1-4	0.5->4	2	0.5-2	-	-	.06-.25
S. aureus	4	4->8	.015-.03	.015-.03	.25-.05	4	1	-
K. pneumoniae	8	8->8	>8	>4	0.5-2	-	-	.06-.16
A. baumannii	24	.25-0.5	4->4	1->8	1-16	-	-	1-2->16
P. aeruginosa	20	8->8	0.5->4	4->8	8->16	-	-	1-2
E. coli	8	1-4	>4	4->8	.25-0.5	-	-	.06-.25

Figure 1: PLG0206 eliminates ESKAPE biofilms from within 30 minutes.



906 An Engineered Antimicrobial Peptide, PLG0206, Reduces Biofilm Mass and Increases Survival in a Rabbit Model of Staphylococcus aureus Periprosthetic Joint Infection

Authors Kimberly M Brothers, Jonathan B Mandell, Masashi Taguchi, Dana M Parker, Peter G Alexander, Despina Dobbins, David B Huang, Nicholas Pachuda, Kenneth L Urish

Background and Rationale Periprosthetic joint infections (PJI) are associated with antibiotic-tolerant S. aureus biofilms. PLG0206, a new class of broad-spectrum antimicrobials, has rapid activity against biofilms and does not have significant local or systemic toxicity in animal models.

Study Question The objective of this study is to evaluate the efficacy of PLG0206 as an adjuvant during a DAIR (Debridement and Antibiotics with Implant Retention) procedure for PJI in a S. aureus PJI rabbit model.

Methods A rabbit PJI model with a tibial implant was inoculated at 2x106 CFU/ml. At 2 days post infection (DPI), the joint space was reopened, irrigated, debrided, and treated with 0.5, 1, and 2 mg/ml PLG0206 for either 5, 7.5, or 15 minutes. Rabbits were then euthanized and quantitative culture on the implant and tibia was performed. For the survival study, at 2 DPI rabbits were treated with 1 mg/ml PLG0206 for 15 minutes and survival was monitored up to a period of 28 days. Animals were treated with cefazolin for a period of 5 days starting at 2 DPI (Fig 1B).

Results Implants removed at 2 DPI and treated with 1 mg/ml and 2 mg/ml PLG0206 for 15 minutes had a significant reduction in bacterial biofilm burden, over 100-fold (lower horizontal dashed line; *p<0.05), compared to I&D alone implants (Fig 1A). In the survival study, rabbits were treated with cefazolin, PLG0206, or both. I&D alone rabbits all succumbed to infection by 4 DPI (Fig 1B). Rabbits treated with PLG0206 had 0% survival by day 8. Cefazolin treated rabbits (Fig 1B) had 0% survival by day 14. The combination treatment group of systemic cefazolin and PLG0206 had 63% survival at day 28 (p<0.05), three weeks after discontinuation of antibiotics (vertical dashed line).

Discussion PLG0206 had a 2 log10 reduction in bacterial biofilm burden. I&D alone or DAIR (I&D with cefazolin) rabbits had 100% mortality. Rabbits with combination therapy (I&D, cefazolin, and PLG0206) had a 63% survival. These studies identify PLG0206 in combination with cefazolin as a promising new therapy for treatment of PJI. In a large animal model of S. aureus PJI results in 100% mortality when antibiotics are discontinued.

Conclusion In a large animal model of PJI, we have demonstrated adjuvant care with PLG0206, a new class of broad-spectrum antimicrobials, has high activity against biofilm and results in disease free survival.

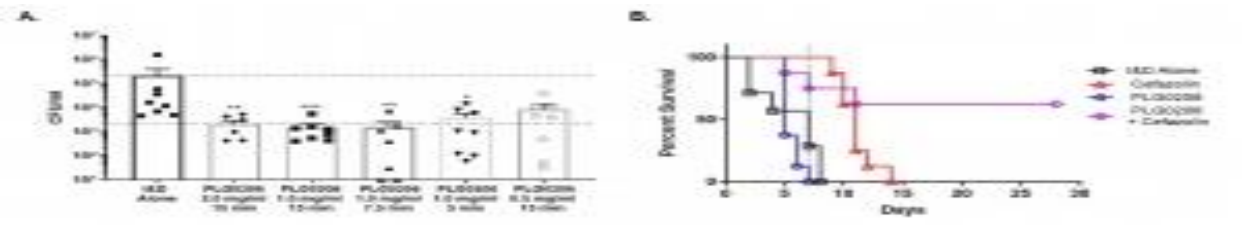


Figure 1
A. In Vivo intra-articular treatment of PJI with PLG0206 for 15 minutes reduces S. aureus biofilm *p<0.05 **p<0.01 ***p<0.001
B. Treatment with cefazolin systemically and PLG0206 intraoperatively results in increased survival

907 Methicillin resistance in Staphylococcus aureus is media dependent

Authors Charles G Gish, Jonathan B Mandell , Kimberly M Brothers, John A Koch, Kenneth L Urish

Background and Rationale Methicillin-resistant Staphylococcus aureus (MRSA) infections are an increasing problem in the United States health care system with increases from 2% up to 50% of all S. aureus infections classified as MRSA from 1974 to present. The S. aureus mecA gene is responsible for resistance to beta-lactam antibiotics, which include penicillin, amoxicillin, and cefazolin.

Study Question The purpose of this study was to test conditions that lower methicillin resistance.

Methods MRSA lab strains and 9 MRSA periprosthetic joint infection clinical isolates were tested. Minimum inhibitory concentrations (MIC) of planktonic bacteria were determined using Clinical and Laboratory Standards Institute (CLSI) protocol in Mueller Hinton Broth (MHB), Tryptic Soy Broth (TSB), Fetal Bovine Serum (FBS), and 10% FBS + Dulbeccoâ€™s Modified Eagle Medium (10% FBS + DMEM). Mouse peritonitis survival experiments were also conducted. An overnight culture of MRSA USA300 JE2 was diluted to 1.0E10 CFU/ml in MHB and FBS. To create an infection model, 100 Âµl was administered by intraperitoneal injection into C57BL/6J mice. Cefazolin and vancomycin were immediately administered at 50 mg/kg and 100 mg/kg respectively and mice were monitored for up to 3 days post-infection.

Results There was a significant increase ($p<0.01$ Fig.1B) in sensitivity to cefazolin as media was changed from standard culture media to more physiologically relevant media. To test this phenotype in vivo, we used a mouse infection model. Mice inoculated with MRSA USA300 JE2 cultured in FBS rather than MHB had a significantly higher survival rate when treated with cefazolin ($p<0.001$ Fig.1C-D).

Discussion Varying resistance to cefazolin was observed in different media conditions. In MHB, the media used in clinical microbiology labs to determine antibiotic resistance, MRSA isolates demonstrated the expected phenotype of resistance to cefazolin. This phenotype was reversed when these same strains were cultured in serum, where MRSA isolates became completely sensitive to cefazolin. These results were replicated in vivo. This supports clinical studies demonstrating improved efficacy when MRSA infections are treated with combination therapy of vancomycin and cefazolin as compared to vancomycin treatment alone.

Conclusion These results suggest a component of serum alters mecA gene expression.

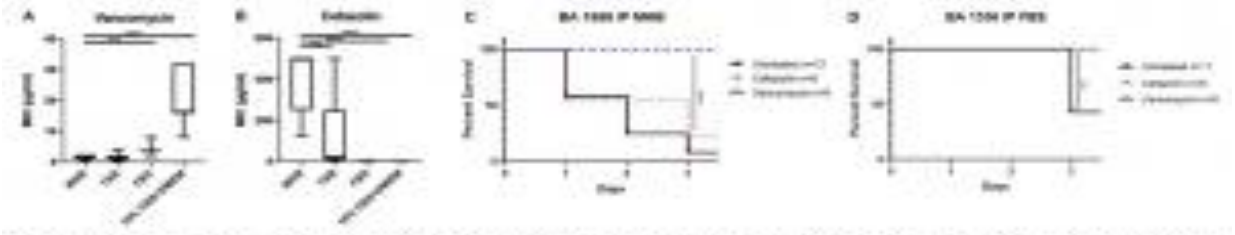


Figure 1: MICs of planktonically grown MRSA for vancomycin (A) and cefazolin (B) in varying media conditions. $^{**}p<0.01$ $^{***}p<0.001$ $^{****}p<0.0001$. Kaplan Meier plot of C57BL/6J mice infected with MRSA BAA-1556 USA 300 JE2 resuspended in MHB (C) or FBS (D). Immediately after infection mice were given no treatment, vancomycin, or cefazolin and survival monitored for up to 3 days.

908 The Joint Microenvironment Decreases MRSA Resistance to Cefazolin

Authors Charles G Gish, Dana M Parker, kimberly M Brothers, Kenneth L Urish

Background and Rationale Methicillin-resistant Staphylococcus aureus (MRSA) remains a significant contributor to periprosthetic joint infection (PJI) following knee and hip arthroplasties. MRSA is clinically identified through CLSI antibiotic susceptibility testing in standard laboratory medium Mueller-Hinton broth (MHB). Recent studies have shown that antibiotic susceptibility can change based on the type of media used for testing.

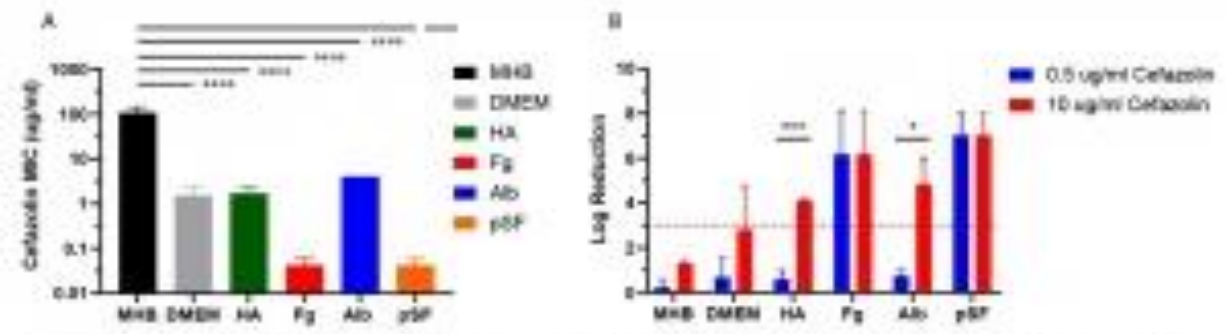
Study Question We questioned whether MRSA susceptibility to first generation cephalosporins could be altered in media replicating the joint microenvironment.

Methods Pseudo synovial fluid (pSF) was prepared by combining 3 mg/ml Hyaluronic Acid (HA), 9 mg/ml Fibrinogen (Fg), and 10 mg/ml Albumin (Alb) in Dulbeccoâ€™s Modified Eagle Medium supplemented with 5% Non-Essential Amino Acids (DMEM) [3]. Each component was also tested individually at the stated concentration in DMEM. The minimum inhibitory concentration (MIC) of MRSA strain BAA-1556 USA 300 JE2 was assessed using the broth microdilution method according to CLSI protocol [4]. Cefazolin was tested at concentrations ranging from 0.016 Âµg/ml to 64 Âµg/ml. The MIC was determined after 24 hours of incubation at 37â„ƒ using PrestoBlueâ„¢ (Gibco) viability reagent according to the manufacturer's instructions. All experiments were performed in triplicate.

Results The average cefazolin MIC (Fig. 1A) was 1.5 Âµg/ml in DMEM, 1.7 Âµg/ml in HA, 0.042 Âµg/ml in Fg, 4.0 Âµg/ml in Alb, and 0.042 Âµg/ml in pSF. All MHB MICs were greater than or equal to 64 Âµg/ml. Both the 0.5 Âµg/ml and 10 Âµg/ml doses of cefazolin eradicated all bacteria in Fg and pSF (Fig. 1B), while only the 10 Âµg/ml dose achieved a 3-log reduction in the other pseudo synovial fluid media components.

Discussion Fibrinogen appears to contribute to cefazolin susceptibility as it was the only one of the three pSF components to significantly lower the MIC in comparison to DMEM (p=0.01 Fig. 1A). Furthermore, no statistical difference was observed between Fg and pSF bacterial reduction at both doses of cefazolin tested (Fig. 1B). Investigating MRSAâ€™s changing susceptibility to first generation cephalosporins may lead to new treatment strategies.

Conclusion Growing MRSA in media replicating the host joint microenvironment significantly reduced its cefazolin MIC compared to MHB (p<0.0001 Fig. 1A).



909 Mapping Bacterial Biofilm on Explanted Orthopedic Hardware: An Analysis of 14 Consecutive Cases

Authors Jacob R Brooks, Matthew Pigott, Douglas Chonko, Anne Sullivan, Kelly Moore, Paul Stoodley

Background and Rationale Hardware implanted during primary total joint arthroplasty (TJA) carries a serious risk for postoperative periprosthetic joint infection (PJI), which can cause devastating patient and financial complications. Though biofilm formation on foreign materials is well-known, there is a significant gap in addressing whether certain areas of a prosthetic joint articulation may be more susceptible to biofilm formation than others.

Study Question This studyâ€™s intent was to identify specific locations on explanted orthopedic hardware that are more prone to bacterial attachment and subsequent biofilm formation using a novel implant culturing method (ICM).

Methods Fifty-three components from fourteen surgical cases involving hip and knee TJA revision were retrieved. The ICM produced a thin brain heart infusion agar coating over components followed by incubation and observation of colony outgrowth over nine days. Presence of growth was recorded, organisms were identified by 16s rRNA sequencing, and locations of outgrowth were analyzed for biofilm accumulation patterns. Outcomes were compared with clinical culturing results and Musculoskeletal Infection Society criteria for PJI diagnosis.

Results The ICM paralleled clinical culturing methods with a sensitivity of 100% and specificity of 57.1%. When compared to MSIS criteria, sensitivity remained at 100% while specificity increased to 80%. Biofilm accumulation was mainly patchy and heterogenous, though the non-articulating surface between the tibial tray and polyethylene insert showed consistent growth in all possible knee cases. On individual components, ridges and edges consistently harbored biofilm, while growth elsewhere was case-dependent.

Discussion The ICM displays promise in both identifying biofilm on culture-negative PJIs and uncovering patterns of growth on total knee prostheses. Consistent growth in the sub-micron space between the tibial tray and polyethylene insert may suggest this region as a protected area from diffusing antibiotics and host defense mechanisms. Biofilm formation observed here and near the edges of the knee locking mechanism may indicate room for improvement during debridement, antibiotics, and implant retention procedures.

Conclusion The ICM consistently identified microbial growth with a high sensitivity and successfully localized biofilm to edges, contour changes, and the specific non-articulating space between the tibial tray and polyethylene insert.

910 Synovial fluid absolute neutrophil count a promising marker for diagnosing periprosthetic joint infection

Authors Alisina Shahi, Ali Oliashirazi, Tae W Kim, Javad Parvizi

Background and Rationale With no gold standard for diagnosing periprosthetic joint infection (PJI) clinicians who encounter a suspected PJI case have to use a combination of tests. Several studies have indicated the importance of absolute neutrophil count (ANC) in systemic infections. However, this test has not yet been investigated in synovial fluid (SF).

Study Question What is the role of SFANC in diagnosing PJI? How does it perform compared to SFPMN% and SFWBC?

Methods We conducted a retrospective multicenter study reviewing the clinical records of patients undergoing revision surgery from 2017 to 2020. Patients who had full set of SFWBC, SFPMN%, and SFANC were included in the study. Our cohort consists of 231 patients that were divided into two groups: aseptic revisions (N=136) and septic revisions (N=95). Sensitivity, specificity, positive and negative likelihood ratio (LR), and diagnostic odds ratio (DOR) were calculated for each test. The cutoff for SF absolute PMN was calculated using the Youdenâ€™s Index (>1950 cells/Î¼L).

Results SFANC had a sensitivity of 88.4%, specificity of 85.2%, positive and negative likelihood ratio of 6.0 and 0.1, and a DOR of 44.2 (95% confidence interval [CI]: 20.1-97.3). SF WBC showed 84.2% sensitivity, 83.8 specificity, 5.2 +LR, 0.1 â€“LR, and 27.6 (95%CI: 13.5-56.5) DOR. Synovial PMN% had a sensitivity of 80.0%, a specificity of 80.8%, + and â€“ LR of 4.1 and 0.2 respectively, and a DOR of 16.9 (95%CI: 8.7-32.7). SFANC with an area under the curve (AUC) of 0.93 was a significantly better predictor of PJI than both SF WBC (AUC=0.91, p=0.007) and SF PMN% (AUC=0.88, p=0.016). The AUC was comparable for SF WBC and SF PMN, p=0.16 .

Discussion Our data showed that SFANC is more specific and more sensitive than both SF PMN% and WBC. This can be due to the fact that ANC takes band cells into account whereas both PMN% and WBC fail to count them in, especially when automated cell count machines are used. AFANC is more capable of showing infection in its early stages or when there is a slow growing organism that does not strongly elicit the immune system.

Conclusion Based on the findings of the current study, it appears that SFANC has a better performance for diagnosing PJI than SFWBC and SFPMN%. Considering that this test is reported as part of the routine synovial fluid analysis at no added cost, we recommend that the orthopaedic community to consider this test in diagnostic work up for PJI.

911 Hardware removal due to infection after open reduction and internal fixation: trends and predictors.

Authors Alisina Shahi, Ali Oliashirazi

Background and Rationale Hardware removal due to infection is one of the major causes failure following open reduction and internal fixation (ORIF).

Study Question The aim of this study was to determine trends and predictors of infection-related hardware removal following ORIF of extremities using a nationally representat

Methods Nationwide Inpatient Sample data from 2006 to 2017 was used to identify cases of ORIF following upper and lower extremity fractures, as well as cases that underwent infection-related hardware removal following ORIF. Multivariate analysis was performed to identify independent predictors of infection-related hardware removal, controlling for patient demographics and comorbidities, hospital characteristics, site of fracture, and year.

Results For all ORIF procedures, the highest rate of hardware removal related to infection was observed in tarsal fractures (6.86%), followed by tibial (4.35%) and carpal (4.17%) fractures. Hardware removal rates due to infection increased in all fractures except radial/ulnar fractures. Tarsal fractures (odds ratio (OR)=1.05, 95% confidence interval (CI): 1.03-1.08, P<0.001), tibial fractures (OR=1.04, 95% CI: 1.03-1.06, P<0.001) and those patients with diabetes mellitus (OR=2.73, 95% CI: 2.36-2.94, P<0.001), liver disease (OR=2.03, 95% CI: 1.74- 2.35, P<0.001), and rheumatoid arthritis (OR=2.05, 95% CI: 1.98-2.28 P<0.001) were the main predictors of infection-related removals; females were less likely to undergo removal due to infection (OR= 0.59, 95% CI: 0.57-0.64 P<0.001).

Discussion Hardware removal rates due to infection increased in all fractures except radial/ulnar fractures. Diabetes, liver disease, and rheumatoid arthritis were important predictors of infection-related hardware removal. The study identified some risk factors for hardware related infection following ORIF, such as diabetes, liver disease, and rheumatoid arthritis, that should be studied further in an attempt to implement strategies to reduce rate of infection following ORIF.

Conclusion Surgeons should be cognizant of these trends. Given the fact that rate of hardware removal due to infection was higher in patients with comorbidities, post operative medical management of these patients is key to potentially decrease the likelihood of failure.

912 Onoderaâ€™s prognostic nutritional index a valuable measure in predicting complications after TKA

Authors Alisina Shahi, Tae W kim, Matthew Brown, Ali Oliashirazi

Background and Rationale The best marker for assessing nutritional status prior to total knee arthroplasty (TKA) remains unknown. Serum Albumin has been widely studied as a marker for nutritional status. However, there are a lot of studies that have debunked the accuracy of this test. In an effort to increase the yield of Albumin in demonstrating the nutritional status of the patients authors have tried to combine it with serum ESR and/or CRP which has increased the yield to some extend but it is still far from perfect.

Study Question The purpose of this study was to investigate the utility of Onoderaâ€™s prognostic nutritional index (OPNI) in predicting early complications following TKA, and to determine the threshold above which the risk of complications increase significantly.

Methods This prospective multi-center study evaluated primary TKAs. The OPNI was measured in patients within 14 days of surgery. Complications were assessed for 12 weeks from surgery and included prosthetic joint infection (PJI), wound complications, re-admission, and re-operation. The Youdenâ€™s index was used to determine the cut-off for OPNI and albumin. Multiple regression model was also performed using the Charlson comorbidity index to compare the outcomes using OPNI and albumin levels as independent variables.

Results Overall, 1325 patients (562 males, 763 females) were included in the study. OPNI cutoff score of 45.1 was determined as the optimal threshold associated with complications. Patients with lower OPNI (<45.1) were 9.8 times more likely to develop PJI compared to patients with higher OPNI (p=0.001). Re-admission and re-operation rates were 4.6 and 4.2 times higher in patients with OPNI below the threshold (p = 0.017 and p = 0.005, respectively). These complications remained statistically significant in multiple regression analysis. Unlike OPNI, albumin failed to show a significant association with complications (cutoff: 38.2 g/L).

Discussion OPNI is a valid and an excellent predictor of complications following TKA. It better reflects the nutritional status, has greater predictive power for complications, and can determine whether the body is in anabolic or catabolic status.

Conclusion Based on these findings, we recommend screening of all patients undergoing TKA using OPNI and for those who have a score lower than 45.1 the risk of surgery should be carefully weighed against its benefit and consider nutritional optimization.

914 Total Knee Arthroplasty Can Save Lungs

Authors Alisina Shahi, Ali Oliashirazi, Lawrence Miller

Background and Rationale Total knee arthroplasty (TKA) is a life-changing event. Many patients stop smoking prior to their elective surgery as part of preoperative optimization. However, it is unknown how many of these patients relapse to smoking after their surgery.

Study Question The aim of this study was to investigate the incidence of smoking relapse and its association with periprosthetic joint infection (PJI) in a large non-select cohort of patients.

Methods We conducted a multicenter study and retrospectively identified patients who underwent primary TKA between 2000 and 2020. Patients were stratified into four groups: current smokers (A), former smokers (B), ceased smoking for the procedure (C), and nonsmokers (D). Patients were followed for at least two years and the relapsed cases were identified. The association between smoking status and PJI was investigated using multivariate regression analysis.

Results 16,322 patients were identified who underwent 19,986 total knee arthroplasties during the study period. Of these patients, 1,352(8.2%) were current smokers, 4,522(27.7%) were former smokers, 3,575(21.9%) ceased smoking for their procedure, and 6,873(42.1%) were nonsmokers. Current smokers were significantly more likely than nonsmokers to undergo reoperation for infection (odds ratio[OR],2.12[95%confidence interval(CI),1.42-3.25];p=0.04), and former smokers were at no increased risk (OR,1.12[95%CI,0.63-1.45];p=0.71). Of group C patients only 1,258(35.1%) had relapse within two years after surgery. The rate of infection was significantly higher in patients who returned to smoking compared to those who didnâ€™t (5.0% vs. 0.4%; OR:2.1[95% CI, 1.53 to 2.44]).

Discussion Based on our finding majority of patients who stopped smoking did not have a relapse within two years after surgery. It appears like that TKA not only can improve patientsâ€™ functionality but also is a turning point that prevents future smoking in majority of the patients. Smoking is a major risk factor for PJI and patients who return to smoking are at higher risk.

Conclusion When patients undergo life changing events like TKA, not only it improves their physical function but also gives them an opportunity to build better life style habits. It is imperative to educate the patients on the consequences of smoking and provide them with tools to help them quite.

916 Assessment of Staphylococcal Clinical Isolates from Periprosthetic Joint Infections for Potential Bacteriophage Therapy

Authors Brian J De Palma, Sumon Nandi, Waqas Chaudhry, Martin Lee, Aaron J Johnson, James B Doub

Background and Rationale Bacteriophage therapy is a potential adjunctive treatment for periprosthetic joint infections (PJIs) given the capabilities of bacteriophages to degrade biofilms, self-replicate, and lyse bacteria. However, many aspects of this therapeutic are ill-defined, and the narrow spectrum of bacteriophage activity along with limited available bacteriophage strains curb potential use for specific bacteria such as Staphylococcus aureus at the present time. Therefore, the aim of this study was to determine the feasibility of using bacteriophages for PJI by (1) categorizing the causative organisms in hip and knee PJI at a tertiary academic center and (2) evaluating in vitro activity of a group of bacteriophages against clinical S. aureus PJI isolates.

Study Question 1. What are the most common causative organisms in hip and knee PJI at a tertiary academic center?

2. Will a library of bacteriophages inhibit growth in vitro of historic clinical S. aureus PJI isolates?

Methods Patients with chronic hip or knee PJI after undergoing the first stage of a 2-stage revision protocol from 2017 to 2020 were identified retrospectively by a query of the hospital billing database. The causative pathogens in 129 cases were reviewed and categorized. From this cohort, preserved S. aureus isolates were tested against a library of 15 staphylococcal bacteriophages to evaluate for bacterial growth inhibition over 48 hours.

Results S. aureus was the most common pathogen causing PJI (26% [33] of 129 cases). Of 29 S. aureus samples that were analyzed for bacteriophage activity, 97% showed adequate growth inhibition of the predominant planktonic colonies by at least 1 bacteriophage strain. However, 24% of the 29 samples demonstrated additional smaller, slower-growing S. aureus colonies, none of which had adequate growth inhibition by any of the initial 14 bacteriophages. Of 5 secondary colonies that underwent subsequent testing with another bacteriophage with enhanced biofilm activity, 4 showed adequate growth inhibition.

Discussion Bacteriophage therapy is a potential novel adjunct treatment for PJI. The results of this study suggest the need for in vitro testing of bacteriophage therapeutics against both planktonic and stationary states of a clinical isolate.

Conclusion This study provides preliminary preclinical evidence of the potential usefulness of bacteriophage therapy in PJI treatment.

917 An externally validated algorithm for prediction of in-hospital and ninety-day mortality after spinal epidural abscess

Authors Akash A Shah, Aditya V Karhade, Olivier Q Groot, Thomas E Olson, Joseph H Schwab

Background and Rationale Despite advances in diagnosis and treatment, mortality rates remain unacceptably high for patients with spinal epidural abscess (SEA). Given the low incidence and limited follow-up of patients with SEA, studies predicting mortality associated with SEA remain scarce. The SORG Orthopaedic Research Group previously developed a machine learning algorithm for pre-operative prediction of short-term mortality in patients with SEA, available as an open-access web application: https://sorg-apps.shinyapps.io/seamortality/.

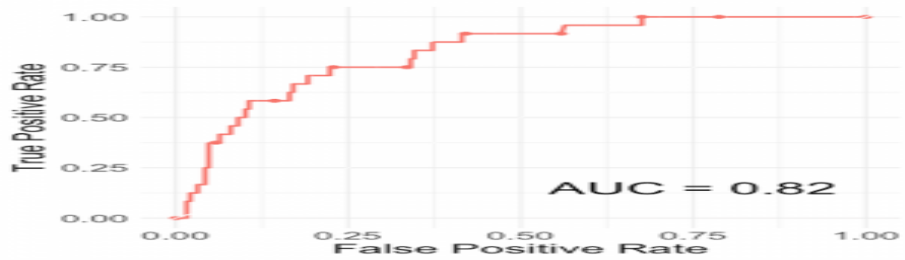
Study Question Is the SORG algorithm for short-term mortality after SEA externally valid on an independent and geographically distinct patient population?

Methods Adult patients diagnosed with SEA at a tertiary care academic medical center between 2003-2020 were included. The primary outcome was mortality within admission or within 90 days of discharge. The SORG algorithm for short-term mortality in SEA was tested on the external validation cohort. Discrimination of the algorithm on the validation cohort was assessed with the area under the receiver operating characteristic curve (AUROC). Calibration was assessed with calibration slope, calibration intercept, and Brier score. Decision curve analysis was also performed.

Results A total of 212 patients were included in the validation cohort. There were 36 cases (17.0%) of in-hospital or 90-day mortality. The SORG stochastic gradient boosting algorithm for in-hospital and ninety-day mortality performed excellently on the validation cohort with AUROC of 0.82 (Figure 1). The algorithm was well-calibrated with a calibration slope of 0.96, calibration intercept of -0.08, and Brier score of 0.09. The SORG algorithm showed greater net benefit than the default strategy of changing management for no patients or for all patients, resulting in a greater balance of true positives than false positives.

Discussion With a contemporary, geographically distinct cohort, we report successful external validation of the SORG algorithm for short-term mortality in patients with SEA - displaying excellent discrimination and calibration on an external cohort. Accurate prediction of mortality risk in patients with SEA may improve pre-operative counseling, as well as influence management and post-discharge surveillance to reduce risk of short-term mortality for SEA.

Conclusion The SORG algorithm for prediction of short-term mortality after SEA is externally valid.



918 An externally validated algorithm predicts failure of non-operative management for spinal epidural abscess

Authors Akash A Shah, Aditya V Karhade, Olivier Q Groot, Thomas E Olson, Joseph H Schwab

Background and Rationale While spinal epidural abscess (SEA) was historically considered a surgical emergency, medical management for select cases has grown in prevalence. Given the poor neurologic outcomes and increased mortality rates observed in patients who fail non-operative management, it would be of utility to determine which patients are at high risk of treatment failure. The SORG Orthopaedic Research Group previously developed a machine learning algorithm for prediction of treatment failure in patients treated non-operatively.

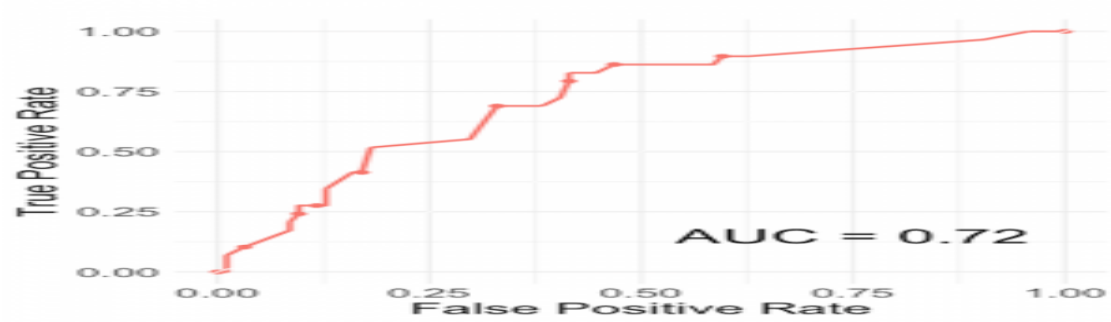
Study Question Is the SORG algorithm for SEA non-operative management failure externally valid on an independent patient cohort?

Methods Adult patients with SEA treated non-operatively at a tertiary care academic medical center between 2003-2020 were included. The primary outcome was treatment failure defined as neurologic deterioration, radiologic progression, or persistent symptoms despite antibiotic therapy. Discrimination of the algorithm on the validation cohort was assessed with the area under the receiver operating characteristic curve (AUROC). We assess calibration with calibration slope, calibration intercept, and Brier score. Decision curve analysis was performed.

Results A total of 123 patients were included in the validation cohort, with 29 cases (23.6%) of treatment failure. The SORG elastic-net penalized logistic regression model for treatment failure performed excellently on the validation cohort with an AUROC of 0.72 (Figure 1). The algorithm was well-calibrated with a calibration slope of 0.50 and calibration intercept of -0.94. The Brier score was 0.20. On decision curve analysis, the algorithm resulted in a greater balance of true positives than false positives.

Discussion Accurate prediction of non-operative management failure is crucial given the risk of clinical deterioration associated with SEA treatment failure. We report successful external validation of the SORG algorithm for non-operative management failure for SEA. This model displays excellent discrimination and calibration when tested on an external cohort. This tool is available as web application: https://sorg-apps.shinyapps.io/seanonop/. Accurate prediction of treatment failure risk may facilitate pre-operative patient counseling and expectation-setting, guiding management choices and improving shared decision-making.

Conclusion The SORG algorithm predicting non-operative management failure for SEA is externally valid.



920 Culture Results Cannot Always Be Relied on During Revision Total Joint Arthroplasty: A Multicenter Study

Authors Graham S Goh, Saad Tarabichi, Colin M Baker, Luigi Zanna, Mustafa Citak, Javad Parvizi

Background and Rationale The 2018 ICM definition allows for false-positive cultures in noninfected cases, since the major criterion constitutes two separate cultures of the same organism. While literature has focused on the diagnosis and treatment of culture-negative PJI, the rate of positive cultures in aseptic revision TJA is less well studied, and it remains unclear whether these organisms represent true contaminants or a possible low-grade infection that could adversely influence outcomes following revision surgery.

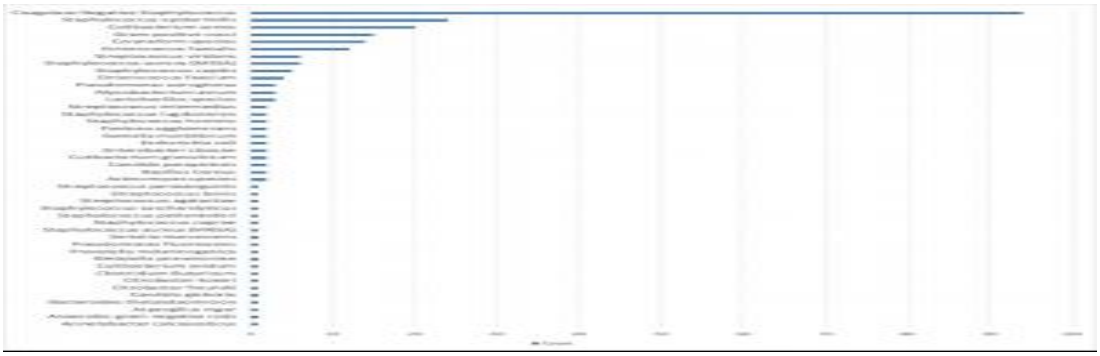
Study Question The hypothesis of this study was that in a portion of patients undergoing revision arthroplasty for aseptic failure, microbial cultures may isolate an organism(s) that may be left untreated by antimicrobials.

Methods This retrospective, multicenter study reviewed all patients who underwent revision TJA two tertiary referral centers in North America and Germany from 2000 to 2017. Patients were categorized as aseptic if they were appropriately investigated preoperatively and did not meet the 2018 International Consensus Meeting (ICM) criteria. In the aseptic revision cohort, patients with a single positive culture or multiple cultures positive for different organisms (â€œorganism-positiveâ€) and patients who had negative intraoperative cultures (â€œorganism-negativeâ€) were compared based on demographics, comorbidities, operative details, subsequent reoperations and periprosthetic joint infection (PJI).

Results In total, 3,234 ICM-negative aseptic revision TJAs were included, of which 215 patients (6.6%) were organism-positive; 196 (91.2%) had a single positive culture and 19 (8.8%) were positive for two or more distinct organisms (i.e. polymicrobial). The most prevalent organisms were Coagulase-Negative Staphylococci (37.5%), Staphylococcus epidermidis (9.6%) and Cutibacterium acnes (8.0%). Demographics and operative details were comparable between the groups. Using multiple regression, there was no association between culture positivity and the rate of reoperation or PJI.

Discussion Isolation of organisms by culture in patients undergoing revision for aseptic failure was not uncommon.

Conclusion As long as these patients were appropriately investigated preoperatively and PJI was excluded, these findings suggest that culture results may be ignored without subjecting patients to additional antimicrobial treatment.



921 Serum Glucose Variability Increases the Risk of Complications Following Aseptic Revision Hip and Knee Arthroplasty

Authors Graham S Goh, Ilan Small, Terence L Thomas, Mohammad S Abdelaal, Noam Shohat, Javad Parvizi

Background and Rationale Increased serum glucose variability has been proposed as a risk factor for perioperative morbidity and mortality. Given the greater surgical complexity and complication risk of revision total joint arthroplasty (TJA), previous findings may not be generalizable to the revision population.

Study Question This study investigated the association between glucose variability and postoperative complications following aseptic revision TJA.

Methods We identified 1,983 patients who underwent aseptic revision TJA (636 knees, 1347 hips) between 2001and 2019. Patients with â‰¥2 postoperative glucose values per day or â‰¥3 values during hospitalization were included in this study. Glucose variability was assessed using the coefficient of variation (COV). Outcomes included length of stay, 90-day complications, mortality and periprosthetic joint infection (PJI) as defined by the 2018 International Consensus Meeting criteria. Multiple regression was used to determine the association between glucose variability and each endpoint, using COV as a continuous and categorical variable (i.e. COV tertiles).

Results Patients with high glycemic variability were at 1.7 times increased risk of 90-day complications (OR 1.664, 95% CI 1.266-2.188, p<0.001) and 2 times increased risk of PJI at minimum 1 year follow-up (OR 1.984, 95% CI 1.270-3.100, p=0.003). These risks increased by 22% (OR 1.022, 95% CI 1.012â€“1.032, p<0.001) and 18% (OR 1.018, 95% CI 1.003-1.034, p=0.013) for every 10-percentage-point increase in COV, respectively. Patients with higher glucose variability also had a longer length of stay (beta 1.028, 95% CI 0.590-1.466, p<0.001). These associations were independent of age, sex, BMI, Charlson comorbidity index, joint, operative time, history of diabetes and mean glucose levels.

Discussion Higher glucose variability was associated with an increased risk of medical complications and PJI following aseptic revision TJA.

Conclusion Patients undergoing these complex procedures should have glucose levels monitored closely in the perioperative period. Future studies should evaluate the utility of continuous glucose monitoring in this high-risk population.

Table. Multivariable regression model for the association between glycemic variability (by Coefficient-of-Variation tertiles) and outcome variables

Outcome	Adjusted OR† or beta^	95% CI	p-value
Any complication†			
Tertile 1	Reference		
Tertile 2	1.183	0.916-1.527	0.196
Tertile 3	1.664	1.266-2.188	**<0.001**
Periprosthetic joint infection†			
Tertile 1	Reference		
Tertile 2	1.073	0.732-1.572	0.719
Tertile 3	1.984	1.270-3.100	**0.003**
Mortality†			
Tertile 1	Reference		
Tertile 2	0.936	0.380-2.308	0.886
Tertile 3	1.360	0.473-3.904	0.568
Non-home discharge†			
Tertile 1	Reference		
Tertile 2	0.925	0.716-1.195	0.551
Tertile 3	1.175	0.906-1.524	0.224
Length of stay^			
COV tertile	1.028	0.590-1.466	**<0.001**

† Multivariate logistic regression
^ Multivariate linear regression

922 Disrupting Biofilms from Titanium with a CHG Antimicrobial Irrigation System

Authors Isabel Laubach, Jessica sanders, Marnie Peterson, Carolyn Twomey, Tanya Eberle

Background and Rationale Orthopedic device-related infections can be difficult to treat and decrease the success of surgical interventions. The implant provides a surface for bacterial attachment and biofilm formation, which decreases antimicrobial efficacy. This study was conducted to assess the ability of the Chlorhexidine Gluconate (CHG) Antimicrobial Irrigation System to disrupt biofilms from titanium coupons using an adapted ASTM E2871-19 method, â€œStandard Test Method for Determining Disinfectant Efficacy Against Biofilm Grown in the CDC Biofilm Reactor Using the Single Tube Method.â€

Study Question Can mature biofilms from clinically relevant organisms be disrupted by a CHG Antimicrobial Irrigation System?

Methods CDC Biofilm ReactorÂ® was inoculated with Staphylococcus epidermidis (ATCCÂ® 14990â„¢), methicillin-resistant Staphylococcus aureus (ATCCÂ® 43300â„¢), Pseudomonas aeruginosa (ATCCÂ® 15442â„¢), or Escherichia coli (ATCCÂ® 25922â„¢). The reactors were run in a batch phase for 24 h, followed by continuous flow phase for an additional 24 h to produce single-species biofilms on titanium coupons. After coupons were washed with PBS to remove planktonic bacteria, growth control coupons were placed into standard sampling solution with 1% Tamol (SST) (neutralizer) or treated with CHG Antimicrobial Irrigation System according to Instructions for Use (IFU) followed by a 60 sec dwell or no dwell. Coupons were rinsed with normal saline following treatment and placed in SST. Then coupons were sonicated and vortexed to release bacteria and plated for enumeration. A coupon from each group was fixed for SEM imaging.

Results The CHG Antimicrobial Irrigation System disrupted biofilms of all organisms from titanium coupons with the greatest log reduction per coupon in the 60 sec dwell treatment group (log10 reduction 2.02 to 4.56 CFU/coupon from controls) (Table). Overall, S. epidermidis and E. coli biofilms had the greatest reductions in bacterial densities. SEM images confirmed biofilm disruption from the titanium surface.

Discussion A 99% reduction of biofilm in clinically relevant organisms was achieved in an in vitro test method using a CDC biofilm reactor and adapted ASTM E2781-19 single tube method when tested per the Instructions for Use.

Conclusion In all cases, the CHG Antimicrobial Irrigation System disrupted biofilms from titanium coupons, with a greater efficacy demonstrated when the labeled dwell time was applied.

Organism	Log_{10} CFU/coupon for growth control (Mean ± SD)	Log_{10} reduction from growth control (Mean ± SD)		Percent reduction from growth control	
		No dwell	Sixty second dwell	No dwell	Sixty second dwell
P. aeruginosa (ATCC® 15442™)	8.22 ± 0.04	0.99 ± 0.06	2.18 ± 0.03	89.723%	99.347%
MRSA (ATCC® 43300™)	7.91 ± 0.05	1.76 ± 0.06	2.02 ± 0.10	98.262%	99.022%
S. epidermidis (ATCC® 14990™)	7.18 ± 0.01	2.99 ± 0.57	4.56 ± 0.70	99.765%	99.995%
E. coli (ATCC® 25922™)	6.34 ± 0.10	2.38 ± 0.31	2.91 ± 0.79	99.500%	99.707%

924 Development of a PJI microJoint Bioreactor for the study of Bacteriophage Activity

Authors Beth A Knapick , Dana M Parker, Kimberly M Brothers, Peter G Alexander, James Doub, Kenneth L Urish

Background and Rationale Periprosthetic joint infection (PJI) is the most severe complication in total knee arthroplasty (TKA) and the largest cause of TKA revision (25%) with a 5 year mortality of 20%. Bacteriophage therapy is a promising new approach for treating chronic PJI. Ensuring lytic activity of a phage therapeutic to a clinical isolate from the patient is necessary as phages bind specific surface receptors that can have large variations in the same species. In PJI, bacteria exist in multiple phenotypic variations in synovial fluid, implant, soft tissues, and bone.

Study Question The objective of this study was to test phage treatment in different knee joint microenvironments.

Methods Staphylococcus aureus (MSSA Newman and SH1000) were used for all experiments. A microJoint bioreactor was developed that enables multi-component culture under these specific joint microenvironments (Fig 1a). S. aureus was cultured for 48 hours in separate compartments containing a 6 mm Kirschner wire implant, a 1 cm piece of mouse bone, a 1 cm piece of mouse tissue, and pseudosynovial fluid. 1 x 10^6 colony forming units (CFU) S. aureus was added to each chamber. A biofilm was allowed to develop over a period of two days. After 48 hours, 1x10^9 PFU Mallokai phage was added to the compartment and let dwell for 24 hours. Colony forming unit analysis was used to determine bacterial burden pre- and post-phage treatment.

Results Newman planktonic bacteria was observed to proliferate and populate the tissues in each compartment, forming an identifiable biofilm (Fig1B). In the Newman strain background, Mallokai phage treatment resulted in a 6.3 log10 reduction in Kirschner wire, a 8.5 log10 reduction in bone, a 5.6 log10 reduction in synovial tissue, and a 4.2 log10 reduction in synovial fluid bacterial burden (Fig 1C). Similar results were observed with SH1000

Discussion We utilized the proven bioreactor design to form a PJI microJoint consisting of a 4-chamber configuration, maintained by a closed-loop and tissue specific maintenance medium where chambers are interconnected by a common flow. A robust biofilm formed over a period of 2 days. Mallokai phage treatment had a greater than 3 log10 reduction in biofilm bacterial burden in each of the different microJoint compartments.

Conclusion We can simulate PJI and biofilm formation in different joint micro-environments and therapeutic eradication by phage

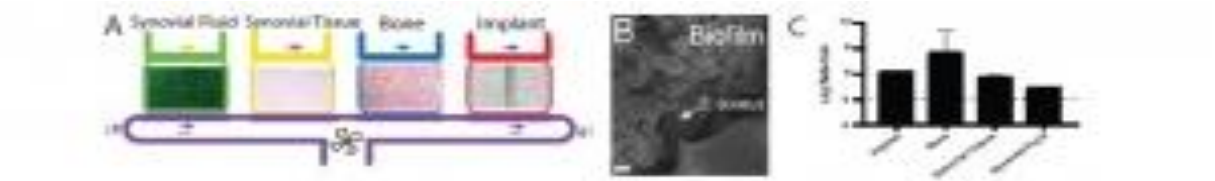


Figure 1. A) Diagram of microJoint tissue chip. Potential flow directions indicated by arrows. B) SEM of Newman biofilm on implant in bioreactor chamber. C) Bioreactor log reduction in CFUs after treatment with phage ····· denotes 3-log$_{10}$ reduction

925 Incidence of Unexpected Positive Sonication Results in Presumed Aseptic Knee and Hip Revision Arthroplasty

Authors Alan Wilson, Stuti Patel, Johannes Plate, Michael O'Malley, Brian A Klatt

Background and Rationale There is an approximately 9% prevalence of unexpected positive intra-operative cultures (UPC) in aseptic revision THA and TKA with data suggesting reduced revision-free survival and infection-free survival in patients with >2 UPCs. Implant-sonicate cultures are used as an adjunct diagnostic tool for identification of infectious organisms at the time of revision surgery and have been shown to improve diagnostic sensitivity for detecting prosthetic joint infection (PJI). However, the incidence and significance of isolated positive sonication results in patients undergoing aseptic revisions remains unclear.

Study Question We evaluated the rate of positive sonication results in patients undergoing presumed aseptic THA or TKA revision and its relation to incidence of subsequent re-revision.

Methods A retrospective single-center study was performed that included patients who underwent aseptic revision TKA or THA from 2016-2020. Medical records were reviewed to collect patient demographics, surgical history, pre-operative and outcome data. Primary outcome was incidence of positive sonication results. Secondary outcome included all-cause re-revision as well as incidence of subsequent prosthetic joint infection at a minimum follow-up of 1year.

Results Incidence of unexpected positive sonication results growing 1 or more colony forming units (CFU) was 21%, with 5% having > 5CFU (7% for revision THA and 3 % TKA) from 424 aseptic revision cases. In 208 patients (96 THA, 112 TKA) with 1 year follow-up, the rate of all-cause re-revision was noted to be higher in the positive group(29 v 22.5%, p=0.34). The rate of subsequent PJI was noted to be 6.25% in patients with positive sonication results compared to 2.75% in those with negative sonication(p = 0.43). Incidence of infection was found to be12.5% for patients with sonication growing >5CFU (12.5% v 4%, p=0.44).

Discussion Incidence of unexpected positive sonication results was higher than the incidence of UPC that has previously been reported. This could be due to the inherent advantage of sonication technique in identifying a broader spectrum of infectious agents. The rate of infection was not significant between the groups.

Conclusion While positive sonication results are associated with a higher incidence of revision and PJI, further studies with a larger sample size are needed to better evaluate the true prognosis of isolated positive sonication results.

926 mazEF toxin anti-toxin mediated regulation of Staphylococcus aureus biofilm growth and antibiotic tolerance

Authors Jonathan B Mandell, Charles Gish, Dana Parker, Kimberly Brothers, Kenneth L Urish

Background and Rationale Staphylococcus aureus biofilms form when bacterial cells adhere to surfaces and form densely populated sessile colonies. As such, traditional antibiotics are largely ineffective against S. aureus biofilms and physical removal is very difficult. The MazEF toxin-antitoxin system comprises the stable cellular toxin MazF and the labile antitoxin MazE which directly inhibits MazF. In gram-positive species like S. aureus, the role of the mazEF gene is controversial and its physiologic function in the disease process from acute to chronic infection is not well understood.

Study Question To determine biofilm growth and antibiotic sensitivity of a MRSA lacking mazEF expression.

Methods Strains tested were wild type MRSA USA300 JE2, JE2 mutant lacking mazEF expression using transponson mutagenesis (Î”mazEF), as well as the mazEF mutant with mazEF expression added back in trans. Planktonic growth and biofilm formation of all strains were determined in standard laboratory culture broth (Mueller-Hinton Broth- MHB), fetal bovine serum (FBS), or pseudo-synovial fluid (SYN). Biofilm formation on implant metal was determined after implant sonication for 30 minutes, serial dilution of sonication fluid, and colony forming unit quantification on TSA II blood agar plates. Biofilms were additionally treated with vancomycin or cefazolin for over 24 hours to determine tolerance to clinical antibiotics.

Results Planktonic cell growth was not significantly altered between JE2 WT, Î”mazEF, and complemented strains in all three media conditions. Planktonic cell growth was comparable between MHB and FBS over 24 hours, while cells in SYN (pseudo synovial fluid) demonstrated less growth and increased persistence. Î”mazEF displayed significantly increased biofilm formation on metal implants over 48 hours compared to WT and complemented strains in all three media conditions. When treated with cefazolin the MRSA JE2 Î”mazEF displayed sensitivity while WT and complemented strains were resistant. Î”mazEF biofilms displayed significantly decreased antibiotic tolerance to both vancomycin and cefazolin in comparison to WT and complement biofilms.

Discussion The mechanism behind S. aureus biofilm antibiotic tolerance and its ability to establish a chronic infection remains unknown.

Conclusion The toxin-antitoxin system mazEF acts to inhibit biofilm formation and promote biofilm antibiotic tolerance, which allows S. aureus to transition

927 Serum D-Dimer: A Promising Marker to Guide Timing of Reimplantation

Authors Saad Tarabichi, Graham S Goh, Colin M Baker, Karan Goswami, steven Yacovelli, Javad Parvizi

Background and Rationale Two-stage exchange arthroplasty remains the gold standard treatment for periprosthetic joint infection (PJI). Despite multiple attempts, no reliable marker to determine infection eradication and the optimal time of reimplantation has been identified. The purpose of this study was to assess the diagnostic utility of serum D-dimer and other serum biomarkers in predicting successful eradication of infection following reimplantation.

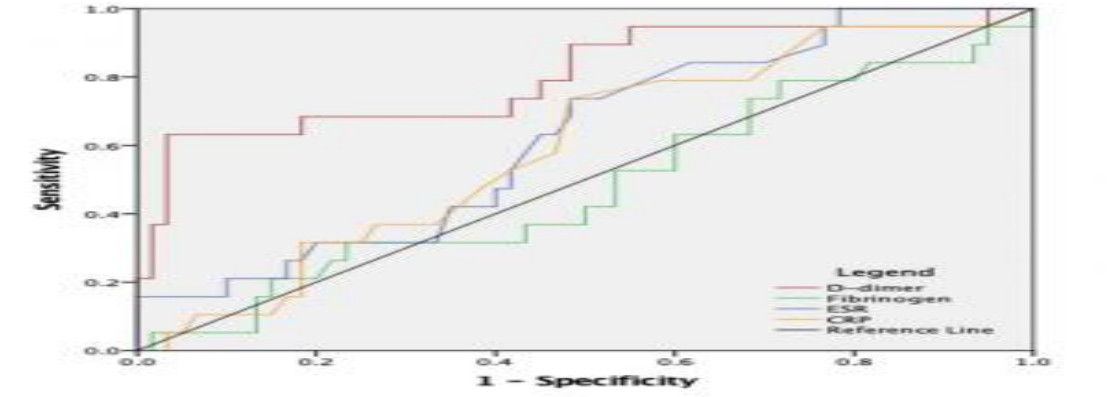
Study Question Can Serum D-dimer predict failure following reimplantation?

Methods This prospective study enrolled 142 patients undergoing second-stage reimplantation between November 2015 and December 2020. All patients met the 2018 International Consensus Meeting criteria for PJI. Serum D-dimer, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured prior to reimplantation. Treatment success was defined using the Musculoskeletal Infection Society Outcome-Reporting Tool. Receiver operating characteristic curves were used to assess the diagnostic accuracy of D-dimer, ESR, and CRP in predicting failure following reimplantation at minimum 1-year follow-up.

Results A total of 121 patients (85%) completed follow-up. Treatment failure following reimplantation occurred in 31 patients (25.6%) at mean follow-up of 3.2 years (range, 1.0â€“5.7). Mean D-dimer was significantly higher in the treatment failure group (2102 ng/mL vs. 830 ng/mL), whereas mean ESR and CRP were not significantly different between the groups. D-dimer demonstrated the best diagnostic utility (area under the curve [AUC] 0.760, sensitivity 58.1%, specificity 93.3%), outperforming both ESR (AUC 0.583, sensitivity 62.1%, specificity 56.8%) and CRP (AUC 0.548, sensitivity 66.7%, specificity 52.3%). Using the Youden index, a D-dimer level of â‰¥1604 ng/mL was identified as the optimal cutoff that predicted failure following reimplantation.

Discussion Serum D-dimer was superior to ESR and CRP in assessing control of infection after the first stage of a two-stage protocol for PJI and could serve as a reliable marker for predicting failure following reimplantation.

Conclusion Further studies with larger cohorts are needed to evaluate its role in determining the optimal timing of reimplantation.



928 Serum D-dimer: An Excellent Screening Test for Periprosthetic Joint Infection

Authors Saad Tarabichi, Graham S Goh, Colin M Baker, Emanuele Chisari, Alisina Shahi, Javad Parvizi

Background and Rationale No single test has demonstrated absolute accuracy in the diagnosis of periprosthetic joint infection (PJI). Serum markers are often used as screening tools to avoid unnecessary joint aspiration in cases with a low pretest probability of infection. This study aimed to determine the utility of serum D-dimer both as a diagnostic marker and as a screening test for PJI in patients undergoing revision arthroplasty.

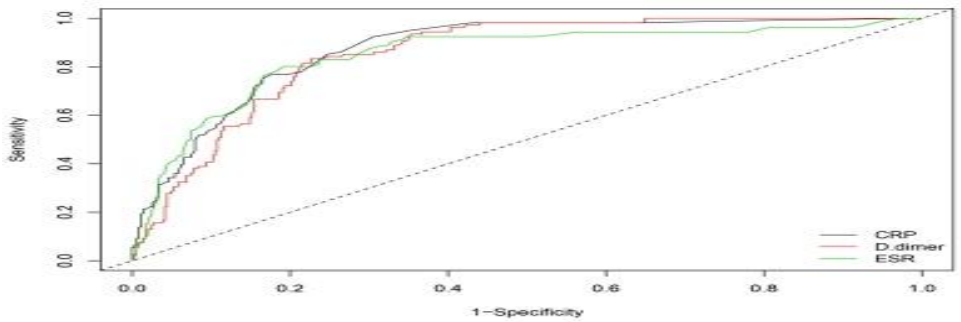
Study Question Does Serum D-dimer outperform CRP and ESR as a screening test for PJI in patients undergoing revision arthroplasty?

Methods This prospective study enrolled 503 patients undergoing revision hip or knee arthroplasty between May 2017 and August 2021. PJI was defined using the 2018 International Consensus Meeting (ICM) criteria. Serum D-dimer, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured preoperatively. Twenty patients had an inconclusive ICM score and were excluded. Receiver operating characteristic curves were used to assess the utility of each biomarker in the diagnosis of PJI. Additional analyses maximizing sensitivity were performed to determine the optimal cutoff of each marker when used as a screening test.

Results Of the 483 included patients, 111 (29%) were ICM positive and 372 (71%) were ICM negative. All three serum markers, D-dimer (area under the curve [AUC] 0.853, sensitivity 83.3%, specificity 77.3%), CRP (AUC 0.873, sensitivity 92.6%, specificity 69.3%) and ESR (AUC 0.848, sensitivity 80.2%, specificity 80.8%), demonstrated comparable diagnostic accuracy for the diagnosis of PJI. When maximizing sensitivity to 100%, D-dimer demonstrated the best diagnostic utility (AUC 0.853, specificity 35.1%), outperforming both ESR (AUC 0.848, specificity 2.8%) and CRP (AUC 0.873, specificity 0%). A serum D-dimer level of â‰¥244 ng/mL was identified as the optimal cutoff for use as a screening test.

Discussion All three serum markers demonstrated similar diagnostic accuracy for PJI. However, after maximizing sensitivity in order to determine which biomarker performed best as a screening test, serum D-dimer was the most specific.

Conclusion Although serum D-dimer demonstrated similar diagnostic accuracy as ESR and CRP, it outperformed both aforementioned markers when used as a screening test for PJI. Nonetheless, additional studies with larger cohorts are needed to validate these findings.



929 When Do Cultures First Turn Positive in Patients with PJI?

Authors Saad Tarabichi, luigi zanna, Qudratullah qadiri, graham S goh, Mustafa Citak, javad Parvizi

Background and Rationale Despite its well-established limitations, culture remains the gold standard for microbial identification in periprosthetic joint infection (PJI). However, there is still no benchmark for the time-to-positivity (TTP) on culture for specific microorganisms. This study aimed to establish normative TTP data for pathogens commonly encountered in PJI.

Study Question Can we establish normative TTP data for pathogens commonly encountered in PJI?

Methods This retrospective multicenter study reviewed all patients who underwent hip or knee revision arthroplasty from February 2016 to August 2021 at two tertiary centers in the United States and Germany. Patients were excluded if they did not meet the 2018 International Consensus Meeting (ICM) criteria for PJI. TTP on culture media was recorded for each sample taken intraoperatively. Two-tailed t-tests and analysis-of-variance were used to compare the mean TTP between gram-positive and gram-negative organisms, different microbial species, and different specimen types.

Results A total of 538 patients with PJI (as defined by ICM criteria) were included. The mean number of positive cultures per patient was 4.33 (range 1-12). Gram-negative organisms (n=225) grew significantly faster on culture than their gram-positive (n=1,774) counterparts (2.9 days vs 4.0 days). Methicillin-resistant staphylococcus aureus (TTP=2.29 days; n=85) demonstrated the fastest TTP, followed by methicillin-sensitive staphylococcus aureus (TTP=2.67 days; n=393), gram-negative rods (TTP=2.69 days; n=163), streptococcus species (TTP=3.13 days; n=230), staphylococcus epidermidis (TTP=4.5 days; n=555), cutibacterium acnes (TTP=7.18 days; n=197), and candida albicans (TTP=10.3 days; n=37). When evaluating mean TTP based on the type of specimen, synovial fluid (TTP=2.31 days; n=109) exhibited the shortest TTP, followed by soft tissue (TTP= 4.0 days; n=1175) and bone (TTP=4.49 days; n=778).

Discussion To our knowledge, this is the first study of its kind that has aimed to identify the TTP of different microorganisms that are commonly encountered in PJI. Methicillin-resistant staphylococcus aureus demonstrated the fastest TTP, while slow-growing candida albicans demonstrated the slowest.

Conclusion To our knowledge, this is the first study to provide normative data on the TTP of common microorganisms that are known to cause PJI. Nonetheless, additional studies with larger cohorts are needed to validate these benchmarks.

931 Utility of Synovial Biomarkers in the Diagnosis of Acute PJI

Authors Saad Tarabichi, Graham S Goh, Colin M baker, Matthew B Sherman, Diana Fernandez-Rodriguez, Javad Parvizi

Background and Rationale The diagnosis of periprosthetic joint infection (PJI), particularly during the early postoperative period, remains challenging. Existing literature evaluating the diagnostic utility of biomarkers for acute PJI has been limited by small sample sizes and the use of outdated diagnostic criteria. This study aimed to assess the accuracy of synovial biomarkers in the detection of acute PJI.

Study Question What is the utility of synovial biomarkers in the diagnosis of acute PJI?

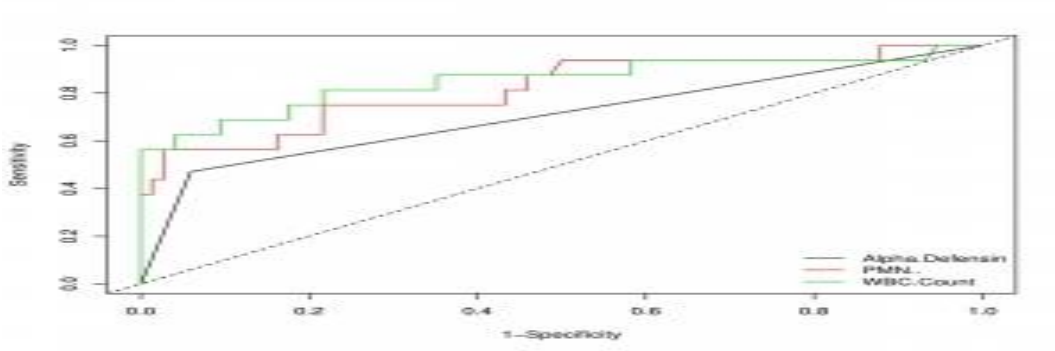
Methods This retrospective study identified 106 patients that underwent a joint aspiration within 90 days of the index hip or knee arthroplasty. Acute PJI was defined using the 2018 International Consensus Meeting (ICM) criteria. Five patients had an inconclusive ICM-score and were excluded. Receiver operating characteristic curves were used to assess the utility of white blood cell count (WBC), polymorphonuclear leukocyte percentage (PMN%) and Alpha-Defensin in the diagnosis of PJI.

Results Of the 101 patients included, 17 (16.8%) were ICM-positive and 84 (83.2%) were ICM-negative.

WBC (area under the curve [AUC] 0.850, sensitivity 81.3%, specificity 78.4%) and PMN% (AUC 0.817, sensitivity 56.3%, specificity 97.3%) demonstrated superior accuracy compared to Alpha-Defensin (AUC 0.706, sensitivity 47.1%, specificity 94.0%) for diagnosis of acute PJI. Additionally, the combination of WBC/PMN% exhibited the highest accuracy in the diagnosis of acute PJI (AUC 0.851, sensitivity 81.3%, specificity 80.0%).

Discussion The combination of WBC count and PMN% demonstrated the highest diagnostic utility for the diagnosis of acute PJI. While the utility of alpha-defensin in the diagnosis of chronic PJI is well-established, it demonstrated poor sensitivity for the diagnosis of acute PJI.

Conclusion Conventional synovial biomarkers such as WBC and PMN% demonstrated excellent accuracy in the diagnosis of acute PJI. While Alpha-Defensin demonstrated high specificity, its poor sensitivity undermines its value in this setting. Further studies with larger cohorts are needed to validate these findings.



932 Utility of Synovial Biomarkers in Predicting Failure following Reimplantation

Authors Saad Tarabichi, Graham S Goh, Irfan A Khan, Colin M Baker, Javad Parvizi

Background and Rationale Two-stage exchange arthroplasty remains the preferred treatment for chronic periprosthetic joint infection (PJI) that has a 20-30% failure rate. There are no accurate metrics that can help with optimal time of reimplantation. The purpose of this study was to assess the diagnostic utility of common synovial biomarkers in predicting successful control of infection following completion of two-stage exchange arthroplasty.

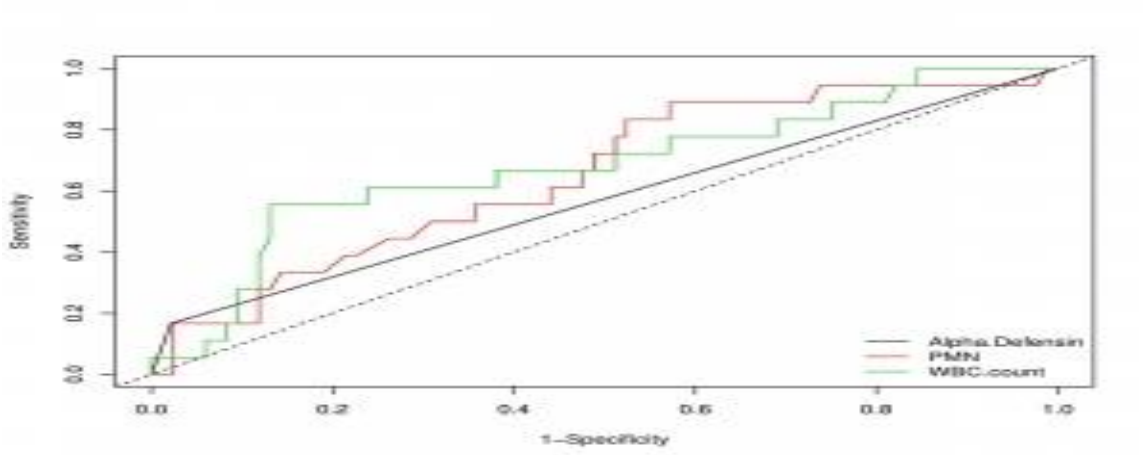
Study Question Can Synovial Biomarkers Predict Failure following Reimplantation?

Methods This retrospective study identified 125 patients undergoing second-stage hip or knee reimplantation between January 2013 and March 2021. All patients had an aspiration prior to reimplantation. Treatment success and failure were defined using the Musculoskeletal Infection Society Outcome-Reporting Tool. Receiver operating characteristic curves were used to assess the diagnostic accuracy of white blood cell count (WBC), polymorphonuclear leukocyte percentage (PMN%), and Alpha-Defensin in predicting failure following reimplantation at minimum 1-year follow-up.

Results A total of 102 (81.6%) patients completed follow-up. Treatment failure following reimplantation occurred in 18 patients (17.6%) at a mean follow-up of 3.4 years (range, 1â€“5.9). WBC (area under the curve [AUC] 0.680, 55.6% sensitivity, 86.9% specificity) and PMN% (AUC 0.651, sensitivity 88.9%, specificity 42.9%) demonstrated superior accuracy compared to Alpha-Defensin (AUC 0.572, sensitivity 16.7%, specificity 97.8%). Alpha-Defensin was negative in 83.3% of patients that subsequently failed treatment. Using the Youden index, WBC â‰¥1,898 cells/ÂµL and PMN% â‰¥40.3 were identified as optimal cutoffs that predicted failure following reimplantation.

Discussion Existing synovial biomarkers did not demonstrate high prognostic utility for predicting failure following reimplantation. However, the WBC count and PMN% cutoffs established in the present study may help determine infection eradication and optimal timing of reimplantation.

Conclusion Although synovial markers could not predict treatment failure with definitive accuracy, WBC and PMN% could help to guide timing of reimplantation. Future studies should explore the use of newer synovial markers for the assessment of infection eradication following two-stage exchange arthroplasty.



934 Polymicrobial PJI Failures: Reinfection or Persistence?

Authors Emanuele Chisari, Leanne Ludwick, Nicolas Piuzzi, Craig Della Valle, Carlos Higuera, Javad Parvizi

Background and Rationale The management of chronic hip and knee periprosthetic joint infection (PJI) involves surgical intervention and antibiotic treatment. This treatment is known to fail in about 30% of patients in the first two years after surgery. In case of reinfection, there is no conclusive data to determine if the infection is as a result of an organism that was present previously or a new organism. Data using next generation sequencing (NGS) suggest that PJI is caused by multiple organisms but is considered monomicrobial due to the limitation of culture in isolating all infective organisms.

Study Question Are failed two-stage exchanges the result of an organism that was originally detected by NGS or a new organism?

Methods A multicenter retrospective study including data from three different PJI referral centers was designed. Cases of polymicrobial PJI at the time of resection surgery (first stage) from 2000 to 2019 were included. Patients who failed at a later time point were defined and the microbiological data was scrutinized. Statistical analysis consisted of descriptive statistics.

Results A total of 83 polymicrobial PJI, treated with a two stage exchange, were included. Fifteen of 83 patients (18.07%) had cultures positive at reimplantation. Of these, 8 (53%) patients reported one of the organisms retrieved at the time of the resection despite a prolonged course of antibiotic treatment targeted towards that organism. Additionally, 24 out of total number of patients (28.91%) had an additional procedure between resection and reimplantation (i.e. spacer exchange or washout). A subgroup analysis of the 59 that did not have a third procedure in the two-stage exchange showed 11 (18%) had a positive culture at reimplantation. Of these, 7 (63%) were due to the same organisms cultured at resection.

Discussion Culture-positive polymicrobial PJI is a good model to study multiple organisms in chronic PJI infections.

Conclusion In the present study, we report that most infections at the time of reimplantation, despite antimicrobial treatment, are represented by the persistence of an organism isolated at the time of the first surgery. Multiple surgeries, including spacer exchange and washout can reduce the bioburden in the joint, with unclear effect on the overall success rate.

935 Is Joint Aspiration Needed before Reimplantation?

Authors Emanuele Chisari, Leanne Ludwick, Taylor D'Amore, Jenna Mandel, Brendan Gleason, Javad Parvizi

Background and Rationale The management of hip and knee periprosthetic joint infection (PJI) involves both surgical intervention and antibiotic treatment. In the first two years, this treatment is known to fail in about 30% of patients. Currently, there is no consensus on how to diagnose possible residual infection before reimplantation. Many surgeons rely on joint aspiration prior to performing the reimplantation surgery.

Study Question Is the use of routine joint aspiration of any value before reimplantation?

Methods A retrospective cohort study using data from a large PJI referral center was designed. Cases of chronic and acute PJI treated with a two-stage exchange from 2000 to 2019 were included. PJIs were defined according to the 2018 ICM criteria. Success was defined according to the 2019 MSIS criteria. Statistical analysis consisted of descriptive statistics and logistic regression modeling. Patients were divided into three groups: (1) patients who had both serum and synovial markers before reimplantation, (2) patients who had serum markers but had a dry tap at the time of joint aspiration, (3) patients who did not undergo aspiration before reimplantation.

Results A total of 501 patients were included. 147 (29.3%) were part of group 1, 70 (13.9%) in group 2 and 284 (56.6%) in group 3. No difference in body mass index, Charlson comorbidity index, or sex were retrieved among the three groups. Success rates did not differ among the three groups (73% vs. 76.1 vs. 68%; p=0.488). The mean time to reimplantation was shorter for group 3 (131Â±115 vs. 129Â±98.5 vs. 94.2Â±145 days; p<0.001). When acute and chronic PJI were analyzed as subgroup analyses, similar results were retrieved.

Discussion Based on the current data, it appears that joint aspiration prior to reimplantation continues to yield minimal fluid in a large number of patients (dry tap). In addition, obtaining joint fluid prior to reimplantation does not appear to impact the outcome of two-stage exchange arthroplasty.

Conclusion The current study, despite all its limitations, suggests that routine aspiration of joints with a spacer in place and prior to reimplantation may not be needed. The findings of this study should be examined in a prospective and randomized manner.

937 New Era in Understanding Periprosthetic joint infections: Microbiome, Antigen Trafficking and The Breach in Gut Epithelia Barrier

Authors Emanuele Chisari, Jeongeun Cho, Marjan Wouthuyzen-Bakker , Javad Parvizi

Background and Rationale A growing number of recent investigations on the human genome, gut microbiome, and proteomics suggests that the loss of mucosal barrier function, particularly in the gastrointestinal tract, may substantially affect antigen trafficking, ultimately influencing the close bidirectional interaction between the gut microbiome and the immune system. This cross-talk is highly influential in shaping the host immune system and ultimately clinical infections.

Study Question Is a change in microbiome and/or breach in GI epithelial barrier partially responsible for development of periprosthetic joint infections (PJI)?

Methods Multiple biomarkers of gut barrier disruption were tested in parallel in plasma samples collected as part of a prospective cohort study of patients undergoing revision arthroplasty for aseptic failures or PJI (As defined by the 2018 ICM criteria). All blood samples were collected before any antibiotic was administered. Samples were tested for Zonulin, soluble CD14 (sCD14), and lipopolysaccharide (LPS) using commercially available enzyme-linked immunosorbent assays. Statistical analysis consisted of descriptive statistics, Mann-Whitney t-test, and Kruskal-Wallis test.

Results A total of 134 patients were consented and included in the study. 44 were classified as PJI (30 chronic and 14 acute), and 90 as aseptic failures (26 primaries and 64 aseptic revisions). Both Zonulin and sCD14, but not LPS, were found to be significantly increased in the PJI group compared to non-infected cases ($p<0.001$; $p=0.003$). Higher levels of Zonulin were found in acute infections compared to chronic PJI ($p=0.005$

Discussion This prospective ongoing study reveals a possible link between gut permeability and the â€˜gut-immune-joint axisâ€™ in PJI.

Conclusion If this association continues to be born out with larger cohort recruitment and more in-depth analysis, it would have an immense implication in managing patients with PJI. In addition to administering antimicrobials, patients with PJI and other orthopedic infections may require gastrointestinal modulators such as pro and prebiotics.

938 Periprosthetic Joint Infection and the Trojan Horse Theory: Examining the Role of Gut Dysbiosis and Epithelial Integrity

Authors Emanuele Chisari, Jeongeun Cho, Marjan Wouthuyzen-Bakker , Javad Parvizi

Background and Rationale Surgical site infections are uncommon yet dreadful complication after total joint arthroplasty. Emerging evidence suggested a role for the gut microbiome in the pathogenesis of such infections as a reservoir of opportunistic pathogens.

Study Question Does the gut microbiome have a role in the pathogenesis of surgical site infections?

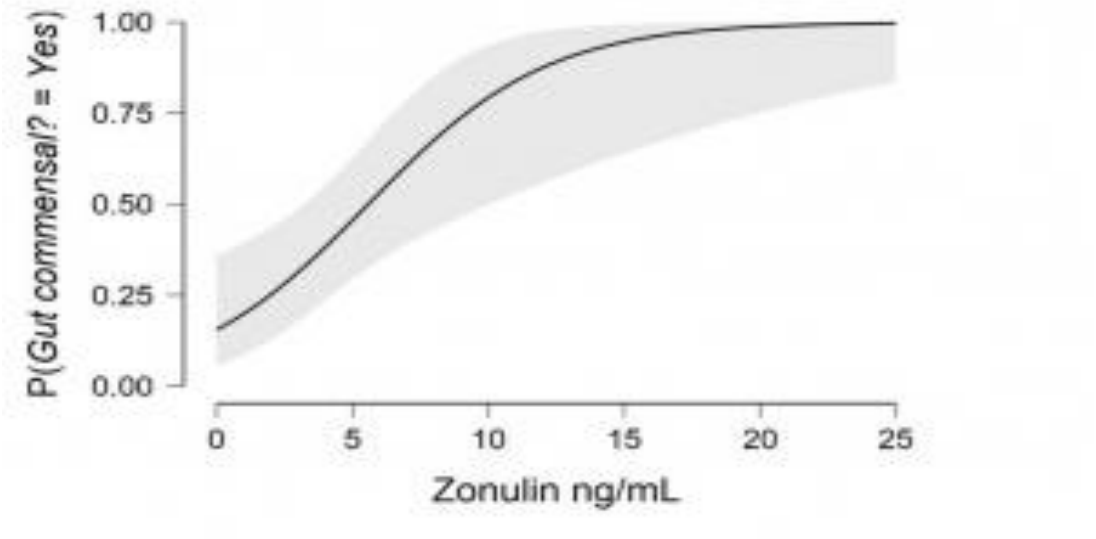
Methods A secondary analysis of an ongoing trial looking at gut dysbiosis and periprosthetic joint infections was performed on patients that had next-generation sequencing done as part of their workup. Gut permeability and dysbiosis was measured using known biomarker such as Zonulin. Statystical analysis consisted of descriptive statistics and logistic regression modeling

Results Among the cohort of 46 (47.8% female) patients, with a mean age of 68.47 years (range, 40 to 91) and a mean BMI 31.15 Â± 6.49 kg/m2, 38 patients underwent revision for PJI (29 chronic and 9 acute infections), and 8 patients were classified as aseptic failures. Then, review of each of the bacteria retrieved was performed. Those known to be gut commensal based on available literature were noted. When regression modeling was performed, Zonulin levels were found to be associated with an increased probability of a similar finding (Estimate: 0.377, OR: 1. 458; p=0.001)

Discussion In our study, we report the first clinical evidence of the translocation of bacteria from the gut to the joint in surgical site infections. In particular, when evaluating the microbiological profile of the NGS signal, a great number of known gut commensals were seen in patients with highly permeable dysbiosis gut

Conclusion Manipulation of the guy microbiome may become part of an essential and comprehensive approach for management of patients with PJI.

Figure 1. Conditional estimates plot based on bi-variable logistic regression is provided.



939 Cutibacterium acnes Native Vertebral Osteomyelitis: A Case Series

Authors Matteo Passerini, Julian Maamari, Don Bambino Geno Tai, Zelalem Temesgen, Aaron J Tande, Elie F Berbari

Background and Rationale Recovering Cutibacterium acnes from spine tissue is often interpreted as a contaminant. However, its role in spine pathology is increasingly being recognized, especially for hardware-associated infections. There is a paucity of data regarding its role in native vertebral osteomyelitis (NVO).

Study Question What are the clinical features, optimal therapy, and outcome of patients with C. acnes NVO?

Methods We identified adults with at least a single positive spine culture for C. acnes from 2011 to 2021 at Mayo Clinic, Rochester (MN). C.acnes NVO is defined as either a) two spine cultures positive for C. acnes AND radiological and clinical suspicion of NVO; or b) one spine culture positive for C. acnes AND radiological and clinical suspicion of NVO AND improvement after treatment. We excluded patients with hardware or polymicrobial infection. We collected data about demographics, clinical presentation, radiological and microbiological findings, treatment, and outcomes.

Results Among 267 patients with at least one positive spine culture, 16 met our criteria for C. acnes VO. The data collected are summarized in Table 1. Back pain was present in all cases, whereas only one patient had fever. Nine patients (56.3%) had a previous spinal procedure, and two (12.5%) a recent trauma. The median time to onset of symptoms after surgery or trauma was 80 days (IQR 26-165). The median time for spine culture positivity was 5 days (range 3-13). Two patients underwent surgical debridement, 2 received upfront oral antibiotics, and 1 patient switched to oral therapy within one week. The treatment success rate was 100% at a median follow-up of 41 months (IQR 18-76).

Discussion The results of our cohort reflect the indolent nature of a C. acnes NVO. Although the median time to detection was 5 days, one sample required 13 days, suggesting that a prolonged incubation period may be warranted when suspecting C. acnes NVO. Similar to NVO caused by other organisms, most patients were successfully managed with a course of antimicrobial therapy without surgery. Oral antimicrobial therapy may be an attractive choice, but further studies are needed.

Conclusion Clinicians should consider C. acnes in the differential diagnosis of NVO, especially in the setting of recent spinal surgery or injection. Prolonged incubation of spinal cultures is suggested for improved detection. Treatment with parenteral beta-lactams is effective, but targeted oral therapy may be a valid alternative.

940 Synovial CRP is a Useful Adjunct for Diagnosis of Periprosthetic Joint Infection

Authors Colin M Baker, Graham S Goh, Saad Tarabichi, Noam Shohat, Javad Parvizi

Background and Rationale The diagnostic utility of synovial C-reactive protein (CRP) has been debated for a while. Existing studies were limited by small sample sizes and used outdated criteria for periprosthetic joint infection (PJI). Furthermore, the relationship between synovial and serum CRP has rarely been investigated in the setting of PJI.

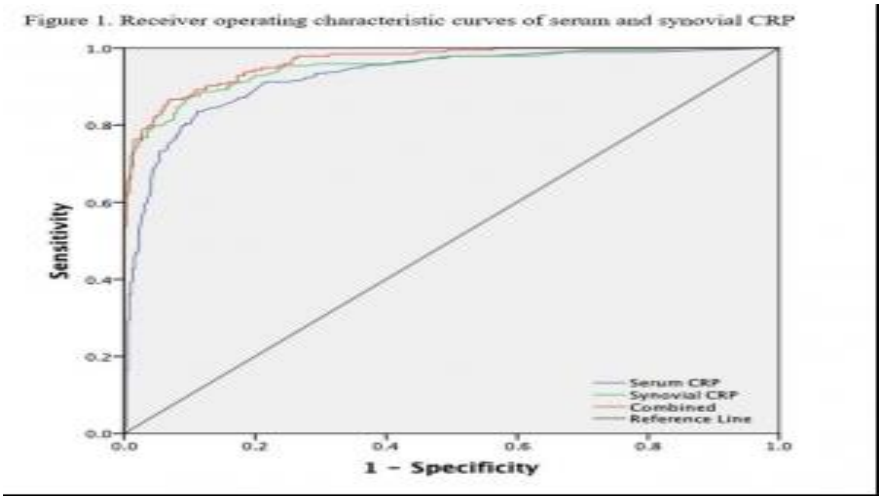
Study Question What is the diagnostic utility of synovial CRP and its relationship with serum CRP and other common biomarkers?

Methods Between 2014 and 2021, 621 patients who underwent evaluation for PJI prior to revision arthroplasty were reviewed. Biomarkers including serum CRP and erythrocyte sedimentation rate (ESR), synovial CRP, polymorphonuclear leukocyte percentage (PMN%), white blood cell count (WBC) and alpha-defensin were evaluated using the 2018 International Consensus Meeting (ICM) criteria.

Results In total, 194 patients had PJI, 394 were considered aseptic failures and 33 were inconclusive. Synovial CRP showed an area under the curve (AUC) of 0.951 (95% CI, 0.932â€“0.970) with 74.2% sensitivity and 98.0% specificity, whereas serum CRP had an AUC of 0.926 (95% CI, 0.903â€“0.949) with 83.5% sensitivity and 88.3% specificity. There was good correlation between synovial and serum CRP (R=0.703; 95% CI, 0.604â€“0.785). The combination of serum and synovial CRP yielded a significantly higher AUC than that obtained when using serum CRP alone (AUC 0.964 vs. 0.926, p=0.016).

Discussion Synovial CRP demonstrated excellent accuracy when used to determine the presence of PJI.

Conclusion There was still good correlation between serum and synovial CRP levels in revision arthroplasty patients. These findings support the routine use of synovial CRP in the evaluation of PJI.



941 Closed Suction Drains after Revision for Infected TJA May Not be Necessary

Authors Farideh Najafi, Michael Meghpara, Jonah M Stein, Matthew Sherman, Nicholas V Peterson, Camilo Restrepo, Javad Parvizi

Background and Rationale There are numerous level-1 studies that demonstrate closed suction drainage (CSD) have little to no benefit after routine primary total joint arthroplasty (TJA). There is little data on the role of CSDs after revision TJA. Compared to primary TJA, revision TJAs are more complex procedures with longer operative times and greater potential for dead space and hematoma formation. CSD may therefore prove beneficial in revision TJA.

Study Question Is there any clinical advantage to the use of closed suction drainage after revision for infected TJ?

Methods We conducted a retrospective cohort study between 2007 and 2021 of patients undergoing revision TJA for infection. Primary outcome was rate of allogeneic blood transfusion, and secondary outcomes included total blood loss (TBL), length of stay and wound complications (hematoma, infection, and dehiscence). Patients undergoing revision surgery for reasons other than infection or those with incomplete data set were excluded. A total of 594 patients were identified that included 111 patients utilizing CSD and 483 patients without CSD after revision for infected hip and knee surgery. The Gross formula was used to calculate TBL.

Results There were no significant differences in rates of post-operative blood transfusion, TBL, and wound complications (hematoma, infection, and dehiscence) between the two groups (p =0.376, 0.591, 1.000, 0.469, 1.000 respectively). Higher rates of transfusion were associated with increasing operation time. Lower rates of transfusion were associated with revision TKA. When adjusted for demographic confounding variables, there was no difference in rates of transfusion between groups (OR 0.97, 95% CI 0.61 â€“ 1.55, p = 0.909). Also adjusted regression analysis for demographic variables, showed no difference in rates of blood loss between groups (estimate 77.37 mL, 95% CI -408.13 â€“ 562.86, p = 0.755). Patients receiving CSD had shorter hospital stay vs. patients without CSD (6.35 days vs. 7.71 days, p = 0.035).

Discussion The current study revealed that routine use of CSD after revision TJA for infection does not provide much clinical benefit.

Conclusion There is a role for CSD usage in a select group of patients.

942 Low Dose Aspirin for VTEp Results in Lower PJI Rates

Authors Farideh Najafi, Joseph K Kendal, Nicholas V Peterson, Kerri-Anne Ciesielka, Diana Fernandez-Rodriguea , Camilo Restrepo, Javad Parvizi, Nicholas M Bernthal

Background and Rationale The use of Aspirin as VTE prophylaxis, has shown to have anti-staphylococcal and anti-biofilm role. Optimal ASA dosage would facilitate antimicrobial effects while avoiding over-aggressive inhibition of platelet antimicrobial function.

Study Question What is the rate of PJI after TJA in patients receiving low-dose ASA (81mg bid), in comparison to high-dose ASA (325mg bid)?

Methods We conducted a retrospective cohort study between 2008 and 2020. Eligible patients were older than 18 years, undergoing primary TJA, had a minimum follow-up of 30 days and received a full course of ASA post-operatively as VTE prophylaxis. Patientsâ€™ records were reviewed for PJI, according to MSIS criteria. Entries were excluded if patients underwent a revision arthroplasty, had a previous history of coagulopathy or ASA regimen was not completed.

Results In total, 15,825 patients were identified, 8,761 patients received low-dose ASA, and 7,064 patients received high-dose ASA. More patients in the low-dose ASA cohort had a history of diabetes mellitus (7.1% vs. 2.53%, p <0.001). Patients receiving high-dose ASA had a higher rate of PJI vs. patients receiving low-dose ASA (0.35% vs. 0.10%, p = 0.001). This relationship was maintained when comparing subgroups comprising TKA (0.32% vs. 0.06%, p = 0.019) or THA (0.38% vs. 0.14%, p = 0.035) solely, and accounting for potentially confounding demographic variables (OR 3.37, 95% CI 1.58 - 8.04, p = 0.003). There were no statistically significant differences in rates of post-operative MI, CVA, GI ulceration or hemorrhage. ROC/AUC analysis of platelet count as a variable for the development of PJI in both cohorts revealed no significant association.

Discussion There were no statistically significant differences in rates of post-operative MI, CVA, GI ulceration or hemorrhage. ROC/AUC analysis of platelet count as a variable for the development of PJI in both cohorts revealed no significant association.

Conclusion Low dose ASA had a lower rate of PJI compared to high-dose ASA

943 Sterile Back Table in the OR Can Harbor Infective Pathogens

Authors Farideh Najafi, Diana FernÃ¡ndez-RodrÃ-guez , Javad Parvizi

Background and Rationale One important factor for SSI prevention is implementation of ultraclean OR. This study designed to evaluate back-table sterility during TJA.

Study Question Is the back-table, because of being out of surgeonâ€™s view for the most part, contaminated during surgical procedures?

Methods This prospective study includes 52 patients undergoing primary TJA between November 2021 and December 2021. A total of 4 swabs (two air and two table) obtained for each case, at conclusion of surgery and prior to drapes take-down. One swab from each set sent for culture and the other for NGS analysis.

Results Among 104 swabs sampling back-table, a total of 13 (12.5%) isolated organisms. Of these, 7 isolated by culture and 6 by NGS. No microorganisms isolated by both culture and NGS from back-table swabs. Among 104 swabs sampling air, a total of 11 (10.6%) isolated organisms. Of these, 6 isolated by culture and 5 by NGS. In 4/104 swabs both culture and NGS isolated organisms from air swabs. 13/104 back-table and air swabs were culture positive. While more than one pathogen was identified in two air swabs; all back-table swabs were monomicrobial by culture. Pathogens identified from 11/104 swabs by NGS; more than one pathogen identified in four swabs (2 air and 2 back-table).

Discussion All organisms isolated by culture and/or NGS are known pathogens that can cause SSI or PJI. Although none of patients in this study developed infection, this study was not powered to investigate effect of back-table contamination on subsequent infection.

Conclusion Findings of this study raise an important issue in that surgical field, including sterile table set-up for instruments is not â€œsterileâ€ and can harbor pathogens. Contamination of surgical field and OR air should always be considered and efforts should be made to minimize their entry into surgical site.

947 Rate of Recurrent Infections and Implant Removal After Initial Debridement in Spine Surgery

Authors Anthony A Oyekan, Dominic Ridolfi, Aaron Zheng, Audrey Chang, Noel Bien Carlos, Ryan Lin, Brandon Couch, Melissa Tang, Joon Y Lee, Jeremy D Shaw

Background and Rationale Surgical site infections (SSIs) in spine surgery are associated with increased morbidity, hospital length of stay, and reoperation. Treatment frequently requires the removal of implants. Despite the abundant literature on infection rates, there is limited data on the rate of infection recurrence after index treatment or implant removal rates.

Study Question What is the rate of infection recurrence and implant removal after initial debridement in spine surgery?

Methods A retrospective review of a prospectively collected database was performed with IRB approval. All patients who underwent spine surgery performed by two fellowship-trained spine surgeons at a single institution between July 2017 to July 2021 were included. Patients less than 90 days since surgery or pre-operative spinal infection were excluded. Infection was defined as gram stain or culture-confirmed growth of organisms from an operative debridement. Recurrent infection was defined as failure of operative debridement and at least four weeks of antibiotics before a repeat operative debridement was required. Chi-square analysis and two-tailed unpaired t-tests were used. $p < 0.05$ was considered significant.

Results Nine hundred and thirty-three subjects (469 M, 464 F; age 56 Â± 15 years) were identified. Post-operative infection patients (n = 19, 9 M, 10 F; age 63 Â± 19 years, BMI 29.2 Â± 7.9, CCI 2.2 Â± 2.7) were older (p = 0.035) and had a greater CCI (p = 0.046) than non-infected patients (n = 914, 460 M, 454 F; age 56 Â± 15 years, BMI 31.0 Â± 7.5, CCI 0.9 Â± 1.5) despite no differences in gender (p = 0.798), BMI (p = 0.343) or revision procedure (p = 0.174). The rate of post-operative infection requiring debridement was 2.03%. Three patients (15.79%) had a recurrent infection and 3 patients (16.67%) with prior instrumentation required removal of implants during operative debridement. 47.37% of infections required multiple debridements. The average number of debridements needed to clear an infection was 1.6 Â± 0.8.

Discussion Spine SSIs frequently require multiple revision procedures for eradication of infection despite antibiotic therapy and debridement. Our findings are a reference for surgeons who may be counseling patients on infection and researchers evaluating spine SSI.

Conclusion Recurrent infection and removal of hardware are common complications in spine surgery.

	Infection (n = 19)	No Infection (n = 914)	P-Value
Age	63 ± 19 years	56 ± 15 years	0.035
Male	9	460	0.798
Female	10	454	$\chi^2 = 0.0653$
BMI	29.2 ± 7.9	31.0 ± 7.5	0.343
CCI	2.2 ± 2.7	0.9 ± 1.5	0.046
Primary	14	462	0.175
Revision	5	81	$\chi^2 = 1.8403$
Cervical	8	337	0.266
Thoracic	10	248	$\chi^2 = 1.2359$
Lumbar	8	550	
Trauma	9	212	0.019
Degenerative	10	670	$\chi^2 = 5.4696$

948 Increased Surgical Site Subcutaneous Fat Thickness Is Associated with Infection after Lumbar Laminectomy with Instrumented Fusion

Authors Anthony A Oyekan, James Rooney, Dominic Ridolfi, Jonathan Dalton, Aaron Zheng, Stephen Chen, Melissa Tang, Emmett J Gannon, Joon Lee, Jeremy Shaw

Background and Rationale Spinal wound complications are multifactorial, with identified risk factors including posterior approach, multi-level surgery, comorbidity burden, and obesity. Conventional definitions of obesity rely upon BMI, which cannot account for local fat distribution. The subcutaneous fat to skin-lamina thickness ratio (SQ:SL) has been identified as a stronger predictor than BMI for surgical site infections (SSI) in select spine procedures. Few studies on this correlation exist.

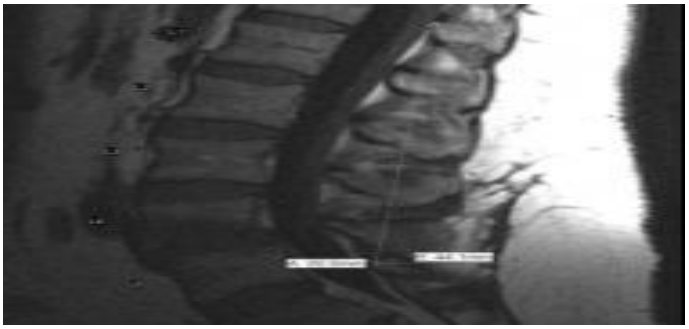
Study Question Is the SQ:SL thickness ratio associated with infection for lumbar laminectomy with fusion?

Methods A retrospective analysis was performed with IRB approval. Patients who underwent elective single or two-level lumbar laminectomy with posterolateral instrumented fusion performed by three fellowship-trained spine surgeons at a single institution between January 2019 to January 2020 were included. Patients with a fracture, infection, tumor, previous surgery, or no lumbar spine MRI were excluded. The SQ:SL thickness ratio was calculated based on mid-sagittal T1-weighted MRI measurements. Subcutaneous fat (SQ) thickness was measured from skin to the dorsal spinous process. Skin lamina (SL) thickness was measured from skin to the ventral lamina. Medical records were reviewed for co-morbidities and surgical outcomes. Pearson correlation was used to assess the relationship between the SQ:SL and SSI.

Results One hundred and thirty-six subjects (41 M, 95 F; age 63 Â± 13 years, BMI 30.9 Â± 6.1, ASA score 2.6 Â± 0.6) with 6 (4.4%) wound complications including 3 (2.2%) infections requiring revision procedure were identified. SQ:SL thickness ratio (r = 0.371; pp =0.002) was associated with and a stronger predictor of infection than BMI (r = 0.235; p = 0.048). The average paraspinal fat thickness was 31.9 Â± 12.6 mm with an average SQ:SL thickness ratio of 0.474 Â± 0.116 mm.

Discussion Increased lumbar surgical site fat may increase the risk of SSI after lumbar laminectomy with fusion. Pre-operative advanced imaging including MRI may be a valuable tool for patient counseling, risk assessment, and optimization.

Conclusion Increased SQ:SL thickness ratio of paraspinal fat measurement is associated with wound complications including SSI requiring revision surgical procedure after short-segment lumbar laminectomy with fusion.



949 Closed Incision Negative Pressure Therapy Reduces Incidence of Re-Operation for Surgical Site Infection in Spine Surgery

Authors Anthony A Oyekan

Background and Rationale Surgical site infections (SSIs) remain a prevalent complication following spine surgery. In some cases, SSIs require re-operations associated with significant morbidity and resource utilization. Closed incision negative pressure therapy (ciNPT) has emerged as a potential tool for reducing the incidence of SSIs, but evidence has been limited to smaller studies.

Study Question Does ciNPT reduce the incidence of surgical site infection?

Methods A retrospective review of a prospectively collected database was performed with IRB approval. All patients who underwent spine surgery with ciNPT performed by two fellowship-trained spine surgeons at a single institution between July 2017 to July 2021 were included. An age and gender-matched cohort of spine surgery patients treated by the same surgeons with traditional dressings between June 2020 to July 2021 were included for comparison. Patients less than 90 days since surgery or pre-operative spinal infection were excluded. Chi-square analysis was used to determine differences in gender and procedure indication (primary vs. revision operation). Two-tailed unpaired t-tests were used to identify differences in continuous variable demographics and complication rate. $p < 0.05$ was considered statistically significant.

Results Nine hundred and six subjects (453 M, 453 F; age 57 Â± 14 years) were identified. ciNPT patients (n = 498, 249 M, 249 F; age 57 Â± 14 years, BMI 31.21 Â± 7.53, CCI 1.6 Â± 1.0) when compared to traditional dressing patients (n = 408, 204 M, 204 F; age 57 Â± 15 years, BMI 30.34 Â± 5.53, CCI 1.2 Â± 0.8) had reduced incidence of wound complication requiring revision (1.20% vs. 3.19%, p = 0.048) and wound infection requiring revision (0.40% vs 1.96%, p = 0.036) within 90 days despite increased BMI (p = 0.042) and no other differences in co-morbidities or surgical indication (p > 0.05).

Discussion Closed incision negative pressure therapy may be an effective tool for reducing the incidence of re-operation in spine surgery due to wound complication or infection. A cost analysis is needed to ascertain the financial implications of this finding.

Conclusion ciNPT in spine surgery is associated with decreased incidence of revision for infection or wound complication

Infection Rate			
	Traditional Dressing	ciNPT	P-Value
All Cases (n = 966)	1.96%	0.40%	0.036
Trauma (n = 185)	3.45%	0%	0.159
Degenerative (n = 662)	1.99%	0%	0.014
Cervical Primary (n = 318)	0.81%	0%	0.319
Cervical Revision (n = 21)	12.50%	0%	0.351
Thoracic Primary (n = 220)	1.33%	0%	0.321
Thoracic Revision (n = 26)	0%	0%	-
Lumbar Primary (n = 485)	2.09%	0.81%	0.242
Lumbar Revision (n = 52)	3.45%	0.00%	0.326

950 Direct anterior approach in primary THA increases the risk of reoperation for superficial infection but not deep prosthetic joint infection compared to posterolateral approach

Authors Brian P Chalmers, Simarjeet Puri, Adam Watkins, Agnes D Cororaton, Andy O Miller, Alberto Carli, Michael Alexiades

Background and Rationale While the direct anterior approach (DAA) has been associated with higher rates of superficial infection and wound healing difficulties compared to other approaches, there remains inconsistent data about the association of surgical approach and periprosthetic joint infection (PJI). As such, we sought to evaluate the risk of reoperation for superficial and deep infection in a multivariate model.

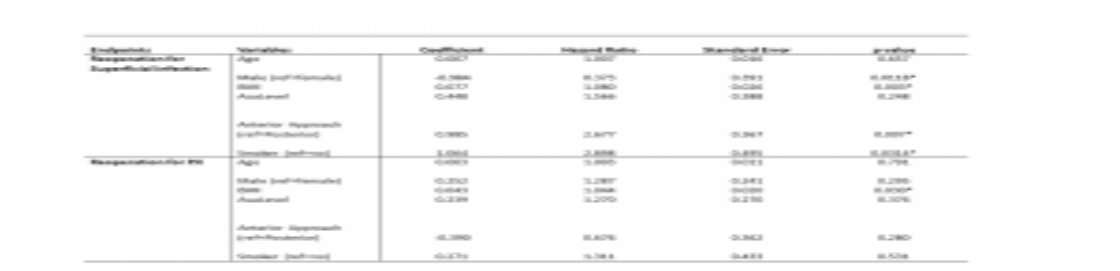
Study Question In a multivariate model controlling for potential confounders including age, sex, smoking status, ASA class, and BMI, is there an association in the incidence of reoperation for superficial and deep infection between DAA and the posterior approach (PA) in patients undergoing primary THA?

Methods We reviewed 16,500 primary THAs, collecting data on surgical approach and any reoperations for superficial infection (n=36) or PJI (n=70). With reoperation for superficial infection and PJI as separate endpoints, we used Kaplan Meier (KM) survivorship analysis to assess survivorship free from reoperation and built Cox Proportional Hazards multivariate models to assess risk factors for reoperation.

Results Between DAA (N=3,351) and PA (N= 13,149) cohorts, rates of superficial infection (0.4% vs 0.2%, respectively) and PJI (0.3% vs 0.5%, respectively) were low and 2-year survivorship free from reoperation for superficial infection (99.6% vs 99.8%) and PJI (99.4% vs 99.7%) were excellent. The risk of developing superficial infection increased with high BMI (hazard ratio (HR)=1.08 per unit increase, p=0.003), direct anterior approach (HR=2.67, p=0.007), and smoking status (HR=2.899, p=0.031) (Table 1). The risk of developing PJI increased with the high BMI (HR=0.043, p=0.03), but not surgical approach (HR= -0.391, p=0.28) (Table 1).

Discussion Overall, we found a low incidence of reoperation for superficial infection and PJI with DAA and PLA THA. In our Cox proportional hazards models, we identified high BMI, smoking status, and DAA as independent risk factors for superficial infection reoperation. However, only BMI, not surgical approach, was associated with a higher incidence of reoperation for PJI.

Conclusion Elevated BMI was a strong risk factor for reoperation for both PJI and superficial infection regardless of surgical approach. Compared to PLA, DAA independently increases risk of reoperation for superficial infection but not PJI.



951 Diagnostic Utility and Thresholds for Commonly Obtained Serum and Synovial Markers prior to Reimplantation in Periprosthetic Joint Infection

Authors Abhijit Seetharam, Julian E Dilley, R. Michael Meneghini, Michael M Kheir

Background and Rationale Diagnosis of persistent periprosthetic joint infection (PJI) during two-stage exchange is critical for determining appropriate timing for reimplantation. However, the diagnostic accuracy and threshold values of routine serum and synovial markers prior to reimplantation remains unclear.

Study Question The purpose of this study was to evaluate the diagnostic performance of several commonly obtained serum and synovial markers including recently studied markers absolute neutrophil count (ANC) and neutrophil-to-lymphocyte ratio (NLR), and to define thresholds for PJI diagnosis to better guide reimplantation.

Methods This was a retrospective review of 249 patients who underwent two-stage exchange with antibiotic spacers for PJI. Charts were reviewed for most recent synovial and serum aspiration data obtained when patients had spacers but prior to planned reimplantation. Synovial makers included white blood cell count (WBC), polymorphonuclear percentage (PMN%), NLR, and ANC. Serum markers included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), WBC, PMN%, NLR, and ANC. The collected markers had their utility in diagnosing PJI examined by area under the curve analysis (AUC). Pairwise comparisons of AUCs were performed for serum and synovial markers.

Results Serum CRP had the highest AUC of all studied markers (0.863). The threshold for serum CRP was 3.1 mg/dL, which provided a sensitivity of 65.3% and specificity of 78.9%. Serum ESR had an â€œacceptableâ€ AUC of 0.749, however all other serum markers qualified as â€œpoorâ€ tests. Synovial ANC had the highest AUC of all synovial makers (0.772), with a cutoff of 3,802 cells/uL, but it did not significantly outperform synovial WBC, PMN%, or NLR, which all had acceptable AUCs.

Discussion The results show serum CRP to have excellent diagnostic utility for diagnosis of persistent PJI in revision total joint arthroplasty with antibiotic spacers, however serum ESR and all synovial markers studied had acceptable AUCs to aid in the diagnosis. The study also defines diagnostic thresholds for many commonly obtained synovial and serum markers in spacer arthroplasty.

Conclusion There is no marker that can currently be used alone to diagnose PJI in these patients, but rather a combination of these markers along with the overall clinical picture should be reconciled together to make the final diagnosis.

952 Histologic mapping of Staphylococcus Aureus infection in an established PJI cemented hemiarthroplasty hip rat model at acute and chronic stages

Authors Hesham Abdelbary

Background and Rationale PJI is a challenge that continue to face arthroplasty surgeons today. Developing a reproducible animal model that is clinically relevant is a critical step towards developing new therapeutics for PJI. This step is not well presented in the literature.

Study Question 1) Can bacterial spread be histologically mapped at acute and chronic stages. 2) What are the histologic features of infected peri-implant tissues at acute and chronic stages. These two questions will be addressed on the femoral and acetabular sides.

Methods Using Sprague-Dawley rats we performed a left hip cemented hemiarthroplasty via a posterior approach under general anesthesia. A total of 6 rats were included in the study, with six being used for the control group and six for the infected group. In the infection cohort, the hip joint was inoculated with 5x109 CFU/mL of S. aureus Xen36 prior to closure of the capsule at the time of surgery. Three rats were sacrificed at 3 days post infection and three rats were sacrificed at 13 days post infection. The femurs and acetabula were harvested at euthanasia and were analyzed histologically. Hematoxylin and eosin (H&E) and Massonâ€™s trichrome (MT) stains were utilized to assess polymorphonuclear cells (PMN) and fibrosis. Immunohistochemistry (IHC) were used to localize S. aureus and osteoclasts within femur and acetabulum tissues.

Results Histological analysis revealed significant differences between 3 days (acute) and 13 days (chronic) infection time points. The chronic infection group showed significantly increased PMN counts, osteoclastic activity as well as tissue fibrosis on the femoral and acetabular sides, . These histologic changes resemble changes seen in chronic PJI in the clinical setting. On the acetabular, IHC demonstrated the bacterial spread starting within the cotyloid fossa at 3 days, and progressing deep within the periacetabular cancellous bone at 13 days.

Discussion In order to address gaps in fundamental PJI knowledge, we have designed a clinically relevant PJI hip model in Sprague-Dawley rats using cemented 3D-printed titanium hip implants and performed a detailed histologic analysis of peri-implant tissue at acute and chronic stages of infection.

Conclusion This model can provide insight into why certain surgical strategies like debridement, antibiotics and implant retention may be associated with high failure rates in hemiarthroplasty.

953 Synovial Fluid Microorganism Antigen Testing Demonstrates Good Nationwide Performance

Authors Carl Deirmengian, Brett Levine, Alex McLaren, Alvin Ong, Pearl Paranjape

Background and Rationale The increasing recognition of culture-negative periprosthetic joint infection (PJI) has prompted the development of alternative methods to detect pathogens. An antigen immunoassay panel (AIP), similar to the rapid strep test for Strep throat, has become clinically available to identify staphylococcus, candida, and enterococcus in synovial fluid (MID test, CD Laboratories, Zimmer Biomet, Towson, MD).

Study Question 1) What are the sensitivity, specificity, and false positive rate for AIP. 2) What is the rate of AIP detection of microorganisms in the setting of culture-negative PJI, and 3) What are the diagnostic predictive values of AIP for PJI.

Methods 59,557 synovial fluid samples being tested for PJI, from 2,290 institutions across the USA, were analyzed in a centralized CLIA laboratory (CD Laboratories) from 2017 to 2021. All samples underwent a complete set of synovial fluid tests, including CRP, alpha-defensin, WBCs, PMN%, culture, and AIP. Samples were classified as Aseptic-43,619, Inconclusive-4,323, or Infected-11,615 by applying this data to the 2018 ICM definition of PJI.

Results 1)The AIP panel demonstrated a sensitivity of 93.6%, specificity of 98.7%, and false-positive rate of 1.25% in the detection of PJI caused by target organisms (staphylococcus, candida, and enterococcus). The subpanel specificity for staphylococcus, candida, or enterococcus was 92.2%, 92.0%, and 97.7%, respectively.

2)The AIP detected microorganisms in 49.6% of 3,644 infected samples that were culture-negative, versus 1.25% of 43,619 aseptic samples.

3)The positive and negative predictive values of the AIP for the diagnosis of PJI were 93.8% and 92.9%.

Discussion With diagnostic performance comparable to other antigen tests commonly used in medicine, this synovial fluid immunoassay panel serves as an effective adjunct to traditional fluid culture, providing more timely pathogen detection (AIP: 6 hrs. vs. Culture: 7-14 days).

Conclusion The synovial fluid AIP, as a method to detect the presence of a microorganism, yields excellent predictive value for PJI, exhibits a very low false-positive rate, and detects a microorganism in roughly half of all culture-negative PJI.

955 Pharmacokinetic Profile of 7-Day Local Irrigation of Vancomycin and Tobramycin for Treatment of Periprosthetic Joint Infection

Authors Kevin Warner, Brian de Beaubien , Bradley Reddick, Kenneth Urish, Bryan Springer

Background and Rationale Available antimicrobial treatment modalities for periprosthetic joint infection (PJI) often fail secondary to variable pharmacokinetics and inability to reach pharmacodynamic targets. The variable pharmacokinetics are associated with significant risks including host toxicity and antimicrobial resistance.

Study Question What is the systemic absorption, distribution, metabolism, elimination and safety of 7-day local irrigation using vancomycin and tobramycin to treat PJI?

Methods A multicenter prospective trial of 7-day two-stage exchange arthroplasty for PJI was conducted in 15 subjects (14 knee/1 hip). Mean age was 69.3 years (55.2-78.6), mean creatinine clearance (CrCl) utilizing adjusted body weight was 82.6ml/min (27.7-159.6). Mean weight was 100.3kg (40.8-147.8). Mean body mass index (BMI) was 35.5kg/m2 (17.0-51.0). The 7-day irrigation included 80mg tobramycin in 50mL 0.9% NaCl (1600mcg/mL) daily with 2-hour soak followed by 30min. negative pressure to actively drain the site, then followed by hourly irrigation using 125mg of vancomycin in 50mL 0.9% NaCl (2500mcg/mL) with 30min. soak followed by 30min. negative pressure (21 cycles/day). Antibiotic serum concentrations were obtained daily. PK was evaluated utilizing population means.

Results Total absorption of vancomycin was 29%, accumulation index (RAC) 1.2, vancomycin clearance 6.3L/hr, and half-life ~9.5h. Mean vancomycin concentration at steady state was 5.2mcg/mL (max. 19.0). Tobramycin concentrations were not detectable in most subjects (max. 1.6mcg/mL).

Mean serum creatinine was 0.9mg/dL (0.5-1.2) pre-operatively, peaked at 1.0mg/dL and was 0.9mg/dL (0.4-1.2) on day 7. Mean c-reactive protein was 7.3 mg/dL (1.5-30.0) pre-operatively, peaked at 7.4mg/dL and was 3.4 mg/dL (0.3-15.6) on day 7. Mean blood urea nitrogen (BUN) was 17mg/dL (9-31) pre-operatively, peaked at 17mg/dL and was 14mg/dL (6-23) on day 7. All subjects were successfully reimplanted 7 days post-Stage 1 surgery, and 14/15 (93%) were infection free at 1 year. No acute kidney injury, treatment-related or unexpected adverse events occurred.

Discussion Local irrigation of vancomycin and tobramycin was highly effective and produced systemic levels at or below what are considered safe therapeutic ranges.

Conclusion Seven-day antimicrobial irrigation provided reliable pharmacodynamic target attainment at the site of infection with a safe pharmacokinetic profile.

956 A New Tool for C. acnes Detection: Antigen Immunoassay

Authors Krista Toler, Pearl Paranjape, Alex McLaren, Carl Deirmengian

Background and Rationale The management of Cutibacterium acnes shoulder infection has been frustrated by controversy regarding isolated positive culture in the absence of an inflammatory host response. Recently, a synovial fluid C. acnes antigen immunoassay (CAI), similar to the rapid test for Strep throat, has become available for clinical testing, providing an additional tool for the detection of C. acnes in synovial fluid.

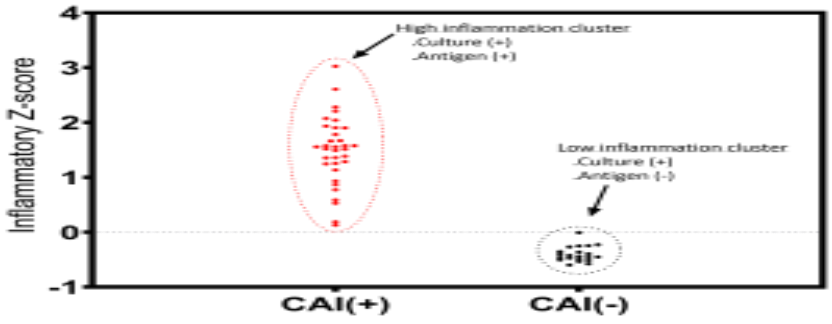
Study Question What are the relationships between inflammation, culture results, and CAI results in synovial fluid samples from the shoulder that are culture-positive for C. acnes?.

Methods 1,827 synovial fluid samples being tested for native (N=564) or periprosthetic (N=1263) shoulder infection, from 428 institutions across the USA, were analyzed in a centralized CLIA laboratory (CD Laboratories, Zimmer Biomet, Towson, MD) from 2018 to 2021. Samples underwent a set of synovial fluid tests, including culture, CAI test, and biomarkers including CRP, alpha-defensin, neutrophil elastase, WBCs, and PMN%. The results of all synovial fluid biomarker results were combined to calculate one standardized inflammatory Z-score per sample. The relationship between the inflammatory Z score, culture results, and the CAI test results was evaluated.

Results Among 231 shoulder fluid samples yielding positive cultures, 55 (24%) yielded C. acnes. Calculation of the inflammatory Z-score for these 55 culture-positive samples revealed two non-overlapping sample clusters. A non-inflammatory cluster of 21 samples exhibited a mean inflammatory Z score of -0.40 (range: -0.60 to -0.01) and all tested negative for antigen by CAI. A high inflammatory cluster of 34 samples exhibited a mean inflammatory Z-score of 1.48 (range: 0.13 to 3.02) and all tested positive for antigen by CAI. The CAI test and Z-score differences between sample clusters yielded $p<0.0001$ for both comparisons.

Discussion This study demonstrates that C. acnes antigen is only detectable in culture-positive synovial fluid when there is an associated host inflammatory response. Clinical outcome studies are necessary to demonstrate whether these findings are sufficient to differentiate between true positive vs. false-positive C. acnes culture results.

Conclusion C. acnes culture-positive synovial fluid samples from the shoulder can be categorized into two distinct clusters: 1) CAI and host inflammation positive vs. 2) CAI and host inflammation negative.



958 The Impact of Specimen Transport Time on Synovial Fluid Culture is Minimal

Authors Krista Toler, Van Thai-Paquette, Alex McLaren, Carl Deirmengian

Background and Rationale There has been ongoing concern in the field of arthroplasty that specimen transport delays may reduce the likelihood of pathogen growth in laboratory culture. However, synovial fluid samples collected in the office, and sometimes in a hospital setting, often require transport to a third-party central or specialty laboratory, causing delays in the initiation of culture incubation.

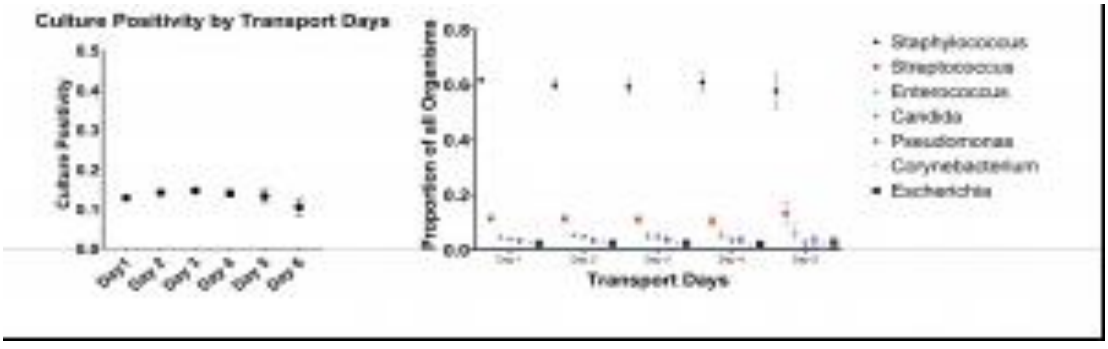
Study Question What is the impact of transportation delay on 1) The culture positive rate of submitted synovial fluid samples and 2) the observed organism proportions of culture-positive synovial fluid samples.

Methods A retrospective review of one clinical laboratoryâ€™s (CD Laboratories, Zimmer Biomet, Towson, MD) testing results from 2015-2021 was conducted. A total of 147,246 synovial fluid samples from knee and hip arthroplasties, from 2,932 different US institutions, were submitted for laboratory testing including synovial fluid culture (blood culture bottles). Transport time was calculated as days from the sample aspiration date to synovial fluid testing date, and this study included samples with a transport time of 1 to 6 days. The overall culture positivity and the proportion of major organism genera was evaluated as a function of transportation time.

Results The laboratory received 72.2% (N=106,346) of samples within 1 day after aspiration, which decreased in an exponential trend to a low of 0.4% (N=636) of samples received on day 6 after aspiration. Samples with 2 to 3 days of transport had a marginally higher mean rate of culture positivity than day 1 samples with an overall difference of 1.5% (14.3% vs. 12.8%; $p<0.0001$). Samples with a transport time of 5 or 6 days had a mean culture positivity that was not different than that observed among day 1 samples (12.6% vs. 12.8%; $p=0.75$). Analysis of the top 7 organism genera as a function of transport days revealed minimal proportional changes over 6 days.

Discussion While the authors of this study advocate for short transport times as a best practice to expedite diagnosis, it appears that concern regarding the degradation of culture results due to synovial fluid transportation are unwarranted.

Conclusion Synovial fluid culture exhibited reasonably consistent positivity and organism profiles for at least 1 to 6 days of transport time to the destination laboratory, with differences that appear to have minimal clinical importance.



960 Synovial Absolute Neutrophil Count is an Accurate Diagnostic Marker for Prosthetic Joint Infection in Revision Total Joint Arthroplasty

Authors Abhijit Seetharam, Julian E Dilley, R. Michael Meneghini, Michael M Kheir

Background and Rationale Diagnosis of prosthetic joint infection (PJI) in revision total joint arthroplasty (TJA) remains a challenge without a single gold-standard test shown to have 100% sensitivity and specificity. Timely and reliable diagnostic tests that are readily available to all clinicians are still needed.

Study Question The purpose of this study is to determine the accuracy of easily attainable synovial and serum biomarkers, including recently studied neutrophil-to-lymphocyte (NLR) and absolute neutrophil count (ANC), in diagnosis of PJI in revision TJA, and to define new thresholds for PJI diagnosis in this context.

Methods This was a retrospective review was of 149 cases of revision total joint arthroplasty who underwent aspiration for PJI or aseptic reasons. Charts were reviewed for synovial and serum markers including white blood cell count (WBC), polymorphonuclear percentage (PMN%), NLR, ANC, serum erythrocyte sedimentation rate (ESR), and serum C-reactive protein (CRP). The collected markers had their utility in diagnosing PJI examined by area under the curve analysis (AUC). Pairwise comparisons of AUCs were performed for serum and synovial markers. Youdenâ€™s test was used to determine diagnostic threshold values for all studied biomarkers.

Results Synovial ANC had a highest AUC of all studied markers (0.84) with a positive diagnostic value of >3,082 cells/uL, sensitivity of 73%, and specificity of 84%. AUCs for synovial WBC, NLR, and PMN% were 0.831, 0.802, and 0.791 respectively, all qualifying as â€œgoodâ€ or â€œacceptableâ€ tests. In direct comparison, synovial ANC significantly outperformed synovial PMN% (p = 0.039) but did not significantly outperform synovial WBC or NLR. For serum biomarkers, only CRP was considered to have an â€œacceptableâ€ AUC (0.714), with all other serum markers qualifying as â€œpoorâ€ tests. No serum biomarker significant outperformed any of the others.

Discussion Synovial ANC was the best performing biomarker for diagnosis of PJI in revision total joint arthroplasty. Synovial markers overall were more accurate compared to serum markers, which were found to have limited utility in this context.

Conclusion Accurate diagnosis of PJI in patients with previous revisions remains challenging, and use of readily available markers such as synovial ANC can help provide additional diagnostic value in these patients.

961 Absolute Neutrophil Count: a Marker for Diagnosis of Chronic Periprosthetic Joint Infection

Authors Troy D Bornes, Allina A Nocon, Jonathan S Yu, John Rezkalla, Mark P Youssef, David J Mayman, Alberto V Carli, Peter K Sculco

Background and Rationale Establishing the diagnosis of periprosthetic joint infection (PJI) is challenging. Diagnostic criteria commonly include synovial white blood cell (WBC) count and polymorphonuclear neutrophil (PMN) percentage. Elevations in these markers suggest the presence of PJI. However, it is currently unclear whether PJI is present if levels are discordant with one marker elevated and the other within normal limits. Our objective was to evaluate synovial absolute neutrophil count (ANC) in the diagnosis of chronic PJI in this population.

Study Question 1. How does ANC compare to other markers in the diagnosis of chronic PJI and in patients with discordance following total hip arthroplasty (THA) or total knee arthroplasty (TKA)?
2. What is the frequency of WBC/PMN discordance?

Methods This retrospective study included 472 patients treated with revision THA or TKA. Chronic PJI was defined using the 2013 International Consensus Meeting criteria. Patients with discordance between WBC and PMN were identified. ANC was calculated as: ANC = synovial WBC x PMN%. ANC thresholds were generated using data-driven and the literature-derived estimates. ANC was compared to other markers (synovial WBC and PMN; serum ESR and CRP) using receiver operating characteristic (ROC) curves, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results There were 193 patients with chronic PJI and 279 patients with no infection. Based on ROC curves, ANC and WBC performed better in the diagnosis of chronic PJI than PMN, ESR, and CRP. Discordance occurred in 11.9% of patients. In patients with discordance, an ANC threshold of 975 cells/ÂµL had a sensitivity of 92.9% and NPV of 88.9%, while a threshold of 3819 cells/ÂµL had a specificity of 87.5% and PPV of 66.7% (Fig. 1). These values appeared to be superior to other markers. In the entire study population of 472 patients, an ANC threshold of 2983 cells/ÂµL yielded optimal balance between sensitivity, specificity, PPV, and NPV.

Discussion A diagnostic algorithm for use in patients with WBC/PMN discordance was generated using thresholds of 975 cells/ÂµL and 3819 cells/ÂµL (Fig. 1). An ANC threshold of 2983 cells/ÂµL effectively diagnosed chronic PJI in the study population of 472 patients.

Conclusion ANC performed well in predicting chronic PJI and could have utility in patients with discordance between WBC count and PMN percentage. Discordance occurred in 12% of patients.

Figure 1

Diagnosis of Chronic Periprosthetic Joint Infection in Patients with Discordance Between WBC Count and PMN Percentage

Marker	Threshold	Sensitivity	Specificity	PPV	NPV	Driver
ANC	1850 cells/µL	21.4%	95.8%	75.0%	67.7%	Data
	3819 cells/µL	42.9%	87.5%	66.7%	72.4%	Data
	2983 cells/µL	50.0%	75.0%	53.9%	72.0%	Data
	2400 cells/µL	64.3%	66.7%	52.9%	76.2%	Literature
	1950 cells/µL	71.4%	54.2%	47.7%	76.5%	Literature
	975 cells/µL	92.9%	33.3%	44.8%	88.9%	Literature
WBC	3000 cells/µL	64.3%	45.8%	40.9%	68.8%	Literature
PMN	80%	35.7%	54.2%	31.3%	59.1%	Literature
ESR	30 mm/h	78.5%	71.4%	64.7%	83.3%	Literature
CRP	1 mg/dL	92.9%	61.9%	61.9%	92.9%	Literature

*Abbreviations: ANC, absolute neutrophil count; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMN, polymorphonuclear neutrophil; WBC, white blood cell

962 Effect of Vitamin D Status and Repletion on Postoperative Total Joint Arthroplasty Complications

Authors Daniel L Lamanna, Nattaly E Greene, Prabhavi Denagamage, Brielle J Antonelli, Antonia F Chen

Background and Rationale Research has demonstrated that patients undergoing total joint arthroplasty (TJA) are often vitamin D3 insufficient (serum levels <30 ng/mL), which has been associated with increased risk of postoperative complications. There exist no clear guidelines on how to best optimize patients prior to surgery with regards to vitamin D levels.

Study Question This trial aimed to investigate if preoperative correction of hypovitaminosis D in subjects scheduled for primary elective hip/knee TJA may reduce 3-month postoperative complications including readmission, reoperation, and periprosthetic joint infection (PJI).

Methods Eligible TJA patients with serum vitamin D concentrations >30 ng/mL formed the control group, and those with levels between 10 â€“ 30 ng/mL were randomized to a low or high dose supplementation. Serum vitamin D levels were measured on the date of surgery for supplemented patients, and were followed up at 3 months. Data were compared between the supplementation groups and the control group using t-tests. Fisherâ€™s exact test determined if there was a difference in emergency department visits between supplemented groups.

Results Control patients had a mean preoperative vitamin D level of 42.23 ng/mLÂ±10.76. Participants randomized to the low-dose supplementation regimen had a mean preoperative vitamin D level of 21.67 ng/mLÂ±5.37 and a postoperative level of 33.8 ng/mLÂ±7.73. Participants randomized to the high-dose regimen had a preoperative vitamin D level of 24.08 ng/mLÂ±4.54 and a postoperative level of 33.8 ng/mLÂ±11.52.

The t-statistic was 1.19 for the association between preoperative vitamin D levels and supplementation regimen (p=0.25), and 0.01 for the association between postoperative vitamin D levels and supplementation regimen (p=0.99). The t-statistic for change in preoperative to postoperative vitamin D levels among low-dose patients was 4.09 (p=0.0027), and 2.33 for this change among high-dose patients (p=0.053).

Among the low-dose regimen patients, 2 patients (16.67%) went to the ED and among high-dose regimen patients, one (8.33%) went to the ED. There were no readmissions, reoperations, or PJIs.

Discussion Low vitamin D patients supplemented with the low-dose regimen experienced an average of a 12.14 ng/mL increase in vitamin D levels from pre- to postoperation.

Conclusion Both supplementation regimens increased serum vitamin D to sufficient levels in low vitamin D patients.

963 Diagnosing prosthetic joint infection in total hip arthroplasty: a comparison of fluoroscopic- and ultrasound-guided hip aspiration

Authors Emily Boes, Michael J Archibeck, John C Wheelwright, Brenna Blackburn, Masaru Teramoto, Daniel Cushman

Background and Rationale Image guided aspiration of total hip arthroplasty (THA) is commonly performed to assist in the diagnosis of prosthetic joint infection (PJI). The superiority of fluoroscopy or ultrasound as the imaging modality of choice remains controversial.

Study Question Is fluoroscopic- or ultrasound-guided aspiration more likely to result in the acquisition of synovial fluid when aspirating a total hip replacement? Does the sensitivity and specificity differ between fluoroscopic- and ultrasound-guided total hip aspiration in the diagnosis of PJI?

Methods All THA aspirations performed between 2014 and 2021 were reviewed. The outcome of the aspiration was recorded as well as the volume of fluid obtained if successful. The diagnosis of PJI was determined using 2018 MSIS criteria and by culture results (Table 1). Acute PJI (<12 weeks) was excluded from analysis in the first method due to differing cell count thresholds. Dry taps and aspirations with no subsequent surgery were excluded in the second analysis. Analyses were performed using studentâ€™s t-test for continuous variables and chi-squared and Fisherâ€™s Exact test for categorical variables. Statistical significance was defined as $p<0.05$.

Results A total of 291 THA aspirations were performed. After exclusion for incomplete data, 290 aspirations were included in the analysis (155 with fluoroscopic guidance and 135 with ultrasound guidance). More dry taps (<0.5cc) occurred in the fluoroscopic-guided cohort (44%) than ultrasound-guided cohort (31%) ($p=0.026$). When successful, more total fluid was obtained in the ultrasound-guided cohort (mean 13.1 mL vs 9.5 mL, $p<0.03$). Using MSIS criteria to diagnose PJI, sensitivity was 0.51 for fluoroscopic- and 0.77 for ultrasound-guided aspirations ($p=0.01$), and specificity was 0.97 and 0.99, respectively ($p=0.35$). Using culture data to diagnose PJI, sensitivity was 0.44 and 0.67, respectively ($p=0.02$), and specificity was 0.88 and 0.96, respectively ($p=0.36$).

Discussion Ultrasound-guided aspiration obtains more fluid and yields fewer dry taps than fluoroscopic-guided aspiration of THA. Ultrasound-guided aspiration is more sensitive in diagnosing PJI than fluoroscopic-guided aspiration using 2018 MSIS criteria or culture data alone to diagnose THA infection.

Conclusion Given these findings, ultrasound guidance should be considered the aspiration imaging modality of choice in the diagnosis of PJI of the hip.

2018 MSIS Criteria		
	+ MSIS major or minor criteria ≥6 post-op	- MSIS major and minor criteria <6 post-op
+ aspiration culture or MSIS minor criteria ≥6 pre-op	21 fluoro 24 ultrasound (TP)	3 fluoro 1 ultrasound (FP)
- aspiration culture and MSIS minor criteria <6 pre-op	20 fluoro 7 ultrasound (FN)	109 fluoro 102 ultrasound (TN)
Culture Data		
	+ intra-operative culture	- intra-operative culture
+ aspiration culture	12 fluoro 18 ultrasound (TP)	3 fluoro 1 ultrasound (FP)
- aspiration culture	15 fluoro 9 ultrasound (FN)	22 fluoro 22 ultrasound (TN)

964 E coli Periprosthetic Joint Infections: Poor Infection Clearance at One Year

Authors Breanna A Polascik, Mikhail A Bethell, Damon V Briggs, Kwabena Adu-Kwarteng, Billy I Kim, Edward F Hendershot, William A Jiranek, Jessica L Seidelman, Thorsten M Seyler

Background and Rationale Escherichia Coli (E coli) is a gram-negative rod that can cause devastating periprosthetic joint infections (PJIs) in patients with total hip and knee replacements (THA/TKA). Minimal literature exists on outcomes of E coli PJIs.

Study Question What are the outcomes of E coli PJI in patients with THA or TKA?

Methods Retrospective review of our institutionâ€™s electronic medical record from 2009-2020 identified 21 patients that met MusculoSkeletal Infection Society criteria for E coli hip or knee PJI. Primary outcome was 1-year infection clearance - eradication of infection off antibiotics with no further surgeries for 1 year after completion of standard postoperative antibiotics. Minimum followup was 1 year.

Results We analyzed 21 patients (mean age 66.6 yrs, 47.6% male, 23.8% nonWhite, 38.1% knee PJIs). There were 11 acute, 8 acute hematogenous (AH), and 2 chronic PJIs. Several patients had recent gastrointestinal/urinary tract surgery (14.3%), recurrent urinary tract infections (9.5%), or â‰¥1 E coli urine culture â‰¤1 mo pre-PJI (14.3%). Surgical treatments included DAIR (66.7%), 2-stage revision (14.3%), Girdlestone/Resection Arthroplasty (G/RA; 14.3%), and fusion (4.8%), with 7.1%, 100%, 66.7%, and 100% 1-year infection clearance, respectively, and 33.3% 1-year infection clearance overall (p=.001). Common reasons for treatment failure were reinfection requiring surgery (57.1%) and chronic antibiotics (38.1%). Patients clear at 1 year had a longer mean time from most recent surgery to index PJI surgery (48.7 vs 7mo;p=.043) and more AH than acute or chronic infections (54.6% vs 27.3% vs 18.2%;p=.0412). Patients who were not clear at 1 year had more acute infections (80% vs 20% AH;p=.0412). The E coli PJI persisted in 23.8% of patients. Outcomes at final followup included G/RA (28.6%), original prosthetic (28.6%), new prosthetic (19%), above knee amputation (9.5%), destination spacer (9.5%), and arthrodesis (4.8%).

Discussion E coli PJI 1-year infection clearance is poor, with DAIR being the most common yet least effective surgical treatment. This may be due to the persistence of E coli biofilms, which may be better removed with prosthetic-extracting surgeries. Also, most E coli PJIs occurred postoperatively as opposed to hematogenously, as is sometimes assumed.

Conclusion E coli PJI 1-year infection clearance is poor.

969 Staphylococcal aggregate morphology and protection from antibiotics is dependent on unique mechanisms arising from various postsurgical joint composition and fluid motion

Authors Amelia M Staats, Peter W Burback, Daniel Li, Anne Sullivan , Paul Stoodley

Background and Rationale Considerable progress has been made toward elucidating the mechanism of staphylococcal aggregation in synovial fluid in the context of prosthetic joint infection. The size and rapidity of aggregate formation is determined by the composition and movement of synovial fluid in the joint cavity. Here we characterize the pathogenic implications of various aggregate morphologies arising from condition-dependent mechanisms.

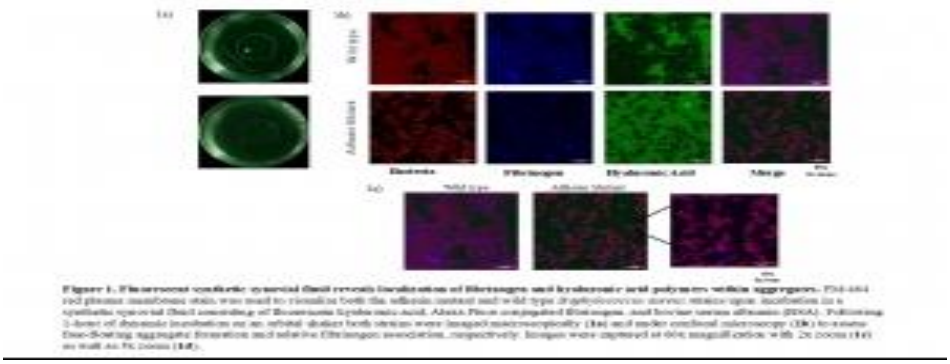
Study Question How does the joint environment influence bacterial aggregation and subsequent protection from antibiotic challenge?

Methods Aggregate morphology was assessed following incubation in several potential postsurgical joint conditions using microscopy. By inclusion of fluorescently-labeled synovial fluid polymers, we mapped their spatial arrangement and proximity to the aggregated bacteria (Fig. 1). Conferred protection was determined by challenging the aggregates with antimicrobials.

Results The dynamically-formed, macroscopic aggregates, were highly recalcitrant to antibiotic challenge. The formation of such aggregates required direct bacterial interaction with host fibrinogen through a polymer bridging mechanism. Under shear, a combination of high concentrations of hyaluronic acid and bovine serum albumin were capable of stimulating an entropy-driven form of aggregation termed â€œdepletion aggregationâ€. The resulting aggregates also displayed an antibiotic tolerant phenotype relative to planktonic cells.

Discussion The synovial fluid aggregate phenotype is dependent on the polymers occupying the joint environment as well as the presence or absence of fluid flow. The relative abundance of fibrinogen, hyaluronic acid, and albumin will determine the primary mechanism of aggregation. Aggregates formed with fibrinogen integration under shear are protected from antibiotics, indicating patient ambulation may play a role in bacterial survival. Alternatively, aggregates formed through a depletion mechanism also display recalcitrance. We suspect that aggregate formation in the joint cavity is dually mediated by both mechanisms acting synergistically to enhance bacterial protection.

Conclusion We report that synovial fluid-induced aggregation can occur through distinct mechanisms depending on the state of the joint environment. The resulting phenotypes confer protection from antibiotics to different degrees.



970 Mitochondrial Response to In Vivo Prosthetic Joint Infection (PJI)

Authors Nour Bouji, Matthew Dietz

Background and Rationale A significant cause of orthopaedic morbidity and mortality is prosthetic joint infection. Mitochondria are recognized as the â€œcell's powerhouseâ€, but they also play crucial roles in infection response and, when not functioning properly, have been linked to an increased risk of mortality from sepsis. There is no research investigating the influence of PJI on mitochondrial function and the interplay between the immune system and the infecting organism, posing a significant barrier to improving treatment outcomes for these patients.

Study Question The purpose of this study is to evaluate the impact of simulated PJI on mitochondrial function.

Methods Using an established prosthetic implant-associated in vivo model, tissues were harvested from the surgical limb of methicillin-sensitive Staphylococcus aureus (ATCC 25923) implant-associated infection model (n=6) versus the non-infected implant model (n=6) at postoperative day 20. To evaluate overall mitochondrial function and health, we performed mitochondrial coupling assays in isolated mitochondria to collect oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) in each group. Electron flow was also measured through the mitochondrial ETC complexes to reflect their activity in each group.

Results On postoperative day 20, CFU/g tissues were quantified showing 5x10^9 CFU/g in the infected joint model and 10^1 CFU/g in the non-infected group (p=0.33). Baseline respiration was not different between both groups (p = 0.28); however, maximal respiration and oxygen consumption due to ATP synthesis were significantly lower in isolated mitochondria from the infected limbs reflecting muscle fatiguability in the PJI model (p = 0.04). Complex I, III, IV, and V activity was assessed showing no difference (all groups p > 0.1) between groups.

Discussion The infected group demonstrated the preservation of complex activity with a shift toward a more glycolytic pathway with a lower OCR and greater ECAR in this group. This is the first step in understanding the altered mitochondrial function in the setting of in vivo PJI. Further understanding the mechanism underlying it could increase treatment success and allow researchers to look at ways to mitigate these changes.

Conclusion The involvement of PJI in the generation of oxidative tissue damage in mammalian cells is highlighted in this study in order to investigate treatment options for reducing the impact of infection on mitochondrial function.

971 Diagnosing Prosthetic Joint Infection in patients with Inflammatory Arthritis

Authors Susan M Goodman, Insa Mannstadt, Kathleen Tam, Alina Nocon, Deanna Jannat-Khah, Andy Miller, Peter Sculco, Mark Figgie, Alberto Carli

Background and Rationale Prosthetic joint infection (PJI) is a common cause of TKA and THA failure. The risk is 50-80% higher for patients with rheumatoid arthritis (RA) and other inflammatory arthritis (IA). For RA patients, the risk remains high for the lifetime of the joint. Moreover, diagnosis of PJI is difficult in IA given the underlying inflammation typical of the disease. The cardinal features of PJI-synovial leukocytosis, ESR, and CRP- are as likely to be elevated during infections in IA patients, but for IA patients there is considerable overlap in values with those flaring without infections. Waiting for definitive microbiologic cultures can delay diagnosis, imperiling the outcome. We hypothesize that systematic data collection including disease specific, microbiologic, serologic and synovial markers, in patients with IA and PJI, IA undergoing aseptic revision, compared to uninfected IA controls (no hardware) who are flaring, will identify features that can efficiently differentiate diagnosis between PJI in patients with IA.

Study Question This ongoing prospective study seeks to identify clinical, serologic, or synovial markers that can accurately and efficiently diagnose PJI in IA patients to differentiate infection from an active flare.

Methods Clinical data, blood, and synovial fluid were collected from IA patients presenting with flares and a swollen joint (no hardware), PJI (culture negative excluded), or for aseptic hip or knee revision.

Results To date, 38 patients enrolled between 10/21/2020 and 4/28/2022 were majority female (65.5%), mean age 52.7, with RA 52.6% overall. Flare cases were younger (mean age 48.5 years vs aseptic revision 57, PJI 56.6). Table 1 Synovial markers reveal higher WBC (p=0.01) and PMNs (p=0.02) among PJI, while alpha-defensin (p=0.02) was positive in 21% of flares and 6% of aseptic revisions. Blood markers reveal non-significant differences in IL-6, procalcitonin, CRP, and D-dimer among flares, while ESR was higher among PJI.

Discussion Preliminary results reveal important overlap between groups, including synovial WBC, IL-6, CRP, D-Dimer, synovial lymphocytes, procalcitonin and alpha-defensin.

Conclusion Early results indicate a lack of specificity in blood and synovial markers between groups. Additional data including Next-Generation Sequencing may provide more diagnostic precision.

Table 1: Blood and synovial markers*	PJI (n=2) Culture negative excluded	Aseptic revision (n=17)	IA flare (n=19) No prosthesis	p-value
Blood markers (mean, SD)				
Hemoglobin (g/dL)	**9.85 (2.5)**	**12.2 (1.4)**	**13.3 (1.5)**	**0.009**
Platelet (n!)	**389.5 (27.6)**	**243.9 (51.8)**	**299.4 (97.1)**	**0.020**
WBC (n!)	6.70 (0.3)	7.31 (3.1)	8.35 (2.1)	0.427
ESR (mm/hr)	**76.50 (24.8)**	**24.40 (14.8)**	**36.82 (30.9)**	**0.025**
CRP (mg/dL)	2.45 (1.9)	0.95 (0.7)	4.67 (11)	0.346
Positive blood culture (n,%)	0 (0%)	0 (0%)	0 (0%)	1
Procalcitonin (pg/mL)	0.07 (0)	0.07 (0)	1.49 (5.9)	0.583
IL-6 (pg/mL)	3.35 (0.6)	2.10 (0.3)	11.27 (20.1)	0.187
D-dimer (mcg/mL)	0.2 (0)	0.36 (0)	0.39 (0.4)	0.865
Rheumatoid factor positive (n,%)	1 (50%)	3 (17.6%)	7 (36.8%)	0.271
anti-CCP positive (n,%)	1 (50%)	2 (11.8%)	3 (15.8%)	0.423
SARS-CoV-2 IgG positive (n,%)	**0 (0%)**	**1 (5.9%)**	**10 (52.6%)**	**0.004**
Synovial markers (mean, SD)				
WBC (microL)	**37963.5 (27099)**	**1201.9 (1138)**	**13617.4 (15195)**	**0.009**
Polys (%)	**88.0 (8.5)**	**17.33 (17.6)**	**48.75 (30.3)**	**0.003**
Lymphs (%)	6.50 (7.8)	44.8 (7.9)	34.4 (29)	0.129
Culture positive (n,%)	2 (100%)	0 (0%)	0 (0%)	0.001
Alpha-Defensin positive (n,%)	**2 (100%)**	**1 (5.9%)**	**4 (21.1%)**	**0.022**
CRP (mg/L)	11.7 (0)	1.61 (1.6)	10.45 (13.8)	**

*Bold indicates statistical significance
**p-value could not be calculated due to only having one participant in the PJI group.

972 What is the relevance of the presence or absence of effusion around a total knee replacement scheduled for aspiration? When should we perform a lavage?

Authors Bashiar Thejeel, Joseph Nguyen, Alberto Carli, Theodore Miller

Background and Rationale The relevance of the presence of an intra-articular effusion around a total knee arthroplasty (TKA) for diagnosing periprosthetic joint infection (PJI) remains unknown. Furthermore, when fluid cannot be collected during an attempted arthrocentesis, the diagnostic utility of a lavage fluid collection for identifying PJI is poorly understood.

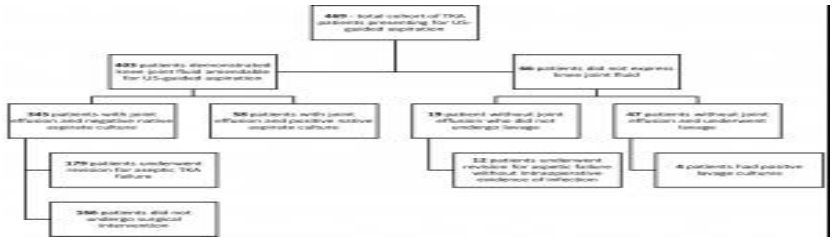
Study Question The purpose of the current study was to 1) to evaluate the clinical outcomes of TKA patients scheduled for image-guided arthrocentesis who did or did not have visible effusions, and 2) to report our experience with lavage fluid collection when clinical concern for infection is present.

Methods A retrospective review was performed of all patients undergoing ultrasound-guided knee arthrocentesis in the presence of primary or revision TKA in our single institution between January 1, 2015 to July 1, 2021. The presence of a joint effusion was recorded for all cases. Patient demographics, comorbidities, serum values, and occurrence (or not) of subsequent surgery following ultrasound and intraoperative cultures were collected. Patients were considered to have clinical concern for underlying infection if they presented with: a prior history of joint infection, fever, positive blood cultures, history of inflammatory arthropathy, or symptoms of swelling, erythema, open wounds or draining sinus.

Results 469 patients were included. Mean age was 67+ 10years, 251 were female. 403 (85.9%) patients had effusions, with 58 (14.3%) having positive cultures and undergoing surgical management. Of the 19 patients without a joint effusion on ultrasound and without clinical concerns for infection, none underwent arthrocentesis, and of the 12/19 that underwent surgical management, 100% had negative intraoperative cultures. Of the 47 patients without a joint effusion, but did have clinical concern for infection, all underwent lavage fluid collection. 4 (8.5%) had positive lavage aspirate cultures and underwent surgical management, while 1 patient with a negative lavage culture did undergo surgery due to a draining sinus being present. With patients without a joint effusion, there was no statistical difference regarding WBC and CRP levels in patients undergoing lavage versus non-lavage.

Discussion Our study findings suggest that patients with 1) a low clinical suspicion of infection and 2) absent effusion on ultrasound can be safely managed without attempted aspiration. If there is clinical concern, lavage and culture was useful for subsequently diagnosing PJI.

Conclusion Total knee replacements with low clinical suspicion of infection do not need to undergo attempted aspiration and saline lavage in the absence of a sonographically visible effusion.



974 Surgical Duration Increases the Risk of Infection Following Total Knee Arthroplasty

Authors Jamie Heimroth, Max L Willinger, Nipun Sodhi, Ariel Henig, Alain Sherman, Jonathan R Danoff

Background and Rationale Risk stratification is commonly used in total joint arthroplasty to optimize patient outcomes and minimize postoperative complications. One modifiable risk factor that can be directly influenced by surgeons is surgical duration, however, under certain circumstances prolonged surgery cannot be avoided. Therefore, the objective of this study is to determine if prolonged surgical duration is associated with postoperative complications.

Study Question The purpose of our study was to determine if surgical duration and tourniquet time during total knee arthroplasty was associated with postoperative surgical site infections

Methods A prospectively collected institutional database from a multicenter healthcare system was queried with ICD-10 codes and manually reviewed for all patients undergoing primary TKA between March 1st 2020 to December 31st 2020. Patient demographics, comorbidities, and infection data were collected. The surgical duration and tourniquet time was calculated for each patient undergoing a TKA and compared against each patientâ€™s rate of PJI or superficial surgical site infection (SSI) rate. PJI was defined based on MSIS criteria, and superficial SSI was defined as any infection that did not meet MSIS criteria.

Results Of the 2,511 patients who underwent primary TKA, 19 were found to have a postoperative infection. The average surgical duration of 120 minutes was associated with a significant increase in infections compared to 103 minutes for TKAs without infection. Patients who developed a surgical site infection had an average tourniquet time of 79 minutes, whereas those without postoperative infections had an average of 62 minutes. Multivariate analysis demonstrated that tourniquet time was significantly associated with an increased risk of infection.

Discussion Our study demonstrates that longer surgical duration and tourniquet time are associated with a greater risk of infection following TKA. While there are many circumstances that can lead to increased surgical time, such as increased BMI and surgeon experience, surgeons should strive to maximize efficiency in the operating room to minimize the risk of postoperative infection.â€¯

Conclusion Longer surgical duration and tourniquet time are increases the risk of infection following a total knee arthroplasty.

Variable	Infection (n = 19)	No Infection (n = 2,492)	p-value
Age (years)	63.00 ± 7.16	66.77 ± 9.02	0.07
BMI (kg/m²)	31.8 ± 6.34	32.24 ± 6.36	0.78
Sex			
Male	11 (1.2%)	924 (98.8%)	0.06
Female	8 (0.5%)	1,568 (99.5%)	
Laterality			
Right	13 (1.0%)	1,237 (99.0%)	0.28
Left	6 (0.5%)	1,199 (99.5%)	
Bilateral	0 (0.0%)	23 (100.0%)	
Operative Time (min)	120.50 ± 31.47	103.44 ± 31.37	**0.02**
Tourniquet Time (min)	78.50 ± 18.44	62.14 ± 24.32	**0.004**

975 Combining Bacteriophage and Vancomycin is More Efficacious in Treating MRSA Aggregates Formed in Human Synovial Fluid Compared to Using Vancomycin or Bacteriophage Alone

Authors Mariam Taha, Hesham Abdelbary

Background and Rationale Failure rate of standard treatment for Periprosthetic joint infection (PJI)is estimated to be around 40% at two years post revision surgery. A major clinical challenge contributing to treatment failure and antibiotics tolerance is the biofilm formation. Lytic bacteriophages (phages) can target biofilm associated bacteria at localized sites of infection by penetrating and disrupting biofilm matrices.

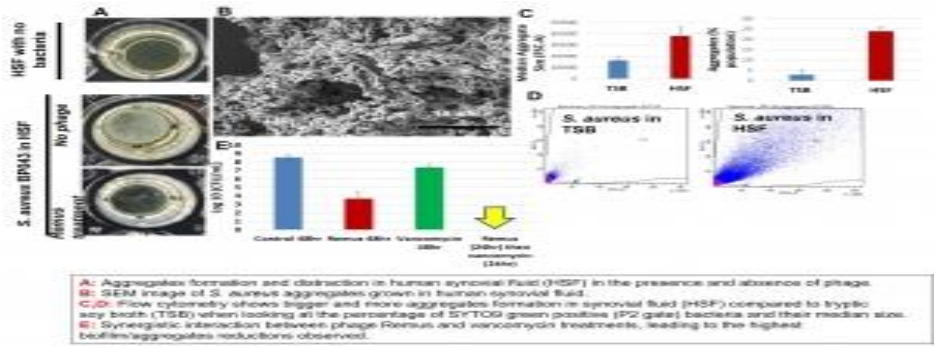
Study Question The aim of this study is to test if phage has better antimicrobial effect than vancomycin against Staphylococcus aureus biofilm aggregates in human synovial fluid.

Methods S. aureus BP043 was utilized in this study. This strain is a PJI clinical isolate, methicillin resistant (MRSA) and biofilm-former. Phage Remus, a lytic phage known to infect S. aureus, was used. S. aureus BP043 was grown in human synovial fluid in 96-well for 24hr. Then the already established S. aureus biofilm aggregates were treated with: a) phage Remus at 4x109 PFU/mL, 48hr, b) vancomycin, 500 ug/mL (sub- minimal biofilm eradication concentration), 48hr, or c) phage Remus, 24hr followed by vancomycin for another 24hr, at 37oC. Then, bacterial survival was assessed by plating on tryptic soy agar plates. Aggregates formation in synovial fluid was assessed using flow cytometer by measuring their size and comparing it to S. aureus clumping in Tryptic Soy broth (TSB). The aggregates were also examined by scan electron microscopy (SEM). Each experiment had two technical repetitions and at least two different human synovial fluids.

Results Phage Remus resulted in more than 56% reduction in viable S. aureus residing in the synovial fluid aggregates, compared to the control aggregates with no treatment (p=0.015). Additionally, Remus is more powerful in breaking BP043 aggregates and eliminating viable bacteria compared to vancomycin (p=0.02). Moreover, combining phage Remus followed by vancomycin is more efficacious in reducing bacterial load than using Remus or vancomycin alone (p=0.023, p<0.001, respectively).

Discussion We demonstrated synergistic interaction between the phage (Remus) and vancomycin, leading to better clearance of synovial fluid aggregates of the S. aureus MRSA isolate.

Conclusion This work is aimed at gathering preclinical evidence for using phage as a new therapeutic avenue to treat PJI.



A: Aggregates formation and distraction in human synovial fluid (HSF) in the presence and absence of phage.
B: SEM image of S. aureus aggregates grown in human synovial fluid.
C,D: Flow cytometry shows bigger and more aggregates formation in synovial fluid (HSF) compared to tryptic soy broth (TSB) when looking at the percentage of SYTO9 green positive (P2 gate) bacteria and their median size.
E: Synergistic interaction between phage Remus and vancomycin treatments, leading to the highest biofilm/aggregates reductions observed.

976 Recurrent prosthetic joint infection is associated with host grade and infecting bacteria

Authors Floriane Ngako Kameni, Jessica P Hampton, Joanne Y Zhou, James I Huddleston III, William J Maloney, Stuart B Goodman, Emilie Cheung, Matthew Miller, Derek F Amanatullah

Background and Rationale Some patients require multiple antibiotic-impregnated spacers for prosthetic joint infection (PJI). We compared the host factors and demographics of those who successfully cleared a PJI for two years or more following insertion of a single spacer with those who failed to clear their infection and required more than one spacer.

Study Question Are host grade and infecting bacteria associated with recurrence of prosthetic joint infection?

Methods A retrospective chart review was performed on ninety-two patients (38 hip, 47 knee, 7 shoulder) who had a resection and placement of an antibiotic spacer between 2009-2020 to treat a PJI meeting Musculoskeletal Infection Society (MSIS) criteria and with a minimum 2-year follow-up after the resection. Sixty-seven (73%) received only one spacer prior to infection-free re-implantation. Twenty-five (27%) continued to be infected and had a repeat spacer within 2 years of their original resection. McPherson host grade and infecting organism at initial resection were compared between patients who received a single spacer and patients receiving multiple spacers using Fisher's Exact test.

Results Patients receiving multiple spacers had a 2.7-times greater chance of being host grade B/C compared to those receiving a single spacer. Single-spacer patients had 2.7-times higher odds of being grade A than those receiving multiple spacers. Of the sixty-eight organisms isolated from the 67 single-spacer patients, coagulase-negative Staphylococcus was the most common isolate (22/68, 32%). Of the thirty-three different organisms isolated from the initial resection of 25 multiple-spacer patients, coagulase-negative Staphylococcus was present in one (1/33, 3%), with instead methicillin-sensitive Staphylococcus aureus as the most common isolate (10/33, 30.3%). Three (3/67, 4.5%) single-spacer patients had polymicrobial infections whereas eight (8/25, 24%) did so in the multiple-spacer group.

Discussion Healthier hosts, as graded by McPherson criteria, were more likely to have successful re-implantation after PJI. There were no significant associations with demographic factors and recurrence.

Conclusion Recurrent infection after two-stage revision arthroplasty is associated with B/C host grades. Successful re-implantation for PJI is associated with A host grade and infection with coagulase-negative Staphylococcus.

978 Defining the Role of Synovial Alpha-Defensin in the Diagnosis of Periprosthetic Joint Infection

Authors Nathanael D Heckmann, Jennifer C Wang, Paul Won, Brian C Chung, Lucas Mayer, Alexander B Christ, Donald B Longjohn, Daniel A Oakes, Jay R Lieberman

Background and Rationale Although the synovial alpha-defensin (AD) test has been previously shown to outperform other biomarkers in diagnosing periprosthetic joint infections (PJI), its role and reliability for this are not well-defined.

Study Question This study aims to examine the diagnostic utility of this test during PJI workup.

Methods A retrospective review was conducted to identify adults who underwent joint aspiration for PJI workup following primary total hip (THA) or knee arthroplasty (TKA) at a single institution. Patients who were aspirated with a spacer in place and who had incomplete data elements were excluded. If multiple aspirations were performed, only results from the initial aspiration were included. Cases were categorized based on the 2018 MSIS criteria as definitive, inconclusive, or negative for PJI. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each MSIS criteria were determined. The proportion of patients whose PJI diagnosis was contingent on a positive synovial AD was calculated.

Results Overall, 204 patients (11.3% THA, 88.7% TKA) were included with an average age of 68.7Â±11.0 years. Of the 27 patients who met the major criteria, 24 (96.0%) tested positive for AD (AD missing: n=2). Of the remaining 177 patients, 100 did not meet minor criteria, 98 (100.0%) of whom tested negative for AD and none tested positive (AD missing: n=2). Among the 37 patients who met minor criteria, 33 tested positive for AD (91.7%) and 3 (8.3%) did not (AD missing: n=1). The remaining 40 patients were deemed inconclusive preoperatively based on MSIS criteria. Of the 177 patients that failed to meet major criteria, 59 (33.3%) were deemed inconclusive before including AD results. A positive AD test resulted in 15 (25.4%) of these patients obtaining a definitive PJI diagnosis. The sensitivity, specificity, PPV, and NPV of AD in this cohort were 92.0%, 92.5%, 97.1%, and 80.7%, respectively.

Discussion Synovial AD results generally (97.9%) match the diagnosis derived using the MSIS criteria. Notably, the AD test identified a PJI in 25.4% of patients that had an inconclusive diagnosis using other criteria. Overall, AD testing for PJI demonstrated high specificity and PPV when compared to other laboratory tests.

Conclusion These results suggest AD should not be used routinely to diagnose a PJI, but only in cases when the diagnosis is inconclusive using other criteria.

980 Incidence of PJI Following Extensor Mechanism Reconstruction in TKA Patients

Authors Colin M Baker, Peter Gold, Qudratullah S Qadiri, Andrew Hughes, Paul M Courtney

Background and Rationale Extensor mechanism disruption is a devastating development following total knee arthroplasty (TKA). Surgeons often choose to perform extensor mechanism reconstruction (EMR) utilizing either allograft or synthetic mesh. Failure rates following EMR are often high and the development of peri-prosthetic joint infection (PJI) is not uncommon. Little has been written about the clinical course in patients with PJI after EMR.

Study Question The aim of this study was to report on the incidence of PJI following extensor mechanism reconstruction in patients with a history of TKA. Additionally, we aimed to present the clinical outcomes in patients who developed a subsequent infection.

Methods This retrospective study identified seventy-eight patients who underwent extensor mechanism reconstruction following TKA between 2008 and 2020 at a single institution. Patient demographics, the reason for surgery, surgical details, history of PJI, development of subsequent infection, and clinical outcomes were recorded. The primary endpoint was failure due to PJI.

Results A total of 49 allograft (25 extensor mechanism allograft, 24 achilles tendon allograft) and 29 mesh reconstructions were performed. There was no significant difference between groups with regard to age or BMI. The incidence of subsequent PJI was similar between groups (26.5% allograft, 20.7% synthetic). Overall, 28/49 (57.1%) allograft and 14/29 (48.3%) mesh reconstructions failed. 3 patients who developed PJI ultimately required arthrodesis and 3 more eventually had the affected leg amputated. Patients with a history of PJI were not associated with higher rates of subsequent PJI following EMR.

Discussion Extensor mechanism disruption is a complex issue following TKA. Failure rates were similar between EMR with allograft and synthetic mesh. Furthermore, the incidence of PJI was relatively high. Little has been published regarding the poor outcomes seen in patients who develop this feared complication. Approximately one-third of patients who developed an infection ultimately underwent a salvage procedure.

Conclusion The development of PJI following extensor mechanism reconstruction was relatively common. Both allograft and synthetic mesh reconstructions demonstrated similar results with regard to the incidence of PJI after surgery. Further large-scale studies are needed to properly evaluate outcomes in this setting.

982 Low Friction Spacers for Two-Stage Exchange Show Decreased Bacterial Colonization Compared to Cement Molds and Static Spacers

Authors Brandon K Couch, Alan E Wilson, Frank J Plate, Brian A Klatt, Michael J O'Malley

Background and Rationale Patients undergoing two-stage exchange arthroplasty for chronic periprosthetic joint infection (PJI) with metal femur and all-polyethylene tibia low friction spacers benefit from improved knee function and some patients ultimately elect to defer reimplantation. While low friction spacers have shown similar reinfection rates following reimplantation, concerns remain regarding the implantation of real components due the potential of biofilm formation.

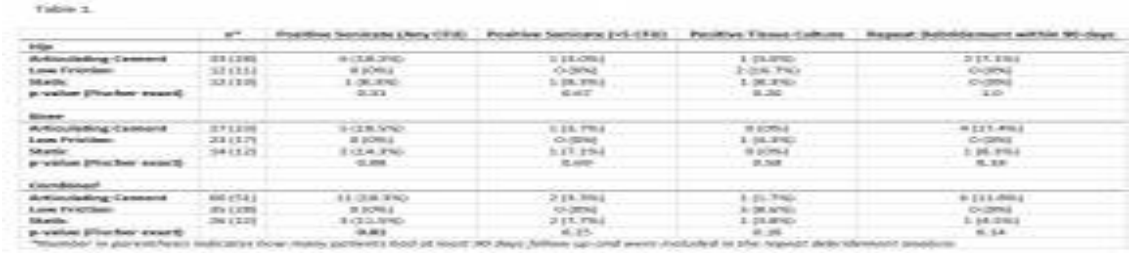
Study Question This study sought to compare sonication fluid cultures (SFC) from explanted low friction, articulating cement, and static spacers to determine whether low friction spacers have a higher risk for bacterial colonization.

Methods A retrospective single-center study was performed that included all patients who completed two-stage exchange arthroplasty for treatment of Musculoskeletal Infection Society (MSIS) defined hip or knee PJI from 01/2016 to 02/2022. All explanted spacer components were sent for SFC. Patient demographics, laboratory values, and clinical outcomes were recorded from the medical record. The primary end point was positive SFC. Repeat debridement within 90 days was a secondary end point.

Results A total of 121 patients (57 hips, 64 knees) completed a two-stage revision for PJI. Sixty (49.6%) patients received an articulating cement spacer, 35 (28.9%) received a low friction spacer, and 26 (21.5%) received a static spacer. No positive SFCs were identified in the low friction group compared to 18.3% with articulating cement and 11.5% with static spacers (p=0.01). No patients who received a low friction spacer required repeat debridement within 90 days while 11.8% with articulating cement spacers and 4.5% with static spacers required repeat debridement (Table 1).

Discussion Low friction spacers provide functional benefits to the patient and facilitate second-stage surgery without compromising the treatment of PJI. The results of this study suggest that low friction spacers may be used in both hip and knee PJI without an increased risk of spacer bacterial colonization or need for repeat debridement when compared to articulating cement and static spacers.

Conclusion Low friction spacers showed decreased bacterial colonization compared to other spacer types supporting the use of low-friction spacers following resection TKA and THA for the treatment of PJI.



984 The Majority of Biofilm Studies in Orthopedic Surgery Lack Direct Visualization of Biofilm and Utilize and In Vitro Study Design: Results of a Systematic Review

Authors Daniel A Driscoll, Tyler K Khilnani, Ajay Premkumar, Sita Nirumpama Nishtala, Mathias P Bostrom, Alberto V Carli

Background and Rationale The development of biofilm by bacteria is central to the pathogenesis of surgical site infections following orthopedic surgery. Consequently, biofilm research has exploded in popularity in the field of orthopedic surgery. The goal of this study was to evaluate the quality of currently available orthopedic literature pertaining to the study of biofilm.

Study Question 1. What percentage of biofilm studies in orthopedics derive results from in vitro, animal, or clinical sources? 2. What percentage of biofilm studies in orthopedics use direct visualization techniques to identify biofilm?

Methods A literature search was conducted in PubMed and then adapted for use in Embase and the Cochrane Library databases. The initial search was run with no limitations in place on April 27, 2020 and updated on April 12, 2022. Studies were stratified into in vitro, in vivo (animal), and clinical (human) studies. Studies that evaluated biofilm in an orthopaedic context were included. Clinical studies were included only if biofilm was confirmed by a quantification or visualization technique. Studies were evaluated and classified based on study design, biofilm quantification and visualization techniques, and bacterial characteristics.

Results A total of 206 articles were identified. 59 articles were included after screening. 32 articles (54%) studied techniques for biofilm eradication, 12 articles (20%) studied materials for prevention of biofilm formation, and 16 studies (27%) studied biofilm in a context other than eradication or prevention. In vitro testing was most commonly utilized (35 articles, 59%). 16 studies (27%) studied human-based biofilm and 9 (15%) studied animal-based biofilm. 61% of all articles (n=36) did not use any technique to visualize biofilm. 31 studies (52%) defined biofilm maturity as at least 72 hours of growth. Biofilm quantification was described in all qualifying studies.

Discussion The majority of published orthopedic studies pertaining to biofilm utilize in vitro models and fail to utilize direct visualization techniques. To date, there are no research standards or recommendations for how to assess biofilm.

Conclusion The orthopedic literature is inconsistent in how biofilm is studied. Animal models and clinical retrieval studies must be prioritized to confirm that in vitro findings are translationally relevant.

985 Combined DAIR and PhotothermAA Gel Decreases Implant Biofilm Burden and Soft Tissue Infection in a Rabbit Model of PJI, A Pilot Study

Authors Anabelle Visperas, Nathalie B Milbrandt, Pedro J Rullan, Yu Hsin Tsai, Zhifei Ye, Dehau Jiang, Nicolas S Piuzzi, Alison K Klika, Anna Cristina S Samia, Carlos A Higuera

Background and Rationale In periprosthetic joint infection (PJI), bacteria are protected by a biofilm matrix making treatment challenging. PhotothermAA gel is a combination of two anti-biofilm methods, D-amino acids and hyperthermia via laser heated gold nanoparticles that in vitro completely eradicates 2-week old biofilm and significantly decreases implant biofilm coverage immediately after treatment in vivo.

Study Question Can combined PhotothermAA gel and debridement, antibiotics, and implant retention (DAIR) decrease implant biofilm burden and soft tissue infection for a prolonged time in a knee PJI model?

Methods Rabbits were fitted with a titanium knee implant and inoculated with 5x10^6 CFU Staphylococcus aureus. At two weeks, rabbits were randomized into three treatment groupsâ€“sham (n=2), DAIR (n=2), or DAIR+PhotothermAA gel (n=3). For DAIR treatment, rabbits underwent irrigation with normal saline and debridement. For DAIR+PhotothermAA gel treatment, rabbits underwent irrigation and debridement plus PhotothermAA gel for two hours, laser heated and washed out. Those that underwent DAIR received cefazolin for two weeks after treatment. Tissue and implant were collected two weeks after treatment for cultures (n=4/animal) and biofilm coverage, respectively. For biofilm coverage, implants were prepared for scanning electron microscopy (SEM). Four standardized images were taken of the implant surface at 1500x and percent coverage was calculated using the Trainable Weka Segmentation plugin in Fiji. Tissues were sonicated and incubated for one week then plated overnight for cultures and colony forming units (CFU).

Results Implants isolated two weeks after treatment with PhotothermAA gel+DAIR had significantly less biofilm coverage compared to sham or DAIR ($p<0.0001$; Figure 1A). Periprosthetic tissue and synovial fluid contained less culturable bacteria compared to sham or DAIR ($p<0.0117$; Figure 1B) and reduced CFU ($p<0.0001$, Figure 1C).

Discussion A decrease in both implant biofilm coverage and bacterial burden were apparent after treatment with PhotothermAA gel+DAIR when analyzed two weeks after treatment. While the numbers of rabbits in this study are low, data were consistent within each group.

Conclusion PhotothermAA gel and laser treatment decreases biofilm coverage and bacterial burden in a rabbit model of PJI in this pilot study and therefore warrants additional studies to further test its efficacy.

986 Do antiseptic irrigation solutions have different efficacies on different orthopedic surfaces against staphylococcal biofilm? An in-vitro evaluation

Authors Tyler K Khilnani, Zachary J Coles, Christina A Chao, Mathias P Bostrom, Alberto V Carli

Background and Rationale Surgical site irrigation with antiseptic solutions is commonly utilized during total joint arthroplasty to reduce the risk of and treat periprosthetic joint infection (PJI). The effect of these solutions on orthopedic surfaces such as porous titanium and polymethylmethacrylate have been recently evaluated. However, to date, very little is known regarding the efficacy of these irrigants on biomaterials utilized in total knee arthroplasty including Cobalt-Chrome (CC) and oxidized Zirconium (OxZr).

Study Question Which antiseptic solution is most effective in eradicating established biofilm in an in vitro model of PJI on commonly used orthopedic surfaces in total knee arthroplasty?

Methods MSSA biofilm was grown on identically sized CC and OxZr coupons for 24- and 72-hour durations to form immature and mature biofilm respectively. Following incubation, coupons were washed with PBS to remove planktonic bacteria, then treated with a single antiseptic solution for 3 minutes. Tested antiseptic solutions included: 10% povidone-iodine (10%PI), a 1:1 mixture of 10% povidone-iodine plus 3% hydrogen peroxide (PI+HP), and 0.35% povidone-iodine (dPI). Controls were washed in PBS without further treatment. Following treatment, samples were sonicated in tryptic soy broth and plated to form countable colony forming units (CFUs). Experiments were performed in quadruplicate and repeated. An antiseptic solution was considered to demonstrate adequate efficacy if there was a 3-log reduction in CFU counts compared to controls.

Results On 24-hour biofilm, PI+HP demonstrated complete bacterial eradication on both OxZr and CC, 10% PI demonstrated clinical efficacy on both surfaces, and dPI showed no clinical efficacy on either surface. On 72-hour biofilm, both 10% PI and PI+HP exhibited complete eradication of biofilm on OxZr and CC while dPI showed no clinical efficacy on either surface.

Discussion Similar to our previous work on porous titanium and polymethylmethacrylate, we identified that 10% PI with or without HP was effective in reducing immature and mature biofilm on both CC and OxZr. dPI proved to not be an effective treatment option for established biofilm.

Conclusion Povidone-iodine should not be diluted when utilized to treat MSSA biofilm on Cobalt Chrome and Oxidized Zirconium. Further in vivo evaluation is needed.

987 Financial Burden of Septic Total Hip Arthroplasty Revisions Compared to Aseptic Ones â€“ Call for New Procedural Coding?

Authors Jesus Villa, Tejbir Pannu, Robert Eysler, Alison Klika, Carlos Higuera-Rueda

Background and Rationale In a consecutive series, we sought to compare length of stay (LOS) and in-hospital charges associated with different revision types employed to treat periprosthetic joint infections (PJI) after total hip arthroplasty (THA) with those of aseptic revisions.

Study Question (1) Is LOS longer for septic revisions? (2) Are septic revisions more expensive? And (3) how do different septic revision types compare with aseptic revisions in terms of LOS and charges?

Methods Retrospective review of 1334 consecutive hip/knee revisions performed by 7 surgeons in a single institution (2015-2020). Exclusions: partial-arthroplasty/open reduction and internal fixation, conversions, bilateral revisions performed on same admission, Girdlestones, fusions, and procedures superficial to the deep fascia. After review of the operative note and radiographs and/or office notes, 602 unilateral THA revisions (477 patients) were identified for statistical analyses. Demographics including age, gender, race, ethnicity, BMI, and ASA were collected. Revisions were set apart in 6 groups: (1) aseptic (control) (n=371), (2) irrigation & debridement (I&D) for PJI w/wo insert exchange (n=11), (3) explantation w/wo spacer (n=144), (4) spacer-exchange (n=7), (5) second-stage reimplantation (n=59), and (6) single-stage reimplantation (n=10). In-hospital professional (i.e., surgeon, anesthesiologist, consulting physicians) and technical (i.e., room and bed, imaging, labs, implants, nursing) charges per case were provided by Enterprise Analytics. Total charges (professional+technical) were calculated. Alpha was set at 0.05.

Results Overall, BMI was significantly higher in septic revisions (n=231) than in aseptic ones (mean 30 vs. 28 Kg/m2, respectively, p<0.001). A higher proportion of males was found in septic revisions than in the aseptic group (61.5% vs. 44.5%, p<0.001). Other demographics were not significantly different. Septic revisions had longer LOS (6.3 Â± SD4.7 vs. 3.3 Â± SD2.9 days, p<0.001) and 43% higher total in-hospital charges (p<0.001). LOS and relative charges of different revision types are shown in Table 1.

Discussion Septic revisions have longer LOS and are significantly more expensive. In particular, explantations are 56% more expensive than the average aseptic revision.

Conclusion For PJI treatment, from the financial standpoint only, single-stage reimplantations represent by far the best value for society. Adjustment in reimbursement is needed as current coding does not reflect real cost, particularly of septic revisions.

Table 1. Average hospital length of stay (days) and relative percentage change in hospital charges of different types of septic hip revisions when compared to aseptic revisions (control group, reference value=1).

Variables	Aseptic Revisions (control) n=371	Irrigation & Debridement (I&D) n=11	Explantation w/wo Spacer n=144	Spacer-exchange n=7	Second-stage Reimplantation n=59	Single-stage Reimplantation n=10	p value (ANOVA) All Groups
Hospital Length of Stay (Mean ± SD, Days)	3.3 ± 2.9	**8.1 ± 3.2***	**7.1 ± 4.8***	**10.9 ± 10.8***	3.4 ± 1.8	**7.0 ± 3.2***	<0.001
Professional In-hospital Charges	1	153%	**131%***	165%	99%	129%	<0.001
Technical In-hospital Charges	1	127%	**165%***	**178%***	114%	**151%***	<0.001
Total In-hospital Charges	1	129%	**156%***	**169%***	111%	146%	<0.001

*** Significantly different (p<0.05) in Post Hoc Tests (Tukey HSD) comparisons with aseptic revisions (control group).** The mean charges in US dollars of the different types of septic revisions are shown as a proportion of the charges found in aseptic revisions (control group, reference value=1). For example, when a mean septic charge and an aseptic charge are equal, the percentage is 100%. However, if a septic charge is higher than the aseptic charge, then the percentage is >100%. The percentage will be <100% when the septic charge is lower than the aseptic one. SD: Standard deviation.

988 Irrigation and Brush Sonication remove mature staphylococcal biofilm on clinical orthopedic implants: An in-vitro evaluation

Authors Zachary J Coles, Christina A Chao, Tyler K Khilnani, Mathias P Bostrom, Alberto V Carli

Background and Rationale The use of intraoperative irrigation is commonplace in surgery, often utilized to clear blood, debris, and microbes from the surgical wound. Recently, mechanical brushing on implants has been recommended as a method of removing implant biofilm in the setting of periprosthetic joint infection (PJI). Despite this recommendation, little evidence exists to demonstrate that brushing can remove biofilm from orthopedic surfaces.

Study Question Does mechanical agitation through use of sonication reduce bacterial load and biomass within biofilm formed on tibial base plates (TBPs)? Are these effects synergistic with surgical lavage?

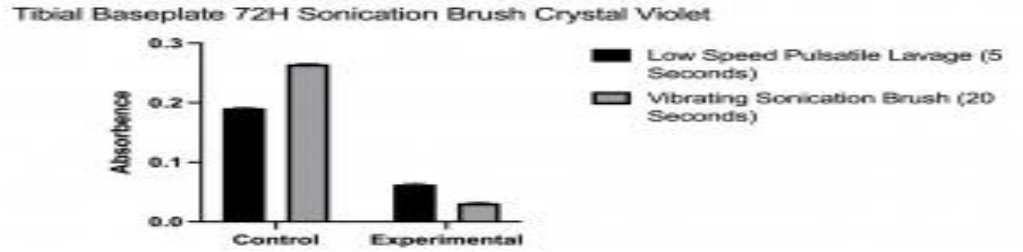
Methods Four never implanted, identically sized, right sided TBPs (Persona; Zimmer-Biomet) underwent keel removal with a diamond saw, passivated in 25% nitric acid, and autoclaved. Pilot experiments using MSSA inoculations with 45mL of 10^7 CFU/ml were performed to confirm that mature (72-hour) biofilms could be reliably established. Confirmation of TPB sterilization prior to re-use was also verified.

72-hour biofilm-coated TBPs were treated with 5 seconds of saline gravity lavage (irrigation tubing), 5 seconds of low-speed pulsatile lavage (Pulsavac Plus; Zimmer-Biomet), and 20 seconds of direct contact with a custom frequency sonication brush. Irrigation sources were fixed at 5 inches above the TBP. Experiments were performed in triplicate, with one TBP kept as a positive control. TBPs were either sonicated and plated to count colony forming units (CFUs) or stained in 0.1% crystal violet to quantify biofilm biomass.

Results Low-speed pulsatile lavage treatment on mature 72-hour biofilm reduced CFUs by 52% compared to controls. Both treatment with low-speed lavage and sonication brushing on mature 72-hour biofilm reduced crystal violet absorbance by 67% and 88% respectively. Gravity lavage on immature 24-hour biofilm reduced crystal violet absorbance by 82% compared to controls. Additional trials with various treatments are ongoing.

Discussion Utilization of irrigation and mechanical methods of removing biofilm from implants is an understudied area despite its prevalent clinical use. The effect of mechanical treatment through sonication shows promise in removing biofilm from topographically complex orthopedic devices.

Conclusion Physical debridement, either by lavage or mechanical means, appears to help reduce biofilm on tibial baseplates. Further evaluation is needed.



989 Financial Burden of Septic Total Knee Arthroplasty Revisions Compared to Aseptic Ones â€“ Call for New Procedural Coding?

Authors Jesus M Villa, Tejbir S Pannu, Robert B Eysler, Alison Klika, Wael K Barsoum, Carlos A Higuera

Background and Rationale In a consecutive series, we sought to compare length of stay (LOS) and in-hospital charges associated with different revision types employed to treat periprosthetic joint infections (PJI) in total knee arthroplasty (TKA) with those of aseptic revisions.

Study Question (1) Is LOS longer for septic revisions? (2) Are septic revisions more expensive? And (3) how do different septic revision types compare with aseptic revisions in terms of LOS and charges?

Methods Retrospective review of 1334 consecutive hip/knee revisions performed by 7 surgeons in a single institution (2015-2020). Exclusions: partial-arthroplasty/open reduction and internal fixation, conversions, bilateral revisions performed on same admission, Girdlestones, fusions, and procedures superficial to the deep fascia. After review of the operative note and radiographs and/or office notes, 653 unilateral TKA revisions (512 patients) were identified for statistical analyses. Demographics including age, gender, race, ethnicity, BMI, and ASA were collected. Revisions were set apart in 6 groups: (1) aseptic (control) (n=393), (2) irrigation & debridement (I&D) for PJI w/wo insert exchange (n=30), (3) explantation w/wo spacer (n=166), (4) spacer-exchange (n=7), (5) second-stage reimplantation (n=51), and (6) single-stage reimplantation (n=6). In-hospital professional (i.e., surgeon, anesthesiologist, consulting physicians) and technical (i.e., room and bed, imaging, labs, implants, nursing) charges per case were provided by Enterprise Analytics. Total charges (professional+technical) were calculated. Alpha was set at 0.05.

Results Overall, a higher proportion of males was found in septic revisions (n=260) than in the aseptic group (52.7% vs. 41.2%, p=0.05) and a higher proportion of ASA 3 cases was present in the septic group than in the aseptic one (60.8% vs. 45.3%, p<0.001). Other demographics were not significantly different. Septic revisions had longer LOS (6.8 Â± SD5.8 vs. 2.3 Â± SD1.5 days, p<0.001) and 42% higher total in-hospital charges (p<0.001). LOS and relative charges of different revision types are shown in Table 1.

Discussion Septic revisions have longer LOS and are significantly more expensive. Particularly, explantations are 57% more expensive than the average aseptic revision.

Conclusion For PJI treatment, from the financial standpoint only, single-stage reimplantations represent by far the best value for society. Adjustment in reimbursement is needed as current coding does not reflect real cost, particularly of septic revisions.

Table 1. Average hospital length of stay (days) and relative percentage change in hospital charges of different types of septic knee revisions when compared to aseptic revisions (control group, reference value=1).

Variables	Aseptic Revisions (control) n=393	Irrigation & Debridement (I&D) n=30	Explantation w/wo Spacer n=166	Spacer-exchange n=7	Second-stage Reimplantation n=51	Single-stage Reimplantation n=6	p value (ANOVA) All Groups
Hospital Length of Stay (Mean ± SD, Days)	2.3 ± 1.5	5.2 ± 2.2*	8.1 ± 6.7*	6.7 ± 4.2*	3.8 ± 2.3	4.0 ± 1.8	<.001
Professional In-hospital Charges	1	105%	197%*	226%	113%	137%	<.001
Technical In-hospital Charges	1	88%	149%*	123%	127%*	140%	<.001
Total In-hospital Charges	1	91%	157%*	141%	125%	140%	<.001

* **Significantly different (p<0.05) in Post Hoc Tests (Tukey HSD) comparisons with aseptic revisions (control group).** The mean charges in US dollars of the different types of septic revisions are shown as a proportion of the charges found in aseptic revisions (control) group, reference value=1). For example, when a mean septic charge and an aseptic charge are equal, the percentage is 100%. However, if a septic charge is higher than the aseptic charge, then the percentage is >100%. The percentage will be <100% when the septic charge is lower than the aseptic one. SD: Standard deviation.

990 Establishment of a Novel Gram-Negative Prosthetic Joint Infection Rat Model Using Uncemented Hip Hemiarthroplasty

Authors Mazen M Ibrahim, Hesham Abdelbary

Background and Rationale Gram-negative prosthetic joint infections (GN-PJI) present unique challenges in management due to their distinct pathogenesis of biofilm formation on implant surfaces. The purpose of this study is to establish a clinically representative GN-PJI model that can reliably recapitulate biofilm formation on titanium implant surface in vivo. I hypothesized that biofilm formation on an implant surface will affect its ability to osseointegrate.

Study Question Can we reliably recapitulate biofilm formation on titanium implant surface in vivo utilizing a clinically representative GN-PJI model?

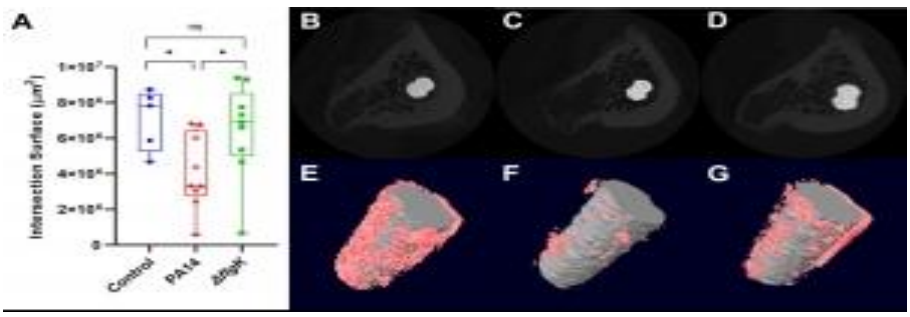
Does implant loosening correlate with biofilm formation on the implant surface?

Methods The model was developed using 3D-printed titanium hip implants, to replace the femoral head of male Sprague-Dawley rats. GN-PJI was induced using two bioluminescent Pseudomonas aeruginosa strains: a reference strain (PA14-lux) and a mutant biofilm-defective strain (DflgK-lux). Infection was monitored in real-time using the in vivo imaging system (IVIS) and Magnetic Resonance Imaging (MRI). Bacterial loads on implant surface and in periprosthetic tissues were quantified utilizing viable-colony-count. Field-emission scanning-electron-microscopy (FE-SEM) of the explanted implants was used to visualize the biofilm formation at the bone-implant-interface. The implant stability, as an outcome, was directly assessed by quantifying the osseointegration in vitro using microCT scan, and indirectly assessed by identifying the gait pattern changes using DigiGaitTM system in vivo.

Results Localized infection was established within the hip joint and was followed by IVIS in real-time. The difference in the bacterial load and biofilm formation between PA14-lux and DflgK-lux was quantified by viable-colony-count and visualized utilizing the FE-SEM. This difference in the ability to persist in the model between the two strains was reflected in the gait pattern and implant osseointegration.

Discussion We developed a novel uncemented hip hemiarthroplasty, GN-PJI rat model. To date, the proposed in vivo biofilm-based model is the most clinically representative for GN-PJI since animals can bear weight on the implant and poor osseointegration correlates with biofilm formation. In addition, localized PJI was detected by various modalities.

Conclusion This model will allow for more reliable testing of novel biofilm-targeting therapeutics.



997 Streptococcal Periprosthetic Joint Infections: Prognosis and Outcomes

Authors Colleen Wixted, Andy Schwartz, Billy Kim, Isabel Prado, Breanna Polascik, Edward Hendershot, Michael Bolognesi, William Jiranek, Jessica Seidelman, Thorsten Seyler

Background and Rationale Streptococcus species is a common pathogen family in periprosthetic joint infection (PJI); however, few studies have focused on the microbe-specific outcome of these infections with significant variation with regard to reported outcomes.

Study Question What are the clinical presentations and outcomes of streptococcal PJI?

Methods Retrospective review of a single institutionâ€™s PJI database identified 54 cases (21 hips, 33 knees) of streptococcal PJI. Infection clearance was defined as no surgical treatment for reinfection or suppressive antibiotic therapy (SAT). Patient demographics, treatment regimen, and outcomes were collected for a minimum of 1 year from index PJI surgery.

Results The cohort was 68.5% male with mean age of 68.0 years (SD: 8.9), mean Elixhauser Comorbidity score of 7.4 (SD: 4.4), and 38.9% had diabetes mellitus type II. The most common species was Group B Streptococcus (GBS) (n=23, 42.6%). Surgical treatment for PJI included DAIR (n=30), 1-stage exchange (n=3), 2-stage exchange (n=18), and resection arthroplasty/amputation (n=3) without any significant differences for infection clearance between groups. Overall, 51.9% of patients were cleared of their infection at 1 year. At the time of final follow-up treatment failures included 12/54 (22.2%) patients who required surgery for reinfection, 9/56 (23.3%) patients on SAT, and 2/56 (3.6%) patients who died before their 1-year postoperative follow-up. Overall, the estimated 5-year survival rate for streptococcal PJI was 0.66 [95% CI: 0.49-0.89].

Discussion Treatment success was suboptimal for streptococcal PJI, with only slightly more than 50% of patients successfully clearing their infection. This falls on the lower end of treatment success rates found in the literature, suggesting Streptococcus may be more difficult to eradicate than previously thought.

Conclusion Streptococcal PJI was most often caused by GBS in this cohort. A majority of patients were treated with DAIR, but there were no differences with regard to infection clearance at 1 year among treatment groups. Only 51.9% of patients overall were infection free at 1-year, and the estimated survival rate was 0.66.

999 Far from perfect: Synovial fluid next-generation sequencing (NGS) in diagnosing periprosthetic joint infection

Authors Tejbir S Pannu, Jesus M Villa, Preston Grieco, Jorge Manrique, Aldo Riesgo

Background and Rationale Next-generation sequencing (NGS) is being increasingly preferred for accurate detection of infecting organism in periprosthetic joint infection (PJI). With this molecular technique, results can be obtained in less than 24 hours as compared to ample time needed in culturing organisms. Nevertheless, adult reconstructive surgeons ordering NGS in PJI workup at our institution grew concerns about inadequacies of this test in identifying organisms, which led to this investigation.

Study Question To test the accuracy of NGS to diagnose PJI with 2018 ICM PJI definition (â€œgold standardâ€) and assess the concordance of this technique with cultures in identifying infecting organisms.

Methods A retrospective review was performed on consecutive 100 NGS tests ordered from 01/2020 to 04/2022 by 4 surgeons in a single institution to diagnose PJI. All patients had a synovial fluid aspiration for NGS and other results incorporated in 2018 ICM PJI criteria. PJI diagnostic workup was performed before the following operations (hips=22; knees=78): revision joint arthroplasties (n=86), or reimplantations (n=14). To assess accuracy for PJI diagnosis, NGS (+) and NGS (-) test results were compared with 2018 ICM PJI definition (â€œstandardâ€). To further evaluate the ability to identify organisms, NGS was analyzed against cultures which had an identified infecting organism. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results With 2018 ICM PJI definition as a â€œgold standardâ€, NGS demonstrated poor sensitivity (59%) and NPV (60.3%), but high specificity (91.4%) and PPV (91%). On comparing NGS with culture results, predictive measures dropped down, specificity (77%) more so than poorer sensitivity (57.8%) (Figure 1). Out of 38 synovial fluid/tissue samples in which infecting organism was cultured, NGS failed to identify 16 of 38 (false negative rate=42.1%). Phenotypically identical organisms were isolated from at least two separate samples from the joint in 50% of these false negatives cases (major criteria for diagnosis of PJI). In 14 tests before reimplantation, NGS missed 3 of 6 culture positive cases with known organisms.

Discussion Synovial fluid NGS has poor sensitivity for PJI diagnosis and fails to identify infecting organisms confirmed on cultures from the prosthetic joint.

Conclusion Synovial fluid NGS is a poor rule-out test for PJI and fails to identify organisms confirmed on cultures from the prosthetic joint.

Figure 1. Next-generation sequencing (NGS) in diagnosing periprosthetic hip or knee infection and identifying infecting organisms in culture positive or negative cases.

	2018 ICM (-)	2018 ICM (+)	Total
NGS (-)	32	21	53
NGS (+)	3	30	33
Total	35	51	86

Accuracy = 100 x 30+32/30+32+21+3 = 73%
Sensitivity = 100 x 30/51 = 59%
Specificity = 100 x 32/35 = 91.4%
Positive predictive value = 100 x 30/33 = 91%
Negative predictive value = 100 x 32/53 = 60.3%
Positive Likelihood Ratio = 0.59/1-0.914 = 6.86
Negative Likelihood Ratio = 1-0.59/0.914 = 0.45

	Culture (-)	Culture (+)	Total
NGS (-)	37	16	53
NGS (+)	11	22	33
Total	48	38	86

Accuracy = 100 x 22+37/22+37+11+16 = 68.6%
Sensitivity = 100 x 22/38 = 57.8%
Specificity = 100 x 37/48 = 77%
Positive predictive value = 100 x 22/33 = 66.6%
Negative predictive value = 100 x 37/53 = 70%
Positive Likelihood Ratio = 0.578/1-0.77 = 2.51
Negative Likelihood Ratio = 1-0.578/0.77 = 0.548

1000 Peri-prosthetic Joint Infection in People Who Inject Drugs

Authors Tyler J Humphrey, Alexander M Tatara, Kyle Alpaugh, Christopher M Melnic, Sandra B Nelson

Background and Rationale The rates of total joint arthroplasty TJA) in people with substance use disorder, including injection drug use (IDU), are increasing. People who inject drugs (PWID) are at increased risk of peri-prosthetic joint infection (PJI) although there is high variance reported in case series in the literature. By understanding the risk factors, rate, and outcomes of PJI in PWID, strategies to better mitigate PJI risk in this population can be better developed.

Study Question What are the rates, risk factors, and outcomes of PJI in PWID compared to people who do not inject drugs?

Methods In a retrospective matched cohort study, patients with history of IDU were matched 1:4 with patients without history of IDU using a systems-wide arthroplasty database. Univariate and multivariate modeling was performed to characterize risk factors associated with PJI occurrence. Kaplan-Meier analysis was performed comparing PJI occurrence over time in the two cohorts. PJI treatment outcomes were compared between cohorts.

Results 58 cases of TJA in 41 PWID were matched to 232 TJAs in people without history of IDU. Patients with history of IDU had greater co-morbidities at baseline including congestive heart failure, coronary artery disease, pulmonary disease, mood disorder, viral hepatitis, and HIV infection. PWID had greater PJI rates (29.3% versus 3.4%) and history of IDU had 9-fold increased risk of PJI (OR 9.605, 95% CI 2.781-33.175, p<0.001). There were not significant differences in treatment outcomes between cohorts.

Discussion To our knowledge, this is the largest cohort of PJI in PWID. Compared to matched controls, PWID had greater co-morbidities and higher rates of PJI with IDU being the single highest risk factor among those analyzed in this study. While not statistically significant, PWID tended to have more cases of late PJI and bacteremia associated with their PJI, suggesting that hematogenous infection is a major contributor in this population.

Conclusion As the opioid epidemic continues, the population of people who inject drugs is likely to increase which continues to present challenges in the field of arthroplasty. There is a clinical need to improve PJI outcomes in this vulnerable patient population and future efforts to study PWID-focused multidisciplinary care in the pre-, peri-, and post-operative settings may provide benefit.

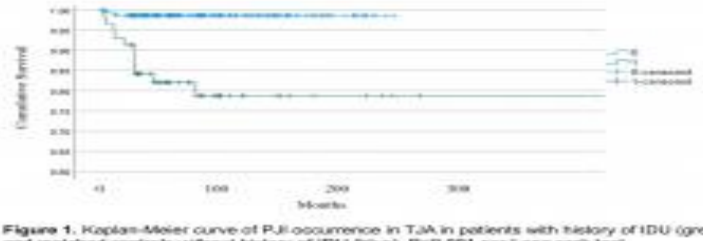


Figure 1. Kaplan-Meier curve of PJI occurrence in TJA in patients with history of IDU (green) and matched controls without history of IDU (blue). P<0.001 per Long rank test.

1002 Do delta changes in synovial WBC count and PMN% anticipate the outcome of reimplantation?

Authors Tejbir S Pannu, Jesus M Villa, Joseph Palmer, Nicolas Piuzzi, Aldo M Riesgo, Carlos A Higuera

Background and Rationale Synovial WBC-count and PMN% values are frequently used to determine infection control at the time of reimplantation but the diagnostic utility of change in these parameters from pre-explantation to pre-reimplantation is unidentified yet.

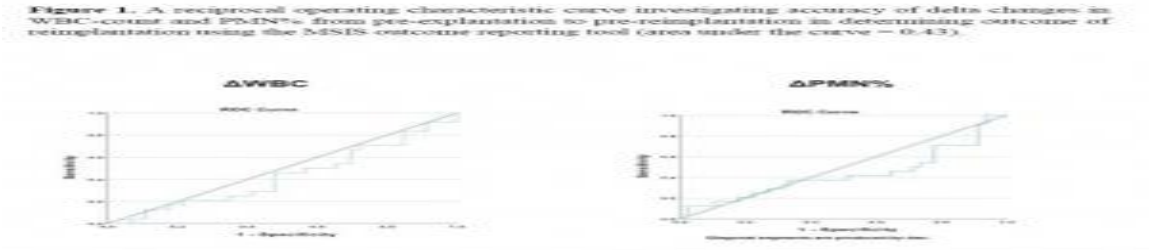
Study Question To investigate the role of delta change in WBC-count and PMN% in anticipating outcome of reimplantation.

Methods A retrospective review was performed on a consecutive series of 133 two-stage revisions for periprosthetic joint infection (PJI) performed by 15 surgeons at two institutions [2014 to 2020]. The minimum follow-up was 1 year. Out of 133, 63 cases with missing synovial aspiration results were excluded. Thus, 70 reimplantations were analyzed. The outcome of reimplantation was defined by MSIS outcome-reporting tool: Tier 1 (infection control with no continued antibiotics), Tier 2 (infection control with suppressive antibiotics), vs Tier 3 (need for reoperation or spacer retention), and Tier 4 (death). Based on non-normal distribution of data, non-parametric tests, Mann-Whitney-U tests were conducted to compare delta change in synovial parameters of Tier 1/2 vs Tier 3/4. Receiver-operating-characteristic (ROC) curves were plotted.

Results The median time to reimplantation was 94.5 days (interquartile range=79.5 to 167.25 days). Demographics, except for American Society of Anesthesiologistsâ€™ grade (p=0.031) were not significantly different between the cases which resulted in MSIS-Tier 1/2 and MSIS-Tier 3/4 outcomes. On comparing changes from pre-explantation to pre-reimplantation values between MSIS Tier 1/2 and Tier 3/4, there were no significant differences in the mean ranks of Î”WBC-count (37.2 vs 32.2; U=472; p=0.322) and Î”PMN% (36.6 vs 31.9; U=467.5; p=0.361). ROC-curve analyses generated results opposite to our hypothesis that increased delta-change [DECREMENT] in these markers would indicate MSIS Tier 1 or 2 outcome. For both Î”WBC-count and Î”PMN%, area under the curve of 0.43 was obtained, which should be deduced as very poor accuracy (Figure 1).

Discussion Our data shows that delta changes in synovial WBC-count and PMN% from explantation to reimplantation have poor accuracy to diagnose infection control and predict the outcome of reimplantation in two-stage revision.

Conclusion The delta changes in synovial WBC-count and PMN% between explantation and reimplantation do not have any capability to diagnose infection control at the time of reimplantation in two-stage revision.



1004 Hardware Removal Due to Infection after Open Reduction and Internal Fixation: Trends and Predictors

Authors Kelsey Martin, Emily Kleinbart, Kudret Usmani, Alec Kellish, Ali Oliashirazi, Kenneth Graf, Henry Dolch, David A Fuller, Alisina Shahi

Background and Rationale Hardware removal due to infection is a major cause of failure following open reduction and internal fixation (ORIF). Few studies have studied trends and predictors of infection of hardware following ORIF, focusing on the multifactorial mechanism of occurrence.

Study Question The aim of this study was to determine trends and predictors of infection-related hardware removal following ORIF of extremities using a nationally representative database.

Methods Nationwide Inpatient Sample data from 2006 to 2017 was used to identify cases of ORIF following extremity fractures, as well as cases that underwent infection-related hardware removal following ORIF. Multivariate analysis was performed to identify independent predictors of infection-related hardware removal, controlling for patient demographics and comorbidities, hospital characteristics, fracture site, and year.

Results For all ORIF procedures, the highest rate of hardware removal due to infection was in the phalanges/hand (5.61%), phalanges/foot (5.08%), and the radius/ulna (4.85%). Hardware removal rates due to infection decreased during the study interval in all fractures except radial/ulnar fractures. Tarsal/metatarsal fractures (odds ratio (OR)=1.45, 95% confidence interval (CI): 1.02-2.05), and tibial fractures (OR=1.82, 95% CI: 1.45-2.28) were identified as independent predictors of infection-related hardware removal. Male gender (OR=1.67, 95% CI: 1.49-1.87), obesity (OR=1.85, 95% CI: 1.34-2.54), diabetes mellitus (OR=1.69, 95% CI: 1.13-2.54, $P<0.05$), and anemia (OR=1.59, 95% CI: 1.14-2.22) were patient factors associated with increased infection-related removals. Removal of hardware due to infection had a higher total charge associated with the episode of care (mean: $166,041) than non-infection-related hardware removal (mean: $133,110).

Discussion Rates of hardware removal due to infection decreased during the study interval in all fractures except radial/ulnar fractures. Diabetes, liver disease, and rheumatoid arthritis were important predictors of infection-related hardware removal, supporting current literature on patient-related risk factors for post-operative infection.

Conclusion The study identified some risk factors for hardware-related infection following ORIF, such as male gender, diabetes, obesity, and anemia, that should be further studied in an attempt to implement strategies and guidelines to reduce rates of infection following ORIF.

1006 The 2018 ICM definition of periprosthetic hip and knee infection is of no value in determining the outcome of reimplantation in two-stage revision

Authors Tejbir S Pannu, Jesus M Villa, Nicolas Piuzzi, Aldo M Riesgo, Carlos A Higuera

Background and Rationale Determining infection control before reimplantation in a two-stage revision is still a challenging endeavor. Given the pitfalls of 2013 MSIS criteria of periprosthetic joint infection (PJI) in this setting, new 2018 ICM PJI definition was proposed. However, its accuracy to confirm control of infection and anticipate the outcome of reimplantation is unknown.

Study Question To evaluate the accuracy of 2018 ICM PJI definition to diagnose residual infection at the time of reimplantation and predict the outcome.

Methods A retrospective review was done on a consecutive series of 134 two-stage hip or knee revisions indicated for the treatment of PJI, which were performed by 16 surgeons in two institutions (2014-2020). The inclusion criteria comprised the completion of reimplantation, tests for 2018 ICM, and minimum 1-year follow-up. Patients with â€œinconclusiveâ€ 2018 ICM PJI definition scores were excluded. Thus, 123 two-stage revisions (49 hips/74 knees) were included. All cases were categorized into either 2018 ICM positive (+) or negative (-). The outcome of reimplantation was defined by MSIS outcome-reporting tool: success (MSIS-Tier-1/2), and failure (MSIS-Tier-3/4). Sensitivity, specificity, and positive/negative predictive values (PPV/NPV) were calculated. ROC-curve and Kaplan-Meier survival-analysis with log-rank test were performed.

Results There were no significant differences in baseline characteristics between 2018 ICM (+) and 2018 ICM (-) two-stage revisions. Also, mean follow-up duration was not significantly different between the groups (26.2 months vs 21.8 months; p=0.402). The 2018 ICM definition demonstrated very poor sensitivity (16.6%) and PPV (43.7%), but high specificity (88.8%) to determine infection control before reimplantation (Table 1). The area under the curve was 0.472, depicting no ability at all to differentiate successful (MSIS-Tier-1/2) two-stage revisions from failed ones (MSIS-Tier-3/4). On survival analyses, there were no significant differences in failure-free survival between 2018 ICM (+) and 2018 ICM (-) surgeries (33.3 months vs 46.1 months; p-value=0.343).

Discussion 2018 ICM PJI definition shows extremely poor accuracy to identify reimplantations which failed vs those that did not, at a minimum follow up of 1 year.

Conclusion 2018 ICM PJI definition demonstrates minimal value to anticipate the outcome of reimplantation, and seems to fail at the objective the previous 2013 ICM criteria did, prediction of survival of reimplantation in two-stage revision.

Table 1. Results of 2018 ICM definition of periprosthetic hip and knee infection in determining the outcome of reimplantation in two-stage revision.

	MSIS Tier 1/2 (-)	MSIS Tier 3/4 (+)	Total
2018 ICM (-)	72	35	107
2018 ICM (+)	9	7	16
Total	81	42	123

Accuracy = 100 x 7+72/7+72+9+35 = **64.2%**
Sensitivity = 100 x 7/42 = **16.6%**
Specificity = 100 x 72/81 = **88.8%**
Positive predictive value = 100 x 7/16 = **43.7%**
Negative predictive value = 100 x 72/107 = **67.2%**
Positive Likelihood Ratio = 0.166/1-0.888 = **1.48**
Negative Likelihood Ratio = 1-0.166/0.888 = **0.94**

1008 Does performance of D-Dimer for diagnosis of periprosthetic joint infection change with the virulence of infecting organism?

Authors Tejbir Pannu, Jesus Villa, Denise Jimenez, Aldo Riesgo, Carlos Higuera-Rueda

Background and Rationale The ability of plasma D-Dimer in diagnosing periprosthetic joint infection is still debatable. It is unknown if virulence of infecting organism has any impact on the diagnostic accuracy of D-Dimer.

Study Question To assess if performance of D-Dimer in PJI diagnosis changes with the virulence of cultured organism.

Methods We conducted a retrospective review of a consecutive series of 143 revision total hip or knee arthroplasties (THA/TKAs) which had D-Dimer test ordered before surgery. Operations were performed by 3 fellowship-trained surgeons at a single institution (11/2017 to 09/2020). Out of 143, 141 revisions with complete 2013 MSIS PJI criteria were initially included. The 2013 MSIS criteria was used to classify revisions as aseptic vs septic. The culture-negative septic revisions (n=8) were excluded, and 133 revisions (47 hips/86 knees; 67 septic/66 aseptic) were analyzed. Based on culture results, septic revisions were further categorized into â€˜low-virulence (LV; n=40)â€™ and â€˜high-virulence (HV; n=27)â€™. The proposed threshold of D-Dimer (850 ng/mL) was tested against the 2013 MSIS criteria (â€œgold standardâ€) in identifying septic-revisions (LV/HV) from aseptic-revisions. Sensitivity, specificity, likelihood ratios, and positive/negative predictive values (PPV/NPV) were determined. Independent t-tests, Fisher's exact tests, chi-squared tests, and receiver operating characteristic curve analysis were performed.

Results Baseline demographics were not significantly different between LV or HV septic and aseptic cases. D-Dimer showed high sensitivity (97.5%) and NPV (95.4%) in LV septic cases, which appeared to reduce by about 5% in HV septic cases (sensitivity=92.5% and NPV=91.3%). However, this marker had poor overall accuracy (LV=57%; HV=49.4%), low specificity (LV and HV=31.8%) and PPV (LV=46.4%; HV=35.7%) to diagnose PJI (Figure 1). The area under the curve (AUC) was 0.647 and 0.622 in LV and HV vs. aseptic revisions, respectively.

Discussion Plasma D-Dimer shows modest higher sensitivity for diagnosing PJI with low (vs high) virulence organisms, but performs poorly to identify septic from aseptic revision THA/TKAs in the setting of low and high virulence infecting organisms alike.

Conclusion Apart from slight higher sensitivity of D-Dimer for diagnosing PJI with low virulence organisms, overall performance of D-Dimer in PJI diagnosis does not change markedly with the virulence of cultured organism.

Figure 1. Predictive ability of plasma D-dimer to diagnose periprosthetic joint infection for low- and high -virulence (LV/HV) organisms (with 2013 MSIS criteria as a gold standard).

LV	2013 MSIS (-)	2013 MSIS (+)	Total
D-dimer (-)	21	1	22
D-dimer (+)	45	39	84
Total	66	40	106

Accuracy = 100 x 39+21/39+21+45+1= 57%
Sensitivity = 100 x 39/40 = 97.5%
Specificity = 100 x 21/66 = 31.8%
Positive predictive value = 100 x 39/84 = 46.4%
Negative predictive value = 100 x 21/22= 95.4%
Positive Likelihood Ratio = 0.975/1-0.318= 1.43
Negative Likelihood Ratio = 1-0.975/0.318= 0.1

HV	2013 MSIS (-)	2013 MSIS (+)	Total
D-dimer (-)	21	2	23
D-dimer (+)	45	25	70
Total	66	27	93

Accuracy = 100 x 25+21/25+21+45+2= 49.4%
Sensitivity = 100 x 25/27 = 92.5%
Specificity = 100 x 21/66 = 32%
Positive predictive value = 100 x 25/70 = 35.7%
Negative predictive value = 100 x 21/23= 91.3%
Positive Likelihood Ratio = 0.925/1-0.32= 1.36
Negative Likelihood Ratio = 1-0.925/0.32= 0.23

1013 A Multicenter Prospective Investigation on Physical and Mental Health After Girdlestone Resection Arthroplasty

Authors Colleen Wixted, Breanna Polascik, Niall Cochrane, Sean Ryan, Ran Schwarzkopf, Antonia Chen, Thorsten Seyler

Background and Rationale Girdlestone resection arthroplasty is a salvage procedure for patients with periprosthetic joint infection (PJI) of the hip. Although effective at controlling infection and reducing chronic pain, this procedure results in limited post-operative joint function.

Study Question How does Girdlestone resection arthroplasty affect physical function and mental health?

Methods This is a multicenter prospective study conducted at three academic tertiary referral centers. Patients treated with Girdlestone resection arthroplasty for any indication between 1995 and 2021 were eligible to participate. Patient reported outcomes were assessed post-operatively with the Prosthesis Evaluation Questionnaire (PEQ), the PROMIS Global Physical Health, and the PROMIS Global Mental Health surveys. The PEQ consists of four scales (ambulation, frustration, perceived response, social burden) with scores ranging from 0 to 10. The PROMIS measures provide raw scores that generate T scores (mean: 50, SD:10) to enable comparisons to the US general population.

Results Thirty-five patients underwent girdlestone resection arthroplasty and completed all surveys. The average time from procedure to completion of the surveys was 6.0 years. The median scores for the ambulation, frustration, perceived response, and social burden scales of the PEQ were 0.0 [IQR: 0-4.1], 6.0 [3.0-9.3], 9.0 [7.2-10.0], and 7.5 [4.3-9.5], respectively. The median raw score for the PROMIS Global Physical Health was 11.91 [IQR: 9-14], which corresponded to an average T-score of 39.7 (SE: 4.3), 10.3 points below the average score in the US general population. The median raw score for the PROMIS Global Mental Health was 14.0 [IQR: 10.0-16.0], which corresponded to an average T-score of 46.1 (SE: 3.8), 3.9 points below the average score in the US general population.

Discussion Girdlestone resection arthroplasty can have a substantial negative impact on physical function while mental health and social interaction may be only moderately affected; Despite these outcomes, this procedure is necessary in certain salvage scenarios.

Conclusion Using PROMIS survey data, the present study found that physical function after Girdlestone resection arthroplasty falls more than two standard errors below that of the general US population, while their mental health scores were only 1 standard below that of the general population.

1014 Skin microbiome and effect of decolonization

Authors Diana Fernandez-Rodriguez, Jeongeun Cho, Emanuele Chisari, Javad Parvizi

Background and Rationale The most common organisms causing surgical site infection (SSI) arise from skin and mucosal surfaces. Decolonization of the skin prior to a surgical procedure has been shown to be effective in reduction of SSI. The aim of this prospective study was to determine the organism profile of the skin and evaluate the effect of application of a unique antiseptic solution on the skin microbiome.

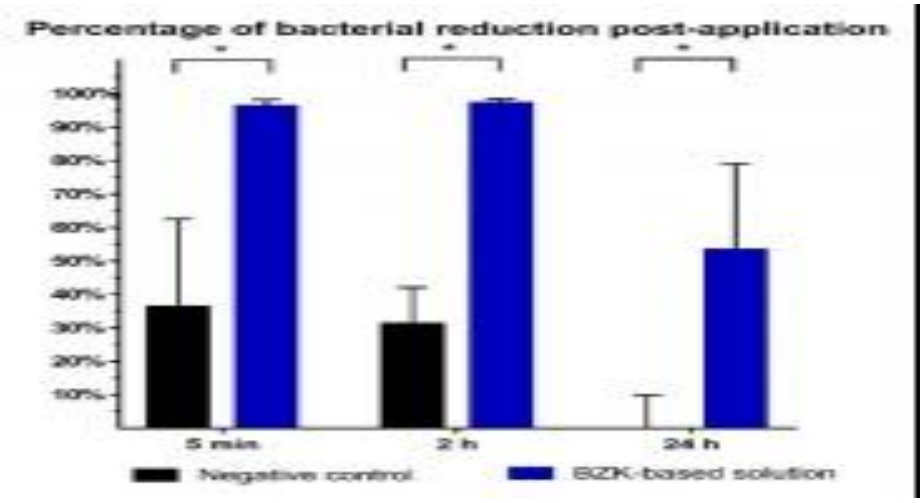
Study Question What is the normal bacterial composition within our skin? What is the efficacy of application of a unique antiseptic solution, containing benzalkonium-chloride, on the skin microbiome?

Methods A total of 50 volunteers were recruited into this study. After randomization one arm of these individuals was cleaned with a wipe that had benzalkonium (BZK) antiseptic solution and the contralateral arm was wiped with PBS. Swab samples of each arm were taken at baseline (prior to application of the agents) and at 3 different timepoints after application (5 min, 2h, and 24h). Skin was protected between 5 min and 2h after application with a sterile wrap. Skin swabs were analyzed for NGS sequencing and culture.

Results The baseline skin bioburden varied greatly among individuals (24 to 32,832 CFU/ml). Bioburden reduction at 5 min was observed in a median of 95.79% vs. 36.26%, after the application of BZK and PBS, respectively. At the 2h after application of BZK, there was still a bacterial reduction of 96.52% (IQR 88.8%-98.56%) and the PBS arm showed a reduction of 31.1% (IQR 0%-56.08%). By 24h, the reduction in bacterial load was 53.26% vs. 0% for BZK and PBS, accordingly.

Discussion Baseline bioburden did not differ between arms ($p=0.61$). A higher effect of bioburden reduction was observed at 5 min after application of BZK, compared to PBS ($p<0.01$). At the 2h after application of BZK, there was still a high bacterial reduction of 96.52% with significant differences compared to the PBS arm (median 31.1%, $p<0.01$). By 24h, the reduction in bacterial load was also higher in the BZK arm ($p<0.01$). The novel antiseptic solution tested during this study has a broad activity against all organisms including fungi and spores.

Conclusion There is a wide difference in the skin microbiome of individuals. Application of BZK-based antiseptic solution led to elimination of the skin flora for up to 2 h after application.



1015 Rapidly Growing Mycobacterial Prosthetic Joint Infections: A Case Series

Authors Eibhlin Higgins, Don Bambino Geno Tai, Omar Abu Saleh, Nancy L wengenack, Aaron J tande

Background and Rationale Nontuberculous mycobacteria (NTM) are ubiquitous environmental organisms which have been associated with a variety of clinical syndromes. They are an extremely rare cause of prosthetic joint infection (PJI). They pose significant therapeutic challenges due to resistance profile of the organisms and toxicity of treatment. However, both diagnostic yield and therapeutic options have improved in recent years thus we sought to review recent cases of rapidly growing mycobacterial (RGM) PJI.

Study Question What are the clinical features, management and outcomes of RGM PJI?

Methods We performed a review of mycobacterial cultures from joint, synovial fluid and periprosthetic tissue from the clinical microbiology laboratory and data from our institutional PJI database. We included isolates positive for RGM from 2010- 2021. PJI was defined as per MSIS criteria.

Results We found 8 cases with mean age of 66 years old (SD 3.8); 4 males and 4 females. 7/8 (87.5%) of cases involved a knee PJI, and one case of hip PJI. Species identified and clinical characteristics of the cohort are summarized in table one.

Six patients underwent two-stage exchange arthroplasty. Of these 6 cases, antibiotic-loaded bone cement with an active agent against NTM were utilized in three cases. Two patients underwent amputation as definitive therapy. Median duration of RGM targeted therapy was 267 days (IQ range 230.0 to 363.8). The median duration of follow up was 3.54 years (IQ range 3.09 to 6.47). 6/8 (75%) of patients experienced an adverse drug reaction. There were no cases of relapsed infection in the cohort at date of last follow up.

Discussion RGM is a rare cause of PJI which may present in immunocompetent hosts as in our cohort. Majority of patients in this cohort did not have systemic symptoms but reported painful joint and/or discharge. Patients demonstrated a chronic course with all having > 4weeks symptoms at presentation. The duration of therapy varied depending on the species isolated and the surgical intervention but prolonged treatment course was utilized in all cases. Majority of patients experience adverse drug reaction during treatment course. Combination surgical and medical therapy resulted in eradication of infection at date of last follow up in all cases.

Conclusion Diagnosis and treatment of RGM PJI is challenging but successful outcome may be achieved with a multimodal patient centric therapeutic approach.

1018 Pseudomonas Prosthetic Joint Infections: Is there a role for monotherapy?

Authors Billy I Kim, Andrew M Schwartz, Colleen Wixted, Isabel Prado, Breanna Polascik, Edward Hendershot, Michael Bolognesi, William Jiranek, Jessica Seidelman, Thorsten M Seyler

Background and Rationale Pseudomonas species are a less common but devastating pathogen family in prosthetic joint infections (PJI). Despite advancements in management, Pseudomonas PJI remains particularly difficult to treat due to fewer antibiotic options and robust biofilm formation. The purpose of this study was to better evaluate outcomes after Pseudomonas PJI treatment.

Study Question What are infection clearance rates for Pseudomonas PJI with respect to host, organism, and treatment factors?

Methods All hip or knee PJIs, at a single institution, with positive Pseudomonas culture were analyzed. 51 patients (29 hips and 22 knees) meeting inclusion criteria were identified. The primary outcome of interest was infection clearance at 1-year after surgical treatment, defined as reassuring aspirate without ongoing antibiotic treatment or death within one year post-operatively. Monomicrobial and polymicrobial infections were evaluated separately.

Results Among monomicrobial PJIs, ten (50.0%) patients were clear of infection at one year post-operatively. Patients treated with 2-stage exchange (n=11) had a 1-year clearance rate of 54.5% compared to 60.0% with DAIR (n=5) and 25.0% with resection or amputation (n=4). Two of six patients treated with fluoroquinolone monotherapy met 1-year infection clearance, despite fluoroquinolone sensitivity, compared to four of five patients meeting 1-year clearance when treated with combined intravenous and oral therapy for at least 6 weeks. Resistance to anti-pseudomonal agents was infrequent (20%, n=4/20), and three of ten mono- and polymicrobial PJI patients with recurrent Pseudomonas PJI developed resistance to anti-pseudomonal therapy. Polymicrobial infections were the most common presentation (54.9%) of Pseudomonas positive PJI with a mortality rate of 46.4% (n=13/28) at a median follow-up of 4.2 years [IQR: 3.4-5.7].

Discussion Infection clearance rate for DAIR and 2-stage exchange were consistent with those reported in prior literature. Our data portrays relatively poor outcomes in patients treated with oral or intravenous monotherapy compared with combination therapy. Additional studies evaluating antibiotic treatment outcomes are warranted.

Conclusion Pseudomonas infections are difficult to eradicate and likely require deviations from classical therapeutic protocols to improve treatment success.

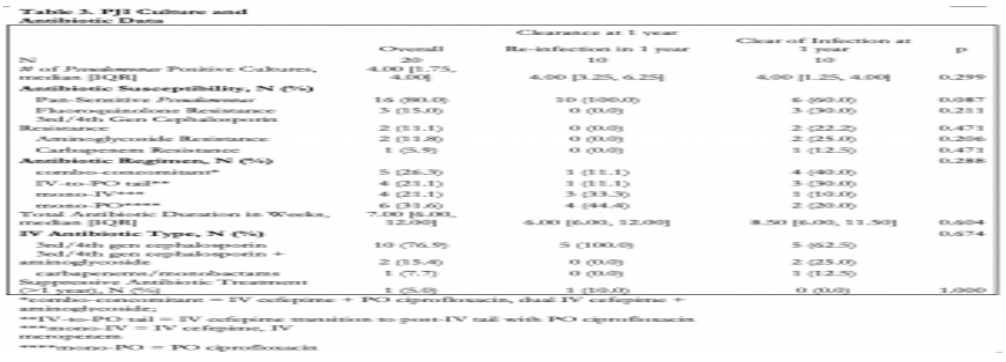


Table 3. PJI Culture and Antibiotic Data

	Overall	Clearance at 1 year: Re-infection in 1 year	Clear of Infection at 1 year	p
N	20	10	10	
# of Pseudomonas Positive Cultures, median [IQR]	4.00 [1.75, 4.00]	4.00 [3.25, 6.25]	4.00 [1.25, 4.00]	0.299
Antibiotic Susceptibility, N (%)				
Pan-Sensitive Pseudomonas	16 (80.0)	10 (100.0)	6 (60.0)	0.087
Fluoroquinolone Resistance	3 (15.0)	0 (0.0)	3 (30.0)	0.231
3rd/4th Gen Cephalosporin Resistance	2 (11.1)	0 (0.0)	2 (22.2)	0.473
Aminoglycoside Resistance	2 (11.8)	0 (0.0)	2 (25.0)	0.286
Carbapenem Resistance	1 (5.9)	0 (0.0)	1 (12.5)	0.473
Antibiotic Regimen, N (%)				0.288
combo-concomitant*	5 (26.3)	3 (33.3)	2 (20.0)	
IV-to-PO sail**	4 (21.1)	3 (33.3)	1 (10.0)	
mono-IV***	4 (21.1)	1 (11.1)	3 (30.0)	
mono-PO****	6 (31.6)	4 (44.4)	2 (20.0)	
Total Antibiotic Duration in Weeks, median [IQR]	7.00 [6.00, 12.00]	6.00 [6.00, 12.00]	8.50 [6.00, 11.50]	0.604
IV Antibiotic Type, N (%)				0.574
3rd/4th gen cephalosporin	10 (76.9)	5 (100.0)	5 (62.5)	
3rd/4th gen cephalosporin + aminoglycoside	2 (15.4)	0 (0.0)	2 (25.0)	
carbapenems/monobactams	1 (7.7)	0 (0.0)	1 (12.5)	
Suppressive Antibiotic Treatment (>1 year), N (%)	1 (5.0)	1 (10.0)	0 (0.0)	1.000

*combo-concomitant = IV cefepime + PO ciprofloxacin, dual IV cefepime + aminoglycoside;
**IV-to-PO sail = IV cefepime transition to post-IV sail with PO ciprofloxacin
***mono-IV = IV cefepime, IV meropenem
****mono-PO = PO ciprofloxacin

1019 Rotational Muscle Flap Coverage for Soft Tissue Defects After Prosthetic Knee Infections

Authors Billy I Kim, Colleen Wixted, Andrew Schwartz, William Jiranek, Sean P Ryan, Thorsten M Seyler

Background and Rationale Soft tissue defects are a devastating complication of prosthetic joint infections (PJI) after total knee arthroplasty (TKA). Rotational flaps are commonly utilized to address these defects with variable reports of success. This study aimed to evaluate outcomes of rotational soft tissue rearrangements in the course of surgical treatment for prosthetic knee infections.

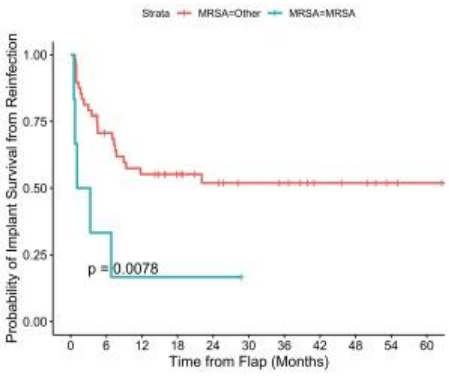
Study Question What is the treatment success rate after muscle flap coverage in prosthetic knee infections and do outcomes vary by infecting pathogen?

Methods 52 cases of rotational muscle flaps for prosthetic knee infection were retrospectively evaluated at a single institution from 2007 - 2020. Muscle flap types included 43 medial and six lateral gastrocnemius, two vastus lateralis, and one anterior tibialis. Minimum follow-up was one year (median: 3.2 years). Primary outcome was recurrent infection requiring additional surgery. Secondary outcomes included final joint outcomes, flap-related complications, and mortality.

Results The one-year survivorship free of reoperation for infection was 44.2% (n=23/52). Univariate cox regression revealed that rheumatoid arthritis diagnosis (HR: 2.79 [CI: 1.24-6.28]) and methicillin-resistant Staphylococcus aureus (HR: 3.47 [CI: 1.30-9.27]) infections were associated with recurrent infection. Coagulase-negative Staphylococcus (CoNS) infections had a lower risk for recurrent infection compared to other infections (HR: 0.21 [CI: 0.05-0.89]). Final joint outcome was amputation in 16 (30.8%) patients, arthrodesis in two (3.8%), and definitive treatment with an articulating spacer in 12 (23.1%). Most common flap complications were wound dehiscence (n=6, 11.5%) and flap failure requiring fasciocutaneous advancement or secondary muscle flap coverage (n=4, 7.8%). Mortality rate at last follow-up was 26.9%.

Discussion Patient outcomes varied by infecting pathogen, with MRSA demonstrating increased and CoNS demonstrating decreased risk for returning to the operating room for infection. Rotational muscle flaps for soft tissue coverage of the knee were associated with a high risk of failure, with nearly a third of patients requiring amputation at last follow-up.

Conclusion When considering surgical options for limb salvage, patients should be counseled on the risks for recurrent infections, amputation, and flap-related complications after flap coverage.



1020 The Utility of Next Generation Sequencing in Revision TJA

Authors Colin M Baker, Karan Goswami, Saad Tarabichi, Graham S Goh, Javad Parvizi

Background and Rationale Next Generation Sequencing (NGS) has emerged as a promising diagnostic tool for periprosthetic joint infection (PJI). NGS facilitates pathogen identification in the context of culture-negative PJI (CN-PJI); however, the clinical relevance of the polymicrobial genomic signal often generated remains unknown.

Study Question This study aimed to explore: (1) The ability of NGS to identify pathogens in CN-PJI; and (2) determine whether organisms detected by NGS, as part of a prospective observational study, had any role in later failure of patients undergoing revision surgery.

Methods In this prospective study, samples were collected from 452 consecutive patients undergoing revision total hip and knee arthroplasties. Of these, 121 patients had PJI, as defined by the International Consensus Meeting (ICM) criteria, and of these 23 were culture-negative (19%). Additionally, 23 patients had inconclusive findings while 308 patients were found to be not infected. Synovial fluid, deep tissue, and swabs were obtained at the time of surgery and sent for NGS and culture/MALDI-TOF. Treatment failure was assessed using the Delphi criteria. In cases of re-operation, organisms present were confirmed by culture. Concordance of the infecting pathogen(s) at failure with the NGS analysis at the initial stage CN-PJI procedure was determined.

Results Among 23 patients with CN-PJI, NGS identified organisms in 11 cases. Twelve cases were both culture and NGS-negative. NGS detected more than one organism in 5 of the 11 CN-PJI cases. Additionally, 2/4 (50%) of aseptic revisions failed from an organism identified via NGS at the initial procedure.

Discussion CN-PJI presents a difficult challenge for treating surgeons. Results from this study suggest that NGS may be useful in identifying organisms that are not isolated using conventional techniques. Additionally, NGS may have utility in identifying organisms in cases that were initially presumed to be aseptic revisions and then later fail due to PJI.

Conclusion CN-PJI is often associated with polymicrobial metagenomic organism profile. Our findings suggest some cases of PJI may be polymicrobial and escape detection using conventional culture.

1022 Childs-Pugh Class B/C Increases Risk of Early Mortality in HCV Patients Undergoing Elective TJA Regardless of Treatment Status

Authors Kyle H Cichos, Antonia F Chen, Erik N Hansen, Eric Jordan, Kian Niknam, Gerald McGwin Jr, Elie S Ghanem

Background and Rationale Patients with Hepatitis C (HCV) undergoing primary elective total joint arthroplasty (TJA) are at increased risk of postoperative complications.

Study Question The aim of this study was to determine risk factors for early (2-year) mortality in HCV patients undergoing elective total joint arthroplasty.

Methods A retrospective review at 3 tertiary academic medical centers, identifyied all patients with HCV undergoing primary elective TJA from 2005-2019 with a minimum 2-year follow-up. After exclusion criteria, 169 patients were included. Outcomes and confounding variables were compared between the early mortality (16 patients) and survival patients (153 patients). Multivariable regression analysis was performed for risk factors of early mortality incorporating all significant preoperative variables. The mean follow-up duration was 53 months (SD 29).

Results There was no difference between the groups in age, BMI, liver fibrosis stage, liver fibrosis activity level, liver fibrosis stage, ALT, HCV genotype, viral load, HCV treatment status and treatment type, MELD level, ASA score, TXA use, anesthesia type, operative duration, blood loss, blood transfusion rate, ICU stay, or comorbidities including cirrhosis with the exception of male sex (p=0.03), undergoing THA vs TKA (p=0.04), AST levels (p=0.02), PVD (p=0.009), ESRD (p=0.01), HF (p=0.002), and COPD (p=0.005), all increased in early mortality group. There was no difference between the groups in 90-day or 1-year surgical complications, including dislocation, mechanical revision, periprosthetic fracture, and PJI. HCV patients with Childs-Pugh Class B/C were at independently increased risk of early (2-year) mortality (OR 29.24, 95% CI 4.90-174.44, $p<0.001$) compared to those with Childs-Pugh Class A. No other variables from univariate analysis were independently associated with early mortality.

Discussion HCV patients that are Childs-Pugh Class B/C at time of elective TJA are 29 times more likely to pass away within 2 years of surgery than those who are Childs-Pugh Class A, regardless of liver function, cirrhosis, age, MELD level, and HCV treatment or viral load status.

Conclusion Surgeons should counsel these HCV patients preoperatively of their significantly increased risk of early mortality after surgery independent of HCV treatment and viral load status, and carefully consider the risk/reward of elective surgery in these patients.

1023 Sarcopenia Increases the Risk of Mortality but not SSI after Acetabular ORIF

Authors Kyle H Cichos, Gerald McGwin Jr, Elie S Ghanem

Background and Rationale Sarcopenia is a surrogate for malnutrition and has been shown to predict post-surgical complications in many surgical fields.

Study Question The purpose of this study is to determine whether sarcopenia or sarcopenic obesity increase the risk of SSI or other complications after operative treatment of acetabular fractures.

Methods 941 patients undergoing operative fixation of acetabular fractures at our level I trauma center treated from 2010-2019 were identified prior to exclusion. The final cohort included 765 patients with an average follow-up of 35 months (6-141 months). Patient demographics, comorbidities, operative and in-hospital variables were compared between patients with sarcopenia and those without. Sarcopenia was defined by skeletal muscle index (SMI) measured on CT scan at L3 level for males <55.4 cm2/m2 and females <38.5 cm2/m2.

Results 140 patients (18.3%) had sarcopenia at the time of injury. The groups differed in baseline characteristics associated with age (sarcopenic: 51 years vs non-sarcopenic: 38 years, p <0.001), including fracture classification (p<0.001) and injury energy: low (7% vs 1%, p<0.001). There was no difference in ICU stay, intraoperative blood transfusion, HO prophylaxis, intrawound antibiotics prior to closure, pelvic artery embolization, GU/bladder or abdominal organ injury, IV drug use, tobacco use, LOS, and ISS. The sarcopenic group had decreased operative duration (183 vs 227 min, p<0.001), blood loss (510 vs 600 mL, p=0.01), BMI (26 vs 32, p<0.001), and TXA use (18% vs 27%, p=0.03). The sarcopenic group was more likely to be male (90% vs 64%, p<0.001). There was no difference between the sarcopenic and non-sarcopenic groups in 1-year outcomes including: dislocation, revision ORIF, HO formation, wound dehiscence/draining (11% vs 12%, p=1.00, deep SSI (5% vs 7%, p=0.36), or FRI (6% vs 9%, p=0.25), and there was no difference between in overall risk of conversion THA (14% vs 17%, p=0.39). The sarcopenic group did have increased risk of mortality at 1-year (9% vs 1%, p <0.001) and were more likely to be discharged to skilled nursing facility (p<0.001).

Discussion Sarcopenia increases the risk of 1-year mortality after acetabular fracture fixation, but does not impact the risk of SSI, FRI, or other postoperative complications.

Conclusion Further analyses are required to stratify the cohort based on age and to assess the effect of sarcopenic obesity on outcomes of these patients.

1025 History of COVID-19 Infection and the Risk of post-operative VTE after Primary Total Joint Arthroplasty

Authors Nick Ogrinc, Hannah Szapary , Alexander Farid , David Novikov , Antonia F Chen , Michael Kain

Background and Rationale Acute infections of COVID-19 are associated with a hypercoagulable state and an increased risk of thromboembolic complications, with venous thromboembolism (VTE) rates of 22.7% for intensive care unit (ICU) patients and 10.4% outside the ICU.5 Anticoagulation therapy is important for minimizing disease severity of COVID-19. One multicenter observational study suggested increased VTE in surgical patients who previously had COVID-19 infection (2.0%) compared to patients who never had COVID-19 (1.4%).1 Some institutions have begun accounting for COVID-19 as a potential risk factor for post-operative VTE occurrence. Hip fracture patients positive for COVID-19 had a mortality rate of 30.5% and VTE rate of 13.4%.2 There is a significant clinical need to understand if there is a relationship between historical COVID-19 infection and post-operative VTE occurrence to inform anticoagulation prophylaxis regimens following total joint arthroplasty (TJA).

Study Question Do patients who had a positive Sars-CoV-2 test one year prior to their elective primary TJA have an increased risk of postoperative VTE events?

Methods A retrospective study on primary TJA patients was performed at two academic hospitals between 8/1/2020 and 11/30/2021. Patients were excluded if they were <18yo, prisoners, or underwent revision TJA. The primary outcomes were postoperative VTE events and cardiopulmonary complications in relation to prior COVID-19 infection.

Results 1034 patients underwent surgery during the study period, and 187 patients presented with a COVID positive test prior to surgery. Of the COVID-19 positive patients, there were only 3 VTE events (1.6%, 2 lower extremity deep vein thromboses and 1 pulmonary embolism). These 3 patients all underwent total hip arthroplasty and 2 of the 3 had a second infection of COVID-19 three months after surgery. Of the COVID-19 positive patients, 3 patients experienced cardiopulmonary events (1 transient ischemic attack, 1 myocardial infarction, and 1 cardiac arrest).

Discussion In this multicenter study review of 187 patients with a positive COVID-19 test prior to elective TJA, the presence of a prior positive COVID-19 infection does not appear to increase the risk of VTE or cardiopulmonary events for primary TJA.

Conclusion VTE and cardiopulmonary events did not increase in COVID-19 positive primary TJA patients.

1026 Treatment Outcomes of Fungal Periprosthetic Joint Infection

Authors Carl L Herndon, Rory Metcalf, Bryan D Springer, Thomas K Fehring, Susan M Odum, Jesse E Otero, Taylor M Rowe

Background and Rationale Periprosthetic joint infection (PJI) after total joint arthroplasty (TJA) is a challenging complication for surgeons and patients alike. Most PJIs are due to gram-positive bacteria; however, the burden of fungal organisms may represent ~1% of all PJI and is more difficult to treat. The current evidence reports poor success rates of small case series. Fungi are typically opportunistic pathogens and patients with fungal PJI are believed to be immunocompromised with decreased cellular immunity. Additionally, fungal biofilms are more complex than those formed by other pathogens and convey additional drug resistance and difficulty in treatment. Due to these factors, the treatment failure is common with 2-year infection-free success reported as low as 38% for hips and 76% for knees in one series.

Study Question What is the failure rate of patients treated with a 2-stage exchange for fungal PJI and what are the risk factors for failure?

Methods A retrospective query of our institutional PJI registry identified 49 patients treated with 2-stage exchange for fungal PJI with a minimum 1-year follow-up. Patient demographics, clinical characteristics, and surgical characteristics were collected. The primary outcome was failure defined as re-operation for infection due to any organism following the index surgery for fungal PJI. Of the 49, patients, 8 patients were excluded for a final followup of less than 1-year.

Results The overall failure rate was 48.8% (20/41). A higher proportion of patients with local extremity grade C failed treatment, and every patient that failed had a host grade of 2 or 3. These results did not reach statistical significance. The average number of prior surgeries, prior arthroplasty surgeries, and time from resection to reimplantation were similar between groups.

Discussion This represents the largest cohort of fungal PJI patients reported in the literature to date. This data supports other literature in that failure rates remain high despite surgical treatment.

Conclusion Fungal PJI remains a rare but devastating diagnosis, and treatment failures continue to remain high. Additional research is needed to further understand fungal PJI and improve care for these patients.

	Overall (n = 41)	Failure		P Value
		Yes (n = 20)	No (n = 21)	
Local Extremity Grade, n (%)				
A: Uncompromised (no compromising factors)	3 (7.1%)	2 (10.0%)	1 (4.8%)	
B: Compromised (1-2 compromising factors)	23 (57.1%)	8 (40.0%)	15 (71.4%)	0.069
C: Significant compromise (> 2 compromising factors)	15 (35.7%)	10 (50.0%)	5 (23.8%)	
MSIS Systemic Host Grade, n(%)				
1: Uncompromised (no compromising factors)	2 (4.8%)	0 (0%)	2 (9.5%)	
2: Compromised (1-2 compromising factors)	26 (61.9%)	16 (80.0%)	9 (42.9%)	0.121
3: Significant compromise (>2 compromising factors)	13 (31.0%)	4 (20.0%)	9 (42.9%)	
Number of prior surgeries, Median (IQR)	5 (2, 4)	3 (2, 4)	3 (2, 4)	0.722
Number of prior arthoplasty surgeries, Median (IQR)	1 (1, 2)	1.5 (1, 2)	1 (1, 2)	0.594
Time from Resection to Reimplantation (Months), Median (IQR)	4 (3, 10)	9 (5, 17)	7 (3, 4)	0.137

1027 Non-Eluting Zimmer Bactiguard Implant Coating Provides Early Protection Against Infection in a Murine Model of Periprosthetic Joint Infection (PJI)

Authors Zeinab Mamouei, Christopher D Hamad, Nicholas V Peterson, Joseph K Kendal, Alan Li, Jeremiah Taylor, Abdulrahman Almalouhi, Aaron Kavanaugh, Fabrizio Billi, Nicholas M Bernthal

Background and Rationale PJI is a morbid complication of total joint arthroplasty requiring multiple surgeries and intensive medical management. Currently, a multi-modal approach of prophylactic antibiotics, intraoperative field sterility, surgical wound irrigation, and intrawound vancomycin powder are used to prevent PJI, but breakthrough cases still occur. Implant coatings could provide additional protection against early biofilm formation on implants. Bactiguard is a noble metal coating consisting of silver, gold, and palladium that generates a pico-current dispersion force to prevent microbial adhesion. Bactiguard is an FDA approved coating currently used on urinary catheters to prevent infection.

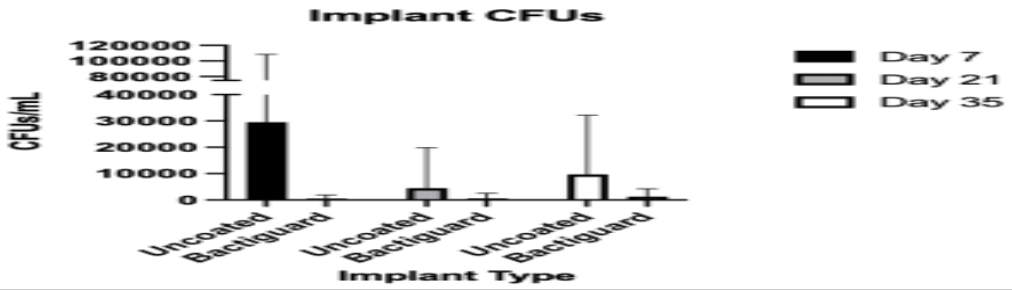
Study Question Does Bactiguard coating technology help prevent implant associated infection (IAI) in a murine model of PJI?

Methods An established mouse model of PJI was utilized. A 6x.8mm Bactiguard or uncoated pin were implanted retrograde into the distal femur of a 10-week-old C57BL/6 mouse and inoculated with 1E3 CFUs of S. aureus (Xen36) or sterile saline. Bacterial burden was longitudinally measured in vivo by quantifying bacterial bioluminescence using an IVIS Spectrum. Animals were sacrificed on post-operative days (PODs) 7, 21, and 35 to collect implants and harvest tissue for CFU analyses. Additional implants were harvested on PODs 7 and 35 for scanning electron microscopy (SEM) analysis.

Results There was no difference in in vivo bioluminescence between Bactiguard and uncoated pins. Bactiguard coated pins had significantly lower CFUs compared to that of uncoated pins on POD7 ($p=0.0085$). There were no significant differences in CFUs on PODs 21 and 35. On SEM, there were fewer staphylococci observed on Bactiguard coated implants harvested on POD7 compared to uncoated pins. On POD35, there were no observed differences between groups on SEM.

Discussion Despite extensive soft-tissue infection seen on in vivo bioluminescence, non-eluting Bactiguard coating provides protection against bacterial colonization of implants on POD7, which is observed on CFUs and SEM. Bactiguard technology may be helpful in conjunction with current multi-modal approaches to help prevent PJI caused by microbial contamination at the time of surgery.

Conclusion Bactiguard coating helps decrease bacterial colonization on implants seven days after surgery in a murine model of PJI.



1028 Similar 90-day surgical site infection rates between robotic-assisted and manual total knee arthroplasty: A large patient cohort

Authors Antonia F Chen, Laura Scholl, Todd Gutowski, Sietske Witvoet, Daniele De Massari

Background and Rationale Robotic-assisted total knee arthroplasty (RA-TKA) has demonstrated improved accuracy to plan, decreased pain, shorter length of stay, and increased satisfaction compared to manual TKA. However, few large-scale studies have been conducted comparing complication rates between manual and RA-TKA.

Study Question The purpose of this study was to compare the 90-day surgical site infection (SSI) and complication rate between manual and RA-TKA.

Methods A retrospective study was conducted evaluating 53,106 TKAs (33,631 manual,19,475 RA) performed from 1/2017-12/2020 at 93 different hospitals. 90-day post-operative complications were classified based on the Clinical Classification Software categorization applied for ICD-10 diagnosis codes. All-cause 90-day readmission rates were computed for the two cohorts and a univariate followed by a multivariable logistic regression analysis was conducted to reveal the factors impacting the 90-day readmission rate. Complication rates were compared between manual and RA-TKA cohorts using Fisherâ€™s exact test analysis for the following categories: deep vein thrombosis, pulmonary embolism, pain management, SSI (deep, superficial, deep & superficial, and pin site), transfusion/injection and venous thromboembolism (VTE).

Results Deep and superficial SSI were not associated with RA-TKA ($p>0.05$) or other factors ($p>0.05$) including patient gender, surgical year, surgical side, anesthesia type, or blood transfusions (Table 1). Deep and superficial SSI were associated with Elixhauser score ($p<0.0001$). There were no pin site infections reported for any RA-TKA.

When considering all cause 90-day readmission, the multivariable logistic regression analysis revealed a significant relationship of patientâ€™s age ($p<0.001$), gender ($p=0.13$), surgery year ($p=0.012$), length of stay ($p<0.001$) and Elixhauser score ($p<0.001$). There was no difference in all-cause 90-day readmission rate between manual and RA techniques (2.7% vs 2.8%, respectively, $p=0.08$). However, the manual cohort had significantly higher VTE ($p=0.008$) compared to RA-TKA (Table 1).

Discussion This study identified that RA-TKA had no difference in SSI rates and significantly less VTE at 90-days postoperatively. Further studies are needed to elucidate differences between manual and RA-TKA cases.

Conclusion RA-TKA had similar SSI rates to manual TKA and significantly less VTE at 90-days postoperatively.

Table 1. Complication rate based on ICD10 codes associated with 90-day readmission. Fisher's exact test was applied for corresponding p-values reported in the table.

Complication	Robotic-assisted	Manual	p-value
Pain Management	0.067	0.074	0.867
Transfusion/Injection	0.000	0.000	1.000
Venous thromboembolism (VTE)	0.056	0.134	0.008*
Deep vein thrombosis (DVT)	0.010	0.039	0.065
Pulmonary embolism (PE)	0.046	0.089	0.096
Deep Infection	0.003	0.003	0.515
Superficial Infection	0.001	0.000	0.253
Deep & Superficial Infection	0.004	0.004	1.000
Pin Site Infection	0.000	0.000	---

Where * represents p<0.05

1029 Characterizing the Local Immune Environment in a Murine Model of Periprosthetic Joint Infection (PJI)

Authors Christopher D Hamad, Joseph K Kendal, Zeinab Mamouei, Nicholas V Peterson, Alan Li, Jeremiah Taylor, Abdulrahman Almalouhi, Parsa Asachi, Micheal R Yeaman, Nicholas M Bernthal

Background and Rationale PJI is a morbid complication of total joint arthroplasty requiring multiple surgeries and intensive medical management. The formation of an immunosuppressive immune microenvironment (IME) may drive the development of chronic infection in PJI. To identify novel immunotherapies, we must elucidate the cellular mechanisms that promote immunosuppression in PJI.

Study Question What local cytokine and cellular changes occur throughout time in a murine model of PJI?

Methods An established mouse model of PJI was utilized. A titanium pin was implanted retrograde into a mouse femur and inoculated with 1E3 CFUs of S. aureus (Xen36) or sterile saline (sham). Negative control mice that did not undergo surgery were included. 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. Flow cytometric analyses was used to quantify innate and adaptive immune populations, and co-expression of relevant immunosuppressive surface markers (PD-1, PD-L1 and CSF-1R).

Results 14/32 cytokines were significantly elevated in infected mice. Cytokines that peak on PODs 1 or 3 include G-CSF, IL-1b, CXCL-1, CXCL-2, and IL-2. Cytokines that peak on PODs 7 or 14 include IL-1a, IL-6, IL-17, RANTES, CCL-3, CCL-4, CXCL-9, and CXCL-10. Only Eotaxin peaked on POD21. Cytokine responses begin waning by POD21. Percent neutrophils and macrophages were lower in infected and sham animals compared to that of negative control. T-cells were highest in infected animals on POD1, but decreased below negative control by POD3. Myeloid derived suppressor cells (MDSCs) were highest in infected animals on PODs 7 and 14. PD-L1+ CSF-1R+ macrophages and MDSCs were highest in infected animals on POD7.

Discussion In a murine model of PJI, the early cytokine response induces acute neutrophil and monocyte recruitment to replace dead innate immune cells. As chronic inflammation persists, the cytokine milieu promotes cellular immunity in a TH1/TH17 dominated manner, despite a low T-cell number. Chronic PJI promotes the recruitment of MDSCs and immunosuppressive PD-L1+ CSF-1R+ macrophages.

Conclusion PJI induces a pro-inflammatory TH1/TH17 response that fails to eradicate infection. Immunosuppression may be driven by MDSC recruitment and checkpoint blockade and their inhibition may promote clearance of PJI.

1030 Intrawound Vancomycin Powder does not Alter Biologic Stability (Osseointegration) in a Murine Model of Joint Arthroplasty

Authors Christopher D Hamad

Background and Rationale Intrawound vancomycin powder is commonly used at the time of surgery to prevent the development of implant associated infection (IAI) in many orthopaedic settings. However, investigators have demonstrated in vitro that vancomycin is cytotoxic to host cells required for healing such as osteoblasts, fibroblasts, myocytes, and endothelial cells. This data has generated concerns that vancomycin may perturb biologic stability of orthopedic implants. We aim to provide in vivo functional data to fill this knowledge gap.

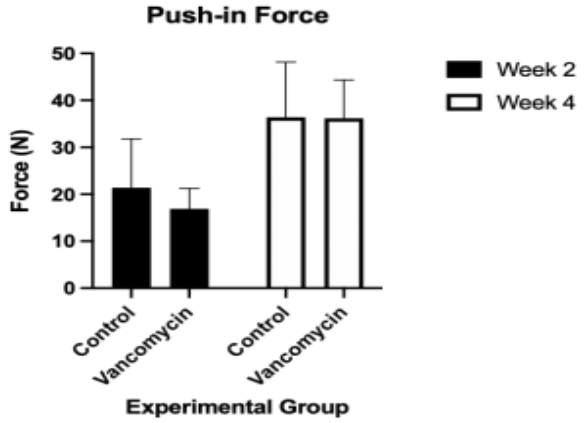
Study Question How does vancomycin affect early and late biologic stability of a titanium implant in a murine model of joint arthroplasty?

Methods A 6x.8mm titanium pin was implanted retrograde into the distal femur of a 10-week-old C57BL/6 mouse. Mice were randomized to receive 4mg of intrawound vancomycin prior to wound closure. Animals were sacrificed at 2 and 4 weeks and femurs were disarticulated, removed, and cleaned of all soft tissue. There were 5 mice in each group at each time point (N=20). Femurs were embedded in a resin block with the distal aspect exposed for â€œpush-inâ€ testing. An Instron instrument was calibrated and used to quantify the force necessary to push-in the titanium implant, effectively disrupting the biologic interface stabilizing metal and bone.

Results he average push-in forces at 2 weeks were 21.4N and 16.9N for control and vancomycin groups, respectively (p=0.6032). The average push-in forces at 4 weeks were 36.4N and 36.175N for control and vancomycin groups, respectively (p=0.9048).

Discussion Vancomycin may decrease implant bony ingrowth 2 weeks after surgery, but this difference in not significant. However, at 4 weeks, there is no difference in Newton force between groups. This data suggests that vancomycinâ€™s in vitro cytotoxicy does not translate to significant long-term changes in in vivo biologic stability.

Conclusion Vancomycin does not significantly impact long-term biologic stability of titanium implants in a murine model of joint arthroplasty.



1032 Permanent articulating spacer versus two-stage exchange for chronic PJI: A propensity-score matched study

Authors Elshaday Belay, Colleen Wixted, Billy Kim, Samuel Wellman, Michael Bolognesi, William Jiranek, Thorsten Seyler

Background and Rationale Although two-stage revision has been proposed as gold standard for PJI treatment, there is limited evidence for the role of an articulating spacer as possible definitive management of chronic PJI.

Study Question Are there differences in clinical outcomes and costs associated with an articulating spacer (1.5-stage) versus a matched 2-stage cohort?

Methods Using an institutional database, a retrospective review was performed from 2016 to 2021 for patients that developed chronic PJI after TKA defined by MSIS criteria. Propensity score matching was performed using a cumulative MSIS score and Elixhauser comorbidity index. Outcomes included VAS pain score, 90-day ED visit, 90-day readmission, unplanned reoperation, reinfection, and costs at one and two-year intervals. Regression analysis was performed to understand independent risk factors for reinfection across both groups.

Results After propensity matching, 118 patients were included for analysis. There was no difference between demographics and baseline characteristics in each group. 93% of 1.5-stage and 90% of 2-stage revision patients met modified MSIS criteria, with no significant difference in either group (p=0.51). 90-day pain scores were lower for 1.5-stage (2.9 vs. 4.6), p=0.0001. There was no significant difference between readmission or reoperation rates. Infection clearance was equivalent at 79.6% for both groups. Two-stage exchange demonstrated an increased cost difference of $26,346 per patient compared to 1.5-stage through 2-years, p=0.0001. Regression analysis for risk factors of reinfection found that perioperative culture-positive result decreased the risk for re-infection after PJI treatment, OR 0.2 (95% Cl 0.04-0.8, p=0.03).

Discussion For high-risk surgical candidates, a permanent articulating spacer technique may preserve knee function, reduce morbidity from second-stage surgery, and lower cost with similar rates of infection clearance as two-stage exchange.

Conclusion Findings from this matched cohort study suggest no differences in baseline characteristics, acute complications, or infection clearance between definitive treatment with an articulating spacer (1.5 stage) and 2-stage exchange. As expected with an additional surgery, the 2-stage cohort had higher costs and 90-day pain scores.

1033 Factors Associated With Periprosthetic Joint Infection in Hip Hemiarthroplasty

Authors Jonathan Bourget-Murray, Isabel Horton, Jared Morris , Antoine Bureau, Simon Garceau, Hesham Abdelbary, George Grammatopoulos

Background and Rationale There currently exists no evidence-based treatment algorithm for managing hemiarthroplasty PJI. With growing evidence suggesting that differences in epidemiology, clinical features, and outcome exists between elective total hip arthroplasty (THA) and hemiarthroplasty patients, these differences may contribute to explain why debridement, antibiotic therapy and implant retention (DAIR) has much lower chances of success with a hemiarthroplasty (22% to 82%) compared to elective THA (72.2%).

Study Question What is the prevalence and treatment outcome of PJI following hemiarthroplasty for hip fracture? What factors are associated with outcome of treatment?

Methods A retrospective review was performed of consecutive patients treated for a hemiarthroplasty PJI between 2010-2021 at an academic, tertiary-referral hospital with a minimum 1-year follow-up. Surgeries performed, by 17 surgeons, included DAIR, and single-stage revision hemiarthroplasty or conversion to THA. Success was defined using the Delphi criteria. The effect of different patient-, surgical- and infection- factors on treatment outcome was determined.

Results Of the 1,666 hemiarthroplasties performed, 44 sustained a PJI (incidence: 2.6%). At a mean follow-up of 4.5 Â± 4.2 years (range, 1.6 weeks-12.9 years), seventeen patients (38.6%) failed initial treatment and required subsequent surgery. One-year mortality was 22.7%. Factors associated with treatment outcome included lower pre-operative hemoglobin level (97.9Â±11.4 vs 107.0Â±16.1; p=0.009), elevated CRP level (99.1Â±63.4 vs. 56.6 Â± 47.1; p=0.030), and type of surgery. There was a lower chance of success with DAIR (11/26, 42.3%) compared to revision hemiarthroplasty (4/6, 66.7%) or revision with conversion to THA (12/12, 100%). In addition, early-onset PJI (â‰¤6 weeks) was associated with a higher likelihood of treatment failure (OR: 3.5 [95% CI, 1.2 to 10.6]; p=0.007) along with patients treated by a non-arthroplasty surgeon (OR: 2.5 [95% CI, 1.2 to 5.3]; p=0.014).

Discussion The findings of this study suggest that performing a revision arthroplasty with conversion to THA should be considered as the initial treatment for hemiarthroplasty PJI.

Conclusion DAIR is associated with poor chances of success and its value is limited. Additional data is required to determine if there are any functional advantages to single-stage revision arthroplasty as an initial treatment option for patients with a hemiarthroplasty PJI.

1034 Re-Infection after 2-Stage Exchange for PJI: Can the Organism be Predicted?

Authors Andrew J Clair, Rory Metcalf, Bryan D Springer, Thomas K Fehring, Susan M Odum, Taylor M Rowe, Jesse E Otero

Background and Rationale Periprosthetic joint infection (PJI) is a rare but devastating complication after total joint arthroplasty. When a two-stage exchange fails to cure or control infection, options are limited, and outcomes are dismal. Efforts to understand mechanisms of septic failure may aid in the prevention of failure in the future. A peculiar observation which has been made repeatedly in patients who fail two-stage exchange is that the re-infecting organism is different from the original infecting organism in 50-80% of occurrences. Understanding the patterns of re-infection, if indeed patterns exist, may offer clues to prevent re-infection.

Study Question Is there an association between the original infecting organism before two-stage exchange for PJI and the organism detected upon failure?

Methods A retrospective query of our institutionâ€™s PJI registry identified 386 patients who underwent a two-stage exchange after total knee arthroplasty (TKA) and total hip arthroplasty (THA) with confirmed chronic bacterial PJI, as defined by MSIS criteria, from January 2010- December 2020. Exclusion criteria included spacer insertion for primary septic arthritis, fungal infections, negative and undocumented PJI cultures. The primary outcome variable was reoperation for re-infection and we compared the index infecting organism to the re-infecting organism for failed 2-stage exchange. Of the 386 patients, there were 223 TKAs (57.8%) and 163 THAs (42.2%).

Results Fifty patients (13%) went on to fail the two-stage exchange, including 35/223 knees (15.7%) and 15/163 hips (9.2%). Of the 50 failures, 27 had a different re-infecting organism (54%), 9 had the same re-infecting organism (18%), 13 were culture negative (26%), and 1 was not collected prior to an amputation (2%). The most common organisms cultured at index 2-stage and at failure were MSSA, MRSA, and coagulase negative staphylococcal species. With these data, there was no discernable patterns of infecting organisms between the index and re-infection surgeries.

Discussion Failure of two-stage exchange frequently occurs with a different organism. Further study is needed to define the relationship between failed two-stage exchange and the infecting organisms to determine patterns.

Conclusion Understanding patterns between the index and failure organisms, and the complex interplay with host factors, will aid in answering the howâ€™s and whyâ€™s of failure and guide prevention and management strategies in the future.

1035 Risk Factors for Surgical Site Infection after Operative Management of Pilon Fractures

Authors Brandon O Boyd, Anthony Wilson, Kyle cichos, Sudarsan Murali, alexander Mihas, David Patch, Gerald McGwin, Michael Johnson, Clay Spitler, Elie Ghanem

Background and Rationale Current operative management of pilon fractures prioritizes initial soft tissue protection with subsequent definitive fixation. Despite concerted efforts, extensive soft tissue damage remains a serious concern as it is associated with postoperative complications such as wound dehiscence and surgical site infection (SSI).

Study Question The purpose of this study is to identify risk factors associated with SSI following operative management of pilon fractures.

Methods A retrospective review of all operatively managed pilon fractures at a single level 1 trauma center from 2014 to 2019 was performed. Minimum six-month follow-up and skeletal maturity was required for inclusion. Patients with amputation prior to definitive fixation were excluded. Patients were grouped based on presence of SSI or no infection. SSI consisted of superficial and/or deep infections (defined as return to the operating room for debridement with positive cultures). Demographics, injury and operative characteristics, and surgical outcomes were compared between the two groups.

Results 279 patients met inclusion criteria, with 40 patients developing SSI (14.3%). Average follow-up was 3.2 years. Patients that developed SSI had a significantly higher proportion of open fractures (47.5% vs 23.4%, $p=0.003$); however, there were no significant differences in Gustilo-Anderson classification or open wound location compared to controls. The SSI group required significantly higher rates of skin grafts (25.00% vs 4.18%, $p<0.001$) and muscle flap coverage (20.0% vs 1.7%, $p<0.001$). Operative time was significantly longer in the SSI group (283.1 vs. 222.3 minutes, $p=0.002$). Patients with SSI displayed significantly higher rates of nonunion at 6-month follow-up when compared to those without SSI (55.0% vs 10.9%, $p<0.001$). There were no significant differences in mechanism of injury, AO/OTA fracture classification, associated ipsilateral lower extremity injuries, bone grafting, surgical approach, or presence of medial column fixation between the two groups

Discussion The present study shows that SSI after pilon fractures has a devastating prognosis, with 55% of patients developing nonunion at 6 months. Future multicenter studies are needed to further investigate risk factors for SSI after operative management of pilon fractures.

Conclusion Risk factors for SSI in these patients included open fracture, receiving soft tissue coverage, and longer operative times.

1036 Subspecialty Training Improves Treatment Success Following Debridement, Antibiotics, and Implant Retention in Total Knee Arthroplasty

Authors Nicholas Tubin , Jonathan Bourget-Murray, Isabel Horton, Antoine Bureau, Hesham Abdelbary, George Grammatopoulos, Simon Garceau, Jared Morris

Background and Rationale Debridement, antibiotics and implant retention (DAIR) is a well-accepted treatment option for acute periprosthetic joint infections (PJI). Failure of initial treatment is associated with inferior outcomes and increased costs. No study has assessed the effect of subspecialty training on the success and outcomes of DAIR for the treatment of PJI after total knee arthroplasty (TKA).

Study Question Does subspecialty training in adult joint reconstruction affect DAIR success for the treatment of PJI after TKA?

Methods All TKA DAIRs performed at our center were retrospectively collected. Two cohorts were created based on whether the DAIR was performed by a fellowship-trained adult joint reconstruction (FT) or non-fellowship-trained (NFT) surgeon. Baseline patient characteristics were collected and compared. Outcomes were collected for each cohort as follows: treatment failure, death during PJI treatment, the total number of PJI surgeries, and soft tissue complications during total PJI treatment. Treatment failure was defined as reoperation for PJI or the need for chronic suppressive antibiotic therapy.

Results A total of 112 patients were identified (FT = 68, NFT = 44). Mean follow up time in months was as follows: FT = 92.1 (47.9) and NFT = 82.6 (47.5). No statistically significant differences were observed between baseline cohort characteristics. Failure of treatment was observed in 34/44 (77.3%) patients in the NFT cohort compared to 39/68 (57.3%), (p = 0.03; OR 2.5, 95% CI 1.1-5.9). Death during the totality of PJI care at our center was as follows: NFT = 13/44 (29.5%) versus FT 11/68 (16.1%), p = 0.09. No other significant differences were observed.

Discussion DAIR after TKA performed by FT resulted in a significantly lower rate of treatment failure, and a trend towards lower mortality during the totality of PJI care was observed. This may potentially be explained by the improved quality of initial surgical debridement. Moreover, more stringent patient selection criteria for DAIR and increased comfort levels with alternative forms of treatment by FT may explain improved success. As such, DAIR for PJI in TKA should not be considered a â€œsimpleâ€ procedure and benefits from subspecialty training.

Conclusion DAIR in TKA performed by FT results in improved successful infection eradication compared to NFT and should be promoted to improve outcomes.

1037 The influence of micro structured surface features on the accumulation of bovine synovial fluid induced aggregates of Staphylococcus aureus

Authors Tripti T Gupta, Niraj K Gupta, Khushi Patel, Paul Stoodley

Background and Rationale Periprosthetic joint infections (PJI) after artificial joint replacement is a major clinical issue that require multiple surgeries and antibiotic interventions. Staphylococcus aureus is a prominent pathogen responsible for causing PJI, with biofilms and aggregates observed on the surface of implanted joint devices and the surrounding tissue. Recent ex vivo observations and in vitro research has shown that staphylococcal strains rapidly form free-floating aggregates in the presence of bovine synovial fluid (BSF) and demonstrate biofilm-like resistance to antimicrobial agents.

Study Question The attachment of these aggregates on micro-structured titanium (Ti) surfaces with varying roughness under shear have not been widely investigated. Thus, this study examined the attachment of free-floating aggregates on a Ti surface with varying roughness.

Methods A flow cell system was used to measure the adhesion kinetics of green fluorescent protein (GFP) labeled S. aureus as single cells and in the aggregative phenotype on flat and rough Ti milled with parallel line patterns for 24 hours.

Results The S. aureus adhesion was significantly higher in the presence of synovial fluid than without synovial fluid (Fig). However, the attachment of S. aureus in the presence and absence of synovial fluid was independent of surface roughness.

Discussion Attachment occurred mainly along the ridges and grooves which co-localized with the deposition of fibrous protein components present in the synovial fluid. In contrast, those fibrous proteins components were not observed on the flat surfaces. The deposition of fibrous proteins in synovial on to the rough surface features of orthopedic implants may facilitate bacterial attachment to these surfaces.

Conclusion Our data provides evidence that the presence of bovine synovial fluid increases the attachment of S. aureus in the form of aggregates by total viable cells. The deposition of fibrinogen, hyaluronic acid, and other proteins on to the micro-structured surfaces with ridges and grooves might have facilitated the bacterial attachment to these surfaces exposed to BSF.

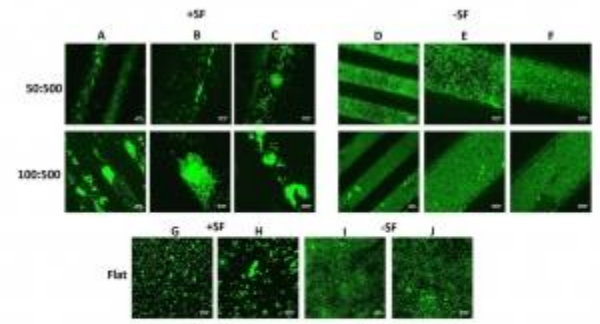


FIG Confocal images of bacteria imaged by GFP attached in the presence (+BSF) and absence of synovial fluid (-BSF) to micro-structured and flat Ti surfaces. The micro-structured patterns were 100 µm depth:500 µm pk-pk distance (100:500), 50 µm depth:500 µm pk-pk distance (50:500). Panel B and E are the ridges and C and F are the grooves of the coupons from A and D respectively. Panel H and J are zoomed-in images. Scale bars are 100 µm.

1038 Does the timing of antibiotic administration affect culture results in resection arthroplasty for PJI?

Authors John Pinski, Rory Metcalf, Jesse E Otero, Susan M Odum, Taylor M Rowe, Thomas K Fehring

Background and Rationale Preoperative aspirations are usually performed off antibiotics for at least 2 weeks to accurately define the infecting organism for targeted antimicrobial therapy during resection arthroplasty for PJI. Similarly, antibiotics are often withheld until intraoperative cultures are obtained during resection arthroplasty for PJI as pre-procedure antibiotics may reduce the sensitivity of cultures.

This has important implications as failures following 2 stage procedures frequently involve different organisms that may have not been identified by cultures obtained during resection. Recent literature suggests that preoperative antibiotics do not affect intraoperative cultures, but the tah sample sizes in these underpowered studies raises concern over these practice changing recommendations.

Study Question Does the timing of antibiotic administration affect the concordance of pre-operative and intraoperative cultures?

Methods Patients treated at the OC PJI Center with resection arthroplasty for PJI were included provided preoperative and intraoperative cultures were available as well as the timing of antibiotic administration either before or after obtaining intraoperative cultures. Patients who failed reimplantation were identified and failure organism documented.

Results 178 patients (181 procedures) were included. 53 patients received antibiotics prior to obtaining intraoperative cultures. 15/53 (28%) had discordant cultures. 9/53 (17%) went on to fail. 8/9 (89%) failed with the same organism. 1/9 (11%) failed with a different organism. In contrast, 128 patients had their antibiotics held until intraoperative cultures were obtained. 26/128 (20%) had discordant cultures. 14/128 (11%) went on to fail. 3/14 (21%) failed with a different organism. 11/14 (79%) failed with the same organism.

Discussion In those patients where antibiotics were withheld until cultures were taken, we noted a lower incidence of discordance between preop aspirations and intraoperative cultures 20% vs. 28% when antibiotics were given. Additionally, the failure rate of reimplantation when antibiotics were withheld was also lower than when antibiotics were given preoperatively (11% vs 17%).

Conclusion If antibiotics are routinely held prior to aspiration, intuitively it seems that the same principle should be observed perioperatively during resection for PJI. A lower discordance and failure rate when antibiotics are withheld supports this principle

1039 Arthroplasty Surgery Alters the Local Immune Composition of the Knee Joint

Authors Kyle H Cichos, Vidya Sagar Hanumanthu, Chander Raman, Elie S Ghanem

Background and Rationale The native knee joint contains 10-20 times more leukocytes than partially replaced knees and 40-50 times a completely replaced knee, but specific cell populations altered have not been studied.

Study Question We aimed to determine how the human innate and adaptive immune cell composition and cytokine profiles of the knee joint microenvironment are altered in replaced knees compared to native knees.

Methods Upon IRB approval, we obtained and synovial fluid from 69 total patients separated into 6 groups: 13 native non-OA, 30 native OA, 9 replaced acute (<6 months), 5 replaced intermediate (6-12 months), 8 replaced chronic (>12 months), and 4 aseptic revision. All samples were analyzed by Flow Cytometry utilizing multidimensional reduction analysis via UMAP and clustering analysis by FastPG and FlowSOM to unbiasedly identify unique populations of cells. Additionally, all samples were analyzed for cytokine/chemokine profiles using 65-Plex ProcartaPlex assays. Cell populations and cytokine/chemokines were compared between each group by ANOVA.

Results Overall, the study groups differed in regulatory T cells, classical monocytes, monocytic-MDSCs, pro-inflammatory macrophages, and CD1c+ dendritic cells (each $p< 0.05$) (increased in all replaced knee groups compared to native non-OA and equal or increased compared to native OA). The groups also differed in B cells, naÃ¯ve CD4 T cells, Th17 cells, CD4 effector memory T cells, mature neutrophils, and low-density neutrophils (each $p< 0.05$) (increased acutely after TKA surgery compared to native non-OA and native OA but return to normal levels by 12 months postop). For the cytokine assays currently processed, the 4 replaced knee groups were combined, showing elevated levels of CXCL5, HGF, IFN-gamma, IL-6, IL-16, CXCL10, CCL2 (MCP-1), CCL8, MDC, TNF-alpha, and VEGF-A compared to the native knee group (combined non-OA and OA) ($p < 0.01$ for all) and a decrease in CX3CL1, CXCL11, IL-3, IL-5, CXCL9, TRAIL ($p < 0.02$ in all cases).

Discussion Arthroplasty surgery results perturbation of the native immune homeostasis of the synovial space via alterations of specific immune cell populations, including Th17 cells, neutrophils, and macrophages, and causes a generally pro-inflammatory cytokine/chemokine profile.

Conclusion Overall, changes in specific immune cell populations may have implications for development of periprosthetic infections at different timepoints after surgery and warrants further study.

1041 Arthroplasty Surgery Impacts the Local Vitamin D Concentration Within the Knee Joint

Authors Kyle H Cichos, Andrzej T Slominski, Elie S Ghanem

Background and Rationale Systemic vitamin D deficiency has been implicated in increasing the risk of PJI. The impact of local synovial vitamin D and non-canonically activated vitamin D has not been investigated in the knee joint.

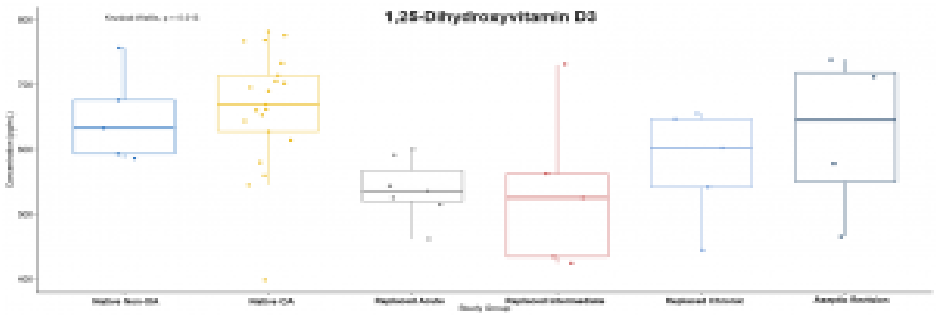
Study Question We aimed to investigate the concentration of synovial vitamin D and metabolites in native knees and compare to post-TKA concentrations at various timepoints.

Methods Upon IRB approval, we obtained blood and synovial fluid from 69 total patients separated into 6 groups: 13 native non-OA, 30 native OA, 9 replaced acute (<6 months), 5 replaced intermediate (6-12 months), 8 replaced chronic (>12 months), and 4 aseptic revision. All samples were analyzed via ELISA assay to quantitate 1,25(OH)2D3 (Calcitriol) and 25(OH)D3 (Calcifediol) and are currently being analyzed by liquid chromatography with tandem mass spectroscopy (LC-MS) to quantitate additional non-canonical vitamin D3 metabolites including 20S(OH)D3 and 20,23(OH)2D3. Vitamin D metabolite levels were compared between each group by ANOVA and post-hoc comparison with Bonferroni correction.

Results Overall, the study groups differed in 1,25(OH)2D3 (Calcitriol) concentration in the synovial fluid (p=0.013). Post-hoc comparison using Bonferroni correction revealed no significant difference between any of the individual groups other than that the replaced acute groupâ€™s mean concentration is significantly decreased compared to the native non-OA groupâ€™s mean concentration (539 pg/mL [SD 47] vs 649 pg/mL [SD70], p=0.008). The groups did not differ in 1,25(OH)2D3 (Calcitriol) concentration systemically in the blood (p=0.07). Analysis of 25(OH)D3 (Calcifediol), 20S(OH)D3, and 20,23(OH)2D3 are currently in process and have not yet been completed for analysis at this time.

Discussion Arthroplasty surgery results in decreased concentrations of active vitamin D (1,25(OH)2D3) locally within the synovial space during the acute postoperative period, but this concentration appears to return to normal over time beyond 1-year postoperatively. There is no difference between the native knee concentration and the concentration in knees undergoing aseptic revision. Additional analysis is underway at this time.

Conclusion Given the known immunomodulatory properties of active vitamin D that increase the innate immune and antimicrobial responses, acute decreases in 1,25-dihydroxyvitamin D3 after TKA surgery may play a role in PJI development within the first year postoperatively.



1042 Mask-wearing practices during COVID-19 do not influence pre-operative S. aureus colonization rates

Authors Cameron G Thomson, Erin S Grawe, Jorge H Figueras, Kimberly A Hasselfeld, Anthony F Guanciale

Background and Rationale Patients with positive pre-operative nasal swabs for Staphylococcus aureus (MRSA and MSSA) are at increased risk for surgical site infection (SSI). Decolonization of the nares pre-operatively appears to reduce this risk. Because S. aureus colonizes the nares and can spread via respiratory droplets, we hypothesized that S. aureus colonization might decrease as a function of mask-wearing requirements.

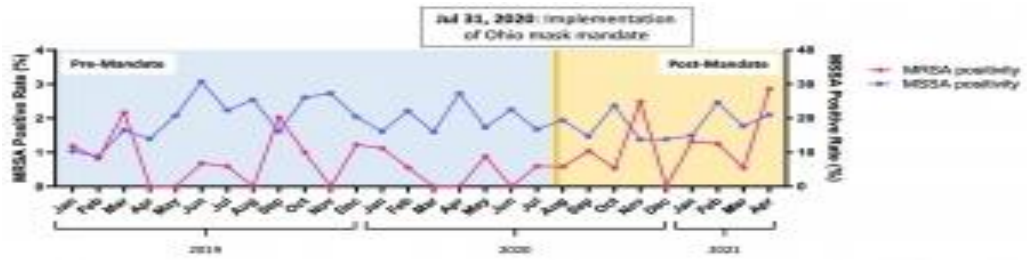
Study Question Here we compared pre-operative S. aureus positivity rates before and after issuance of a state-wide COVID-19 mask mandate in a cohort of 4,317 orthopedic patients.

Methods Electronic medical records for all elective total joint and orthopedic spine cases performed at our institution between January 2019 through April 2021 (N= 5,102) were reviewed for the presence of pre-operative S. aureus screening. Patients with pre-operative S. aureus screening results (N= 4,317) were split into two patient groups, a pre-mandate cohort (N= 2,811: January 1, 2019 â€“ July 31, 2020) and a post-mandate cohort (N= 1,506: August 1, 2020 â€“ April 30, 2021). S. aureus positivity rates were then compared across the two groups.

Results There were no significant differences in S. aureus positivity rates between the pre- and post-mandate cohorts for MRSA (0.7% vs 1.1%, p=0.16) and MSSA (16.3% vs 15.3%, p=0.40). These results did not differ even when adjusted to account for the potential early adoption of mask-wearing practices by some patients at the onset of the COVID-19 pandemic (i.e., March 2020 â€“ July 2020) and prior to the implementation of formal mask-wearing mandates (MRSA: p= 0.64; MSSA: p= 0.36).

Discussion Collectively, the findings reported here represent a paradox when considered in the context of prior work examining SSI rates during the COVID-19 pandemic. Specifically, Losurdo and colleagues (2020) report reduced SSI rates and reasonably speculated that mask-wearing practices may serve as an early preventative measure to reduce post-operative SSI rates. Indeed, this rationale motivated the current research. However, results from this larger cohort demonstrate that pre-operative rates of S. aureus colonization did not change as a function of mask-wearing practices during COVID-19.

Conclusion Our results suggest alternative mechanisms (e.g., hospital social distancing practices, increased exercise and improved self-health practices) may account for an alleged reduction in SSIs.



1049 Utility of Diagnostic Tests Prior to Reimplantation in Patients Undergoing Two-Stage Revision Total Joint Arthroplasty: A Systematic Review and Meta-Analysis

Authors Irfan A Khan, Brandon O Boyd, Antonia F Chen, Nicholas Cortes-Penfield, Thomas G Myers, Timothy S Brown, Gina A Suh, Gerald McGwin, Elie S Ghanem, Yale A Fillingham

Background and Rationale Periprosthetic joint infection (PJI) is a devastating complication following total joint arthroplasty (TJA). While two-stage revision is successful in majority of patients, 12-28% of patients experience treatment failure after reimplantation.

Study Question Given the high failure rate after reimplantation, we sought to answer the following question: What diagnostic biomarkers can predict persistent infection or treatment failure after undergoing two-stage revision for PJI?

Methods The Cochrane Library, PubMed (MEDLINE), and EMBASE were searched for randomized controlled trials, prospective nonrandomized studies, and retrospective studies published prior to October 3rd, 2021, which evaluated the utility of serum/plasma biomarkers (erythrocyte sedimentation rate [ESR], c-reactive protein [CRP], interleukin-6 [IL-6], fibrinogen, d-dimer), synovial biomarkers (white blood cell [WBC] count, neutrophil percentage [PMN %], alpha-defensin [AD], leukocyte esterase [LE], fluid culture), tissue frozen section, tissue culture, and spacer sonication fluid culture at predicting persistent infection or treatment failure after two-stage revision. Risk-of-bias was assessed with the QUADAS-2 tool. Diagnostic accuracy measures included sensitivity, specificity, and diagnostic odds ratio (OR).

Results This systematic review included 47 studies, which consisted of 6,592 diagnostic tests among 3,725 cases of patients undergoing two-stage revision for PJI. Amongst those cases, 605 (16.2%) experienced persistent infection or treatment failure. Synovial LE (sensitivity 0.25 [0.10 â€“ 0.47], specificity 0.99 [0.93 â€“ 1.00], diagnostic OR 18.75 [1.71 â€“ 205.57]), serum IL-6 (sensitivity 0.52 [0.33 â€“ 0.70], specificity 0.92 [0.85 â€“ 0.96], diagnostic OR 16.03 [1.01 â€“ 254.34]), and synovial PMN (sensitivity 0.62 [0.52 â€“ 0.72], specificity 0.76 [0.72 â€“ 0.79], diagnostic OR 6.34 [3.47 â€“ 11.60]) had the highest diagnostic accuracy among the biomarkers.

Discussion This meta-analysis found that no biomarker has optimal diagnostic accuracy for predicting persistent infection or treatment failure after two-stage revision.

Conclusion Given the limited availability of synovial LE and serum IL-6, and the restricted number of studies supporting their use, obtaining a synovial fluid culture prior to reimplantation appears to be the best diagnostic tool prior to reimplantation.

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Alan K. Li, BS(This individual reported nothing to disclose); Submitted on: 11/02/2021

Daniel Li, MD (Columbus, OH)
(This individual reported nothing to disclose); Submitted on: 04/24/2022

Jay R Lieberman, MD, FAAOS (Los Angeles, CA)Submitted on: 05/18/2022
AAOS: Board or committee member
BD Surgiphor: Stock or stock Options
DePuy, A Johnson & Johnson Company: IP royalties; Paid consultant
Hip Innovation Technology: Stock or stock Options
Hip Society: Board or committee member
Musculoskeletal Transplant Foundation: Board or committee member
Saunders/Mosby-Elsevier: Publishing royalties, financial or material support
Western Orthopaedic Association: Board or committee member

Ryan Thomas Lin(This individual reported nothing to disclose); Submitted on: 05/24/2022

Donald B Longjohn, MD, FAAOS, FACS (This individual reported nothing to disclose); Submitted on: 05/31/2022

Sadie Longo, BS (Pittsburgh, PA)(This individual reported nothing to disclose); Submitted on: 07/16/2022

Leanne Ludwick, BS(This individual reported nothing to disclose); Submitted on: 06/22/2022

M

Julian Maamari, MD(This individual reported nothing to disclose); Submitted on: 06/14/2022

William J Maloney, MD, FAAOS (Redwood City, CA)Submitted on: 04/01/2022
AAOS: Board or committee member
Knee Society: Board or committee member
Stryker: IP royalties; Paid consultant
TJO: Stock or stock Options
Western Orthopedic Association: Board or committee member
Zimmer: IP royalties

Zeinab Mamouei, PhD This individual reported nothing to disclose); Submitted on: 07/17/2022

Jenna Mandel, BS(This individual reported nothing to disclose); Submitted on: 06/24/2022

Jonathan Mandell (This individual reported nothing to disclose); Submitted on: 07/16/2022

Insa Maria Mannstadt, BA, BS (New York, NY)Submitted on: 06/03/2022
American Society of Bone and Mineral Research: Board or committee member
Amolyt and Takeda: Paid consultant
Radius: Employee; Stock or stock Options

Jorge Manrique, MD Submitted on: 05/02/2022
Colombian Journal of Orthopedics and Traumatology: Editorial or governing board
International Consensus Meeting on Periprosthetic Joint Infection: Editorial or governing board
Parvizi Surgical Innovations: Stock or stock Options

Kelsey Martin(This individual reported nothing to disclose); Submitted on: 04/07/2022

Daniele De Massari, MSc, PhD (Netherlands)Submitted on: 09/13/2021
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David Jacob Mayman, MD, FAAOS Submitted on: 06/01/2022
Cymedica: Stock or stock Options
Hip Society: Board or committee member
Imagen: Stock or stock Options
Knee Society: Board or committee member
MiCare Path: Stock or stock Options
OrthAlign: IP royalties; Stock or stock Options
Smith & Nephew: IP royalties
Stryker: Paid consultant
Wishbone: Stock or stock Options

Tyler Lee McGee, BS(This individual reported nothing to disclose); Submitted on: 02/01/2022

Gerald McGwin Jr, MS, PhD(This individual reported nothing to disclose); Submitted on: 06/03/2022

Alexander C McLaren, MD, FAAOS*: Submitted on: 10/25/2021
Hayes Diagnostics Inc: Stock or stock Options
Musculoskeletal Infection Society: Board or committee member
Sonoran Biosciences: Stock or stock Options

Michael Marek Meghpara, MD, MBA This individual reported nothing to disclose); Submitted on: 06/23/2022

Christopher Michael Melnic, MD, FAAOS Submitted on: 07/16/2022
Smith & Nephew: Paid consultant

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American Association of Hip and Knee Surgeons: Board or committee member
DJ Orthopaedics: IP royalties; Paid consultant
Emovi: Stock or stock Options
Hip Society: Board or committee member
International Congress for Joint Reconstruction: Board or committee member
Journal of Arthroplasty: Editorial or governing board
KCI: Paid consultant
Kinamed: IP royalties; Paid consultant
Knee Society: Board or committee member
Orthopedics Today: Editorial or governing board
Osteoremedies: IP royalties; Paid consultant
PeekMed: Stock or stock Options
Rory Metcalf, MD, BS (This individual reported nothing to disclose); Submitted on: 05/31/2022

Alexander Mihas, BS(This individual reported nothing to disclose); Submitted on: 10/22/2021

Nathalie Bea Milbrandt (This individual reported nothing to disclose); Submitted on: 05/31/2022

Andy Miller, MD (This individual reported nothing to disclose); Submitted on: 04/08/2022

Lawrence S Miller, MD, FAAOS (This individual reported nothing to disclose); Submitted on: 06/06/2022

Matthew S Miller, MD (This individual reported nothing to disclose); Submitted on: 06/15/2022

Theodore Miller, MD (New York, NY)(This individual reported nothing to disclose); Submitted on: 06/05/2022

Kelly Elizabeth Moore, BS Submitted on: 10/05/2021
Biocomposites Inc.: Paid consultant

Kelly Elizabeth Moore, BS Submitted on: 10/05/2021
Biocomposites Inc.: Paid consultant

Sudarsan Murali, MBA Submitted on: 02/03/2022
OrthoScrews LLC: Stock or stock Options

Thomas G Myers, MD, FAAOS*: Submitted on: 06/27/2022
AAOS: Board or committee member
American Association of Hip and Knee Surgeons: Board or committee member
Journal of Arthroplasty: Editorial or governing board

N

Farideh Najafi, MD(This individual reported nothing to disclose); Submitted on: 04/14/2022

Sumon Nandi, MD, MBA, FAAOS, FACS Submitted on: 05/04/2022
AAOS: Board or committee member
American Association of Hip and Knee Surgeons: Board or committee member
Arthroplasty: Editorial or governing board
Journal of Arthroplasty: Editorial or governing board
Springer: Publishing royalties, financial or material support

Priyanka Vijay Nehete, MPH (Jackson, MS)(This individual reported nothing to disclose); Submitted on: 02/02/2022

Sandra Bliss Nelson, MD (Boston, MA)Submitted on: 07/16/2022
Journal of Bone and Joint Infection: Editorial or governing board
Musculoskeletal Infection Society: Board or committee member
UpToDate: Publishing royalties, financial or material support

Joseph Nguyen, MPH (New York, NY)Submitted on: 10/22/2021
Journal of Women's Sports Medicine: Editorial or governing board
The American Journal of Sports Medicine: Editorial or governing board

Kian Niknam, MS(This individual reported nothing to disclose); Submitted on: 06/08/2022

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Regeneron Pharmaceuticals Inc.: Employee; Stock or stock Options

Allina A Nocon, PhD, MPH (This individual reported nothing to disclose); Submitted on: 06/01/2022

David Novikov, MD(This individual reported nothing to disclose); Submitted on: 07/08/2022

O

Daniel Atherton Oakes, MD, FAAOS Submitted on: 05/31/2022
LimaCorporate: Paid consultant

Susan Marie Odum, PhD (Charlotte, NC)Submitted on: 06/14/2022
AAOS: Board or committee member; Paid consultant
Lumbar Spine Research Society: Board or committee member
PrideOrtho: Board or committee member
Stryker: Paid consultant

Nick Ogrinc, BA (This individual reported nothing to disclose); Submitted on: 07/17/2022

Ali R Oliashirazi, MD, FAAOS (Huntington, WV) Submitted on: 02/01/2022
DePuy, A Johnson & Johnson Company: Paid consultant; Paid presenter or speaker; Research support
Medtronic: Paid consultant
Zimmer: Paid consultant
Thomas Olson, BS(This individual reported nothing to disclose); Submitted on: 10/21/2021

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Smith & Nephew: Paid consultant
Stryker: Paid consultant

Alvin C Ong, MD, FAAOS Submitted on: 06/27/2022
Smith & Nephew: IP royalties; Paid consultant; Research support
Stryker: Paid consultant

Tito Onyekweli (Pittsburgh, PA)(This individual reported nothing to disclose); Submitted on: 07/17/2022

Jesse E Otero, MD, FAAOS (Charlotte, NC)Submitted on: 05/31/2022
American Association of Hip and Knee Surgeons: Board or committee member
DePuy, A Johnson & Johnson Company: Paid consultant; Research support

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P

Nicholas Michael Pachuda, DPM Submitted on: 09/27/2021
Biorez: Paid consultant; Stock or stock Options
GID Bio: Paid consultant; Stock or stock Options
Peptilogics: Employee; Stock or stock Options
Zygofix: Paid consultant; Stock or stock Options

Joseph Palmer, DO(This individual reported nothing to disclose); Submitted on: 05/02/2022

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Journal of Orthopaedic Surgery and Research: Editorial or governing board

Pearl Ravindra Paranjape, MS (Claymont, DE)Submitted on: 06/03/2022
Zimmer: Paid consultant

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Javad Parvizi, MD, FAAOS, FRCS (Philadelphia, PA)Submitted on: 06/23/2022
3M: Research support
Acumed, LLC: Stock or stock Options
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
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

Matteo Passerini, MD(This individual reported nothing to disclose); Submitted on: 06/14/2022

David Albert Patch, MD, MEd(This individual reported nothing to disclose); Submitted on: 04/07/2022

Robin Patel, MD (Rochester, MN)
Submitted on: 07/18/2022
1928 Diagnostics: Paid consultant
Abbott: Paid consultant
Adaptive Phage Therapeutics: Other financial or material support
American Society of Microbiology: Board or committee member
BioFire: Research support

CARB-X: Paid consultant
ContraFect: Research support
Curetis: Paid consultant
Day Zero Diagnostics: Paid consultant
Infectious Diseases Board Review (Faculty): Board or committee member
Mammoth Biosciences: Paid consultant
Mayo Clinic, Rochester MN (my employer): Employee
Netflix: Paid consultant
Pathogenomix: Other financial or material support
PathoQuest: Paid consultant
PhAST: Paid consultant
Qvella: Paid consultant
Selux Diagnostics: Paid consultant
TenNor Therapeutics: Research support
Torus Biosystems: Paid consultant
Up-to-Date: Editorial or governing board
USMLE: Board or committee member

Stuti Patel, MD(This individual reported nothing to disclose); Submitted on: 05/30/2022

Nicholas Peterson(This individual reported nothing to disclose); Submitted on: 05/16/2022

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Matthew Pigott, MD (Columbus, OH)Submitted on: 07/02/2022
DePuy, A Johnson & Johnson Company: Paid consultant

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John Pinski, MD(This individual reported nothing to disclose); Submitted on: 06/01/2022

Nicolas Santiago Piuzzi, MD Submitted on: 06/01/2022
American Association of Hip and Knee Surgeons: Board or committee member
ISCT: Board or committee member
Journal of Hip Surgery: Editorial or governing board
Journal of Knee Surgery: Editorial or governing board
Orthopaedic Research Society: Board or committee member
Osteal Therapeutics: Research support
RegenLab: Research support
Signature Orthopaedics: Research support
Stryker: Paid consultant
Zimmer: Research support

Johannes F Plate, MD, PhD Submitted on: 05/25/2022
American Association of Hip and Knee Surgeons: Board or committee member
Eventum Orthopaedics: Stock or stock Options
Journal of Arthroplasty: Editorial or governing board
Peptilogics: Research support
Smith & Nephew: Paid consultant
VisualDX: Publishing royalties, financial or material support

Breanna Alexa Polascik, BS (This individual reported nothing to disclose); Submitted on: 04/08/2022

Isabel P Prado, MS(This individual reported nothing to disclose); Submitted on: 09/10/2021

Ajay Premkumar, MD, MPH Submitted on: 11/08/2021
Elsevier: Publishing royalties, financial or material support
HSS Journal: Editorial or governing board

Jakrapun Pupaibool, MD, MSc*: (Salt Lake City, UT)
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Simarjeet Puri(This individual reported nothing to disclose); Submitted on: 05/19/2022

Q

Qudratullah Qadiri, BS (This individual reported nothing to disclose); Submitted on: 09/13/2021

R

Chander Raman, PhD (This individual reported nothing to disclose); Submitted on: 07/03/2022

Brad Reddick, DO Submitted on: 06/23/2022
Joint purification systems: Research support
Stryker: Paid consultant; Stock or stock Options

Camilo Restrepo, MD (This individual reported nothing to disclose); Submitted on: 06/07/2022

John Rezkalla, BA, MS(This individual reported nothing to disclose); Submitted on: 07/03/2022

Julie Elizabeth Reznicek, DO (This individual reported nothing to disclose); Submitted on: 07/18/2022

Dominic Tyler Ridolfi, BS(This individual reported nothing to disclose); Submitted on: 06/16/2022

Aldo M Riesgo, MD (Weston, FL) Submitted on: 04/12/2022
Stryker: Paid consultant
Zimmer: Paid consultant

James G Rooney (Pittsburgh, PA)(This individual reported nothing to disclose); Submitted on: 06/15/2022

Taylor M Rowe (Charlotte, NC)(This individual reported nothing to disclose); Submitted on: 05/18/2022

Pedro Javier Rullan, MD(This individual reported nothing to disclose); Submitted on: 07/11/2022

Sean Patrick Ryan, MD Submitted on: 05/29/2022
romtech: Paid consultant

S

Anna Cristina Samia, PhD (This individual reported nothing to disclose); Submitted on: 05/31/2022

Jessica Sanders, MS (This individual reported nothing to disclose); Submitted on:07/17/2022

Meredith Schade, MD* (Hershey, PA)Submitted on: 05/23/2022
MSIS: Board or committee member

Laura Scholl, MS (Mahwah, NJ)Submitted on: 06/15/2022
Stryker: Employee; Stock or stock Options

Joseph Hasbrouck Schwab, MD, FAAOS (Boston, MA)Submitted on: 02/06/2022
Association of Bone and Joint Surgeons: Board or committee member

Musculoskeletal Tumor Society: Board or committee member
North American Spine Society: Board or committee member

Andrew Michael Schwartz, MD Submitted on: 06/01/2022
AAOS Now: Editorial or governing board

Ran Schwarzkopf, MD, FAAOS (New York, NY)Submitted on: 04/27/2022
AAOS: Board or committee member
American Association of Hip and Knee Surgeons: Board or committee member
Arthroplasty Today: Editorial or governing board
Gauss surgical: Stock or stock Options
Intelijoint: Paid consultant; Stock or stock Options
Journal of Arthroplasty: Editorial or governing board
PSI: Stock or stock Options
Smith & Nephew: IP royalties; Paid consultant; Research support

Peter Keyes Sculco, MD Submitted on: 05/24/2022
DePuy, A Johnson & Johnson Company: Paid consultant; Paid presenter or speaker
EOS Imaging: Paid consultant; Paid presenter or speaker
Intellijoint Surgical: Paid consultant; Paid presenter or speaker; Stock or stock Options
Intelljoint Surgical: Research support
Lima Corporate: Paid consultant
Parvizi Surgical Innovation: Stock or stock Options
Zimmer: Paid consultant

Poorani Sekar, MD* (Iowa City, IA)(This individual reported nothing to disclose); Submitted on: 04/07/2022

Abhijit Seetharam, MD(This individual reported nothing to disclose); Submitted on: 05/13/2022

Jessica Seidelman, MD (This individual reported nothing to disclose); Submitted on: 06/30/2022

Thorsten M Seyler, MD, PhD, FAAOS*: (Durham, NC)Submitted on: 07/11/2022
American Association of Hip and Knee Surgeons: Board or committee member
Heraeus: Paid consultant
Lippincott Williams & Wilkins: Publishing royalties, financial or material support
Musculoskeletal Infection Society: Board or committee member
Next Science: Research support
Pattern Health: IP royalties
Restor3d: IP royalties
Smith & Nephew: Paid consultant
Total Joint Orthopedics, Inc.: Paid consultant
Zimmer: Research support

Akash Shah, MD (This individual reported nothing to disclose); Submitted on: 01/28/2022

Neel B Shah, MD Submitted on: 07/16/2022
Peptilogics: Paid consultant

Alisina Shahi, MD, PhD (Philadelphia, PA)Submitted on: 06/10/2022
Bonefoam: Paid consultant

Jeremy Dewitt Shaw, MD, MS (Pittsburgh, PA)Submitted on: 05/03/2022
Editorial Board Member with Operative Techniques in Orthopaedics: Editorial or governing board
Elsevier: Editorial or governing board
Lumbar Spine Research Society: Board or committee member

Alain Emil Sherman, MD, MBA (This individual reported nothing to disclose); Submitted on: 05/31/2022

Matthew Sherman, BS (This individual reported nothing to disclose); Submitted on: 06/21/2022

Dean Shinabarger, PhD (Kalamazoo, MI)Submitted on: 09/20/2021
Allergenis: Stock or stock Options
Microbion Biosciences: Stock or stock Options
Peptilogics: Paid consultant
Pfizer: Stock or stock Options

Noam Shohat, MD(This individual reported nothing to disclose); Submitted on: 06/06/2022

Andrzej Slominski, MD, PhD (This individual reported nothing to disclose); Submitted on: 06/28/2022

Ilan Small (This individual reported nothing to disclose); Submitted on: 07/18/2022

Nipun Sodhi, MD (This individual reported nothing to disclose); Submitted on: 02/14/2022

Clay A Spitler, MD, FAAOS Submitted on: 05/13/2022
AAOS: Board or committee member
AO North America: Board or committee member
AO Trauma: Paid presenter or speaker
Delfi Medical Innovations: Other financial or material support
DePuy, A Johnson & Johnson Company: Paid consultant
Invibio: Paid consultant
Journal of Bone and Joint Surgery - American: Editorial or governing board
KCI: Paid consultant
Orthopaedic Trauma Association: Board or committee member
ROM 3 Rehab LLC: Stock or stock Options
Stryker: Research support
Synthes: Research support

Bryan Donald Springer, MD, FAAOS (Charlotte, NC) Submitted on: 04/30/2022
AJRR: Board or committee member
American Association of Hip and Knee Surgeons: Board or committee member
Arthroplasty Today: Editorial or governing board
Convatec: Paid consultant
ICJR: Board or committee member
Journal bone and joint infection: Editorial or governing board
Journal of Arthroplasty: Editorial or governing board
Osteoremedies: IP royalties; Paid consultant
Stryker: IP royalties; Paid consultant

Amelia M Staats (Columbus, OH)(This individual reported nothing to disclose); Submitted on: 07/18/2022

Jonathan Damien Steckbeck, MBA, PhD (Pittsburgh, PA)Submitted on: 09/27/2021
Peptilogics: Employee; Stock or stock Options

Jonah M Stein (Philadelphia, PA)(This individual reported nothing to disclose); Submitted on: 06/23/2022

Paul Stoodley, PhD (Columbus, OH)Submitted on: 04/07/2022
Azko-Nobel: Research support
Biocomposites: Paid consultant; Research support
Biocomposites Ltd: Paid presenter or speaker
Colgate-Palmolive: Research support
Dyson: Paid consultant
Journal of Orthopaedic Research: Editorial or governing board
Mondelez: Research support

Procter & Gamble: Research support
Unilever: Research support
Zimmer: Paid consultant

Gina Suh, MD (Rochester, MN) Submitted on: 10/22/2021
Adaptive Phage Therapeutics: IP royalties
Adaptive Phage Therapeutics (APT): Research support

Anne C Sullivan, MD, FAAOS Submitted on: 06/07/2022
AAOS: Board or committee member
Aaos practice prep package: Editorial or governing board
Biocomposites, Ltd.: Research support

Hannah Jacqueline Szapary, BS(This individual reported nothing to disclose); Submitted on: 05/13/2022

T

Masashi Taguchi, MD (Japan)(This individual reported nothing to disclose); Submitted on: 06/22/2022

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Musculoskeletal Infection Society: Board or committee member
Wolters Kluwer Health - Lippincott Williams & Wilkins: Publishing royalties, financial or material support

Don Bambino Geno Tai, MD (This individual reported nothing to disclose); Submitted on: 07/17/2022

Kathleen W Tam, MPH (This individual reported nothing to disclose); Submitted on: 03/04/2022

Yunting Melissa Tang (Pittsburgh, PA)(This individual reported nothing to disclose); Submitted on: 07/14/2022

Saad Tarabichi, MD (This individual reported nothing to disclose); Submitted on: 07/16/2022

Alexander Mitchell Tatara, MD, PhD (This individual reported nothing to disclose); Submitted on: 07/07/2022

Jeremiah M Taylor, BS(This individual reported nothing to disclose); Submitted on: 06/01/2022

Zelalem Temesgen (This individual reported nothing to disclose); Submitted on: 07/16/2022

Masaru Teramoto, MPH, PhD (This individual reported nothing to disclose); Submitted on: 05/01/2022

Bashiar Thejeel, MD (This individual reported nothing to disclose); Submitted on: 07/16/2022

Van Thai-Paquette (Claymont, DE)Submitted on: 06/03/2022
Zimmer: Employee

Terence Thomas Jr, BS(This individual reported nothing to disclose); Submitted on: 09/27/2021

Cameron G Thomson, MD (This individual reported nothing to disclose); Submitted on: 10/01/2021

Krista O'Shaughnessey Toler, MBA, MS Submitted on: 06/06/2022
Zimmer: Employee; Stock or stock Options

Yu Hsin Tsai (Cleveland, OH)(This individual reported nothing to disclose); Submitted on: 06/16/2022

Nicholas Tubin, MD (This individual reported nothing to disclose); Submitted on: 05/31/2022

Matthew James Twetten, MA, MBA (This individual reported nothing to disclose);
Submitted on: 07/18/2022

Carolyn L Twomey, BSN Submitted on: 07/17/2022
Irrimax Corporation: Employee
Irrisept Corporation: Other financial or material support; Stock or stock Options

U

Kenneth Urish, MD, PhD, FAAOS Submitted on: 07/01/2022
AAOS: Board or committee member
Adaptive Phage Therapeutics: Paid consultant
ASTM: Board or committee member
Peptilogics: Paid consultant; Research support; Stock or stock Options
Smith & Nephew: Paid consultant; Research support

Kudret Usmani, MD (This individual reported nothing to disclose); Submitted on: 02/06/2022

V

Craig J Della Valle, MD, FAAOS (Chicago, IL)Submitted on: 03/10/2022
Arthritis Foundation: Board or committee member
DePuy, A Johnson & Johnson Company: Paid consultant
Knee Society: Board or committee member
MidAmerica Orthopaedic Association: Board or committee member
Navbit: Stock or stock Options
Orthopedics Today: Editorial or governing board
Orthophor and Surgiphor: Stock or stock Options
Parvizi Surgical Innovations: Stock or stock Options
SLACK Incorporated: Editorial or governing board; Publishing royalties, financial or material support
Smith & Nephew: IP royalties; Research support
Stryker: Research support
Wolters Kluwer Health - Lippincott Williams & Wilkins: Publishing royalties, financial or material support
Zimmer: IP royalties; Paid consultant; Research support

Jesus M Villa, MD (Weston, FL)(This individual reported nothing to disclose); Submitted on: 05/02/2022

Anabelle Visperas, PhD (This individual reported nothing to disclose); Submitted on: 05/31/2022

W

Kevin D. Warner, PharmD (Saginaw, MI)Submitted on: 06/27/2022
Bristol-Myers Squibb: Stock or stock Options
Heron Therapeutics: Paid presenter or speaker
Johnson & Johnson: Stock or stock Options
Osteal Therapeutics: Paid consultant; Stock or stock Options
Pfizer: Stock or stock Options
Stryker: Stock or stock Options
Zimmer: Stock or stock Options

Adam Michael Watkins, BS(This individual reported nothing to disclose); Submitted on: 02/08/2022

Samuel Secord Wellman, MD, FAAOS (Durham, NC)Submitted on: 05/05/2022
American Association of Hip and Knee Surgeons: Board or committee member

Biomet: Research support
DePuy, A Johnson & Johnson Company: Research support
Joint Development, LLC: Stock or stock Options
Journal of Arthroplasty: Editorial or governing board
Medacta: Research support
Smith & Nephew: Paid consultant; Research support
Stryker: Research support
Total Joint Orthopaedics: Paid consultant
Total Joint Orthopedics: IP royalties
Zimmer: Research support

Nancy Wengenack, PhD (This individual reported nothing to disclose); Submitted on: 06/27/2022

John Cade Wheelwright(This individual reported nothing to disclose); Submitted on: 07/12/2022

Marcelle H Wilkinson(This individual reported nothing to disclose); Submitted on: 05/23/2022

Max Willinger, MD (This individual reported nothing to disclose); Submitted on: 05/31/2022

Alan Edward Wilson Jr, MD(This individual reported nothing to disclose); Submitted on: 06/01/2022

Anthony Louis Wilson, MS(This individual reported nothing to disclose); Submitted on: 07/16/2022
Sietske Witvoet, MS (Netherlands)Submitted on: 06/20/2022
Stryker: Employee

Colleen Wixted, BS(This individual reported nothing to disclose); Submitted on: 06/03/2022

Paul Won, BS (Los Angeles, CA)(This individual reported nothing to disclose); Submitted on: 05/31/2022

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Submitted on: 02/01/2022
Zimmer: Unpaid consultant

Y

Steven John Yacovelli (This individual reported nothing to disclose); Submitted on: 07/02/2022

Zhifei Ye, PhD (Cleveland, OH)(This individual reported nothing to disclose); Submitted on: 06/16/2022

Michael Yeaman, PhD (Torrance, CA)Submitted on: 07/04/2022
Alexion: Paid consultant
Genentech-Roche: Paid consultant
Horizon: Paid consultant
Metacin, Inc.: IP royalties; Stock or stock Options

Mark Youssef, BS (New York, NY)(This individual reported nothing to disclose); Submitted on: 07/03/2022

Jonathan S Yu, BS(This individual reported nothing to disclose); Submitted on: 03/04/2022

Z

Luigi Zanna Sr, MD(This individual reported nothing to disclose); Submitted on: 05/27/2022

Aaron Zheng, BS Submitted on: 06/13/2022
Bristol-Myers Squibb: Employee; Stock or stock Options
Johnson & Johnson: Employee; Stock or stock Options

Joanne Zhou, MD(This individual reported nothing to disclose); Submitted on: 06/02/2022