Programme and abstracts

EBJIS2023

41st Annual Meeting of the European Bone and Joint Infection Society

12 -14 October 2023 · Basel · Switzerland

#EBJIS2023

www.ebjis2023.org

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EBJIS 2023

41st Annual Meeting of the European Bone and Joint Infection Society

EBJIS Membership

Join the European Bone and Joint Infection Society now and explore exciting opportunities for volunteering and active involvement in shaping our organization's future.

Member benefits

- Access to all EBJIS Newsletters and the latest updates related to Bone and Joint Infection.
- Access to the EBJIS community that encourages discussion and collaboration between the EBJIS Members on clinical cases.
- Discounted Annual EBJIS Meeting registration fee, which is equivalent to the annual membership fee (130 euros).
- Eligibility to become an EBJIS Fellow, allowing you to apply for the fully-funded annual Travelling Fellowship program at www.ebjis.org/fellowship. Three Travelling Fellowships are granted annually.
- Opportunity to apply for a Country Delegate position, serving to enhance EBJIS promotion in many countries around the world, facilitate connections with interested colleagues, and encourage the growth of Bone and Joint Infection centers in various countries.
- Participation in the EBJIS Annual General Assembly with voting rights on crucial decisions.
- Reduced article processing charges when publishing an open-access article in The Journal of Bone and Joint Infection (JBJI). Visit administrator.copernicus.org/authentication for more details.
- Support from the Executive Committee for organizing scientific meetings and promoting them within our membership and on the EBJIS website.

Annual membership fee: € 130

For further details, contact us here:
info@ebjis.org

For more information and to register as a member of EBJIS please visit our website:

www.ebjis.org/membership

Welcome

Dear colleagues and friends,

On behalf of the EBJIS Executive Committee and the EBJIS 2023 Local Organising Committee, we warmly welcome you to the 41st **Annual Meeting of the European Bone & Joint Infection Society** taking place in Basel.

We are thrilled to present to you the extensive scientific programme built around the conference theme “From the beginnings of the AO foundation to modern treatment concepts in implant-related infections”. Make sure to attend the key sessions with experts from all over the world, as well as the free paper sessions, industry symposia and - not to forget – all the great posters located next to the exhibition.

We hope you all have the occasion to fulfil your educational goals during the three conference days, meet new inspiring colleagues, but also discover a little bit of Basel – a place of exciting contrasts. A city with historical buildings next to modern architecture like Messe Basel build by Herzog & de Meuron. Where a young and dynamic art scene exists alongside world-renowned museums. Cosmopolitan ambience here, lively traditions there. A vibrating place for science, especially in pharma and biomedical engineering.

The conference will again be a hybrid event and will offer online streaming and on-demand access of all sessions to all registered participants.

We wish all conference participants a very pleasant and interesting time.

Welcome to EBJIS 2023 – in Basel and online!

Martin Clauss
EBJIS Treasurer &
EBJIS 2023 Local Chair

Alex Soriano
President of EBJIS

Organisation

The Local Organising Committee

Martin Clauss
Local Chair
Center for Musculoskeletal Infections (ZMSI), Department of Orthopaedic and Trauma Surgery, University Hospital Basel

Yvonne Achermann
Internal Medicine and Infectious Diseases, Hospital Zollikerberg, Zollikerberg

Olivier Borens
Hirslanden Group, Lausanne

Richard Kühl
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Mario Morgenstern
Center for Musculoskeletal Infections (ZMSI), Department of Orthopaedic and Trauma Surgery, University Hospital Basel

Fintan Moriarty
AO Research Institute Davos

Rik Osinga
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Parham Sendi
Institute for Infectious Diseases, University of Bern

The EBJIS Executive Committee

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Hospital Clinic of Barcelona, Department of infectious diseases, Spain

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Orthopedic Hospital Valdoltra, Slovenia

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Martin Clauss
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Marjan Wouthuyzen-Bakker
Ordinary Member
University Medical Center Groningen Department of Medical Microbiology and Infection Prevention, The Netherlands

Irene Sigmund
Ordinary Member
Medical University of Vienna, Austria

General information

Conference website
www.ebjis2023.org

Conference venue
Congress Center Basel
Messepl. 10
4058 Basel
Switzerland

Badges
The conference name badges must always be worn during the conference. Access to the conference venue will not be granted without the name badge issued by the conference organisers.

Entitlements for participants
Admission to all scientific sessions and industry symposia, admission to exhibition, conference bag with programme- and abstract book, CME credits, coffee breaks and lunch, welcome reception on Thursday 12 October, farewell lunch on Saturday 14 October and certificate of attendance.

CME credits
The conference has been accredited with 15 European CME credits (ECMEC) by the European Accreditation Council for Continuing Medical Education (EACCME). Participants who wish to apply for CME credits should go to the registration desk to confirm their attendance each day. You will receive an email with more information and the link to download the certificate after the conference.

Cloakroom
A manned cloakroom will be available by the main entrance during the scheduled programme.

Information for Speakers
Please bring your presentation, on a USB stick, to the Speakers' Preview room located next to session room Sydney. An assistant will help you upload the presentation to the computer. Please make sure to upload your presentation at least 2 hours before your session starts. We do not allow the use of personal laptops for presentations. At the end of the conference, all presentations will be deleted to secure that no copyright issues will arise.

Speakers' Preview room (2nd floor)

Opening hours:

Thursday, 12 October	7:30 - 17:00
Friday, 13 October	7:45 - 17:00
Saturday, 14 October	8:00 - 12:00

WIFI
Free access to the WIFI at the conference venue is provided.

1) Please select "Free-Messe-Basel" and wait until a pop-up window appears
2) Please enter your mobile number and wait for your access code (SMS)
3) Please enter the access code to connect

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Social events

Welcome Reception
Date 12 October 2023
Time 18:30 - 20:00
Place Exhibition area at the conference venue

The reception is included in the registration fee.

EBJIS Conference Dinner
Date 13 October 2023
Time 19:30 - 24:00
Place Restaurant Safran Zunft Basel, Gerbergasse 11

NB: Admission by pre-booked ticket only

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Programme

Thursday, 12 October 2023

Plenary Room: San Francisco (3rd floor)			
07:30		Registration opens	
08:30-08:50		**Opening Session:** ***Welcome by EBJIS President and Local Chair***	**Alex Soriano &** **Martin Clauss**
08:50-09:30		**Key session 1: From the beginnings of the AO foundation to modern treatment concepts in implant-related infections**	**Chairs:** **Alex Soriano &** **Martin Clauss**
		Historical Aspects	Olivier Borens
		The Global Burden of BJI	Len Marais
09:30-10:30		**Key session 2: Biofilm and Beyond - Translation from In-vitro Data to In-vivo Strategies**	**Chairs: Richard Kühl & Fintan Moriarty**
		Phenotyping bacteria in the in-vivo environment	Dirk Bumann
		Imaging and characteristics of bacterial biofilms	Knut Drescher
		New biofilm concepts	Thomas Bjarnsholt
10:30-11:00		***Coffee break / Posters/ Exhibition***	
11:00-12:30		**Free Paper Session A: PJI (9 x 6 min + 2 min)**	**Chairs:** **Yvonne Achermann &** **Andrej Trampuz**
	FP A1	Outcome of Prosthetic Joint Infection (PJI) is more dependent on JS-BACH classification than treatment method	Martin McNally
	FP A2	Incidence of rifampicin-resistance in staphylococcal Periprosthetic Joint Infection: A single-center cohort study on 238 patients	Stergios Lazarinis
	FP A3	Prosthetic Joint Infections due to Candida spp.: A multicenter international observational study	Julie Lourtet
	FP A4	Hospitalizations due to prosthetic joint infection in Spain during the period 2000-2015	Joan Gómez-Junyent
	FP A5	Infection after intracapsular femoral neck fracture – Does antibiotic-loaded bone cement reduce infection risk after hemiarthroplasty and total hip arthroplasty? – Data from the German Arthroplasty Registry	Dominik Szymski
	FP A6	Microbiologic epidemiology of Hip Prosthetic Joint Infections in elderly patients caused by multidrug-resistant gram-negative bacteria: A retrospective cohort	Thomas Stravinkas Durigon
	FP A7	Impact of positive cultures during the second stage of a 2-stage replacement. Systematic review	Marta Sabater Martos
	FP A8	Outcomes of Mega-Endoprosthesis in Lower Limb Periprosthetic Joint Infections: A case-control study	Chukwudubem Anibueze
	FP A9	Revision due to PJI increases risk of perioperative myocardial injury and death in comparison to primary and non-PJI revision arthroplasty	Martin Clauss
12:30-14:00		***Lunch break / Posters/ Exhibition***	
12:45-13:45		**Industry Symposium A** (Please see page 161 for the agenda)	
14:00-15:00		**Key session 3:** **Animal Models in Biofilm Research**	**Chairs:** **Fintan Moriarty &** **Edward Schwarz**
		S. aureus invasion of the osteocyte lacunocanalicular network	Edward Schwarz
		International consensus on basic science in bone and joint infection	Kordo Saeed
		Humanised models of BJI	Gowri Muthukrishnan

Due to CME regulations no industry names or logos are allowed in the scientific programme.
Detailed programme of industry symposia is available on pages 159-171

Thursday, 12 October 2023

Parallel Session Room: Hall Sydney (2nd floor)			
10:30-11:00		***Coffee break / Posters/ Exhibition***	
11:00-12:30		**Free Paper Session B: FRI (10 x 6 min + 2 min)**	**Chairs:** **Volker Alt &** **Christof Wagner**
	FP B1	Fracture-related Infection:Prevalence and application of the new consensus definition in a cohort of 1004 surgically treated ankle fractures	Kristian Pilskog
	FP B2	What is the effect of duration of infection on the success rate of Debridement, Antibiotics and Implant Retention in patients with a Fracture-Related Infection of the lower leg?	Michelle Buijs
	FP B3	Outcomes of fracture-related infections – do organism, depth of involvement, and temporality count?	Janus Wong
	FP B4	Treatment and outcome of Fracture-Related Infection of the clavicle	Laura Bessems
	FP B5	Masquelet technique for infected segmental defects of long bones in a low-resource setting of sub-Saharan Africa: Technical adaptations and outcome	Loïc Fonkoue
	FP B6	The clinical relevance of low-grade infection in the development and management of fracture-related nonunion	Katharina Trenkwalder
	FP B7	Debridement, antibiotics, irrigation, and implant retention in a sheep fracture-related infection model	Claudia Siverino
	FP B8	Management and Outcome following Severe Osteomyelitis due to Pin Site Infections	Florian Frank
	FP B9	Closed-incisional negative pressure wound therapy in post-surgical management of bone and joint infections	Daniele De Meo
	FP B10	A New Classification of Fracture-related Infection	Martin McNally
12:30-14:00		***Lunch break / Posters/ Exhibition***	
12:45-13:45		**Industry Symposium B** (Please see page 163 for the agenda)	

Plenary Room: San Francisco (3rd floor)			
15:00-15:50		**Free Paper Session C: Biofilm Basics / Animals (6 x 6 min + 2 min)**	**Chairs: Richard Kühl & Martin McNally**
	FP C1	The role of macrophages and intracellular survival of Staphylococcus aureus – New insights from direct evaluation of human tissue samples	Benedict Morin
	FP C2	Rethinking the Inoculum Used in Animal Models of Implant-Associated Osteomyelitis – The Formation and Application of Bacterial Aggregates	Katrine Top Hartmann
	FP C3	The Infected Polypropylene Mesh: Which Antiseptic Solution Most Effectively Removes Biofilm?	Alberto Carli
	FP C4	Longitudinal Intravital Imaging to Quantify the "Race for the Surface" Between Host Immune Cell and Bacteria for Orthopaedic Implants with S. aureus Colonization in a Murine Model	Chao Xie
	FP C5	Antibody-drug conjugate therapy against S. aureus implant-associated infection in a murine model	Nis Jørgensen
	FP C6	Emerging roles of the long pentraxin PTX3 in Staphylococcus aureus-dependent osteomyelitis	Valentina Possetti
15:50-16:20		***Coffee break / Posters/ Exhibition***	
16:20-17:20		**Key session 4: Diabetic Foot Infection and Diabetic Foot Osteomyelitis**	**Chairs: Marjan Wouthuyzen-Bakker & Ilker Uçkay**
		40 years of DFI/DFO: What have learned?	Eric Senneville
		Surgery in DFO: Curing the infection and retaining the ability to walk	Javier Aragòn Sanchez
		Antibiotic Stewardship in DFI	Ilker Uçkay
17:25-18:25		**Industry Symposium C** (Please see page 165 for the agenda)	
18:30-20:00		**Welcome Reception in the exhibition area** *(included in the registration fee)*	

Due to CME regulations no industry names or logos are allowed in the scientific programme.
Detailed programme of industry symposia is available on pages 159-171

Parallel Session Room: Hall Sydney (2nd floor)			
15:00-15:50		**Free Paper Session D: Phages / Biofilm (6 x 6 min + 2 min)**	**Chairs: Tristan Ferry & Willem-Jan Metsemakers**
	FP D1	Bacteriophage therapy in orthopedic and cardiovascular surgery: Clinical experience in eight patients with difficult-to-treat infections	Paula Morovic
	FP D2	Synergistic Action of Bacteriophage and Vancomycin in a Co-delivery hydrogel for Localized Treatment of Fracture-Related Infection caused by Methicillin-resistant Staphylococcus aureus	Baixing Chen
	FP D3	Antibacterial activity of new developed multielement nanogranular coatings	Elena De Vecchi
	FP D4	Novel antimicrobial coating on titanium with stable non-antibiotic quaternary ammonium compounds to prevent implant-associated infection	Martijn Riool
	FP D5	Noble metal-based antibacterial implant coatings for articulating implant surfaces	Chris Arts
	FP D6	Short-term Celecoxib Promotes Bone Formation Without Compromising Antibiotic Efficacy in Early Orthopaedic Device-Related Infection: Evidence from a Rat Model	Vuyisa Mdingi
15:50-16:20		***Coffee break / Posters/ Exhibition***	
17:25-18:25		**Industry Symposium D** (Please see page 167 for the agenda)	

Programme

Friday, 13 October 2023

Plenary Room: San Francisco (3rd floor)			
7.45		**Registration opens**	
08:30-09:30		**Key Session 5: Antimicrobials**	**Chairs: Parham Sendi & Tristan Ferry**
		Shorter is better: Where are the limits?	Adrien Lemaignen
		Bone penetration of antibiotics: What we know and don't know	Mats Bue
		Long-acting antibiotics (dalbavancin/oritavancin)	Alex Soriano
		Monitoring of adverse events: Do we get the overall picture?	Florent Valour
09:30-10:30		**Key Session 7: Infection Prevention**	**Chairs: Yvonne Achermann & Irene Sigmund**
		Prevention from the point of view of the infectiologist	Tobias Kramer
		Prevention in open fractures, timing of surgery in complex fractures	Mario Morgenstern
		Prevention in immunosuppressed patients – point of view from a rheumatologist	Ulrich Walker
10:30-11:00		***Coffee break / Posters/ Exhibition***	
11:00-12:30		**Free Paper Session E: Infection Prevention and Risk Factors (9 x 6 min + 2 min)**	**Chairs: Andy Miller & Parham Sendi**
	FP E1	Antibiotic Prophylaxis for Endoprosthetic Replacements Implanted for Musculoskeletal Tumours: An International Survey of Practice	Tariq Azamgarhi
	FP E2	Risk Factors for Fracture-related Infection after Ankle Fracture Surgery	Kristian Pilskog
	FP E3	Bacterial reservoir in deeper skin is a potential source for surgical site and biomaterial-associated infections	Sebastian Zaat
	FP E4	The ORACLE study: Open fracture Risks Associated with infection – A Cohort Longitudinal Evaluation study of 517 open fractures across 20 years	Janus Wong
	FP E5	Risk analysis of periprosthetic knee joint infection (PJI) in total knee arthroplasty after preoperative corticosteroid injection: A systematic review	Daniel Pérez-Prieto
	FP E6	Risk factors and outcome of polymicrobial prosthetic joint infections compared to mono microbial: A single- institution revision of 536 patients	Ignacio Ortiz Martín
	FP E7	Can a Diabetic Foot Ulcer be prevented?	Madhu Tiruveedhula
	FP E8	A 2-Stage Approach in Managing Diabetic Neuropathic Forefoot Ulcers	Madhu Tiruveedhula
	FP E9	Single-stage orthoplastic management of calcaneal osteomyelitis: An analysis of outcomes	Billy Down
12:30-13:45		***Lunch break / Posters / Exhibition***	
12.35-13.35		**Industry Symposium E** (Please see page 169 for the agenda)	
13:45-14:45		**Key Session 8: The non-surgical burden of BJI**	**Chairs: Olivier Borens & Ricardo Sousa**
		Treatment of BJI – really expensive? Impact on public health	Martin Clauss
		Specialised centers – are they really better? Outcome analysis	Lee M. Jeys
		The psychological impact of BJI: an underestimated aspect in the treatment of BJI	Nike Walter

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Parallel Session Room: Hall Sydney (2nd floor)			
08:15-09:15		**Key Session 6: Orthoplastic Surgery – From Split Skin to Tailored Tissue Engineering**	**Chairs: Willem-Jan Metsemakers & Martin McNally**
		Get, set, go... and keep going. Setting up orthoplastics for acute fracture treatment to reduce the risk of bone infection	Sarah Tucker
		Orthoplastic Surgery Concept: How to? The BIPS approach	Rik Osinga
		Soft-tissue reconstruction through ring fixateur: friend or foe?	Alex Ramsden
		Periosteal flaps for osseous non-unions	Heinz Bürger
09:15-10:15		**EBJIS Journal: Journal of Bone and Joint Infection**	
		Report and best papers	Parham Sendi
		Results of MSIS survey	Andy Miller
10:30-12:00		**Country Delegates meeting** (By invitation only)	**Meeting Room Rio**
11:00-12:30		**Free Paper Session F: Antimicrobials (10 x 6 min + 2 min)**	**Chairs: Anna Conen & Jaime Lora-Tamayo**
	FP F1	Amoxicillin in deep-seated samples – quantification of a delicate compound	Joana Erdmann
	FP F2	Steady-State Piperacillin Concentrations in the Proximity of an Orthopedic Implant: A Microdialysis Porcine Study	Johanne Gade Lilleøre
	FP F3	Is délafloxacine a therapeutic option for bone and joint infections? A CRIOGO multicenter retrospective study	Stephane Corvec
	FP F4	Bone and soft tissue concentrations of penicillin - is oral penicillin V non-inferior to intravenous penicillin G?	Hans Christian Rasmussen
	FP F5	Local antibiotic delivery via intra-articular catheter infusion for the treatment of periprosthetic joint infection: A systematic review	Sander Bruyninckx
	FP F6	Struggling with a cefazolin impregnation protocol of bonechips. The effect of the timing of the impregnation and gamma irradiation on the cefazoline release	Guy Putzeys
	FP F7	Extended oral antibiotic prophylaxis – do the same criteria apply to patients undergoing aseptic revision arthroplasty?	Alberto Carli
	FP F8	Monitoring and guidance of patients with prolonged antimicrobial therapy: Filling the gap to improve quality of care	Denise Telgt
	FP F9	Impact of antimicrobial suppression on long-term outcome of streptococcal periprosthetic joint infections	Maria Virginia Dos Santos
	FP F10	Use of Dalbavancin to Facilitate Discharge in the Treatment of Bone and Joint Infections	Tariq Azamgarhi
12:30-14:00		**Editorial board meeting of JBJI** (By invitation only)	**Meeting room Miami**
12.35-13.35		**Industry Symposium F** (Please see page 171 for the agenda)	
13:45-14:45		**Scientific projects from the EBJIS Country Delegates Group**	**Chairs: Charles Vogely & Christof Wagner**
		EBJIS Project – Country Delegates	Christof Wagner
		Septic Arthritis Guidelines	Jeroen Neyt & Christen Ravn
		Health economic burden of periprosthetic joint infections in Europe	Volker Alt
		Impact of positive cultures during the second stage of a 2-stage replacement	Marta Sabater

Plenary Room: San Francisco (3rd floor)			
14:45-15:45		**Free Paper Session G: Outcome and Quality of Life (7 x 6 min + 2 min)**	**Chairs: Rik Osinga & Charles Vogely**
	FP G1	Quality of life in osteomyelitis is significantly worse compared to other chronic diseases	Andrew Hotchen
	FP G2	Frame treatment improves quality of life in osteomyelitis, but only after a period of significant impairment	Florian Frank
	FP G3	Direct hospital costs per case for periprosthethic hip and knee joint infection in Europe – A systematic review	Dominik Szymski
	FP G4	Analysis of multidisciplinary team decision adherence in complex bone, joint and arthroplasty infections	Jaap Hanssen
	FP G5	What Can They Expect? Decreased Quality of Life and Increased Postoperative Complication Rate in Patients with a Fracture-Related Infection of a Long Bone Fracture	Michelle Buijs
	FP G6	The national infection control program PRISS, had no effect on postoperative infections after primary total hip arthroplasty in Sweden	Peter Wildeman
	FP G7	Quality of life and Mortality in Patients Waiting for an Operation for Bone and Joint Infection	Andrew Hotchen
15:45-16:15		***Coffee break / Posters/ Exhibition***	
16:15-17:15		**Free Paper Session I: Diagnostics 1 (7 x 6 min + 2 min)**	**Chairs: Ilker Uçkay & Matteo Ferrari**
	FP I1	Bony sequestrum in chronic osteomyelitis: characteristic on 18F-FDG-PET-CT images.	Ahmed Elsheikh
	FP I2	Novel diagnosis marker of periprosthetic joint infection: A systematic review	Melanie Schindler
	FP I3	Calprotectin: an important synovial marker for the diagnosis of periprosthetic joint infection	Stephane Corvec
	FP I4	Evaluation of an upgraded synovial calprotectin lateral flow assay in unclear cases of hip and knee prosthetic joint infections	Susana Gardete-Hartmann
	FP I5	Inferior diagnostic performance of serum Albumin-Globulin-Ratio in periprosthetic joint infection	Markus Luger
	FP I6	Plasma Fibrinogen is a Promising First-line Screening Biomarker for the Diagnosis of Periprosthetic Joint Infection and Timing of Reimplantation: A Multicenter Retrospective Study	Hang Fang
	FP I7	Synovial fluid viscosity with synovial fluid cell count: a highly sensitive and specific diagnostic tools of prosthetic joint infections	Samo Roskar
17:30-18:45		**EBJIS General Assembly** *(for EBJIS members, by invitation only)*	**Meeting Room Rio**
19:30		**EBJIS Conference Dinner at Restaurant Safran Zunft** *(Admission by pre-booked ticket only)*	Address: Gerbergasse 11

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Parallel Session Room: Hall Sydney (2nd floor)			
14:45-15:45		**Free Paper Session H: Myco and Micro (7 x 6 min + 2 min)**	**Chairs: Marjan Wouthuyzen-Bakker & Parham Sendi**
	FP H1	Tuberculous Arthritis of Native Joints: A systematic review and EBJIS workgroup report	Leonard Marais
	FP H2	The prevalence of mycobacteria in bone and joint samples at a tertiary orthopaedic centre in a setting with a low burden of tuberculosis disease	Antonia Scobie
	FP H3	Microbiological Profile Changes in Sequential Revision Hip and Knee Arthroplasty for Prosthetic Joint Infection	Robert McCulloch
	FP H4	Clinical Outcome And Microbiological Analysis Of Unexpected Positive Intraoperative Cultures In Presumed Aseptic Knee and Hip Revision Arthroplasty – A ten year Retrospective Analysis with a Minimum Follow-Up Of Two Years	Sebastian Simon
	FP H5	Does improvement in preanalytics lead to increased culture yield in patients with periprosthetic infections?	Juliane Käschner
	FP H6	Is an isolated positive sonication fluid culture in revision arthroplasties clinically relevant?	Marjan Wouthuyzen-Bakker
	FP H7	Molecular Epidemiology of community onset methicillin-resistant Staphylococcus aureus causing skin and musculoskeletal infections: An alarming antimicrobial resistance scenario	Stefânia Bazanelli Prebianchi
15:45-16:15		***Coffee break / Posters/ Exhibition***	
16:15-17:15		**Free Paper Session J: Diagnostics 2 (7 x 6 min + 2 min)**	**Chairs: Nora Renz & Christen Ravn**
	FP J1	The predictive value and reliability of ultrasound-guided biopsies for diagnosing periprosthetic shoulder infections	Denise Telgt
	FP J2	The value of preoperative ultrasound-determined fluid film and joint aspiration prior to revision total hip arthroplasty for the diagnosis of periprosthetic hip joint infection	Jennyfer A Mitterer
	FP J3	Genome-based analysis of virulence factors of the genus Cutibacterium isolated from implant-associated infections in Slovenia	Anja Erbeznik
	FP J4	Improving the diagnosis of bone and joint infections: evaluation of 16S rDNA targeted meta-genomics	Tiphaine Roussel-Gaillard
	FP J5	What is the agreement between principles and practice of antibiotic stewardship in the management of diabetic foot infections?	Noémie Reinert
	FP J6	To sonicate or not to sonicate?	Anne Brun Hesselvig
	FP J7	Does high bacterial load in sonication of mobile parts predict failure after DAIR in prosthetic joint infections?	Loris Oehen

Programme

Saturday, 14 October 2023

		Parallel Session room: Sydney	
08:30-09:00		**Travelling Fellowship Report**	**Chair: Ricardo Sousa**
		Presented by: Marianna Faggiani, Italy Mats Bue, Denmark Marti Carles Bernaus Johnson, Spain Wout Veltman, Netherlands	
09:00-10:00		**Key Session 9:** **From Culture-Negative to MDR - Challenges**	**Chairs: Len Marais & Christen Ravn**
		Infection mimikers	Parham Sendi
		Osteomyelitis after gun and war injuries	Maritz Laubscher
		MDR bacteria in bone and joint infections	Efthymia Giannitsioti
10:00-10:30		***Coffee break / Posters/ Exhibition***	
10:30-12:00		**Best Papers Session** **(10 x 6 min + 2 min)**	**Chairs: Irene Sigmund & Alex Soriano**
	BP1	Prevention of prosthetic joint infection using electrical fields. Proof of concept in an experimental in vivo model	Marti Bernaus
	BP2	Implant retention in a rabbit model of delayed fracture-related infection: Successful eradication but impaired bone bone healing compared to early infection	Jan Puetzler
	BP3	May local vancomycin incorporated into bone substitute increase plasma concentrations of vancomycin in patients with osteomyelitis and influence the need to perform more frequent dosage adjustments?	Roger Rojas-Sayol
	BP4	Towards preoperative diagnosis of infected nonunion of femur or tibia with targeted proteomics in blood plasma	Ferdinand Weisemann
	BP5	DAIR to Stop: Suppressive antibiotic treatment after 12 weeks of therapy is not beneficial for acute periprosthetic joint infections	Marjan Wouthuyzen-Bakker
	BP6	Biofilm of Cutibacterium acnes: target of different active substances	Stephane Corvec
	BP7	Sepsis in Periprosthetic Joint Infections - Epidemiology, Risk Factors, and Outcomes	Susanne Bärtl
	BP8	Mental health and experienced physical & psychological impairment in patients with musculoskeletal infections	Katinka Wetzel
	BP9	Extended antimicrobial prophylaxis does not improve outcome of unexpected PJI: A randomized controlled trail	Karin Veerman
	BP10	Development and validation of a synthetic synovial fluid model as diagnostic tool for biofilm-related prosthetic joint infections	Amber De Bleeckere
12:00-12:30		**Honorary lecture:** **The development of the NEJM treatment algorithm in PJI**	**Chairs: Martin Clauss & Ricardo Sousa** **Speakers: Peter Ochsner & Werner Zimmerli**
12:30-12:45		**Closing Remarks & Prizes**	
12:45-14:00		***Farewell lunch with a local flavour***	

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Poster overview

No	Title	Authors
P1	Analysis of the soft tissue data in the 18F-FDG-PET-CT images of appendicular chronic osteomyelitis	Ahmed Elsheikh
P2	Incidence of postoperative hematoma following revision arthroplasty for infection using microporous polysaccharide hemosphere	Gregor Giebel | Marcel Niemann | Andrej Trampuz | Carsten Perka | Ulrich Stöckle | Sebastian Meller
P3	No difference in bacterial contamination of hip capsule sutures and control sutures in hip arthroplasty surgery	Thomas van Schaik | Maurits van Meer | Lex de Jong | Jon Goosen | Matthijs Somford | Job van Susante
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Oral abstracts

[FP A1] OUTCOME OF PROSTHETIC JOINT INFECTION (PJI) IS MORE DEPENDENT ON JS-BACH CLASSIFICATION THAN TREATMENT METHOD

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Aim: To compare outcomes of PJI in relation to treatment method versus classification using the JS-BACH system.

Method: Patients having surgery for EBJIS Criteria Confirmed PJI between 2010-2015 were included. Index surgical procedures were 1-stage or 2-stage revision or debridement and implant retention (DAIR). Patients completed the EuroQol EQ-5D-3L questionnaire and were followed clinically to a median of 4.7 years (IQR 2.7-6.7 years). Patients were stratified using the JS-BACH classification[1] into either 'Uncomplicated', 'Complex' or having 'Limited treatment options', by two separate classifiers, blinded to clinical outcome.

Results: 216 patients met the inclusion criteria. There were 51 patients classified as Uncomplicated (23.6%), 127 (58.8%) as Complex and 38 (17.6%) having Limited treatment options. Patients underwent either DAIR (n=97), 1-stage (n=35) or 2-stage (n=84) revision. Patients classified as Uncomplicated PJI had the lowest risk of recurrence or treatment failure, regardless of index procedure performed. Complex patients were significantly more likely than Uncomplicated patients to have recurrence following 2-stage revision (Odds Ratio 1.85; p=0.040) or DAIR (OR 1.83; p=0.037), but not 1-stage revision (OR 0.518; p=0.675). Limited treatment option patients had the highest recurrence risk regardless of index procedure (1-stage: OR 2.5 p=0.036; 2-stage: OR 3.3 p=0.004; DAIR: OR 3.40 p=0.006).

At one year after surgery, Uncomplicated patients had the highest EQ-index scores (a marker of Quality of Life), with all treatments. Differences in patient-reported outcomes were greater between the JS-BACH classification groups than between the methods of treatment (Table 1).

Conclusions: The JS-BACH classification effectively predicted outcome after three common PJI treatments. Comparing outcomes between treatments, without stratification of the patients, may be misleading as factors other than treatment method have a major effect on outcome. Classification may allow better allocation of individual treatments to provide optimal outcome for patients.

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	Treatment Method			
JS BACH Classification	1 Stage	2 Stage	DAIR	p value*
Uncomplicated	0.917	0.713	0.689	0.379
Complex	0.511	0.500	0.524	0.965
Limited Treatment Options	0.403	0.091	0.437	0.149
p value*	0.001	0.025	0.211	

Table 1. EuroQol EQ-5D-3L mean index scores at one year after treatment of EBJIS Confirmed PJI, stratified by the JS-BACH Classification. *ANOVA for significance between groups.

[FP A2] INCIDENCE OF RIFAMPICIN-RESISTANCE IN STAPHYLOCOCAL PERI-PROSTHETIC JOINT INFECTION: A SINGLE-CENTER COHORT STUDY ON 238 PATIENTS

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Aim: Rifampicin as a biofilm-active antibiotic drug has a significant role in the treatment of peri-prosthetic joint infection (PJI). However, rifampicin resistance is an increasing threat to PJI treatment. This study aimed to evaluate the prevalence of rifampicin resistant staphylococci over time and its association with infection-free survival after PJI in a single centre in Sweden.

Methods: We included 238 PJIs in 238 patients who had undergone PJI revision surgery from 2001 to 2020 on whom the causative bacteria were staphylococci and the agent was tested for rifampicin resistance. Data regarding agents, rifampicin resistance, treatment and outcome was obtained. Kaplan-Meier survival analysis and a Cox regression model with adjustment for age, sex, localisation (hip or knee) and type of prosthesis (primary or revision) were used to calculate infection-free survival rates and adjusted risk ratios (HRs) of the risk of treatment failure. Treatment failure was defined as any reoperation or suppression treatment with antibiotics due to prolonged infection.

Results: Among the included 238 PJIs, 40 rifampicin-resistant staphylococci [93% Coagulase Negative Staphylococci (CoNS)] and 29 treatment failures were identified. The proportion of rifampicin resistant agents decreased from 25% in 2010-2015 to 12% in 2016-2020. The 2-year infection-free survival rates were 79.0% (95% CI 0.66-0.92) for the rifampicin resistant and 90% (95% CI 0.86-0.94) for the rifampicin sensitive group. Patients with PJI caused by rifampicin resistant bacteria had a significantly higher risk of treatment failure than those caused by sensitive bacteria (HR 2.5; 95% CI 1.0–6.2).

Conclusions: The incidence of PJI caused by rifampicin resistant staphylococci decreased in Uppsala, Sweden over the past 20 years. PJI caused by rifampicin-resistant staphylococci has a two-fold risk for treatment failure compared to PJI caused by rifampicin-sensitive staphylococci, which stresses the importance of retaining rifampicin resistance low. Additionally, the increased risk of treatment failure when PJI is caused by a rifampicin-resistant bacteria warrants consideration of a more conservative treatment strategy.

[FP A3] PROSTHETIC JOINT INFECTIONS DUE TO CANDIDA SPP.: A MULTICENTER INTERNATIONAL OBSERVATIONAL STUDY

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Aim: Prosthetic joint infection (PJI) due to ***Candida*** spp. is a severe complication of arthroplasty but is little reported. This study describes Candida PJI epidemiology, management and outcome.

Method: We performed a retrospective, observational multinational study with support of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). Patients diagnosed with PJI due to ***Candida*** spp. between 1990 and 2021 were included. Demographic, clinical, laboratory, imaging, medical/surgical treatment, and outcome data were collected within a standardized database. Treatment failure was defined either as a ***Candida*** infection recurrence, superinfection, or death due to infection.

Results: Data from 151 patients across 18 centers were analyzed. Mean age was 69.5 ± 13.1yo, 78 (51.7%) patients were male, and 21 (13.9%) were immunosuppressed. Site of infection included hip (55.0%), knee (41.7%), shoulder (2.6%), and femur (0.7%). Twenty-five (16.6%) patients were febrile, and 58 (38.4%) had fistula. Mean number of previous surgeries on the same anatomical site was 3.3±2.3. Surgeries were DAIR (33.8%), one-stage exchange (19.9%), two-stage exchange (39.1%), and implant removal (6.0%). Candida species identified were ***C. albicans*** (60.3%), ***C. parapsilosis*** (26.5%), ***C. glabrata*** (7.3%), and ***C. tropicalis*** (5.3%).

Co-infection with bacteria was found in 69 (45.7%) cases. Fluconazole (62.9%) and caspofungin (14.6%) were the main antifungal agents prescribed for 148.6 ± 167.5 days. Favorable outcome was found in 54/144 (37.5%) cases. Failure was associated with the number of previous surgeries (OR 1.249, 95%CI 1.061-1.469; p-value=0.007), while treatment by fluconazole was associated with cure (OR 0.336, 95%CI 0.160-0.707; p-value=0.004).

Conclusions: This study provides epidemiologic and outcome data on ***Candida*** PJIs. Although poor overall, the prognosis did not seem associated with immunosuppression, type of surgery, fungal species or treatment duration.

[FP A4] HOSPITALIZATIONS DUE TO PROSTHETIC JOINT INFECTION IN SPAIN DURING THE PERIOD 2000-2015

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Aim: Prosthetic joint infection (PJI) is a devastating complication of joint replacement, having an impact on morbimortality but also on national health systems and their budgets. The current situation of PJI-related hospitalizations in Spain and their changes over time are unknown. Therefore, we aimed to analyze the hospitalization burden of PJI, including costs and trends in recent decades.

Methods: Retrospective observational study including data from the National Surveillance System for Hospital Data, which includes more than 98% of Spanish hospitals. During the period 2000-2015, hospitalizations due to PJI (ICD-9-CM 996.66) as main diagnosis were included. Epidemiological trends were evaluated during four periods: P1, 2000-2003; P2, 2004-2007; P3, 2008-2011; P4, 2012-2015. Annual hospitalization rates per 100,000 inhabitants and trends were also calculated.

Results: Among 5,721,6725 hospitalizations, 49,835 were PJI related, which represented 8.71/10,000 admissions. We observed a significant increase in the number of PJI-related hospitalizations per 10,000 admissions during the study period: 6.43 P1, 8.53 P2, 9.60 P3, 10.05 P4 (p<0.001). The annual hospitalization rate was 6.9/100,000 inhabitants (95%CI 6.9-7), which also increased over time (p<0.001). The median age was 72 years (IQR 65-78) and 58.12% were women. Hospitalization rates were higher in women (7.95 vs 5.90; p<0.001) and also increased with patients' age (p<0.001). Whereas the median length of stay was 7 days (IQR 7-8) in the global cohort, it was 18 days (IQR 10-31) in those with PJI-related hospitalization; however, the median length of stay in PJI-related hospitalizations decreased during the study period (P1 20 days, P4 16 days, p<0.001). The total cost for the healthcare system was 366 million euros and the median cost per patient was 6937 euros (IQR 3584-10505), which significantly increased from 4804 euros in P1 to 8534 in P4 (p<0.001). The majority of patients (90.32%) were discharged home and the case-fatality rate was 2.70%, without significant differences during the study (p=0.384).

Conclusions: In Spain, PJI-related hospitalizations have increased in recent decades, with higher costs despite the decrease in length of stay. PJI is a first magnitude healthcare problem, which should be prioritized in health systems and budgets.

[FP A5] INFECTION AFTER INTRACAPSULAR FEMORAL NECK FRACTURE –DOES ANTIBIOTIC-LOADED BONE CEMENT REDUCE INFECTION RISK AFTER HEMIARTHROPLASTY AND TOTAL HIP ARTHROPLASTY? – DATA FROM THE GERMAN ARTHROPLASTY REGISTRY

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Aim: The aim of this investigation was to compare risk of infection in both cemented and cementless hemiarthroplasty (HA) as well as total hip arthroplasty (THA) following femoral neck fracture.

Methods: Data collection was performed using the German Arthroplasty Registry (EPRD) In HA and THA following femoral neck fracture fixation method was divided into cemented and cementless protheses and paired according to age, sex, body mass index (BMI), and the Elixhauser score using Mahalanobis distance matching.

Results: Overall in 13,612 cases of intracapsular femoral neck fracture, with 9,110 (66.9 %) HAs and 4502 (33.1 %) THAs were analyzed. Infection rate in HA was significantly reduced in cases with use of antibiotic-loaded cement compared to cementless fixated prosthesis (p=0.013). In patients with THA no statistical difference between cemented and cementless prothesis was registered, however after one year 2.4 % of infections were detected in cementless and 2.1 % in cemented THA. In the subpopulation of HA after one year 1.9 % of infections were registered in cemented and 2.8 % in cementless HA. BMI (p=0.001) and Elixhauser-Comorbidity-Score (p<0.003) were identified as risk factors of PJI, while in THA also cemented prosthesis demonstrated within the first 30 days an increased risk (HR=2.728; p=0.010).

Conclusion: The rate of infection after intracapsular femoral neck fracture was significantly reduced in patients treated by antibiotic-loaded cemented hemiarthroplasty. In particular for patients with multiple risk factors for the development of a PJI the usage of antibiotic-loaded bone cement seems to be a reasonable procedure for prevention of infection.

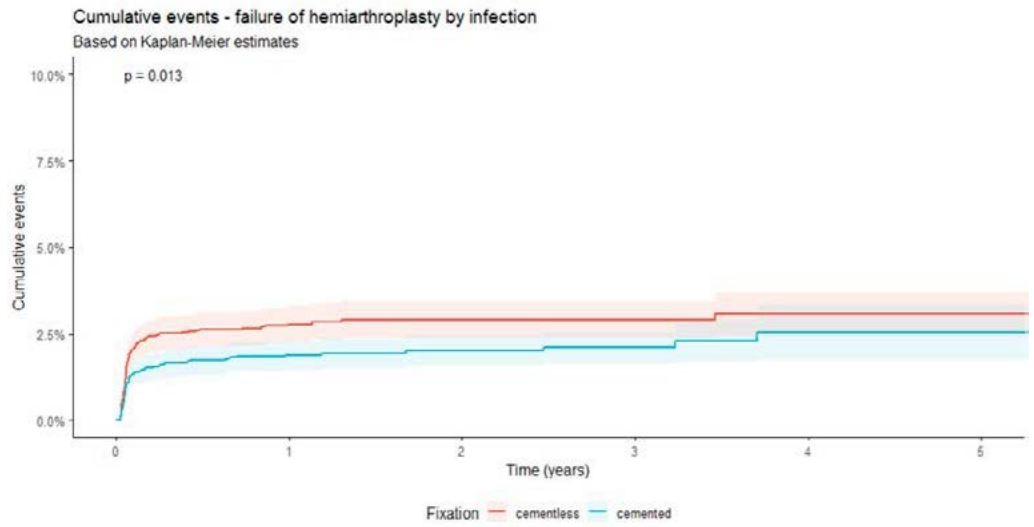

Figure 1: Development of infection in cemented and cementless hemiarthroplasties after femoral neck fractures in a period of 5 years

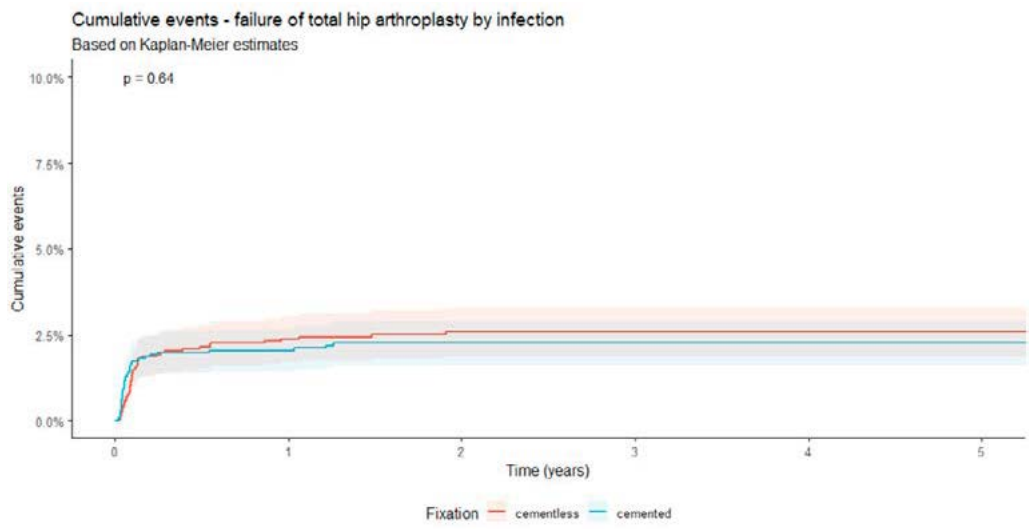

Figure 2: Development of infection in cemented and cementless total hip arthroplasties after femoral neck fractures in a period of 5 years

[FP A6] MICROBIOLOGIC EPIDEMIOLOGY OF HIP PROSTHETIC JOINT INFECTIONS IN ELDERLY PATIENTS CAUSED BY MULTIDRUG-RESISTANT GRAM-NEGATIVE BACTERIA: A RETROSPECTIVE COHORT

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Aim: Currently, gram-negative bacteria (GNB), including multidrug-resistant (MDR-GNB) pathogens, are gaining importance in the aetiology of prosthetic joint infection (PJI). To characterize the antimicrobial resistance patterns of Gram-negative bacteria (GNB) causing hip prosthetic joint infections in elderly patients treated at a Brazilian tertiary academic hospital.

Method: This is a retrospective, cross-sectional study of patients over 60 years of age undergoing hip arthroplasty from 2018 to 2023 at a tertiary academic trauma, which were diagnosed with hip prosthetic joint infection. PJI diagnosed was based on EBJIS criteria, in which intraoperative tissue cultures identified the pathogens. Demographics, reason for arthroplasty, type of implant and susceptibility patterns using disk diffusion method were analysed.

Results: Overall, among 17 elderly patients diagnosed with hip infected arthroplasty, 45 bacterial isolated were identified. Debridement, irrigation, antibiotic and implant retention (DAIR) procedures due to uncontrolled infection occurred in 47.0% (n=8/17), and five patients underwent more than two DAIR surgeries. Tissue cultures yielded eleven different bacterial species, with GNB accounted for 64.4% (n=29/45) of pathogens. ***Klebsiella pneumoniae, Acinetobacter baumannii, Escherichia coli, and Pseudomonas aeruginosa*** were identified in 34.5% (n=10/29), 17.25% (n=5/29), 13.8% (n=4/29), and 13.8% (n=4/29), respectively. In the resistance profile analysis, ***E. coli*** was most sensitive to antibiotics, whereas ***K. pneumoniae*** showed resistance rates higher than 70% for cephalosporins, carbapenems, and quinolones. All ***A. baumannii*** isolates were resistant to meropenem, and 80% of these isolates were resistant to amikacin.

Conclusions: This study emphasizes the role of GNB in the microbiological profile of PJI among elderly patients at a tertiary hospital in a Brazilian centre. The present study portrays a worryingly higher rates of MDR-GNB, mainly to quinolones and cephalosporins resistance which have been the cornerstone of PJI antibiotic treatment. In addition, higher rates carbapenems and aminoglycosides resistance shows a threat to antibiotic treatment of PJI. More global studies need to be carried out to show a likely change in the microbial epidemiology of PJI.

[FP A7] IMPACT OF POSITIVE CULTURES DURING THE SECOND STAGE OF A 2-STAGE REPLACEMENT. SYSTEMATIC REVIEW

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Aim: Two-stage replacement is a frequent procedure in patients with chronic PJI. However, results in the literature after this procedure differ, ranging from 54% to 100% of infection eradication. Positive cultures at reimplantation, when performing the second stage, are perceived as a risk factor for reinfection. This study aims to determine the impact of positive cultures during the second stage on the outcome of patients undergoing a 2-stage septic replacement and the impact of antibiotic holidays between the first and the second stage.

Method: We systematically searched four databases from inception to May 31, 2022. We combined terms related to PJI, joint replacement and culture results. We analysed the risk of failure when positive cultures at second stage and performed a subgroup analysis by antibiotic holiday period.

Results: We included 24 studies with 2387 patients of which 432 had positive cultures during second stage (18.09%). Global failure rate was 18.01% (430 patients). When dividing failure by culture results during second stage, we found that failure in positive group was 37.01% (161/432 patients) and failure in negative group was 13.7% (269/1953 patients). In the meta-analysis (MA) the odds ratio (OR) was 4.047 (95% CI: 2.954-5.544). When performing the subgroup analysis by antibiotic holidays we found that the rate of positive cultures without and with holidays was 21.3% and 16.05%, respectively. Failure rate without holidays was 15% (90/600 patients) and with holidays was 17.3% (202/1165 patients) (p=0.21). Failure in each group was higher when cultures were positive (without holidays, 25% vs 12.2%, p=0.0003, and with holidays 41.1% vs 12.7%, p<0.0001). In the MA we found that those studies in which antibiotic holiday was reported had higher risk of failure when cultures were positive during second stage (OR 4.798 95%IC 3.142-7.325). When studies reported no antibiotic holidays also had a higher risk of failure when cultures where positive (OR 2.225 95%CI 1.103-4.489), though it was lower.

Conclusions: There exists a higher risk of failure after a two-stage septic replacement when cultures are positive during reimplantation. Patients who followed no antibiotic holidays or antibiotic holidays before reimplantation have similar failure rate when cultures are negative. In both groups they have a higher risk of failure when cultures are positive, having higher risk those positive patients in the antibiotic holidays group. Therefore, importance in detecting these patients before reimplantation is crucial to ensure higher survival rates.

[FP A8] OUTCOMES OF MEGA-ENDOPROSTHESIS IN LOWER LIMB PERIPROSTHETIC JOINT INFECTIONS: A CASE-CONTROL STUDY

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Aim: Mega-endoprosthesis over the last two decades have played a significant role in management of non-neoplastic cases for limb salvage for a variety of indications involving bone loss, infection, fracture and failed revision surgery. This is a retrospective case control study comparing outcomes of Mega-Endoprosthesis (MEP) in non-neoplastic cases with periprosthetic joint infections (PJI), with previous history of PJI and aseptic revision. Failure was defined as persistence/recurrence of infection, all cause revision, and antibiotic suppression during the follow up period. Secondary aims were identification of causative organisms, resistance profile and causative factors for revision surgery.

Method: A total of 122 patients undergoing 133 MEPs were identified between January 2012 and December 2020. 60 procedures were categorised as group 1 (infection; 50%), 20 as group 2 (previous history of infection; 16.7%), and 53 controls (no infection; 44.2%). Mean age of the cohort was 70.97 years (37.16-94.17), with a mean follow-up of 44.5 months (0.2-179) including patients lost to follow up.

Results: Overall failure rate was 71/133 53.3% (group 1 39/60 (55.56%), group 2 12/20 (60%) and controls 20/53 (37.7%)). Thirteen patients died in the first 2 years (five in group 1, one in group 2 & seven in controls). The most common postoperative infection was polymicrobial followed by Coagulase Negative Staphylococcus Species (CoNS) and Methicillin Sensitive Staphylococcus aureus (MSSA). Nineteen patients had polymicrobial PJI (Eighteen in group 1 and one in control). CoNS led to postoperative infection in Fifteen patients (six in group 1, five in group 2 and four in control group). MSSA was the pathogen in four patients (three in group-1 and one in the control group). The same organisms were responsible for recurrent infection in fourteen patients in group 1 and one patient in group 2. Limb salvage was achieved in 96.2% overall (95% group 1, 90% group 2, 100% control group).

Conclusions: MEPs in the context of PJI have a significant risk of failure however they play an important role in limb salvage. Patients should be counselled appropriately prior to surgery.

[FP A9] REVISION DUE TO PJI INCREASES RISK OF PERIOPERATIVE MYOCARDIAL INJURY AND DEATH IN COMPARISON TO PRIMARY AND NON-PJI REVISION ARTHROPLASTY

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Aim: Perioperative myocardial infarction/injury (PMI) is a common complication in noncardiac surgery, contributing to postoperative morbidity and mortality. We aimed to identify the risk for PMI in periprosthetic joint infection (PJI) in comparison to primary hip (THA) and knee arthroplasty (TKA) and to non-PJI revision surgery.

Methods: Patients undergoing primary/revision THA/TKA at a University Hospital who were eligible for the institutional PMI screening and response program were prospectively included. Revision arthroplasties were divided into 2 groups (PJI revision and non-PJI revision). PJI was defined according to the EBJIS criteria, and included DAIR, one-stage and two-stage revisions. Non-PJI revisions included partial and/or complete exchange of components. The primary endpoint was PMI, secondary endpoints were major adverse cardiovascular events (MACE) and all-cause mortality within 120 days.

Results: The study population included 673 patients (443 primary THA/TKA, 119 PJI revision, 111 Non-PJI revision) enrolled from 05/2014 to 06/2018. The median age in all groups was 75 years. In primary, non-PJI and PJI revision surgery, 39%, 41% and 50%, respectively were male.

PMI occurred in 12% of patients with primary arthroplasty compared to 20% and 35% in non-PJI and PJI revision, respectively ($p<0.001$ overall), with PJI having a significantly elevated risk over non-PJI revisions ($p=0.014$). Conversely, in MACE (4% primary vs 9% non-PJI vs 12% PJI, $p=0.002$) an all-cause mortality (2% primary vs 4% non-PJI vs 9% PJI, $p<0.001$) no significant difference between PJI and non-PJI revisions was observed. We found no difference for the risk of PMI comparing DAIR vs one-/two-stage PJI revision ($p=0.88$).

In multivariable analysis (primary arthroplasty as reference), significant odds ratios for PMI included PJI (3, 1.7-5.3), coronary artery disease (2.9, 1.9-4.4), chronic heart faiure (1.3, 1.1-1.7) and age (1.1, 1.0-1.1 per each year age). Urgency of surgery, duration of surgery, to the presence of ***Staphylococcus aureus*** were not significant. impact on PMI.

Conclusion: In PJI, PMI and MACE were 3-times, and death 4.5 times, respectively, more frequently observed than in primary arthroplasty. Also, PJI had the highest odds for PMI (3.0). Orthopaedic surgeons should be aware of the high PMI risk when performing revision surgery. This work confirms the importance of a peri-/postpoperative PMI screening and response program in the field of septic surgery.

[FP B1] FRACTURE-RELATED INFECTION: PREVALENCE AND APPLICATION OF THE NEW CONSENSUS DEFINITION IN A COHORT OF 1004 SURGICALLY TREATED ANKLE FRACTURES

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Aim: Surgical treatment of ankle fractures comes with a substantial risk of complications, including infection. An unambiguously definition of fracture-related infections (FRI) has been missing. Recently, FRI has been defined by a consensus group with a diagnostic algorithm containing suggestive and confirmatory criteria. The aim of the current study was to report the prevalence of FRI in patients operated for ankle fractures and to assess the applicability of the diagnostic algorithm from the consensus group.

Method: Records of all patients with surgically treated ankle fractures from 2015 to 2019 were retrospectively reviewed for signs of postoperative infections. Patients with suspected infection were stratified according to ***confirmatory*** or ***suggestive criteria*** of FRI. Rate of FRI among patients with ***confirmatory*** and ***suggestive criteria*** were calculated.

Results: Suspected infection was found in 104 (10%) out of 1004 patients. Among those patients, ***confirmatory criteria*** were met in 76/104 (73%) patients and ***suggestive criteria*** were met in 28/104 (27%) at first evaluation. Patients with clinical confirmatory criteria (N= 76) were diagnosed with FRI. Patients with suggestive criteria were further examined with either bacterial sampling at the outpatient clinic, revision surgery including bacterial sampling, or a wait-and-see approach. Eleven (39%) of the 28 patients had positive cultures and were therefore diagnosed as having FRI at second evaluation. In total 87 (9%) patients were diagnosed with FRI according to the consensus definition. Only 73 (70%) of the 104 patients with suspected FRI had adequate bacterial sampling.

Conclusions: The prevalence of FRI, applying the FRI-consensus criteria, for patients with surgically treated ankle fractures was 9%. Twenty-two percent of patients who met the ***confirmatory criteria*** had negative bacterial cultures. The current study shows that we did not have a systematic approach to patients with suspected FRI as recommended by the consensus group. A systematic approach to adequate bacterial sampling when FRI is suspected is paramount. The consensus definition of FRI and its diagnostic algorithm facilitates such an approach.

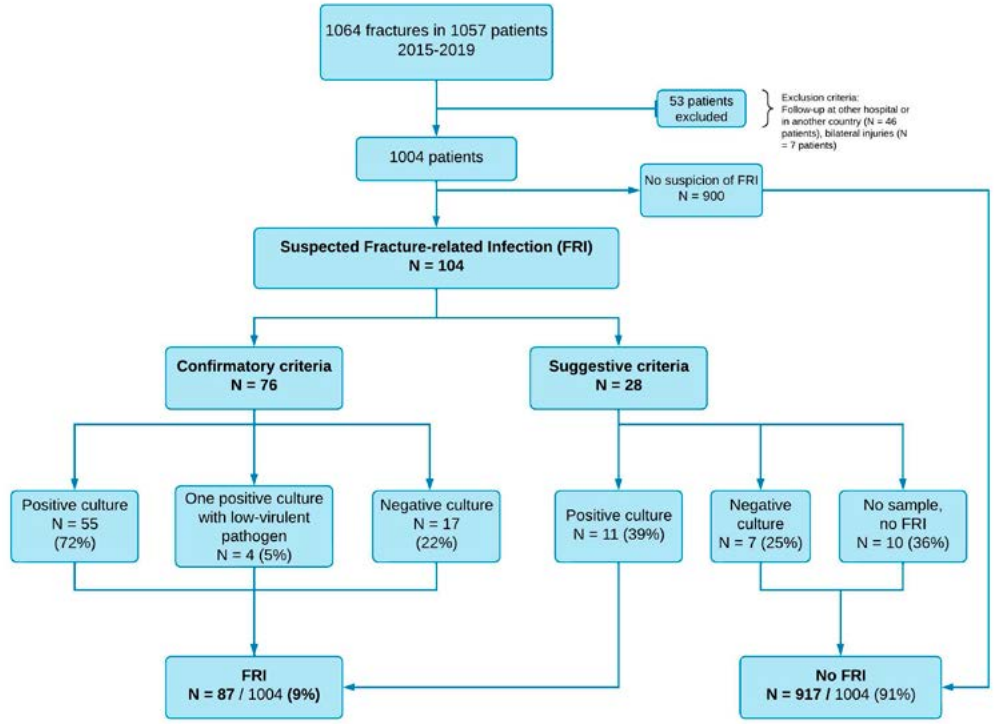

Figure legend: Patient inclusion flow-chart. N – Number of patients. FRI – Fracture-related Infection.

[FP B2] WHAT IS THE EFFECT OF DURATION OF INFECTION ON THE SUCCESS RATE OF DEBRIDEMENT, ANTIBIOTICS AND IMPLANT RETENTION IN PATIENTS WITH A FRACTURE-RELATED INFECTION OF THE LOWER LEG?

Jonathan Sliepen[1], Michelle Buijs[2], Marjan Wouthuyzen-Bakker[3], Melissa Depypere[4], Rob Rentenaar[5], Willem-Jan Metsemakers[6], Geertje Govaert[7], Frank Ijpma[1]

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Aims: Fracture-Related Infection (FRI) is a severe complication caused by microbial infection of bone. It is imperative to gain more insight into the potentials and limitations of Debridement, Antibiotics and Implant Retention (DAIR) to improve FRI treatment. The aims of this study were to: 1) determine how time to surgery affects the success rate of DAIR procedures of the lower leg performed within 12 weeks after the initial fracture fixation operation, 2) determine the recurrence rate of DAIR versus non-DAIR procedures and 3) evaluate whether appropriate systemic antimicrobial therapy affects the success rate of a DAIR procedure.

Methods: This multicentre international retrospective cohort study included patients of at least 18-years of age who developed an FRI of the lower leg within 12 weeks after the initial fracture fixation operation, between January 1st 2015 to July 1st 2020. DAIR success was defined as absence of recurrence of infection, preservation of the affected limb and retention of implants during the initial treatment. The antimicrobial regimen was considered appropriate if the pathogen(s) was susceptible to the given treatment at the correct dose as per guideline. Logistic regression modelling was used to assess factors that could contribute to the DAIR success rate.

Results: A total of 120 patients were included, of whom 70 DAIR patients and 50 non-DAIR patients. Within a median follow-up of 35.5 months, 21.4% of DAIR patients developed a recurrent FRI compared to 12.0% of non-DAIR patients. The DAIR procedure was successful in 45 patients (64.3%). According to the Willenegger and Roth classification, DAIR success was achieved in 66.7% (n=16/24) of patients with an early infection (<2 weeks), 64.4% (n=29/45) of patients with a delayed infection (2-10 weeks) and 0.0% (0/1) of patients with a late infection (>10 weeks). Univariate analysis showed that the duration of infection was not associated with DAIR success in this cohort (p=0.136; OR: 0.977; 95%CI:[0.947-1.007]). However, an appropriate antimicrobial regimen was associated with success of DAIR (p=0.029; OR: 3.231; 95%CI:[1.138-9.506]).

Conclusions: Although the results should be interpreted with caution, an increased duration of infection was not associated with a decreased success rate of a DAIR procedure in patients with FRI of the lower leg. The results of this study highlight the multifactorial contribution to the success of a DAIR procedure and emphasize the importance of adequate antimicrobial treatment. Therefore, time to surgery should not be the only key-factor when considering a DAIR procedure to treat FRI.

[FP B3] OUTCOMES OF FRACTURE-RELATED INFECTIONS – DO ORGANISM, DEPTH OF INVOLVEMENT, AND TEMPORALITY COUNT?

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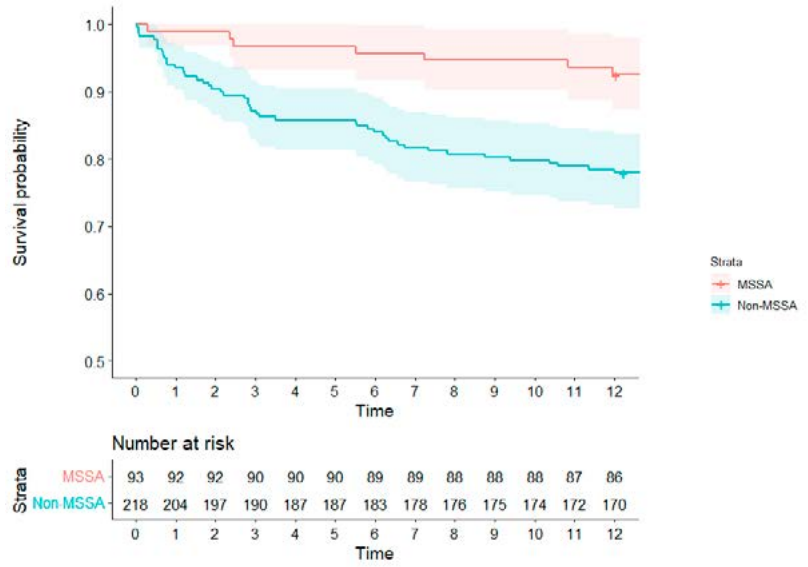
Aim: To determine mortality and outcomes of patients diagnosed with fracture-related infections (FRIs).

Method: FRI patients treated at a trauma centre between 2001 and 2020 were analysed. The primary outcome was 1-year mortality; mortality associations with FRI organism, depth of involvement, and temporality were investigated with multivariable survival analysis. Healthcare-associated and serological outcomes were reported as secondary outcomes.

Results: 311 FRIs with mean age of 67.0 and median Charlson comorbidity index of 0 were analysed. Methicillin-sensitive ***Staphylococcus aureus*** (MSSA) (29.9%) was the most frequently implicated organism. The majority of FRIs were deep infections (62.7%). FRIs were diagnosed at a median of 40 (IQR 15-200) days post index surgery. The mean follow-up was 5.9 years.

One-year mortality amounted to 17.7%. MSSA FRIs were associated with better survival (adj HR 0.34, 95%CI 0.15-0.76, p=0.008). There was no difference in survivorship between deep or superficial FRI (adj HR 0.86, 95%CI 0.62-1.19, p=0.353) or in relation to onset time (adj HR 1.0, 95%CI 0.99-1.00, p=0.943). Implant removal or debridement alone was performed in 61.7% and 17% respectively. Antibiotics was prescribed for 53 (IQR 23-110) days, and patients were hospitalised for 39 (IQR 19-78) days. CRP and ESR normalised in 70.3% (median 46 days) and 53.8% (median 86 days) patients respectively.

Conclusions: Fracture-related infections are associated with significant mortality and morbidity regardless of depth and temporality. Non-MSSA FRIs are associated with inferior survival.



[FP B4] TREATMENT AND OUTCOME OF FRACTURE-RELATED INFECTION OF THE CLAVICLE

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Aim: The number of operatively treated clavicle fractures has increased over the past decades. Consequently, this has led to an increase in secondary procedures required to treat complications such as fracture-related infection (FRI). The primary objective of this study was to assess the clinical and functional outcome of patients treated for FRI of the clavicle. The secondary objectives were to evaluate the healthcare costs and propose a standardized protocol for the surgical management of this complication.

Method: All patients with a clavicle fracture who underwent open reduction and internal fixation (ORIF) between 1 January 2015 and 1 March 2022 were retrospectively evaluated.
This study included patients with an FRI who were diagnosed and treated according to the recommendations of a multidisciplinary team at the University Hospitals Leuven, Belgium.

Results: We evaluated 626 patients with 630 clavicle fractures who underwent ORIF. In total, 28 patients were diagnosed with an FRI. Of these, eight (29%) underwent definitive implant removal, five (18%) underwent debridement, antimicrobial treatment and implant retention, and fourteen patients (50%) had their implant exchanged in either a single-stage procedure, a two-stage procedure or after multiple revisions. One patient (3.6%) underwent resection of the clavicle. Twelve patients (43%) underwent autologous bone grafting (tricortical iliac crest bone graft (n=6), free vascularized fibular graft (n=5), cancellous bone graft (n=1)) to reconstruct the bone defect. The median follow-up was 32.3 (P_{25}-P_{75}: 23.9-51.1) months. Two patients (7.1%) experienced a recurrence of infection. The functional outcome was satisfactory, with 26 out of 28 patients (93%) having full range of motion. The median healthcare cost was € 11.506 (P_{25}-P_{75}: € 7.953-23.798) per patient.

Conclusion: FRI is a serious complication that can occur after the surgical treatment of clavicle fractures. Overall, the outcome of patients treated for FRI of the clavicle is good, when management of this complication is performed by using a multidisciplinary team approach. The median healthcare costs of these patients are up to 3.5 times higher compared to non-infected operatively treated clavicle fractures. Expert opinion considers factors such as the size of the bone defect, the condition of the soft tissue, and patient demand to guide surgical decision making.

[FP B5] MASQUELET TECHNIQUE FOR INFECTED SEGMENTAL DEFECTS OF LONG BONES IN A LOW-RESOURCE SETTING OF SUB-SAHARAN AFRICA: TECHNICAL ADAPTATIONS AND OUTCOME.

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Aim: infected segmental bone defect (ISBD) is frequent in developing countries. The aim of this study was to assess the efficacy of the Masquelet technique in the treatment of ISBD in a low-resource setting.

Patients and Method: We performed a prospective cohort study during the period from 2018 to 2022. Patients with infected bone defect of long bones were included. Management protocol consisted of two stages in all patients. The first stage consisted in debridement, tissues biopsy for microbiological culture, stabilization with external fixator and defect filling with gentamicin cement spacer. The second stage consisted of reconstruction using a cancellous bone autograft alone, or a mixture of autograft with allograft (demineralized bone matrix + tricalcium phosphate) and 1 gram of vancomycin powder. All patients were followed-up for at least one year. The results were assessed based on both objective (clinical and radiographic evaluation) and subjective (limb function and patient satisfaction) criteria. Main outcomes were bone union, reoperation and failure rates, union time, and limb function.

Results: We included 31 patients in this study (80.6% men), with a median age of 35 [9 – 80] years. The tibia was affected in 12 cases and the femur in 15 cases. The median size of bone defect was 4 [1.5 – 12] cm. The most prevalent microorganisms were ***Klebsiella pneumoniae*** and ***Staphylococcus aureus***. The mean interval between both stages was 14 (8 – 36) weeks and the median follow-up period after the second stage was 20 [12-62] months. External fixation was used in both stages in 25(80%) cases. Bone union was achieved in 26 (83.8%) patients of whom 24 without recurrence of infection, over a median time of 9 [6 – 16] months. All patients with a mixed graft (allograft and autograft) impregnated with local antibiotics achieved bone union. Two patients needed reoperation for relapse of infection between both stages, and subsequently achieved bone union without recurrence of infection. There were three cases of failure related to persistent infection or insufficient fixation stability in the second stage.

Conclusions: Masquelet technique is a reliable procedure that can be safely performed in limited resources settings with satisfactory results. The mixture of autograft and allograft when available, all mixed with vancomycin seems to give promising results.

Keywords: Austere environment; infected bone defect; Masquelet technique.

[FP B6] THE CLINICAL RELEVANCE OF LOW-GRADE INFECTION IN THE DEVELOPMENT AND MANAGEMENT OF FRACTURE-RELATED NONUNION

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Aim: Treatment algorithms for fracture-related nonunion depend on the presence or absence of bacterial infection. However, the manifestation of septic nonunion varies. Low-grade infections, unlike manifest infections, lack clinical signs of infection and present similarly to aseptic nonunion. The clinical importance of low-grade infection in nonunion is not entirely clear. Therefore, the aim of this study was to evaluate the clinical relevance of low-grade infection in the development and management of femoral or tibial nonunion.

Method: A prospective, multicenter clinical study enrolled patients with nonunion and regular healed fractures. Preoperatively, complete blood count without differential, C-reactive protein (CRP), and procalcitonin were obtained, clinical signs of infection were recorded, and a suspected septic or aseptic diagnosis was made based on history and clinical examination. During surgical nonunion revision or routine implant removal, tissue samples were collected for microbiology and histopathology, and osteosynthesis material for sonication. Nonunion patients were followed for 12 months. Definitive diagnosis of “septic” or “aseptic” nonunion was made according to diagnostic criteria for fracture-related infection, considering the results of any further revision surgery during follow-up.

Results: 34 patients with regular healed fractures were included. 62 nonunion patients were diagnosed as aseptic, 22 with manifest, and 23 with low-grade infection. The positive predictive value was 88% and the negative predictive value 72% for the suspected diagnosis. The nonunion groups had significantly higher CRP levels than the regular healer group. Differentiation between septic and aseptic nonunion based on blood values was not possible. Low-grade infection demonstrated less frequently histopathologic signs of infection than manifest infection (22% vs. 50%, p=0.048), with 15% of regular healers having histopathologic signs of infection. ***Cutibacterium acnes*** was less present in manifest compared to low-grade infection (p=0.042). Healing rates for septic nonunion involving ***C. acnes*** were significantly lower for manifest infection (20%) than for low-grade infection (100%, p=0.002). Patients with low-grade infection were treated with systemic antibiotics less frequently than patients with manifest infection (p=0.026), with no significant difference in healing rate (83% vs. 62%), which was slightly lower for low-grade infection than for aseptic nonunion (90%).

Conclusions: Low-grade infections play a significant role in nonunion development and are difficult to diagnose preoperatively due to the lack of clinical signs of infection and unremarkable blood counts. However, our results imply that for low-grade infections, antibiotic therapy may not always be mandatory to heal the nonunion. This study was supported by the German Social Accident Insurance (FF-FR0276).

[FP B7] DEBRIDEMENT, ANTIBIOTICS, IRRIGATION, AND IMPLANT RETENTION IN A SHEEP FRACTURE-RELATED INFECTION MODEL

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Aim: Debridement, Antibiotics, Irrigation, and implant Retention (DAIR) is a surgical treatment protocol suitable for some patients with fracture related infection (FRI). Clinically relevant preclinical models of DAIR are scarce and none have been developed in large animals. Therefore, this project aimed to develop a large animal model for FRI including a DAIR approach and compare outcomes after 2 or 5 weeks of infection.

Method: Swiss Alpine sheep (n=8), (2-6 years, 50-80 kg) were included in this study. This study was approved by cantonal Ethical authorities in Chur, Switzerland. A 2 mm osteotomy was created in the tibia and fixed with a 10-hole 5.5 mm steel plate. Subsequently, 2.5 mL of saline solution containing 10^6 CFU/mL of ***Staphylococcus aureus*** MSSA (ATCC 25923) was added over the plate. Sheep were observed for 2 (n=3) or 5 weeks (n=5) until revision surgery, during which visibly infected or necrotic tissues were removed, and the wound flushed with saline. All samples were collected for bacterial quantification. After revision surgery, the sheep were treated systemically for 2 weeks with flucloxacillin and for 4 weeks with rifampicin and cotrimoxazole. After 2 further weeks off antibiotics, the animals were euthanized. Bacteriological culture was performed at the end of the study. Bone cores were isolated from the osteotomy site and processed for Giemsa & Eosin and Brown and Brenn staining. A radiographical examination was performed every second week.

Results: Bacteriological evaluation of the retrieved samples during revision surgery showed no significant difference between the 2 ***vs*** 5 weeks infection periods in term of total CFU counts. At the end of the study, radiographical examination showed callus formation over the osteotomy site in both groups, although the osteotomy was not completely healed in either group. At euthanasia, the 2 weeks infection group showed a higher soft tissue burden compared to the 5 weeks group, whereby the infection in the 5 weeks group was primarily located in the bone and bone marrow.

Conclusions: The large animal model of FRI and DAIR was successfully established. Bacteriological outcomes highlight that the increasing duration of the infection does not change the outcome but the location of the infection from a predominantly soft tissue infection to a deeper bone and intramedullary (IM) channel infection. The debridement of the IM channel could potentially reduce the infection burden by eliminating those bacteria not easily reached by systemic antibiotics, though is not practical using conventional techniques.

[FP B8] MANAGEMENT AND OUTCOME FOLLOWING SEVERE OSTEOMYELITIS DUE TO PIN SITE INFECTIONS

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Aim: Pin track infection (PTI) is a common complication of external fixators. PTI usually presents as superficial infection which is treated conservatively. This study investigated those rare cases of PTI requiring surgery due to persistent osteomyelitis (OM), after pin removal.

Method: In this retrospective cohort study we identified patients who required surgery for an OM after PTI (Checketts-Otterburn Classification Grade 6) between 2011 and 2021. We investigated patient demographics, aetiology of the OM, pathogen and histology, treatment strategies and complications. Infection was confirmed using the 2018 FRI Consensus Definition. Successful outcome was defined as an infection-free interval of at least 24 months following surgery, which was defined as minimum follow-up.

Results: Twenty-seven patients were treated due to a pin site infection with an osteomyelitis (22 tibias, 2 humeri, 2 calcanei, 1 radius). 85% identified as male and the median age was 53.9 years. Eighteen infections followed external fixation of fractures, with 4 cases after Ilizarov deformity correction, 2 cases followed ankle fusion and 3 after traction pin insertion. Fifteen patients were classified as BACH Uncomplicated and 12 were BACH Complex. The median follow-up was 3.99 years (2.00-8.05 years).

Staphylococci were the most common pathogens (16 MSSA, 2 MRSA, 2 CNS). Polymicrobial infections were present in 5 cases (18%).
All surgery was performed in a single stage following the same protocol at one institution. This included deep sampling, debridement, implantation of local antibiotics, culture-specific systemic antibiotics and soft tissue closure. Seven patients required flap coverage (6 local, 1 free flap), which was performed in the same operation.

25 (93%) patients had a successful outcome after surgery. Two had recurrence of infection which was successfully treated by repeat of the protocol. One patient suffered a fracture through the operated site after a fall. This healed without infection recurrence. Wound leakage after local antibiotic treatment was seen in 3/27 (11%) of cases. All resolved without treatment.
After a minimum of 2 years follow up, all patients were infection free at the site of the former osteomyelitis.

Conclusions: OM after PTI is uncommon but has major implications for the patient as 7 out of 27 patients needed flap coverage. This reinforces the need for careful pin placement and pin site care to prevent deep infection. These infections require appropriate surgery, not just curettage. All patients in our cohort were infection-free after a minimum follow-up of 2 years suggesting that this protocol is effective.

[FP B9] CLOSED-INCISIONAL NEGATIVE PRESSURE WOUND THERAPY IN POST-SURGICAL MANAGEMENT OF BONE AND JOINT INFECTIONS

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Aim: There are no studies in literature that analyze the effectiveness of closed-incisional negative pressure wound therapy (ciNPWT) in the treatment of bone and joint infections (BJI). The aim of the study was to evaluate the efficacy and the safety of the application of ciNPWT in the postsurgical wound management of patients with osteoarticular infections.

Method: We conducted a perspective single-center study on patients with BJI treated between 01/2022 and 10/2022 with ciNPWT dressing application at the end of the surgical procedure. All patients were treated by a multidisciplinary team (MDT) approach and operated by the same surgical equipe. Inclusion criteria were: presence of periprosthetic joint infection (PJI), fracture-related infection (FRI), osteomyelitis (OM), septic arthritis (SA) surgically treated, after which ciNPTW was applied over the closed surgical wound. 30 patients (19M, 11F) have been analyzed with mean age of 56,10±17,11 years old; BJIs were all localized in the lower limb (16 PJI, 12 FRI, 1 SA, 1 OM).

Results: We considered the following clinical local pre-operative parameters: presence of fistula (10 patients, 33,33%), presence of erythema (18 patients, 60%), presence of previous flap in the incisional site (7 patients, 23,33%). In 11 cases (36,67%) more than 3 previous surgical procedures were performed in the surgical site. The following surgical procedures were performed: 8 debridement and implants removal, 7 DAIR, 3 one-stage exchange, 6 two-stage exchange, 3 spacer exchange, 3 resection arthroplasty. Nineteen patients (63,34%) showed no occurrence of any local post-operative complication (erythema, hematoma, wound breakdown, wound blister, necrosis). Seven (23,33%) patients showed the presence of one or more postoperative complications that didn't require additional surgery. We observed four (13,33%) failures, defined as the need for further surgical procedures following the onset of a local complication: two patients had a wound breakdown before wound closure and two had a recurrence of infection after an uneventfully wound closure. All failures were within the group of joint infection (PJI+SA) and were affected by a multi drug resistant pathogen.

Conclusions: In our series four patients required further surgery, but only two cases were related to incisional wound problems, that is consistent with aseptic joint revision surgeries data that are available in literature (3.4%-6.9%)[1-2]. Patients affected by BJI are a group with significant high risk of failure and therefore the use of ciNPWT should be considered. However, randomized clinical trials are needed to establish the superiority of the ciNPWT dressing over the standard one.

[FP B10] A NEW CLASSIFICATION OF FRACTURE-RELATED INFECTION

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Aim: To classify Fracture-related Infection (FRI) allowing comparison of clinical studies and to guide decision-making around the main surgical treatment concepts.

Method: An international group of FRI experts met in Lisbon, June 2022 and proposed a new FRI classification. A core group met during the EBJIS Meeting in Graz, 2022 and on-line, to determine the preconditions, purpose, primary factors for inclusion, format and the detailed description of the elements of an FRI Classification.

Results: Historically, FRI was classified by time from injury alone (early, delayed or late). Time produces pathophysiological changes which affect the bone, the soft-tissues and the patient general health, over a continuum. No definitive cut-off is therefore possible. The most important primary factors were characteristics of the fracture (**F**), relevant systemic co-morbidities of the patient (**R**) and impairment of the soft-tissue envelope (**I**). These factors determine FRI severity, choice of treatment method and are predictors of outcome. Hence the **FRI Classification** was designed (Table 1).

The final proposal of the FRI Classification is presented here. The new classification has five stages; from simple cases of infected healed fractures, in healthy individuals with good soft tissues (Stage 1), through unhealed fractures with variable potential for bone healing (Stages 2, 3 or 4) to Stage 5, with no limb-sparing or reconstructive options. In each patient, the most severe stage for any element (**F**, **R** or **I**) gives the definitive stage for that patient. For instance, the need for a free flap (**I**4), over a well-healed fracture (**F**1), in a patient with 2 co-morbidities (**R**2) gives a definitive **FRI**4 for that patient.

Conclusions: This novel approach to FRI classification builds on previous work in osteomyelitis, PJI and chronic medical conditions. It focusses attention on the elements of the disease which need treatment. It now requires validation in large patient cohorts.

Table 1. The FRI Classification

Stage	1	2	3	4	5
Fracture F	Fracture Healed	Fracture Not Healed Good bone healing potential	Fracture Not Healed Poor bone healing potential	Fracture Not Healed Major segmental bone defect	Fracture Not Healed Bone Reconstruction Not Possible
Relevant Patient Factors* R	Fit for Surgery	1 or 2 systemic comorbidities, without end organ damage	3 or more systemic comorbidities without end-organ damage	Systemic comorbidity with end organ damage	Unfit for Surgery or Declines Treatment
Impairment of Soft Tissues I	Robust Direct Wound Closure Possible	Direct Wound closure possible but cover of bone and/or implant is fragile	Soft Tissue Reconstruction is required with local tissue transfer	Soft Tissue Reconstruction is required with free tissue transfer	Soft Tissue Reconstruction Not Possible

*Systemic medical conditions are classified at the time of infection surgery. Patients may present with more severe comorbidities which may be treated and optimised prior to surgery. This may reduce the severity of compromise at the time of surgery.

[FP C1] THE ROLE OF MACROPHAGES AND INTRACELLULAR SURVIVAL OF STAPHYLOCOCCUS AUREUS – NEW INSIGHTS FROM DIRECT EVALUATION OF HUMAN TISSUE SAMPLES

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Aim: *Staphylococcus aureus* (SA) can cause various infections and is associated with high morbidity and mortality rates of up to 40%. Antibiotic treatment often fails to eradicate SA infections even if the causative strain has been tested susceptible *in vitro*. The mechanisms leading to this persistence is still largely unknown. In our work, we to reveal SA interactions with host cells that allow SA to persist at the site of infection.

Method: We established a sampling workflow to receive tissue samples from patients requiring surgical debridement due to SA bone-and joint or soft-tissue infections. We developed a multiplex immunofluorescent staining protocol which allowed us to stain for SA, leukocytes, neutrophils, macrophages, B-cells, T-cells, DAPI and cytoplasmatic marker on the same sample slide. Further, distance of SA to cell nuclei was measured. Interaction of immune cells and SA on a single cell level was investigated with high-resolution 3D microscopy. We then validated our findings applying fluorescence-activated cell sorting (FACS) on digested patient samples. Finally, we aimed to reproduce our *ex vivo* patient results in an *in vitro* co-culture model of primary macrophages and clinical SA strains, where we used live cell microscopy and high-resolution microscopy to visualize SA-immune cell interactions and a gentamicin protection assay to assess viability of SA.

Results: Here, we revealed that CD68+ macrophages were the immune cells closest to SA with a mean distance of 56µm (SD=36.4µm). Counting the amount of SA, we found in total >7000 single SA in nine patients. Two-thirds of SA were located intracellularly. Two-thirds of the affected immune cells with intracellular SA were macrophages. The distribution of intra- to extracellular SA was independent of ongoing antibiotic therapy and underlying infection type. FACS confirmed these findings. In our co-culture model, intracellular SA remained alive for the whole observation period of eight hours and resided in RAB5+ early phagosomes.

Conclusions: Our study suggests an essential role of intracellular survival in macrophages in SA infections. These findings may have major implication for future treatment strategies.

[FP C2] RETHINKING THE INOCULUM USED IN ANIMAL MODELS OF IMPLANT-ASSOCIATED OSTEOMYELITIS – THE FORMATION AND APPLICATION OF BACTERIAL AGGREGATES

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Aim: To make an inoculum for induction of Implant-Associated Osteomyelitis (IAO) in pigs based on bacterial aggregates resembling those found on the human skin, i.e. aggregates of 5-15 µm with low metabolic activity. The aggregates were evaluated and compared to a standard planktonic bacterial inoculum.

Method: The porcine *Staphylococcus aureus* strain S54F9 was cultured in Tryptone Soya Broth for seven days. Subsequently, the culture was filtered through cell strainers with pore sizes of 15 µm and 5 µm, respectively. The fraction of 5-15 µm aggregates in the top of the 5 µm filter was collected as the aggregate-inoculum. The separation of aggregates into different size fractions was evaluated by light microscopy. The metabolism of the aggregate-inoculum and a standard overnight planktonic inoculum was evaluated with isothermal microcalorimetry.In total, six female minipigs were allocated into three groups (n=2), receiving different inoculums. Group A: overnight planktonic inoculum; 10^4 CFU ***S. aureus*** (S54F9), Group B: seven days old 5-15 µm aggregate-inoculum; 10^4 CFU ***S. aureus*** (S54F9), Group C: saline. All inoculums were placed in a pre-drilled implant cavity in the right tibia of the pig and a sterile stainless-steel implant was inserted. The pigs were euthanized seven days after surgery. Postmortem macroscopic pathology, microbiology, computed tomography and histopathology were performed.

Results: The separation of aggregates into different size fractions was done successfully by the filtering method. Isothermal microcalorimetry showed, a delayed Time-to-peak metabolic activity of the aggregate-inoculum compared to the planktonic inoculum. ***S. aureus*** was isolated from subcutis, bone and implants from all animals in groups A and B. Both group A animals showed osteomyelitis at gross inspection with suppuration and sequestration, while groups B and C animals had no macroscopic lesions. From CT scans, both group A animals also showed positive signs of osteomyelitis, i.e., osteolysis, while only one animal in group B did, and none in group C. Histopathological examination of the bones showed more extensive inflammation in group A animals compared to those in group B, which showed more osteoid formation.

Conclusions: Formation and separation of low metabolism bacterial aggregates into different size fractions was possible. The aggregates can be used as inoculum in the porcine IAO model, with microbiological re-isolation from both implants and tissue. Furthermore, the aggregates caused a less aggressive IAO, than the planktonic counterparts. Using aggregated bacteria as inoculum appears to be more relevant to the clinical situation of infecting bacteria.

[FP C3] THE INFECTED POLYPROPYLENE MESH: WHICH ANTISEPTIC SOLUTION MOST EFFECTIVELY REMOVES BIOFILM?

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Aim: Polypropylene (PPE) synthetic mesh is increasingly used in knee arthroplasty surgery to salvage a disrupted extensor mechanism. Despite its clinical success, it is associated with a high rate of periprosthetic joint infection (PJI), which is hypothesized to be caused by bacterial biofilm. The purpose of the current study is to describe the progression of PPE-based biofilm formation over time and to determine if intraoperative antiseptic solutions could be used to effectively remove biofilm when treating PJI.

Method: Commercially available knotted monofilament PPE mesh[1] was cut into 10mm circular shape, immersed in tryptic soy broth (TSB) with methicillin-sensitive staphylococcus aureus and cultured individually in 48-well plates for 10 days to elucidate the biofilm grown on mesh over time. At every 24 hours, a triplicate of samples was retrieved and biofilm on the mesh was dislodged by sonicating at 52 kHz for 15 minutes and quantified by counting colony-forming units (CFUs) after overnight growth. The biofilm growth was also verified using scanning electron microscopy.
The effect of saline and antiseptic solutions was verified by exposing 1) 0.05% chlorohexidine gluconate[2], 2) acetic acid-based mixture[3], 3) diluted povidone-iodine (0.35%), 4) undiluted povidone-iodine (10%)[4], and 5) 1:1 combination of 10% povidone-iodine & 3% hydrogen peroxide on immature and mature biofilms for 3 minutes, created by culturing with bacteria for 24 hours and 72 hours respectively. All experiments were performed in quintuples and repeated. Antiseptic treatments that produced a three-log reduction in CFU counts compared to controls were considered clinically significant.

Results: PPE-mesh produced reliable CFU counts at 24 hours and reached peak growth at 72 hours. For immature biofilm, all formulations of povidone-iodine produced significant reductions in CFU counts compared to controls. Although not meeting the established threshold, saline irrigation removed 86.5% of CFUs, while formulation based on chlorohexidine and acetic acid removed 99.2% and 99.7% respectively. For mature biofilm, formulations based on povidone-iodine and acetic acid produced significant reductions in CFU counts.

Conclusions: Our findings suggest biofilm may form on mesh as early as 24 hours after bacterial exposure. Povidone-iodine formulations were consistently the most effective in removing biofilm on mesh surfaces. We recommend that surgeons consider using an antiseptic solution, preferably povidone-iodine-based, in addition to regular saline lavage when attempting to salvage a PPE mesh in the setting of PJI.

[1]Marlex mesh (CR Bard, Davol Inc, Warwick, RI), [2]Irrisept (Irrimax Corp, Gainesville, FL), [3]Bactisure (Zimmer-Biomet, Warsaw, IN), [4]Aplicare (Inc, Meriden, CT)

[FP C4] LONGITUDINAL INTRAVITAL IMAGING TO QUANTIFY THE "RACE FOR THE SURFACE" BETWEEN HOST IMMUNE CELL AND BACTERIA FOR ORTHOPAEDIC IMPLANTS WITH S. AUREUS COLONIZATION IN A MURINE MODEL

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Title: Longitudinal Intravital Imaging to Quantify the "Race for the Surface" Between Host Immune Cell and Bacteria for Orthopaedic Implants with ***S. aureus*** Colonization in a Murine Model

Aim: To assess ***S. aureus*** vs. host cell colonization of contaminated implants vis intravital multiphoton laser scanning microscopy (IV-MLSM) in a murine model.

Method: All animal experiments were approved by IACUC. A flat stainless steel or titanium L-shaped pin was contaminated with 10^5 CFU of a red fluorescent protein (RFP) expressing strain of USA300LAC, and surgically implanted through the femur of global GFP-transgenic mice. IV-MLSM was performed at 2, 4, and 6 hours post-op. Parallel cross-sectional CFU studies were performed to quantify the bacteria load on the implant at 2,4,6,12,18 and 24 hours.

Results: 1) We developed a high-fidelity reproducible IV-MLSM system to quantify S. aureus and host cell colonization of a bone implant in the mouse femur. Proper placement of all implants were confirmed with in vivo X-rays, and ex vivo photos. We empirically derive the ROI during each imaging session by aggregating the imaged volume which ranges from (636.4um x 636.4um x 151um) = 0.625 +/- 0.014 mm^3 of bone marrow in a global GFP-transgenic mouse.
2) IV-MLSM imaging acquisition of the "race for the surface". *In vitro* MPLSM images of implants partially coated with USA300LAC (RFP-MRSA) were verified by SEM image. Results from IV-MLSM of RFP-MRSA and GFP^+ host cell colonization of the contaminated implants illustrated the mutually exclusive surface coating at 3hrs, which to our knowledge is the first demonstration of "the race for the surface" between bacteria and host cells via intravital microscopy.
3) Quantifying the "race for the surface" with CFU verification of *S. aureus* on the implant. 3D volumetric rendering of the GFP^+ voxels and RFP+ voxels within the ROI were generated in Imaris. The voxel numbers suggeste that the fight for the surface concludes ~3hrs post-infection, and then transitions to an aggressive MRSA proliferation phase. The results of WT control demonstrate a significant increase in CFU by 12hrs post-op for both stainless steel (P<0.01) and titanium (P<0.01).

Conclusions: We developed IV-MLSM to quantify the "Race for the Surface" between host cells and contaminating ***S. aureus*** in a murine femur implant model. This race is remarkably fast, as the implant surface is completely covered with 3hrs, peak bacterial growth on the implant occurs between 2 and 12 hours and is complete by 12hrs.

[FP C5] ANTIBODY-DRUG CONJUGATE THERAPY AGAINST S. AUREUS IMPLANT-ASSOCIATED INFECTION IN A MURINE MODEL

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Aim: Infections represent a serious threat to the successful utilization of implants in modern medicine. Implant-associated infections are difficult to treat, because they involve biofilms that protect bacteria from the immune system and harbour antibiotic-tolerant persister cells.
In this work, we developed an antibody-drug conjugate (ADC) containing the anti-neoplastic drug mitomycin C (MMC) as a novel treatment paradigm for implant-associated infections. MMC was chosen as it is a potent antimicrobial against biofilms and its synthesis into an ADC was chosen to alleviate toxicity. Following development and synthesis of the ADC, stability and release of MMC was measured. We then used the ADC to kill bacteria in suspension and in biofilms, ***in vitro*** and ***in vivo***.

Method: Mitomycin C was conjugated to a commercially available antibody against ***S. aureus*** via a disulfide linkage, with a drug release occurred via thiol-disulfide exchange.
ADC as tested against ***S. aureus*** under various growth conditions (planktonic, persisters and biofilm). ***In vitro*** toxicity of ADC vs MMC was measured using a human cell line (MOLT-4).
Finally, two independent ***in vivo*** experiments were performed in a murine implant-associated osteomyelitis model. In experiment one ADC treatment was compared NaCl, vancomycin and vancomycin + ADC (n=10 for all groups). Subsequently, ADC was compared to NaCl, the antibody used in the ADC construction, MMC and a novel ADC constructed with a non-***S. aureus*** antibody (n=10 for all groups). All treatments were started day 7 post inoculation and were administered for 3 days. CFU enumeration was done following sonication to quantify bacterial load.

Results: Drug release could be triggered on demand with N-acetyl cysteine and release occurred, once in contact with free thiols on ***S. aureus*** cell surface.
The ADCs exhibited a concentration-dependent antimicrobial effect against ***S. aureus*** with doses exceeding 0.5 mg/l reducing amount of CFU to below detection limit ($p < 0.001$). 15 minutes exposure to ADC resulted in an approx. 2 log CFU/ml reduction compared to untreated biofilms ($p < 0.01$).
In vivo ADC treatment was effective compared to NaCl treatment and the vancomycin treatment ($p \leq 0.001$). Further ADC and MMC treatment were comparable in efficacy, but both were superior than NaCl, pure antibody and the non-specific ADC ($p \leq 0.05$). Finally, ***in vitro*** cytotoxicity was significantly lower for ADC than MMC.

Conclusions: In this study we have demonstrated that ADCs can be a novel treatment approach to combat implant-associated infections caused by ***S. aureus***.

[FP C6] EMERGING ROLES OF THE LONG PENTRAXIN PTX3 IN STAPHYLOCOCCUS AUREUS-DEPENDENT OSTEOMYELITIS

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Aim: Osteomyelitis (OM) is a debilitating infection of the bone that originates from hematogenous spreading of microbes or contamination after surgery/fracture. OM is mainly caused by the opportunistic bacterium ***Staphylococcus aureus*** (SA), which can evade the host immune response, acquire antibiotic resistance and chronically colonize the musculoskeletal tissue [1,2], yet the underlying molecular and cellular processes are largely unclear. This study aimed to characterize the pathogenetic mechanisms of SA-OM with a focus on the long pentraxin 3 (PTX3), a soluble pattern recognition molecule and bone tissue component that is emerging as a new player in osteoimmunology [3] and a diagnostic marker of periprosthetic joint infections, a common form of OM[4].

Method: A murine model of OM based on intra-bone injection of SA was developed that closely mimicked surgery/trauma-related OM in humans and allowed addressing the role of PTX3 in gene-modified (***Ptx3***$^{-/-}$) animals. Local and systemic infection and inflammation were assessed via microbiology, flow cytometry, histochemistry and microCT techniques.

Results: SA-injected mice developed chronic infection with measurable levels of viable bone-resident bacteria up until 30 days from microbial challenge. The infection was confined to the treated limbs only and accompanied by extensive tissue remodelling. The bacterial load was higher in WT than ***Ptx3***$^{-/-}$ animals at 6 and 14 days from SA injection. Accordingly, WT mice had enhanced systemic inflammation with expanded innate immune compartment in the spleen and increased serum levels of inflammatory cytokines and chemokines. PTX3 levels were higher in SA- than vehicle (PBS)-injected WT animals both in the serum and bone tissue. Furthermore, administration of a PTX3-targeting antibody reduced the bacterial burden in the bones of SA-injected WT mice.

Conclusions: In a mouse model of SA-OM, genetic deficiency of PTX3 protected from infection and inflammation, pointing to this pentraxin as a crucial player in OM pathogenesis and a novel therapeutic target in bone infections.

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[FP D1] BACTERIOPHAGE THERAPY IN ORTHOPEDIC AND CARDIOVASCULAR SURGERY: CLINICAL EXPERIENCE IN EIGHT PATIENTS WITH DIFFICULT-TO-TREAT INFECTIONS

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Aim: Antibiotics have limited activity in the treatment of multidrug-resistant or chronic biofilm-associated infections, in particular when implants cannot be removed. Lytic bacteriophages can rapidly and selectively kill bacteria, and can be combined with antibiotics. However, clinical experience in patients with surgical infections is limited. We investigated the outcome and safety of local application of bacteriophages in addition to antimicrobial therapy.

Method: 8 patients (2 female and 6 male) with complex orthopedic and cardiovascular infections were included, in whom standard treatment was not feasible or impossible. The treatment was performed in agreement with the Article 37 of the Declaration of Helsinki. Commercial or individually prepared bacteriophages were provided by ELIAVA Institute in Tbilisi, Georgia. Bacteriophages were applied during surgery and continued through drains placed during surgery three times per day for the following 5-14 days. Follow-up ranged from 1 to 28 months.

Results: Median age was 57 years, range 33-75 years. Two patients were diagnosed with a persistent knee arthrodesis infection, one chronic periprosthetic joint infection (PJI), one cardiovascular implantable electronic device (CIED) infection and four patients with left ventricular assist device (LVAD) infection. The isolated pathogens were multi-drug-resistant Pseudomonas aeruginosa (n=3), methicillin-sensitive Staphylococcus aureus (n=4), methicillin-resistant Staphylococcus aureus (MRSA) (n=1) and methicillin-resistant Staphylococcus epidermidis (MRSE) (n=1). 4 infections were polymicrobial.

5 patients underwent surgical debridement with retention of the implant, 1 patient with PJI underwent the exchange of the prosthesis and one patient with LVAD infection was treated conservatively. All patients received intravenous and oral antibiotic therapy and local application of bacteriophages. At follow-up of 12 month, 5 patients were without signs or symptoms of infection, whereas in one patient with LVAD infection, a relapse was observed with emergence of phage-resistant Pseudomonas aeruginosa. In this patient, no surgical revision was performed.

Conclusions: Bacteriophage therapy may represent a valid additional approach, when standard antimicrobial and surgical treatment is not possible or feasible, including in difficult-to-treat infections. In our case series, 5 of 6 patients were infection free after 1 year. Further studies need to address the optimal bacteriophage administration route, concentration, duration of treatment and combination with antimicrobials.

[FP D2] SYNERGISTIC ACTION OF BACTERIOPHAGE AND VANCOMYCIN IN A CO-DELIVERY HYDROGEL FOR LOCALIZED TREATMENT OF FRACTURE-RELATED INFECTION CAUSED BY METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS

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Aim: Bacteriophages are remerging as alternative and adjunctive therapy for fracture-related infection (FRI). However, current administration protocols involve prolonged retention of a percutaneous draining tube with potential risk of developing superinfection. In this study, we applied a cocktail of ***in vitro*** evolved biofilm-targeting phages for Methicillin-resistant ***Staphylococcus aureus*** (MRSA) in a hydrogel platform co-delivering vancomycin. ***In vitro*** synergy and antibiofilm activity was assessed and a subsequent ***in vivo*** study was performed in a mouse FRI model with MRSA.

Method: Two evolved bacteriophages (MRSA-R14 and COL-R23) with improved antibiofilm activity against a clinical isolate (MRSA3) were tested in combination with vancomycin and a carboxymethylcellulose (CMC) hydrogel ***in vitro*** and ***in vivo***. MRSA3 bacterial biofilms were formed on sterile 4 mm sintered porous glass beads at 37 °C for 24 h. Biofilms were exposed to ***i***-phage cocktail (10^7 PFU/ml), ***ii***-vancomycin at concentrations of 0.5, 1, 10 and 100 times the MIC, or ***iii***-combination of phage cocktail and vancomycin. Recovered biofilm cells, were quantified by colony counting. The stability and release profiles of phage cocktail and vancomycin in co-delivery hydrogel were assessed ***in vitro*** for 8 days and 72 hrs, respectively, and subsequently tested in the treatment of 5-day-old MRSA3 infection of a femoral plate osteotomy in mice.

Results: *In vitro*: The cocktail of evolved phages (10^7 PFU/ml, 1:1) combined with 0.5 MIC vancomycin achieved 99.72% reduction in MRSA3 biofilm ***in vitro*** compared to the growth control. This combination was stable in the co-delivery hydrogel over 8 days. The release profile showed that 57% of phages and 80% of vancomycin were released after 72hrs, which was identical to the performance for gels loaded with phage or antibiotic alone. In the ***in vivo*** study, the bacterial load from animals that received co-delivery hydrogel and systemic vancomycin was significantly reduced compared to controls, animals that received systemic vancomycin and animals that received co-delivery hydrogel alone ($p<0.05$).

Conclusions: Our study demonstrates the potential of using evolved phages in combination with vancomycin and hydrogel delivery systems for the treatment of MRSA-related infections. Further research in this area may lead to the development of specific therapies for biofilm-related infection.

[FP D3] ANTIBACTERIAL ACTIVITY OF NEW DEVELOPED MULTIELEMENT NANOGRANULAR COATINGS

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Aim: Antibacterial activity of coatings based on metal and metal oxide nanoparticles (NPs) often depends on materials and biotic targets resulting in a material-specific killing activity of selected Gram-positive and Gram-negative bacteria, including drug-resistant strains. In this perspective, the NPs loading amount, the relative elemental concentration inside the nanogranular building blocks and the deposition method are of paramount importance when the goal is to widen the antimicrobial spectrum, but at the same time to avoid high levels of metal content to limit undesired toxic effects. Aim of the present study was evaluation of the antimicrobial properties of two multielement nanogranular coatings composed of Titanium-Silver and Copper and of Magnesium-Silver and Copper.

Method: Ti-Ag-Cu and Mg-Ag-Cu NPs were deposited on circular cover glasses (VWR) by Supersonic Cluster Beam Deposition. Biofilm-producer strains of ***Staphylococcus aureus*** (methicillin susceptible and resistant), ***Staphylococcus epidermidis*** (methicillin susceptible and resistant), ***Escherichia coli*** (fully susceptible and producer of extended spectrum beta lactamases), and ***Pseudomonas aeruginosa*** (susceptible and multidrug-resistant) were selected. The abilities of the selected strains to adhere, colonize and produce biofilm on the discs coated with Ti-Ag-Cu or Mg-Ag-Cu NPs were compared to uncoated circular cover glasses which were used as growth control. Cytotoxicity was also evaluated in order to assess the biocompatibility of the newly synthesized NPs.

Results: In comparison to uncoated controls, both coatings showed significant anti-adhesive properties against ***S. aureus***, ***S. epidermidis***, and ***E. coli***. Reduction in adhesion to Mg-Ag-Cu coated discs was observed also for ***P. aeruginosa*** isolates, although differences vs uncoated controls did not reach statistical significance. Biofilm formation was reduced on discs coated with Mg-Ag-Cu compared to Ti-Ag-Cu and, again, coatings had a milder effect on ***P. aeruginosa***, probably due to its exceptional capability of attachment and matrix production. These results were confirmed by the evaluation of bacterial colonization on nanoparticles-coated discs by means of confocal laser scanning microscopy. A viability of 95.8% and 89.4% of cells cultured in the presence of Ti-Ag-Cu and Mg-Ag-Cu discs, respectively, when compared to negative controls was observed, thus excluding cytotoxic effects on eukaryotic cells.

Conclusions: The newly synthesized Ti-Ag-Cu and Mg-Ag-Cu coatings are able to limit bacterial adhesion colonization and biofilm production, thus highlighting the safe use of multi-element families of NPs as new strategies against bacterial attachment to the surface of biomedical implants. However, further studies addressing activity against ***P. aeruginosa*** and including a wide number of isolates are warranted.

[FP D4] NOVEL ANTIMICROBIAL COATING ON TITANIUM WITH STABLE NON-ANTIBIOTIC QUATERNARY AMMONIUM COMPOUNDS TO PREVENT IMPLANT-ASSOCIATED INFECTION

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Aim: The use of medical devices has grown significantly over the last decades, and has become a major part of modern medicine and our daily life. Infection of implanted medical devices (biomaterials), like titanium orthopaedic implants, can have disastrous consequences, including removal of the device. For still not well understood reasons, the presence of a foreign body strongly increases susceptibility to infection. These so-called biomaterial-associated infections (BAI) are mainly caused by ***Staphylococcus aureus*** and ***Staphylococcus epidermidis***. Formation of biofilms on the biomaterial surface is generally considered the main reason for these persistent infections, although bacteria may also enter the surrounding tissue and become internalized within host cells. To prevent biofilm formation using a non-antibiotic based strategy, we aimed to develop a novel permanently fixed antimicrobial coating for titanium devices based on stable immobilized quaternary ammonium compounds (QACs).

Method: Medical grade titanium implants (10×4×1 mm) were dip-coated in a solution of 10% (***w/v***) hyperbranched polymer, subsequently in a solution of 30% (***w/v***) polyethyleneimine and 10 mM sodium iodide, using a dip-coater, followed by a washing step for 10 min in ethanol. The QAC-coating was characterized using water contact angle measurements, scanning electron microscopy, FTIR, AFM and XPS. The antimicrobial activity of the coating was evaluated against ***S. aureus*** strain JAR060131 and ***S. epidermidis*** strain ATCC 12228 using the JIS Z 2801:2000 surface microbicidal assay. Lastly, we assessed the ***in vivo*** antimicrobial activity in a mouse subcutaneous implant infection model with ***S. aureus*** administered locally on the QAC-coated implants prior to implantation to mimic contamination during surgery.

Results: Detailed material characterization of the titanium samples showed the presence of a homogenous and stable coating layer at the titanium surface. Moreover, the coating successfully killed ***S. aureus*** and ***S. epidermidis in vitro***. The QAC-coating strongly reduced ***S. aureus*** colonization of the implant surface as well as of the surrounding tissue, with no apparent macroscopic signs of toxicity or inflammation in the peri-implant tissue at 1 and 4 days after implantation.

Conclusions: An antimicrobial coating with stable quaternary ammonium compounds on titanium has been developed which holds promise to prevent BAI. Non-antibiotic-based antimicrobial coatings have great significance in guiding the design of novel antimicrobial coatings in the present, post-antibiotic era.

[FP D5] NOBLE METAL-BASED ANTIBACTERIAL IMPLANT COATINGS FOR ARTICULATING IMPLANT SURFACES

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Aim: Prosthetic joint infections pose a major clinical challenge. Developing novel material surface technologies for orthopedic implants that prevent bacterial adhesion and biofilm formation is essential. Antimicrobial coatings applicable to articulating implant surfaces are limited, due to the articulation mechanics inducing wear, coating degradation, and toxic particle release. Noble metals are known for their antimicrobial activity and high mechanical strength and could be a viable coating alternative for orthopaedic implants [1]. In this study, the potential of thin platinum-based metal alloy coatings was developed, characterized, and tested on cytotoxicity and antibacterial properties.

Method: Three platinum-based metal alloy coatings were sputter-coated on medical-grade polished titanium discs. The coatings were characterized using optical topography and scanning electron microscopy with energy dispersive spectroscopy (SEM/EDS). Ion release was measured using inductively coupled plasma optical emission spectrometry (ICP-OES). Cytotoxicity was tested according to ISO10993-5 using mouse fibroblasts (cell lines L929 and 3T3). Antibacterial surface activity, bacterial adhesion, bacterial proliferation, and biofilm formation were tested with gram-positive Staphylococcus aureus ATCC 25923 and gram-negative Escherichia coli ATCC 25922. Colony forming unit (CFU) counts, live-dead fluorescence staining, and SEM-EDS images were used to assess antibacterial activity.

Results: Three different platinum-based metal alloys consisting of platinum-iridium, platinum-copper, and platinum-zirconium. The coatings were found 80 nm thick, smooth (roughness average < 60 nm), and non-toxic. The platinum-copper coating showed a CFU reduction larger than one logarithm in adherent bacteria compared to uncoated titanium. The other coatings showed a smaller reduction. This data was confirmed by SEM and live-dead fluorescence images, and accordingly, ICP-OES measurements showed low levels of metal ion release from the coatings.

Conclusions: The platinum-copper coating showed low anti-adhesion properties, even with extremely low metal ions released. These platinum-based metal alloy coatings cannot be classified as antimicrobial yet. Further optimization of the coating composition to induce a higher ion release based on the galvanic principle is required and copper looks most promising as the antimicrobial compound of choice.

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[FP D6] SHORT-TERM CELECOXIB PROMOTES BONE FORMATION WITHOUT COMPROMISING ANTIBIOTIC EFFICACY IN EARLY ORTHOPAEDIC DEVICE-RELATED INFECTION: EVIDENCE FROM A RAT MODEL

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Aim: In this study we investigated the effects of non-steroidal anti-inflammatory drugs (NSAIDs) with different cyclooxygenase (COX) selectivity on orthopaedic device-related infections (ODRIs) in a rat model. Specifically, we aimed to measure the impact of NSAID therapy on bone changes, bacterial load, and cytokine levels after treatment with antibiotics. In addition, we compared the effects of long vs short-term celecoxib (a COX-2 inhibitor) treatment on the same outcomes.

Method: Skeletally mature female Wistar rats were implanted with ***Staphylococcus epidermidis***-contaminated polyetheretherketone (PEEK) screws (1.5 x 10^6 CFU per screw) in the proximal right tibia and monitored for 7 days. All animals received subcutaneous antibiotics (rifampicin plus cefazolin) for two weeks from day 7 to 21. In phase I of the study, rats were randomly assigned to receive 28 days of oral treatment with acetylsalicylic acid, ibuprofen, celecoxib, or vehicle control. In phase II, an additional group received seven days of celecoxib treatment from day 0 to 7. After implantation, bone changes were monitored using ***in vivo*** micro-CT and histology. Quantitative bacteriology was performed at euthanasia. Plasma samples were collected to measure cytokine levels at four time points (day 0, 6, 20, and 28).

Results: The combination of antibiotic therapy resulted in treatment success in 85.71% of cases, while the addition of long-term celecoxib treatment reduced it to 45.45%. Long-term celecoxib treatment significantly reduced bone loss (33.85% mean difference [95% CI 14.12-53.58], p=0.0004 on day 6 bone fraction) and periosteal reaction (0.2760 µm mean difference [95% CI 0.2073-0.3448], p<0.0001 on day 14 periosteal thickness) during the early post-infection period compared to the control group. Short-term celecoxib treatment showed similar radiological results, however, there was no significant reduction in treatment success in the celecoxib group (88.9%). No differences in the selected inflammatory markers were observed.

Conclusion: Our findings highlight the potential benefits of short-term use of celecoxib in improving bone fraction during the early post-infection period without impairing the efficacy of antibiotic therapy. This study suggests that celecoxib may be a useful addition to the multimodal approach to pain management in orthopaedic device-related infections.

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[FP E1] ANTIBIOTIC PROPHYLAXIS FOR ENDOPROSTHETIC REPLACEMENTS IMPLANTED FOR MUSCULOSKELETAL TUMOURS: AN INTERNATIONAL SURVEY OF PRACTICE

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Aim: Deep infection following endoprosthetic replacement (EPR) of long bones is a devastating complication occurring in 15% of musculoskeletal tumour patients. The recently published PARITY Trial demonstrated that extending antibiotic prophylaxis from 24 hours to 5 days does not reduce infection rates. However, questions remain about the optimal antibiotic choice and dose.

Method: A 23-question multiple-choice questionnaire was designed and piloted through an iterative feedback process until the final version was agreed by all authors. Open and closed-ended questions were used to gather information on practice and Likert-type scale responses were used to grade responses to ascertain surgeon perceptions and preferences. The online survey was sent to all surgeon delegates of the 34th Annual Meeting of the European Musculo-Skeletal Oncology Society in London in October 2022.

Results: Amongst 61 respondents, 43 were based in Europe and 18 outside of Europe. The majority (48/61) had been in clinical practice over 11 years.

Antibiotic choice

1st or 2nd generation cephalosporins were the first line choice practiced among 49 (80.3%) of respondents. Of these, 39 responded had a 2nd line protocol for beta-lactam allergy which was most commonly clindamycin (18), vancomycin (11) or a combination of a glycopeptide or clindamycin plus gentamicin (4). Respondents changed their first line regimen for radiotherapy in 6/61, chemotherapy in 8/61 and tumour site in 20/61.

Re-dosing

Intraoperative re-dosing intervals of 1st and 2nd generation cephalosporins ranged from 2 to 8 hourly. Re-dosing for blood loss ranged from never to when 2 litres was lost. Of the 47 respondents, 24 said intraoperative re-dosing is always reliably administered.

Duration

Six (10%) of 61 respondent routinely cover the intraoperative period only, whereas 30 (49%) give 24 hours, 16 (give 48 hours or longer and 8 continue until surgical drains are removed. 31 of 61 change duration depending on clinical situation. The most common reasons for changing were patient risk factors, soft tissue status and previous radiotherapy. 40/61 surgeons were aware of the PARITY Trial. When these respondents were asked whether they had changed practice based on PARITY, 10 said yes, 14 said no and 16 said they always give 24 hours anyway.

Conclusions: Amongst an international cohort of orthopaedic oncology surgeons there was a wide variation in practice. Further research should focus on the optimum choice and re-dosing strategy, which have not been defined.

[FP E2] RISK FACTORS FOR FRACTURE-RELATED INFECTION AFTER ANKLE FRACTURE SURGERY

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Aim: Ankle fracture surgery comes with a risk of fracture-related infection (FRI). Identifying risk factors are important in preoperative planning, in management of patients, and for information to the individual patient about their risk of complications. In addition, modifiable factors can be addressed prior to surgery. The aim of the current paper was to identify risk factors for FRI in patients operated for ankle fractures.

Method: A cohort of 1004 patients surgically treated for ankle fractures at Haukeland University hospital in the period of 2015-2019 was studied retrospectively. Patient charts and radiographs were assessed for the diagnosis of FRI. Binary logistic regression was used in analyses of risk factors. Regression coefficients were used to calculate the probability for FRI based on the patients' age and presence of one or more risk factors.

Results: FRI was confirmed in 87 (9%) of 1004 patients. Higher age at operation ($p < 0.001$), congestive heart failure (CHF), $p = 0.006$), peripheral artery disease (PAD, $p = 0.001$), and current smoking ($p = .006$) were identified as risk factors for FRI. PAD and CHF were the risk factors displaying the strongest association with FRI with an adjusted odds ratio of 4.2 (95% CI 1.8-10.1) and 4.7 (95% CI 1.6-14.1) respectively.

Conclusions: The prevalence of FRI was 9% after surgical treatment of ankle fractures. The combination of risk factors found in this study demonstrate the need for a thorough, multidisciplinary, and careful approach when faced with an elderly or frail patient with an ankle fracture. The results of this study help the treating surgeons to inform their patients of the risk of FRI prior to ankle fracture surgery.

Table 2 - Logistic regression model of risk factors for Fracture-related infection

	aOR (95% C.I.)	P-value
Female Sex	0.7 (0.4-1.1)	0.1
Age by 10 year interval	1.3 (1.1-1.5)	<0.001
Current smoking status	2.1 (1.2-3.5)	0,006
Congestive heart failure	4.7 (1.6-14.1)	0,006
Peripheral arterial disease	4.2 (1.8-10.1)	0,001

Logistic model of risk factors for Fracture Related infection. aOR - adjusted Odds Ratio. C.I. - Confidence interval

Table 3 - Probability of developing FRI based on the identified risk factors

	Probability in %
18 year old patient, no risk factors	1
50 year old patient, no risk factors	3
50 year old patient, current smoker	7
70 year old patient, no risk factors	5
80 year old patient, no risk factors	6
80 year old patient, current smoker	12
80 year old patient with heart failure	24
80 year old patient with PAD	26
80 year old patient with PAD and current smoker	37
80 year old patient with heart failure and current smoker	39
80 year old patient with PAD and heart failure	57
80 year old patient with PAD, current smoking and heart failure	73

Calculation of probabilty of developing FRI based on the identified risk factors from Table 2. PAD: Peripheral Artery Disease.

[FP E3] BACTERIAL RESERVOIR IN DEEPER SKIN IS A POTENTIAL SOURCE FOR SURGICAL SITE AND BIOMATERIAL-ASSOCIATED INFECTIONS

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Aim: The origin of surgical site and biomaterial-associated infection is still elusive. Microorganisms contaminating the wound may come from the air, the surgical team, or from the skin of the patient. Prior to surgery the skin of patients is disinfected, but bacteria deeper in the skin (***e.g.*** in sweat glands or sebaceous glands), may not be reached. This study aims to assess a potential role of this intracutaneous bacterial reservoir in biomaterial-associated infection.

Method: To study if cutaneous microbiota colonize the wound when released from the skin upon cutting, we isolated, quantified and identified aerobic and anaerobic bacteria from the skin of 99 patients undergoing trauma surgery, before and after skin disinfection, from the knife blades and from the wound directly after the first cut.

Results: Ninety-nine percent of the patients were culture-positive before disinfection with chlorhexidine. Of these, 40% were still culture-positive after disinfection. Of these, 54% had a positive culture of the wound after the skin cut. Twenty percent of the patients with a negative culture after disinfection, nevertheless had a positive wound culture after cutting the skin. ***Staphylococcus epidermidis*** and ***Cutibacterium acnes*** were the most often cultured bacterial species. In 9%, more than 100 bacterial colonies were cultured from the wound, a dose that may cause biomaterial-associated infections.

Conclusions: Bacteria residing in the skin and not eradicated by disinfection may enter the surgical wound upon cutting, resulting in contamination which may cause a biomaterial-associated infection. Use of two knifes likely reduces the risk of wound contamination.

[FP E4] THE ORACLE STUDY: OPEN FRACTURE RISKS ASSOCIATED WITH INFECTION – A COHORT LONGITUDINAL EVALUATION STUDY OF 517 OPEN FRACTURES ACROSS 20 YEARS

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Aim: Open fractures incur high risk of infection and morbidity. We adopted a data-driven approach to quantify variables associated with open fracture-related infections (FRI), and constructed a nomogram for clinical risk assessment.

Method: Open fractures treated at a trauma centre during a 20-year-period with minimal 6-month-follow-up were investigated, with evaluation of 110 potential confounders. FRI diagnosis was adjudicated by a microbiologist and orthopaedic surgeon per international consensus criteria. Multivariate logistic regression with Cox proportional hazards model was performed.

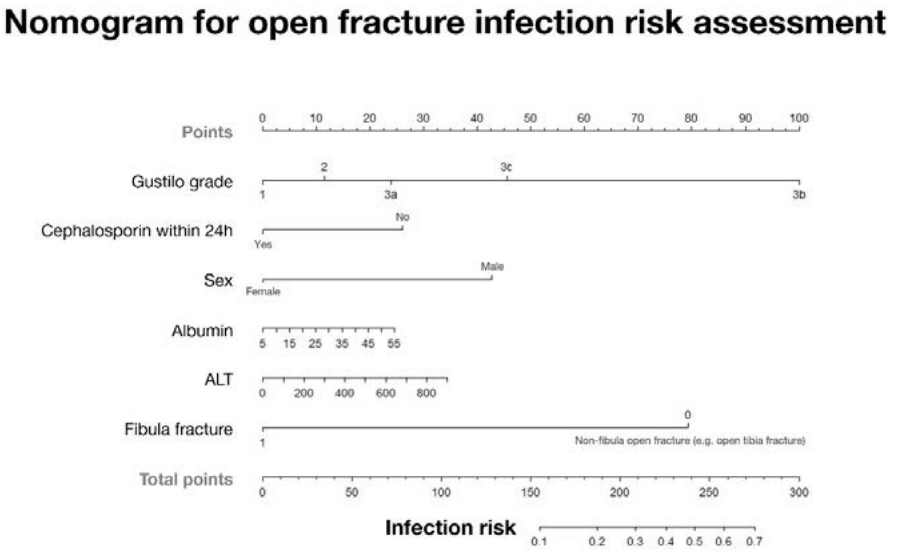
Results: 517 open fractures (359 male, 158 female) were analysed, of which 68 (13.2%) developed infection. Methicillin-resistant ***Staphylococcus aureus*** (N=22, 32%FRI), non-fermenters e.g. ***Pseudomonas aeruginosa*** (N=21,31%FRI), and Enterobacterales (N=19,28%FRI) were most frequently cultured.

Multivariate analysis identified Gustilo IIIB injuries (adj HR 11.2, p<0.001), male sex (adj HR 4.3, p=0.008), and albumin (adj HR 1.1, p=0.015) as significant predictors. Cephalosporin administration within 24 hours was associated with reduced infection risk (adj HR 0.4, p=0.004).

Staphylococcal FRIs were associated with immunocompromise (adj HR 6.5, p=0.019), and blood transfusion (adj HR 1.16, p=0.029). Gram-negative rod infections were associated with higher Charlson comorbidity index (adj HR 1.86, p=0.047), and operation performed after-hours (adj HR 4.8, p=0.006).

A nomogram is presented for ease of clinical risk assessment.

Conclusions: Cephalosporin was associated with decreased risk of infection and should be administered early for open fractures. Patients with comorbidities and after-hours surgery should be given antibiotics effective against Gram negative rods. Vigilance against immunocompromise and judicious blood transfusion could guard against the risk of staphylococcal infection.



[FP E5] RISK ANALYSIS OF PERIPROSTHETIC KNEE JOINT INFECTION (PJI) IN TOTAL KNEE ARTHROPLASTY AFTER PREOPERATIVE CORTICOSTEROID INJECTION: A SYSTEMATIC REVIEW

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Purpose: Intra-articular corticosteroid injection is widely used for symptomatic relief of knee osteoarthritis. However, if pain is not improved which consequences a total knee arthroplasty (TKA), there is a potential risk of post-operative periprosthetic joint infection (PJI). The aim of this study is to investigate whether the use of preoperative intra-articular corticosteroid injection increases the risk of PJI and to investigate a time frame in which the risk of subsequent infection is significantly increased.

Methods: A systematic search was performed in PubMed (Medline), Scopus, and the Cochrane Library. Inclusion criteria were original studies investigating the rate of PJI in patients receiving preoperative intra-articular corticosteroid injection compared to controls.

Results: A total of 380 unique articles were screened. Six studies met the inclusion criteria with 255,627 patients in total. Overall, no statistical significance was observed in the intra-articular infection rate in corticosteroid compared to controls groups. However, intra-articular corticosteroid injections within 3 months prior to TKA were associated with a significantly increased risk of infection (OR: 1.52, 95% CI 1.37-1.67, p < 0.01); this was not observed in the 6 month period (OR: 1.05, 95% CI 0.80-1.39, p = 0.72).

Conclusions: Performing an intra-articular corticosteroid injection within 3 months prior to TKA is associated with a significantly increased risk of PJI. The current evidence supports the safe use of intra-articular corticosteroid injection more than 6 months before TKA. However, additional studies are needed to clarify the risk of PJI after TKA implantation between 3 and 6 months after the last corticoid injection.

[FP E6] RISK FACTORS AND OUTCOME OF POLYMICROBIAL PROSTHETIC JOINT INFECTIONS COMPARED TO MONO MICROBIAL: A SINGLE- INSTITUTION REVISION OF 536 PATIENTS

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Aim To describe the risk factors, microbiology and treatment outcome polymicrobial prosthetic joint infections (PJI) compared to monomicrobial PJI.

Methods Between January 2011 and December 2021, a total of 536 patients were diagnosed with PJI at our institution. Clinical records were revised, and 91(16.9%) had an isolation of two or more pathogens. Age, sex, previous conditions, Charlson comorbidity score, previous surgery, PJI diagnosis and surgical and antibiotic treatment, from the index surgery onwards were reviewed and compared between groups.

Results: Polymicrobial PJI success rate was 57.1%, compared to 85.3% of the monomicrobial PJI(p=0.0036). There were no statistically significative differences between acute and chronic infections. In terms of related risk factors, revision surgery(p=0.0002), fracture(p=0.002), tobacco(p=0.0031) and Body Mass Index (BMI) between 20-25(p=0.0021) were associated to monomicrobial PJI, whereas overweight(p=0.005) and obesity(p=0.02) were linked to polymicrobial PJI. Regarding pathogens, the most common microorganism isolated in monomicrobial was ***S.aureus*** (33.5%), followed by ***S. epidermidis***(20%) and gram negative bacilli (12.2%); while ***S. epidermidis***(56%), gram negative bacilli (41.8%) and ***E.colli*** (30.8%) were the most frequent in the polymicrobial PJI. Enterococci(p=0.0008), ***S. epidermidis***(p=0.007), ***E.colli*** (p=0.0008), gram negative bacilli (p=0.00003) and atypical bacteria (p=0.00001) statistically significative linked to polymicrobial PJI; while ***S.aureus*** (p=0.018) was related to monomicrobial PJI

Conclusion: Polymicrobial PJI showed worse outcome compared to monomicrobial PJI in our cohort. In terms of risk factors, overweight, obesity and some pathogens like gram negative bacilli, atypical bacteria, enterococci, ***S. epidermidis*** and ***E.colli*** were associated with Polymicrobial PJI

[FP E7] CAN A DIABETIC FOOT ULCER BE PREVENTED?

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Aim: The aim of this paper is to analyse the cause of neuropathic diabetic foot ulcers and discuss their preventive measures.

Methods: Review of patients with foot ulcers managed in our diabetic MDT clinics since Feb 2018 were analysed. Based on this observation and review of pertinent literature, following observations were made.

Results: Forefoot- Progressive hindfoot equinus from contraction of gastroc-soleus-tendo-Achilles complex, with additional contraction of tibialis posterior and peroneal longus muscles and, progressive plantar flexed metatarsal heads secondary to claw toe deformity results in increased forefoot plantar pressures. In patients with insensate feet, this result in ulcer formation under the metatarsal heads from shear stress when walking.

Callosity under the metatarsal heads is the earliest clinical sign. Most patients by this time have fixed tightness of the muscle groups as assessed by negative Silfverskiold test. Percutaneous tendo-Achilles lengthening (TAL) has shown to reduce the mid-forefoot plantar pressures by 32% and ulcer healing in 96% of patients within 10 weeks (± 4 weeks). Additional z-lengthening of peroneal longus and tibialis posterior tendons helped in patients with big-toe and 5th metatarsal head ulcers. Proximal metatarsal osteotomies further reduce the forefoot pressures to near normality.

Midfoot- Midfoot ulcers are secondary to rocker-bottom deformity a consequence of Charcot neuroarthropathy (CN). Hindfoot equinus as described and relative osteopenia from neurally mediated increased blood flow (neurovascular theory) and repeated micro-trauma (neurotraumatic theory) result in failure of medial column osseo-ligamentous structures. As the disease progress to the lateral column, the cuboid height drops resulting in a progressive rocker bottom deformity. The skin under this deformity gradually breaks down to ulceration.
In the pre-ulcerative stages of midfoot CN, TAL has shown to stabilise the disease progression and in some patents' regression of the disease process was noted. The lump can excised electively and the foot accommodated in surgical shoes.

Hindfoot- These develop commonly at the pressure areas and bony exostosis in non-ambulatory patients. In ambulatory patients, the most common cause are factors that result in over lengthening of tendo-Achilles such as after TAL, spontaneous tears, or tongue-type fractures.

Conclusions: Early identification of factors that result in plantar skin callosity and treating the deforming forces prevent progression to ulceration. Total contact cast without treatment of these deforming forces results in progression of these callosities to ulceration while in the cast or soon after completion of cast treatment.

[FP E8] A 2-STAGE APPROACH IN MANAGING DIABETIC NEUROPATHIC FOREFOOT ULCERS.

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Aim: To describe a 2-stage treatment pathway for managing neuropathic forefoot ulcers and the safety and efficacy of percutaneous tendo-Achilles lengthening (TAL) in out-patient clinics.

Methods: Forefoot ulcers in patients with diabetic neuropathy are a result of factors that result in increased forefoot plantar pressure. Plantar flexed metatarsal heads secondary to progressive claw toe deformity and hindfoot equinus from changes within the gastrocnemius-soleus-tendo-Achilles complex, with additional contraction of tibialis posterior and peroneal longus, secondary to motor neuropathy results in progressive increase in forefoot plantar pressures.

Consecutive patients, who presented to our Diabetic Foot clinic since February 2019 with forefoot ulcers or recurrent forefoot callosity were treated with TAL in the first instance, and in patients with recurrent or non-healing ulcers, by proximal dorsal closing wedge osteotomy; a 2-stage treatment pathway.

Patients were followed up at 3, 6, and 12 months to assess ulcer healing and recurrence.

Results: One hundred and twelve patients (146 feet) underwent TAL by 3 consultants in the out-patient clinics. Of these, 96 feet were followed for a minimum of 12 months (range 12-36 months). None had infection or wound related problems at the tenotomy sites; complete transection of the tendon was noted in 4 patients (4%) and one-patient developed heel callosity suggestive of over-lengthening.

In 92 feet (96%), the ulcers healed within 10 weeks (± 4 weeks). Additional z-lengthening of peroneal longus and tibialis posterior tendons helped in patients with big-toe and 5th metatarsal head ulcers.

In 12 feet (10%), the ulcer failed to heal or recurred, the MRI scan in these patients showed plantar flexed metatarsals secondary to progressive claw toe deformity. The ulcer in this group healed after surgical offloading with proximal dorsal closing wedge osteotomy. In patients with osteomyelitis, the intramedullary canal was curetted and filled with local antibiotic eluting agents such as Cerament G®. The osteotomy site was stabilised with a percutaneous 1.6mm k-wire.

Conclusion:
The described 2-stage treatment pathway results in long-term healing of neuropathic forefoot ulcers, and in 96% of patients, the ulcer healed after out-patient percutaneous TAL alone. TAL is a safe and effective initial out-patient procedure with improved patient outcomes.

[FP E9] SINGLE-STAGE ORTHOPLASTIC MANAGEMENT OF CALCANEAL OSTEOMYELITIS: AN ANALYSIS OF OUTCOMES

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Aim: This study assesses the outcomes of single stage orthoplastics surgical treatment of chronic osteomyelitis of the calcaneus requiring concurrent soft tissue reconstruction.

Method: We performed a retrospective review of all patients who underwent combined single-stage orthoplastics surgical treatment of calcaneal osteomyelitis between 2008 and 2022. Primary outcome measures were recurrence of osteomyelitis and requirement for amputation. Secondary outcome measures included; flap failure, operative time, length of hospital stay, and number of out-patient appointments.

Results: In total, 33 patients (16 female, mean age 54.4 years (95% confidence interval (CI) 48.8-60.0)) with Cierny and Mader IIIB calcaneal osteomyelitis were included; 20 received a local flap, 13 received a free flap. Fracture-related infection was the most common aetiology of infection (n=13), followed by pressure ulceration (n=6) and diabetic ulceration (n=5). A least one previous surgical intervention had been performed in 23 patients prior to orthoplastic surgery. Polymicrobial infections were present in 20 cases with ***Staphylococcus spp*** the most common isolate (n=17). A local antibiotic carrier was used for dead space management in 27 patients. The median follow-up period was 28 months (range 2-169).

Surgery was successful in 26 cases with seven cases of recurrent osteomyelitis, one of whom required a below-knee amputation. Peripheral vascular disease (Odds Ratio (OR) 39.7 (95% CI 1.7-905.6), p=0.006) and local flap reconstruction (OR 15 (95% CI 0.8-289.6), p=0.027) were risk factors for recurrent infection. Recurrent osteomyelitis was associated with an increased risk of mortality (OR 18.8 (95% CI 1.5-227.8), p=0.004) with a median time to death 22 months (95% CI 0-69). Recurrence was also associated with a lower likelihood of walking independently following surgery (OR 0.14 (95% CI 0.02-0.86), p=0.042), as well as patients wearing their own footwear (OR 0.16 (95% CI 0.02-1.45), p=0.030)

There was a statistically significant difference in mean length of surgery between local flap and free flap reconstruction (181.3 vs 448.4 minutes; p<0.001) but no statistically significant differences in length of hospital stay (12 vs 14 days, p=0.888) or frequency of out-patient appointments (9.1 vs 8.9 appointments, p=0.942).

Conclusions: Single-stage orthoplastic management was associated with 79% eradication of infection and 3% amputation, in this complex and co-morbid patient series. Risk factors for failure after orthoplastic reconstruction were peripheral vascular disease (OR 39.7) and local flap reconstruction (OR 15). Whilst good clinical and functional outcomes can be achieved for patients using this treatment strategy, it requires high levels of both in-patient and out-patient care.

[FP F1] AMOXICILLIN IN DEEP-SEATED SAMPLES – QUANTIFICATION OF A DELICATE COMPOUND

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Aim: Antibiotic concentration at the infected site is a relevant information to gain knowledge about deep-seated infections. The combination of antibiotic therapy and debridement is often indicated to treat these infections. At University Hospital Basel the most frequently administered antibiotic before debridement is amoxicillin in combination with clavulanic acid. Amoxicillin is a fragile beta-lactam antibiotic that brings multiple challenges for its quantification.
As for many sample materials only little material is available, the aim of this work was to establish a sensitive and reliable quantification method for amoxicillin that only requires a small sample mass. We did not quantify clavulanic acid as we focused on the drug with antibiotic action.

Method: Usually discarded sample material during debridement was collected and directly frozen. The thawed tissues were prepared using simple protein precipitation and manual homogenization with micro pestles followed by a matrix cleanup with online solid-phase extraction. Separation was performed by HPLC followed by heated electrospray ionization and tandem mass spectrometry.

Results: During method development, amoxicillin showed partial formation of a covalent methanol adduct when performing protein precipitation. Furthermore, multiple in-source products of amoxicillin during ionization could be observed. Adding an aqueous buffer to the samples before protein precipitation and summing up the signals of amoxicillin and its in-source acetonitrile-sodium-adduct led to successful method validation for a calibration range of 1-51 mg/kg using 10 mg of each tissue sample. The imprecision was < 8% over the entire concentration range and the bias was ≤ 10 %. The quantitative matrix effect was < 6 % in six different tissue samples.
Until now we measured amoxicillin in samples from nine patients with prosthetic joint infection, bursitis, or an abscess who obtained amoxicillin between 5 hours and 15 minutes before sampling and found concentrations between 1.4 and 35 mg/kg.

Conclusions: With this method, we developed a fast, simple, and sensitive quantification assay for amoxicillin in tissue samples with little material that can now be applied to different study samples.

[FP F2] STEADY-STATE PIPERACILLIN CONCENTRATIONS IN THE PROXIMITY OF AN ORTHOPEDIC IMPLANT: A MICRODIALYSIS PORCINE STUDY

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Background and aim: Implant-associated osteomyelitis is one of the most feared complications following orthopedic surgery. Although the risk is low it is crucial to achieve adequate antibiotic concentrations proximate to the implant for a sufficient amount of time to protect the implant surface and ensure tissue integration. The aim of this study was to assess steady-state piperacillin concentrations in the proximity of an orthopedic implant inserted in cancellous bone.

Method: Six female pigs received an intravenous bolus infusion of 4 g/0.5 g piperacillin/tazobactam over 30 min every 6 h. Steady state was assumed achieved in the third dosing interval (12–18 h). Microdialysis catheters were placed in a cannulated screw in the proximal tibial cancellous bone, in cancellous bone next to the screw, and in cancellous bone on the contralateral tibia. Dialysates were collected from time 12 to 18 h and plasma samples were collected as reference.

Results: Time above the minimal inhibitory concentration (*f*T>MIC) was evaluated for MIC of 8 (low target) and 16 µg/mL (high target). For the low piperacillin target (8 µg/mL), comparable mean *f*T>MIC across all the investigated compartments (mean range: 54–74%) was found. For the high target (16 µg/mL), *f*T>MIC was shorter inside the cannulated screw (mean: 16%) than in the cancellous bone next to the screw and plasma (mean range: 49–54%), and similar between the two cancellous bone compartments.

Conclusions: To reach more aggressive piperacillin *f*T>MIC targets in relation to the implant, alternative dosing regimens such as continuous infusion may be considered.

[FP F3] IS DÉLAFLOXACINE A THERAPEUTIC OPTION FOR BONE AND JOINT INFECTIONS? A CRIOGO MULTICENTER RETROSPECTIVE STUDY

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Abstract Background: The treatment of bone and joint infections (BJI) involving multi-drug resistant bacteria remains a challenge. MDR ***Staphylococcus epidermidis*** (MDRSE) clones, resistant to methicillin, clindamycin, levofloxacin, rifampicin and even linezolid, have been reported worldwide. The interest of delafloxacin (DFX), theoretically active on MRSA, remains to be evaluated with respect to MDRSE.

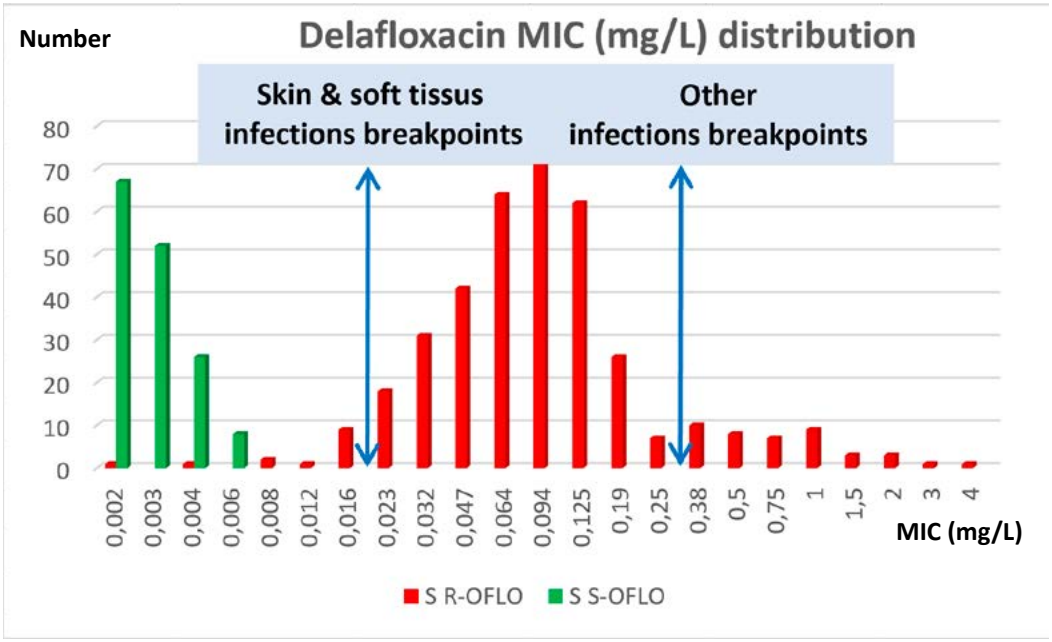
Purpose: Our objective was to evaluate during a retrospective multicenter study the DFX minimal inhibitory concentrations (MICs) and compare its efficacy between ofloxacin-susceptible and ofloxacin-resistant ***S. epidermidis*** clinical strains involved in BJI.

Methods: In this multicenter retrospective study (Reference centers from the West part of France, CRIOGO), 529 strains were collected mostly from BJI. DFX MICs were determined by using a 0.5 Mc Farland bacterial inoculum on Mueller-Hinton agar plates with gradient strips incubated for 24h at 35°C. For ***S. aureus***, breakpoints differentiate skin and soft tissue infections from other infections. Breakpoints followed 2022 EUCAST criteria, with ***S. aureus*** values adopted for ***S. epidermidis.***

Results: Of the 529 strains collected, 355 were from prosthetic infections, 159 from synthetic infections and 15 from non-device infections. 152 strains were susceptible to ofloxacin (110 males ***vs*** 42 females) and 377 resistant (210 ***vs*** 167). As presented in Figure 1, all the ofloxacin-susceptible strains presented a DFX MIC ≤0.006mg/L. Resistant strains presented a double population distribution, with 3.7% categorized susceptible according to skin and soft tissues infections breakpoint, against 88.9% according to other breakpoint infections (0.016 or 0.25mg/L respectively).

Conclusion: DFX shows excellent activity against ofloxacine-susceptible strains. Concerning the ofloxacin-resistant strains, more than 80% strains or less than 10% can be considered as DFX-susceptible depending on the breakpoints used. Further clinical studies are needed to validate the real breakpoints that must be used in MDRSE BJI, allowing a microbiological cure and a favourable clinical outcome.

Figure 1: Comparison of Delafloxacin MIC distribution between *S. epidermidis* ofloxacin-susceptible and ofloxacin-resistant strains involved in bone and joint infections.



[FP F4] BONE AND SOFT TISSUE CONCENTRATIONS OF PENICILLIN - IS ORAL PENICILLIN V NON-INFERIOR TO INTRAVENOUS PENICILLIN G?

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Aim: The β-lactam penicillin is often used in the treatment of soft tissue infections and osteomyelitis caused by penicillin susceptible ***Staphylococcus aureus***. Oral antibiotic treatment has been shown to be non-inferior to intravenous (IV) therapy when used during the first 6 weeks in complex orthopedic infections (OVIVA trial). However, the use of oral β-lactams in osteomyelitis treatment remains a topic of debate due to low and variable bioavailability. The aim was to assess the time for which the unbound penicillin concentration exceeded targeted minimum inhibitory concentrations (*f*T>MIC) in cancellous bone and subcutaneous tissue after IV (penicillin G) and oral (penicillin V) treatment in a porcine microdialysis model.

Method: 12 female pigs (75kg) were assigned to standard clinical regimens of either three doses of IV penicillin G (1.2g) or oral penicillin V (0.8g) every 6h over 18h. Microdialysis catheters were placed for sampling in tibial cancellous bone and adjacent subcutaneous tissue. Data was collected in the first dosing interval (0-6h; prophylactic situation) and the third dosing interval (12-18h; assumed steady state). Plasma samples were collected for reference. MIC targets of 0.125µg/mL (***Staph. aureus*** breakpoint), 0.25µg/mL (***Strep.*** Group A, B, C and G breakpoint) and 0.5µg/mL (4xMIC) were applied.

Results: For all investigated MIC targets, IV penicillin G resulted in a longer mean *f*T>MIC in cancellous bone during the first dosing interval, and in both cancellous bone and subcutaneous tissue during the third dosing interval compared to oral penicillin V. Across compartments, mean *f*T>MIC for IV penicillin G (MIC: 0.125, 0.25 and 0.5µg/mL) were ≥97%, ≥84% and ≥75% during the first dosing interval, and 100%, ≥95% and ≥88%, during the third dosing interval. The mean *f*T>MIC for oral penicillin V were ≥40%, ≥24% and ≥7% during the first dosing interval, and ≥42%, ≥36% and ≥18% during the third dosing interval.

Conclusions: The findings suggest that standard clinical dosing of IV penicillin G provides superior *f*T>MIC in cancellous bone and subcutaneous tissue compared to oral penicillin V, particularly in the third dosing interval. This emphasizes the importance of appropriate route of administration when applying penicillin treatment.

Acknowledgements: Funding was received from The Kirsten and Freddy Johansen Foundation, The Novo Nordisk Foundation, The Beckett Foundation, The Hede Nielsen Family Foundation, King Christian the 10th Foundation, The A.P. Møller Foundation, The Dagmar Marshalls Foundation, and The Carl and Ellen Hertz Foundation.

[FP F5] LOCAL ANTIBIOTIC DELIVERY VIA INTRA-ARTICULAR CATHETER INFUSION FOR THE TREATMENT OF PERIPROSTHETIC JOINT INFECTION: A SYSTEMATIC REVIEW

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Aim: The objective of this systematic review is to evaluate the current evidence for or against this up-and-coming treatment modality.

Method: A comprehensive literature search in accordance with the Preferred Reporting Items for Systematic review and Meta-analysis (PRISMA) guidelines was conducted using PubMed, Embase, MEDLINE and Cochrane databases. Exclusion criteria included patients < 18 years of age, fungal infections, follow-up < 11 months, and a score < 6 on the National Institute of Health quality assessment tool.

Results: 15 articles were included in the final analysis, all level IV case series. The quality of almost all studies was impeded by a retrospective design (14/15), a relative small study population (10 out of 15 studies had less than 50 patients), selection bias and remarkable heterogeneity in terms of catheter type, antibiotic type, dose and duration of intra-articular (IA) antibiotics or techniques of surgical revision. This review included data on 561 periprosthetic joint infections (PJIs) (in 556 patients); 460 were chronic infections and 101 acute infections. The majority was treated with single-stage revision with adjuvant IA antibiotic infusion (429/561, 76.5%), the remaining PJIs were treated with stand-alone IA antibiotic infusion (77/561, 13.7%), DAIR with IA antibiotic infusion (36/561, 6.5%) or two-stage revision with IA antibiotic infusion (19/561, 3.4%). Mean duration of IA antibiotic infusion was 30.4 days (range 3-50), although it should be noted that most patients received a combination of IA and systemic (IV or PO) antibiotics. An overall failure rate of approximately 10% was found. The use of IA antibiotic infusion as a stand-alone treatment was associated with a higher failure rate than using it as an adjuvant treatment. In total 117 complications occurred in 561 joints (20.9%). Of these, 71 were non-catheter-related complications (60.7%) and 46 were catheter-related (39.3%). The most common catheter-related complications were (1) premature loss of the catheter (18/56), (2) elevated blood urea nitrogen (BUN) and creatinine levels (12/56) and (3) developing a fistula (5/56).

Conclusions: Due to the lack of comparative studies the added benefit of IA antibiotic infusion in the treatment of PJI remains uncertain, although it seems likely that it should not be used as a stand-alone treatment. A prospective randomized controlled trial using a well-described infusion protocol is needed to see if the potential benefits justify the increased costs, labour and catheter-related complications of this adjuvant treatment modality.

[FP F6] STRUGGLING WITH A CEFAZOLIN IMPREGNATION PROTOCOL OF BONECHIPS. THE EFFECT OF THE TIMING OF THE IMPREGNATION AND GAMMA IRRADIATION ON THE CEFAZOLINE RELEASE

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Aim: Local antibiotics released through a carrier is a commonly used technique to prevent infection in orthopaedic procedures. An interesting carrier in aseptic bone reconstructive surgery are bone chips impregnated with AB solution. Systemically administered Cefazolin (CFZ) is used for surgical site infection prophylaxis however in vitro study showed that fresh frozen and processed bone chips impregnated with CFZ solution completely release the CFZ within a few hours. On the other hand irradiated freeze-dried bone chips, treated with supercritical CO2 (scCO2) have been shown to be an efficient carrier for the antibiotics vancomycine or tobramycine.
With this pilot study we wanted to investigate if CFZ solution impregnation of bone chips treated with scCO2 shows a more favorable release pattern of CFZ.

Method: The bone chips were prepared using the standard scCO2 protocol and were impregnated with 100 mg/ml cefazolin at different timepoints during the process: before freeze drying (BC type A), after freeze drying (BC type B) and after gamma-irradiation. 0.5g of the impregnated bone grafts were incubated with 5ml of fetal calf serum (FCS) at 37°C. At 2, 4, 6, 8 and 24h of incubation 200µl of eluate was taken for analysis. After 24h the remaining FCS was removed, bone grafts were washed and new FCS (5ml) was added. Consecutive eluate samples were taken at 48, 72 and 96h of incubation.
The concentration of CFZ in the eluates was measured with the validated UPLC-DAD method. Analysis was performed in triplicate.

Results: The mean concentration of CFZ in the eluate obtained from BC type A incubated for 2h was higher compared to BC type B, respectively 581 mg/l and 297 mg/l. However, the elution profile is the same for both types: the CFZ concentration in the eluates drops within the first 24h from 581 mg/l to 365 mg/l (37%) for BC type A and from 297 mg/l to 132 mg/l (56%) for BC type B. After 24h no further significant CFZ release is seen. Impregnation of the bone chips before or after gamma irradiation did not affect this elution profile.

Conclusions: Bone chips treated with scCO2 show a comparable elution pattern compared to non-scCO2 treated bone chips. AB release depends on the properties of the AB, making it impossible to copy the same impregnation protocol for different antibiotics. The stability of CFZ in solution at 37°C and its release are a major concern when establishing an impregnation protocol with CFZ.

[FP F7] EXTENDED ORAL ANTIBIOTIC PROPHYLAXIS – DO THE SAME CRITERIA APPLY TO PATIENTS UNDERGOING ASEPTIC REVISION ARTHROPLASTY?

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Aim: Prosthetic joint infection (PJI) is a devastating and costly complication of total joint arthroplasty (TJA). Use of extended oral antibiotic prophylaxis (EOAP) has become increasingly popular in the United States following a highly publicized study (Inabathula et al) from a single center demonstrating a significant protective effect (81% reduction) against PJI in 'high-risk' patients. However, these results have not been reproduced elsewhere and EOAP use directly conflicts with current antibiotic stewardship efforts. In order to study the role of EOAP in PJI prevention, consensus is needed for what defines 'high-risk' patients. The revision TJA (rTJA) population is an appropriate group to study due to having a higher incidence of PJI. The purpose of the current study was to rigorously determine which preoperative conditions described by Inabathula et al. (referred to as Inabathula criteria (IBC)) confer a higher rate of PJI in patients undergoing aseptic rTJA.

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

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

Conclusions: Over half of rTJA patients meet IBC and could be eligible to receive EOAP in the United States. However, the specific presence of active smoking, BMI>35, CKD, and diabetes mellitus appear to be responsible for the increased risk of PJI. Prospective studies investigating EOAP use for patients with these specific conditions are urgently needed to prevent unnecessary antibiotic use.

[FP F8] MONITORING AND GUIDANCE OF PATIENTS WITH PROLONGED ANTIMICROBIAL THERAPY: FILLING THE GAP TO IMPROVE QUALITY OF CARE

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Aim: Bone and joint infection requires antimicrobial treatment for 6 to 12 weeks. When patients are well prepared and instructed regarding their therapy, they are more likely to have less side effects and improved compliance. Although side effects are common, this coaching is often not routinely performed when oral treatment is given. We developed a monitoring and guidance program for our outpatients who are on long term antimicrobial therapy, in which we can early signal side effects and treatment failure and coach the patients in their journey of infection treatment.

Method: In our tertiary referral centre for orthopaedic infections, we started the outpatient monitoring of antimicrobial treatment (OMAT)- team for patients who will receive antimicrobial therapy for >2 weeks. Before discharge, our trained nurse gives instruction to the patient. Within 3 days after hospital discharge the patient is contacted by phone to, if necessary, clarify ambiguities in monitoring set up. During this contact, the nurse checks for side effects, addresses logistic problems regarding laboratory monitoring or future appointments and coaches patients for other questions. The patient is instructed how to recognize and who to contact in case of red flags and problems possibly related to the treatment. This is repeated after every laboratory check-up. Supervision is performed by an infectious disease specialist in close collaboration with the patient's surgeon.

Results: The OMAT-team started in October 2020 and consists of 3 trained nurses and 3 ID specialist. In one year, 453 patients were proactively monitored for a mean of 11 weeks. Routinely, laboratory measurements were performed 1 week after the start of therapy and every 3-4 weeks thereafter, which resulted in 2711 contacts per year. In total, 64% of the patients reported side effects and 13% needed one or more extra laboratory measurement. This led to 40 additional outpatient consultations by the ID specialist because of complications of treatment and a switch of the antimicrobial agent in 31% of the patients.

Conclusions: OMAT seems to improve the early signalling of complications regarding treatment, which is likely to improve compliance. The OMAT-team serves as a easy to access team to discuss any problem regarding antimicrobial therapy. Being proactive, the OMAT-team intervenes in an early stage of problems regarding side effects, logistics of the treatment and possible treatment failure. Future analysis of our data will show to what extend this will lead to prevention of re-hospitalization and improvement of success rate.

[FP F9] IMPACT OF ANTIMICROBIAL SUPPRESSION ON LONG-TERM OUTCOME OF STREPTOCOCCAL PERIPROSTHETIC JOINT INFECTIONS

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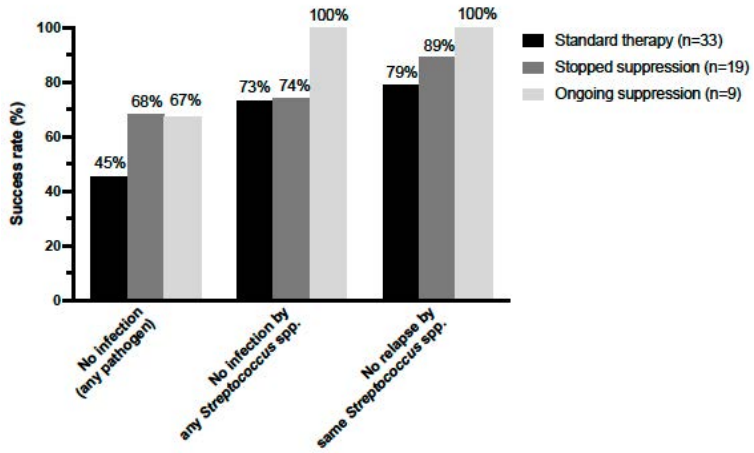
[3]*Inselspital Bern, Department of Infectious Diseases, Bern, Switzerland*

Aim: Antimicrobial suppression has shown significantly improved outcomes in streptococcal periprosthetic joint infection (PJI) at short-term follow up compared to 12-week antimicrobial therapy. Here we assessed the impact of suppression on the long-term outcome and compared it to standard 12-week therapy.

Method: Consecutive patients with streptococcal PJI (defined by EBJIS criteria) treated 2009-2020 were prospectively included and allocated into standard and suppression (> 6 months) treatment group. Episodes with early (within 12 weeks, n=3) or fatal failure (n=3) and/or follow-up <2 years (n=8) were excluded. Rates of infection-free, streptococcal infection-free and relapse-free status were assessed.

Results: Sixty-one PJI episodes (36 knee, 24 hip and one shoulder prosthesis) of patients with a median age of 71.3 (35-91) years were included. Twenty-six (43%) were females. Predominant pathogens were ***S. agalactiae*** (n=19), ***S. dysgalactiae*** (n=18) and ***S. mitis/oralis*** (n=12). Two-stage exchange (n=28) and prosthesis retention (n=19) were the main surgical strategies. Standard treatment was administered in 33 patients and suppression in 28, of whom 9 had ongoing treatment and 19 had discontinued antibiotics at time of follow-up. Used oral antibiotics for suppression were amoxicillin (n=27), doxycycline (n=5) and clindamycin (n=3); 4 switched primary antibiotic due to side effects. The median follow-up time was 4.3 (0.3-13.3) years. At time of follow-up 15/33 patients (45%) were infection-free with standard therapy and 19/28 patients (67%) with suppression (p=0.121). Different success rates are depicted in the figure. Infection with any ***Streptococcus*** spp. was observed in 9/18 (50%) failures with standard treatment, 5/6 (83%) failures after discontinuing suppression and none during suppression. All failures in patients with ongoing suppression were caused by gram-negative rods.

Conclusion: At long-term follow-up, the success rate was no longer superior with suppression compared to standard treatment. Nevertheless, suppression successfully prevented PJI caused by streptococci, however, one third of them experienced a new PJI with gram-negative rods.



[FP F10] USE OF DALBAVANCIN TO FACILITATE DISCHARGE IN THE TREATMENT OF BONE AND JOINT INFECTIONS

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Aim: Dalbavancin is a lipoglycopeptide with a half-life of 14 days (range 6.1 to 18.4), significantly longer than other antimicrobials, which avoids the need for daily antibiotic dosing. This multicentre observational study aims to describe the use of dalbavancin to facilitate discharge in treating bone and joint infections.

Method: All adult patients treated with dalbavancin from January 2017 to September 2022 in two UK bone infection units were included.
Data collected through a standardised data collection form included:

- Clinical and microbiological characteristics.
- Antimicrobial susceptibilities.
- Hospital length of stay.
- Complications.
- Patient suitability for hypothetical treatment options, such as Outpatient Parenteral Antibiotic Team (OPAT)
- Clinical outcome.

Treatment-related costs were calculated for dalbavancin and the preferred hypothetical treatment option that would have been administered for the same duration. The costs were subtracted to calculate the cost difference.
Clinical outcome was defined as definite failure in accordance with the OVIVA Trial protocol.

Results:
Twenty-four patients were included: 10 males and 14 females, with a median age of 53 (IQR 43-73). Eleven were prosthetic joints, seven septic arthritis: five were other orthopaedic-related implant infections, and one was spondylodiscitis. In 15 cases, the infecting organism was coagulase-negative staphylococci, and nine were due to Staphylococcus aureus.

Reason for dalbavancin
The reasons for choosing dalbavancin over alternatives were to facilitate discharge:

- Necessity
- Due to poor adherence (11)
- Or lack of viable OPAT options due to antibiotic resistance or intolerance (5) Or,
- Convenience
    - To avoid the need for OPAT (8)

Dalbavancin was initiated at 1500mg after a median of 12 days (IQR 9–21) of in-hospital antimicrobial therapy. Subsequent dalbavancin doses were based on clinical decisions and ranged from 1000mg to 1500mg.

Outcome
Overall, 14 patients (70.1%) were infection-free after a median follow-up of 12.1 months (IQR, 6.1 – 19.4).

No patients developed an adverse drug reaction.

Healthcare benefits
Switching to dalbavancin reduced treatment costs by a median of £4197 (IQR 1368 - 6694) compared with the preferred theoretical alternatives. A median of 31 hospital days (IQR 23–47) was avoided among patients who would have required a prolonged inpatient stay.

Conclusions: Dalbavancin can safely facilitate outpatient treatment in patients with limited oral options and in whom OPAT is unsuitable. Dalbavancin is cost-effective compared with the alternative of an inpatient stay.

[FP G1] QUALITY OF LIFE IN OSTEOMYELITIS IS SIGNIFICANTLY WORSE COMPARED TO OTHER CHRONIC DISEASES

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Aim: Patient quality of life (QoL) in untreated bone infection was compared to other chronic conditions and stratified by disease severity.

Method: Patients referred for treatment of osteomyelitis (including fracture related infection) were identified prospectively between 2019 and 2023. Patients with confirmed infection completed the EuroQol EQ-5D-5L questionnaire. Clinicians blinded to EQ-index score, grouped patients according to JS-BACH Classification into 'Uncomplicated', 'Complex' or 'Limited treatment options'. A systematic review of the literature was performed of other conditions that have been stratified using EQ-index score.

Results: 257 patients were referred, and 219 had suspected osteomyelitis. 196 patients had long bone infection and reported an average EQ-index score of 0.455 (SD 0.343). 23 patients with pelvic osteomyelitis had an average EQ-index score of 0.098 (SD 0.308). EQ-index scores for other chronic conditions ranged from 0.382 (SD 0.374) in stroke to 0.950 (SD 0.140) in Gaucher's disease. In 8,960 patients with no underlying comorbidity, EQ-index score was reported as 0.904 (SD 0.156). Compared to these conditions, patients with bone infection, in particular those with pelvic osteomyelitis, had amongst the lowest self-reported quality of life scores (Figure 1).
In long bone infection, 41 cases (21.0%) were 'Uncomplicated', 136 (69.4%) 'Complex' and 19 (9.7%) with 'Limited treatment options available'. Within classification stratification, patients with 'Uncomplicated' long bone infections reported a mean EQ-index score of 0.618 (SD 0.227) which was significantly higher compared to 'Complex' (EQ-index: 0.410 SD 0.359, p=0.004) and 'Limited treatment options available' (EQ-index: 0.400 SD 0.346, p=0.007) (Fig. 1).

Conclusions:
Bone and joint infections have a significant impact on patient quality of life. It is much worse when compared to other common chronic conditions, including malignancy, cardiovascular and neurological diseases. This has not been previously reported but may focus attention on the need for more investment in this patient group.

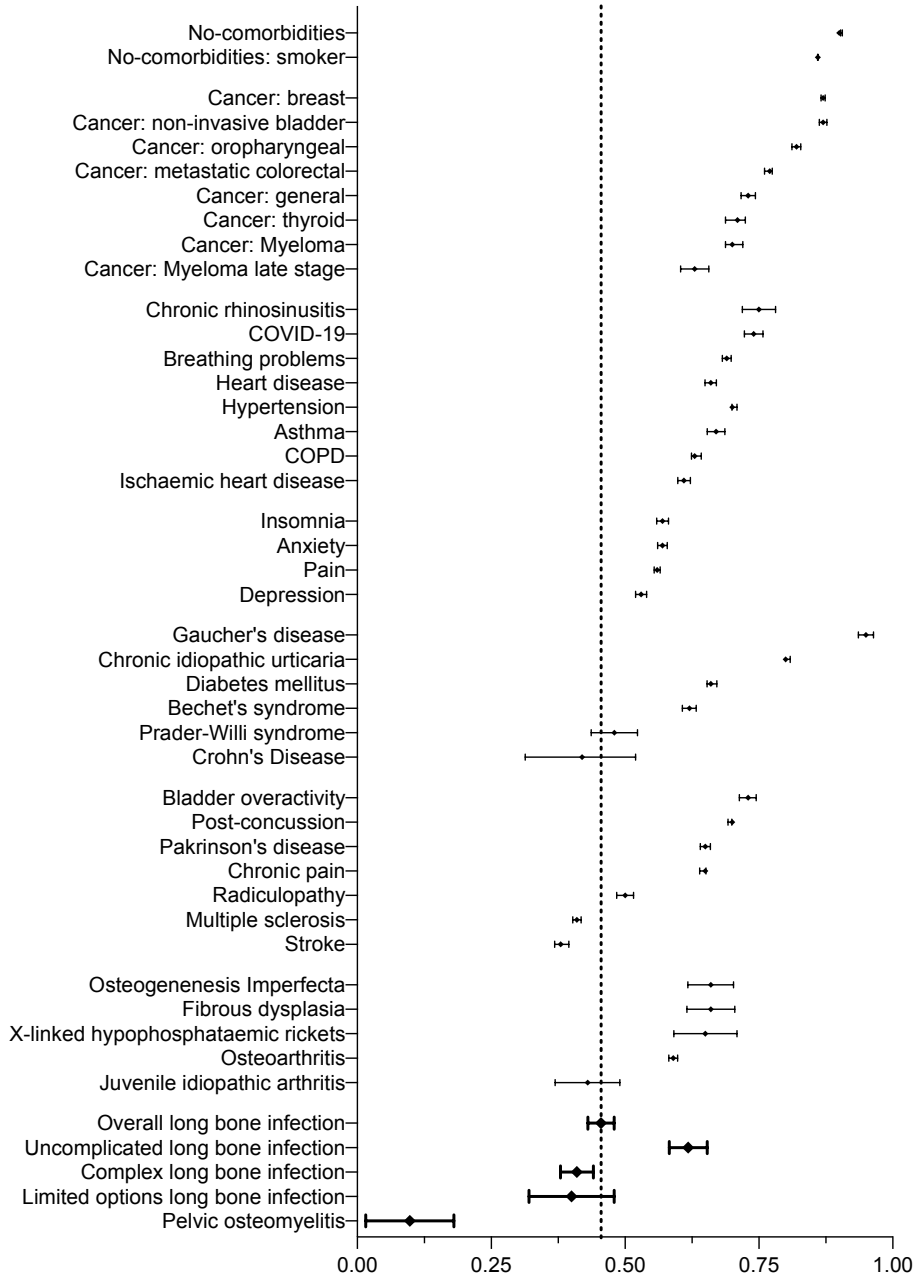

Fig.1 - Summary of available EQ-5D-5L index scores across a range of medical conditions compared to long bone infection and pelvic osteomyelitis (Endo. = endocrine; BJI = bone and joint infection; Psych. = psychological). Dotted line = average for long bone infection.

[FP G2] FRAME TREATMENT IMPROVES QUALITY OF LIFE IN OSTEOMYELITIS, BUT ONLY AFTER A PERIOD OF SIGNIFICANT IMPAIRMENT

Florian Frank[1], Andrew Hotchen[1], Christen Ravn[2], Vicky Pullinger[1], Katherine Eley[1], David Stubbs[1], Jamie Ferguson[1], Martin McNally[1]

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Aim: This study assessed quality of life (QoL) in patients having external fixation for treatment of osteomyelitis and fracture-related infection (OM/FRI).

Method: Patients who had surgery for OM/FRI and who completed the EuroQoL EQ-5D-5L or EQ-5D-3L questionnaires, were identified between 2010 and 2020. Patients were followed-up for 2 years after surgery. QoL was compared between patients who had either an Ilizarov frame or a monolateral external fixator with those who did not receive external fixation.

Results: 165 patients were included. Of these, 37 (22.4%) underwent application of external fixation which included 23 circular frames and 14 monolateral external fixators. Patients in the frame group had more BACH 'Complex' infections (34/37; 91.9%), compared to non-frame patients (57/81; 70.3%).

Pre-operatively, the mean EQ-index score for patients planned to receive a frame (0.278 SD 0.427) was worse compared to other treatments (0.453 SD 0.338, p=0.083). At 6 weeks after surgery, the EQ-index score remained significantly lower in frame patients compared to non-frame patients (frame: 0.379 SD 0.363; no frame: 0.608 SD 0.326, p=0.016). By 6 months, 26/37 patients had undergone frame removal. The patients who had frames ***in situ*** at 6 months had lower EQ-index scores when compared to patients who had their frames removed (frame ***in situ***: 0.187 SD 0.213; frame removed 0.674 SD 0.206, p=0.076) (figure 1). At one year, 36/37 (97.3%) patients had their frame removed. QoL had greatly improved, to levels similar to non-frame patients (no frame: 0.652 SD 0.357; frame removed: 0.657 SD 0.247, p=0.949).

Conclusions: Frame treatment impacts patient QoL, especially in those with frames ***in situ*** for more than 6 months. However, following frame removal, patients report similar QoL to those who did not undergo treatment using an external fixator. This underlines the need for close and professional patient support during frame treatment for bone infection.

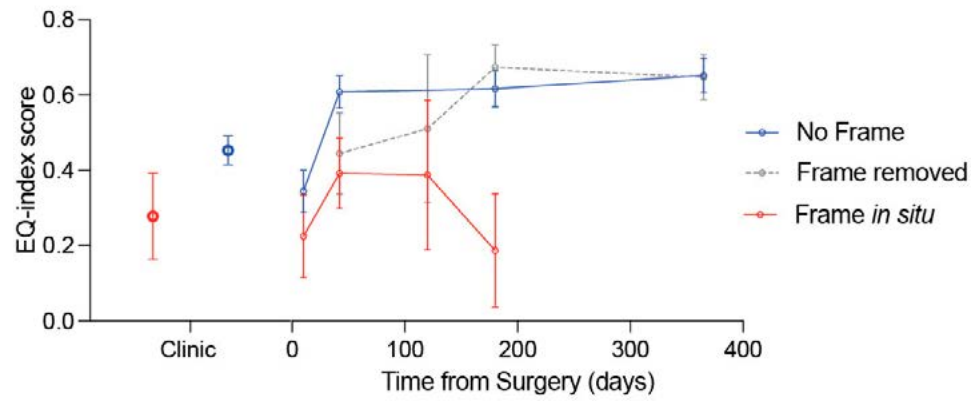

Figure 1 – Graph demonstrating the change in EQ-index score over time from surgery. Grey dotted line = patients after frame removal. Blue line = no frame, Red line = patients with frame.

[FP G3] DIRECT HOSPITAL COSTS PER CASE FOR PERIPROSTHETHIC HIP AND KNEE JOINT INFECTION IN EUROPE – A SYSTEMATIC REVIEW

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Aim: The number of periprosthetic joint infections (PJI) is increasing due to ageing population and increasing numbers of arthroplasty procedures and treatment is costly. Aim of the study was to analyze the direct healthcare costs of PJI in Europe for total hip arthroplasties (THA) and total knee arthroplasties (TKA).

Method: A systematic review in PubMed with search of direct costs of PJI in European countries was performed. Thereby the term ***cost* AND (infection OR PJI) AND (prosthesis OR knee OR hip OR "TKA" OR "THA" OR arthroplast*)*** was combined with each European country to detect relevant publications. Publications with definition of performed procedure and joint localization were included into further analysis. The mean value of direct healthcare cost was calculated for the respective joint and the respective operation performed.

Results: Screening revealed 1,274 eligible publications. After review of abstracts and full-texts n=11 manuscripts were included into final analysis (Figure 1). The mean combined direct hospital costs for revision for PJI after TKA and THA was 26,311€. Mean costs for revision procedures for PJI after TKA were 24,617€. Direct costs for TKA-PJI treated with debridement, antibiotics and implant retention (DAIR) were on average 10,121€. For two-stage revisions in knee arthroplasties total average costs were 30,829€. Referring to revision surgery for PJI in THA, the mean hospital costs in Europe were 28,005€. For a DAIR procedure direct healthcare costs of 5,528€ were identified. Two-stage revision cost on average 31,217€.

Conclusions: PJIs are associated with significant direct healthcare costs. The financial burden of up to 30,000 € per case underlines the impact of the disease for European health care system. However, the number of detailed reports on PJI costs is limited and the quality of the literature is limited. There is a strong need for more detailed financial data on the costs of PJI treatment.

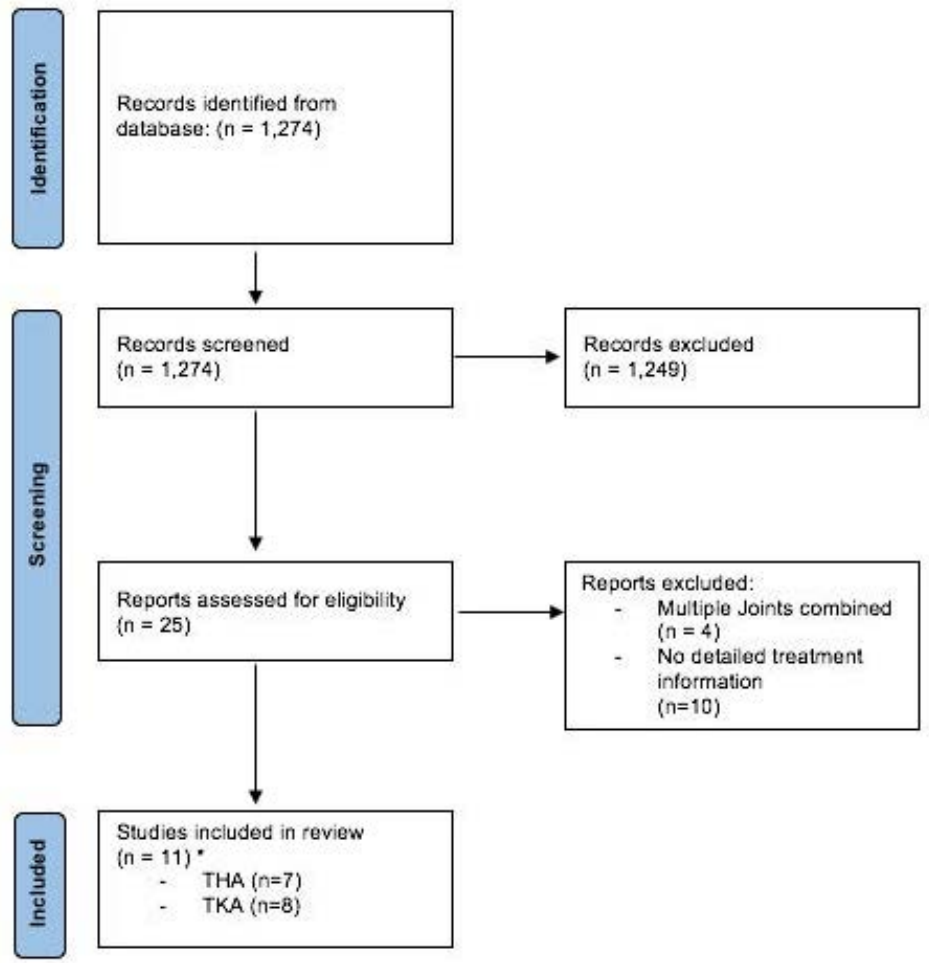

Figure 1: PRISMA flow diagram presenting the process of identification, screening, eligibility, and final inclusion of relevant articles. (* some studies reporting costs for THA and TKA)

[FP G4] ANALYSIS OF MULTIDISCIPLINARY TEAM DECISION ADHERENCE IN COMPLEX BONE, JOINT AND ARTHROPLASTY INFECTIONS

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Aim: Multidisciplinary team (MDT) meetings for patients with prosthetic joint infections (PJI) are increasingly being implemented aiming to optimize care and treatment. Although current data and rationale suggest a clear benefit, the precise effects of MDT meetings in this field are lacking. Therefore we aimed to analyze the context, content and evolution of MDT meetings together with the adherence to MDT decisions in our institution. Based on the results, recommendations were formulated to further improve the general implementation of MDTs for PJI and other complex bone and joint infections (BJI).

Method: A cohort study was conducted including all patients with complex BJI including PJI who were discussed during MDT meetings between 2015 and 2022 in a tertiary care hospital. Data were obtained from electronic patient records. Baseline patient characteristics, causative micro-organisms, therapeutic strategy and MDT decisions were collected. MDT decisions were compared with the actual treatment received by patients and in case of non-adherence the characteristics of this decision were analyzed.

Results: The analysis included 1321 MDTM case discussions and decisions on 509 patients collected from 329 MDT meetings. Of these decisions, 51% concerned PJI, 15% fracture related infections and spinal implant infections and 34% non-implant related BJI. Debridement, Antibiotics and Implant Retention was performed in 28% of patients. The average number of patients discussed per meeting increased from 2,7 to 5,5. The number of discussed BJIs other than PJI increased from 31 to 123 patients per year.

The overall MDT decision non-adherence rate was 7,9% and constant. In 72% of these decisions this was the choice of the physician treating the patient. In 15% of cases this was due to new clinical information, in 51% because of a different insight than the MDT and in 28% no considerations were reported. Non-adherence concerned both surgical and antibiotic therapy as diagnostic procedures.

Conclusions: Over the years, the scope of MDT meetings evolved from PJI only to all complex BJI. Most of the decisions made by the MDT were adhered to in clinical practice. Non-adherence to MDT decisions was the choice of the treating physician in the majority of cases and due to a different insight than the MDT. To further improve the quality of MDT meetings, we recommend: (a) standardizing clinical information presented at the MDT, (b) encouragement of feedback to the MDT and (c) refraining from discussing patients whose treating physician is not present at the meeting.

[FP G5] WHAT CAN THEY EXPECT? DECREASED QUALITY OF LIFE AND INCREASED POSTOPERATIVE COMPLICATION RATE IN PATIENTS WITH A FRACTURE-RELATED INFECTION OF A LONG BONE FRACTURE

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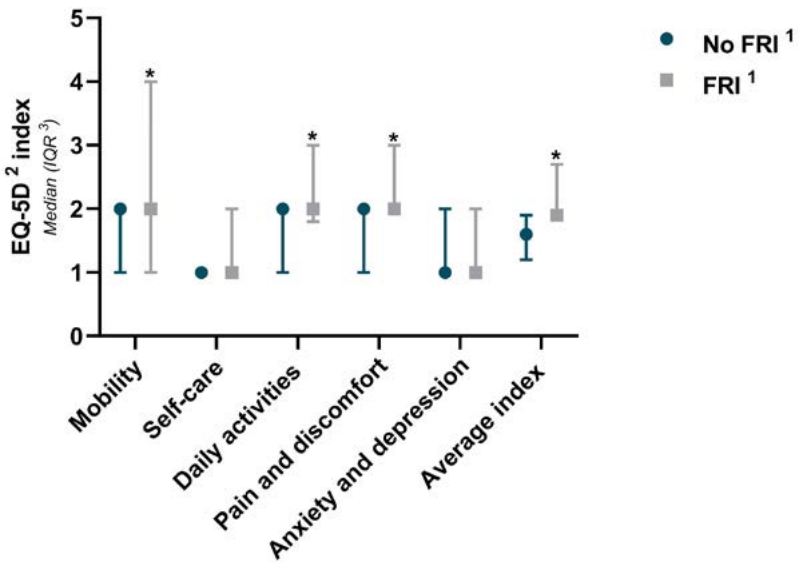
Aim: By gaining insight into the Quality of Life (QoL) and occurrence of complications, critical facets in the care for patients with Fracture-Related Infection (FRI) can be mitigated. Therefore, the aims of this study were to 1) determine the QoL in FRI patients in comparison to non-FRI patients and 2) describe the incidence of complications in both FRI and non-FRI patients.

Method: An ambidirectional cohort study was conducted in a level-1 trauma centre between January 1st 2016 and November 1st 2021. All patients who underwent surgical stabilisation of a long bone fracture were eligible for inclusion. Patients with an Injury Severity Score (ISS) ≥16 or incomplete follow-up were excluded. QoL was assessed through the use of EuroQol five-dimension questionnaires twelve months post-injury.

Results: A total of 134 patients were included, of whom 38 (28%) FRI patients and 96 (72%) non-FRI patients. In comparison to non-FRI patients, FRI patients scored significantly worse on the QoL assessment regarding the average index (p=0.007), and the subjects' mobility (p=0.00), daily activities (p=0.010) and pain (p=0.009) (Figure 1). During the median follow-up of 14.5 months (interquartile range 9.5-26.5), patients developed other complications besides FRI in 42% (n=56) of cases, with a total of 93 individual complications. A complication rate of 74% (n=28/38) was reported in FRI patients with 57 distinctive complications. The complications nonunion (30%, n=17/57), infection other than FRI (16%, n=9/57) and implant failure (12%, n=7/57) were the most frequently described in the FRI group.

Conclusions: As a result of this study, FRI patients can be better counselled regarding the potential physical and mental consequences of their disease. FRI patients can be informed that they are more likely to endure challenges in daily life due to a decreased QoL and that a 74% chance of developing a postoperative complication was seen in this cohort.



Description of the figure
Figure 1. Visual overview of the Quality of Life assessment.
[1] Fracture-Related Infection, [2] EuroQol five-dimension, [3] Interquartile range, * Statistically significant variables

[FP G6] THE NATIONAL INFECTION CONTROL PROGRAM PRISS, HAD NO EFFECT ON POSTOPERATIVE INFECTIONS AFTER PRIMARY TOTAL HIP ARTHROPLASTY IN SWEDEN

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Aim: Prosthetic joint infection (PJI) is a serious complication following total hip arthroplasty (THA) entailing increased mortality, decreased quality of life, and high healthcare costs. In 2009 a nationwide, multidisciplinary infection control program was launched in Sweden, PRISS, which aimed to reduce the PJI burden by 50%.
The primary aim was to investigate whether the PRISS project reduced PJI incidence after primary THA; the secondary aim was to evaluate other possible benefits of PRISS, such as shorter time to diagnosis.

Method: We obtained data on patients undergoing primary THA in Sweden (n = 45,723 patients, 49,946 THAs), 2012–2014. Using personal identity numbers, this cohort was matched with the Swedish Prescribed Drug Registry. Medical records of patients with ≥4 weeks antibiotic consumption were reviewed to verify PJI diagnosis (n = 2240, 2569 THAs).

Results: The cumulative incidence of PJI following the PRISS project was 1.2% [95% CI 1.1-1.3] as compared to 0.9% [95% CI 0.8-1.0] before. Cox regression models for the PJI incidence post PRISS indicates there were no statistical significance difference versus pre PRISS (HR 1.1 [95% CI 0.9-1.3]. There were similar time to PJI diagnosis after the PRISS project 24 vs 23 days (p=0.5).

Conclusions: Despite the comprehensive nationwide PRISS project, Swedish PJI incidence was higher after the project and time to diagnosis remained unchanged. Factors contributing to PJI, such as increasing obesity, higher ASA class, and more fractures as indications, explain the PJI increase among primary THA patients.

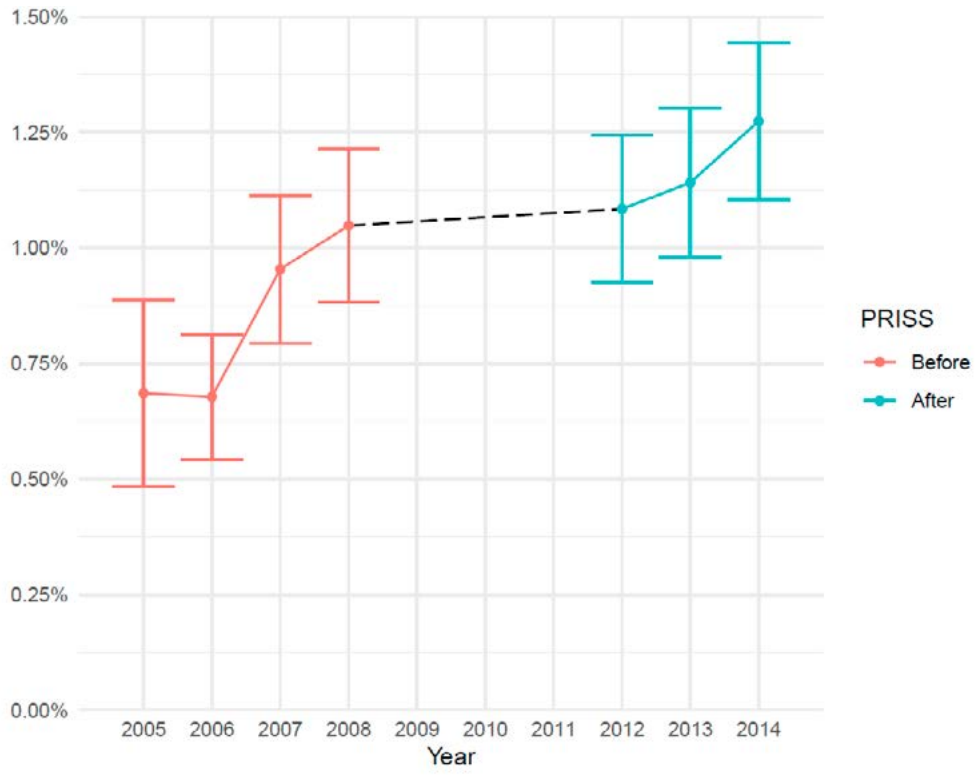

Figure 2. Trend of cumulative prosthetic joint infection incidence pre and post PRISS, 2005-2014.

[FP G7] QUALITY OF LIFE AND MORTALITY IN PATIENTS WAITING FOR AN OPERATION FOR BONE AND JOINT INFECTION

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Aim: To investigate the impact of waiting for surgical treatment for bone and joint infection (BJI) on patient self-reported quality of life (QoL).

Method: Patients presenting to clinic between January 2019 and February 2020 completed the EuroQol EQ-5D-5L questionnaire. Patients were divided into three groups: surgery performed; on the waiting list for surgery; or decision for non-operative management. All patients were followed-up for 2 years. The EQ-index score was calculated and change from presentation to 1-year and 2-year follow-up was compared across the 3 groups. Mortality at final follow-up was measured in all groups.

Results: 188 patients were included. Of these, 98 had an operation performed, 50 were on the waiting list for surgery but did not receive an operation and 40 were treated non-operatively. At presentation, all three groups had similar EQ-5D-5L index scores (surgery:0.412 SD0.351; waiting list:0.510 SD0.320; non-operative management: 0.467 SD0.354; p=0.269). There was a significant improvement in QoL in patients who underwent surgery when compared to their pre-operative state (mean increase of EQ-index score +0.241 in the first year (SD0.333, p<0.001) and +0.259 (SD0.294, p<0.001) in the second year (Fig. 1). Patients on the waiting list for surgery had a small time-dependent decrease in EQ-index score at 1 year (-0.077, SD0.282, p=0.188) and 2 years (-0.140, SD0.359, p=0.401). Patients treated non-operatively had similar changes in EQ-index scores at 1 year (-0.052, SD0.309, p=0.561) and 2 years (-0.146, SD 0.234, p=0.221). Patients who had surgery had significantly better QoL at 2-years after treatment compared to other groups (mean EQ-index scores: surgery performed 0.671 vs. waiting list 0.431, p<0.001; surgery performed vs. non-operative management 0.348, p<0.001) (Fig. 1).

Mortality in the operated group was 3.1%, which was similar to patients who were on the waiting list for surgery (6.5%, p=0.394) but lower than patients who were non-operatively managed (14.7%, p=0.014).

Conclusions: The Covid-19 pandemic created long waiting times for some patients. Selecting patients with BJI who can safely wait for surgery is difficult. QoL for patients with BJI deteriorates over time if surgery is delayed or not performed. When patients decline surgery, they should be counselled that their QoL is likely to be impaired over time. The relationship between waiting time and mortality merits further study.

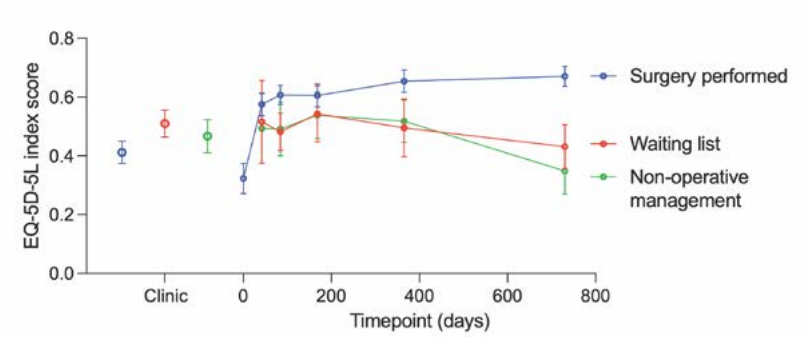

Figure 1 – Plot demonstrating clinic EQ-index score and then either after surgery (blue line); when patients are on the waiting list for surgery (red line); or for patients treated non-operatively (green line).

[FP H1] TUBERCULOUS ARTHRITIS OF NATIVE JOINTS: A SYSTEMATIC REVIEW AND EBJIS WORKGROUP REPORT

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Aim: The aim of this systematic review was to assess the existing published data on tuberculous arthritis involving native joints in adults aged 18 years and older. The specific research questions focused on the diagnosis and management of the disease.

Method: This study was performed in accordance with the guidelines provided in the Preferred Reporting Items for Systematic reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR). A systematic literature search was undertaken of Pubmed, Web of Science, Scopus and the Cochrane library. Only studies published in English since 1970 were considered. Case series involving less than 10 patients, systematic and narrative reviews, and laboratory or animal studies were excluded. We also excluded reports of TB infections not involving a "native joint" and tuberculosis of the spine. The level of evidence and strength of recommendations was performed in accordance with the GRADE system.

Results: The systematic review of the literature yielded 2023 potential sources. Following deduplication, screening and full-text review, 20 data sources involving 573 patients from nine countries, were included. There was considerable variation amongst the studies in terms of the approach to diagnosis and management. The most common method used to confirm the diagnosis was microbiological culture of tissue obtained by biopsy, with positive findings in 93% of cases. Medical management involved a median 12 months of antitubercular treatment (IQR 8-16; range 4-18 months). Duration of pre-operative treatment ranged from two to 12 weeks in duration. Surgery was performed in approximately 87% of patients and varied from arthroscopic debridement to complete synovectomy combined with total joint arthroplasty. When arthroplasty and arthrodesis cases are excluded, 80% of patients received an open or arthroscopic debridement. The mean follow-up time of all studies was 26 months, with most studies demonstrating a minimum follow-up of at least six-months (range 3-112 months). Recurrence rates were reported in most studies, with an overall average recurrence rate of 7,4% (35 of 475).

Conclusions: The current literature on TB arthritis highlights the need for the establishment of standardised diagnostic criteria. Further research is needed to define the optimal approach to medical and surgical treatment. The role of early debridement in active tuberculous arthritis needs to be explored further. Specifically, comparative studies are required to address the questions around use of medical treatment alone versus in combination with surgical intervention.

[FP H2] THE PREVALENCE OF MYCOBACTERIA IN BONE AND JOINT SAMPLES AT A TERTIARY ORTHOPAEDIC CENTRE IN A SETTING WITH A LOW BURDEN OF TUBERCULOSIS DISEASE

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Aim: At our tertiary orthopaedic centre, mycobacterial cultures are routinely performed on bone and joint samples sent for bacterial culture. We have previously described the prevalence ***Mycobacterium tuberculosis*** Complex (MTBC) in these samples. Here, we describe the prevalence of non-tuberculous mycobacteria (NTM). We calculate the number needed to test to identify one previously undiagnosed mycobacterial bone or joint infection.

Methods: Samples taken during a single procedure were pooled in one BACTEC MGIT culture. From laboratory records, we ascertained the number of mycobacterial cultures performed, the number positive for MTBC or NTM, and characteristics of individuals from whom mycobacteria were isolated. We collected the same data from 100 individuals with negative mycobacterial cultures. Results presented here are from interim analysis.

Results: Excluding sample types that were clearly not bone or joint samples, 6162 mycobacterial cultures were performed between 4 July 2017 and 30 September 2022. Twenty-two patients had MTBC and 6 patients had NTM newly isolated from bone or joint samples placed in mycobacterial culture, with a further patient having both ***M. tuberculosis*** and ***M. avium*** isolated. In both patients with ***M. abscessus***, the organism also grew in routine bacterial cultures. In one further patient, ***M. fortuitum*** was isolated from a sample not put into mycobacterial culture.
To identify one new mycobacterial infection of bone or joint (MTBC or NTM) that would not be detected with routine bacterial cultures, 228 (95% CI 157 – 346) mycobacterial cultures were needed. The laboratory cost per additional patient identified using MGIT cultures was £10,955 (95% CI £7537 - £16,612).

Mycobacterial cultures were much less likely to be positive in samples taken from prosthetic joints. They were more likely to be positive in spinal samples and in samples taken from patients with suspected sarcoma. In patients for whom we had contemporaneous histological specimens, these demonstrated granulomatous inflammation in 86% (18/21) of patients from whom MTBC had been isolated but in none of the four patients from whom only NTM was isolated. Ascertaining the clinical significance of NTM isolates is challenging, although in 2/8 cases the same organism was isolated following repeat sampling.

Conclusions: Targeted rather than routine mycobacterial culture of bone and joint specimens should be considered in settings with a low burden of tuberculosis. NTM are rarely isolated from bone and joint specimens at our centre and fast growers may be isolated using routine bacterial culture.

[FP H3] MICROBIOLOGICAL PROFILE CHANGES IN SEQUENTIAL REVISION HIP AND KNEE ARTHROPLASTY FOR PROSTHETIC JOINT INFECTION

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Introduction: A proportion of patients with hip and knee prosthetic joint infection (PJI) undergo multiple revisions with the aim of eradicating infection and improving quality of life. The aim of this study was to describe the microbiology cultured from multiply revised hip and knee replacement procedures to guide antimicrobial therapy at the time of surgery.

Patients and Methods: Consecutive patients were retrospectively identified from databases at two specialist orthopaedic centres in the United Kingdom between 2011 and 2019. Patient were included who had undergone repeat revision total knee replacement (TKR) or total hip replacement (THR) for infection, following an initial failed revision for infection.

Results: 106 patients were identified, of which 74 underwent revision TKR and 32 underwent revision THR. Mean age at first revision was 67 years (SD 10). Charlson Comorbidity Index was ≤2 for 31 patients, 3-4 for 57 patients, and ≥5 for 18 patients. All patients underwent ≥2 revisions, 73 patients received 3, 47 patients received 4, 31 patients received 5, and 21 patients received ≥6. After six revisions, 90% of patients cultured different organisms than the initial revision, and 53% of organisms were multi-drug resistant species. The most frequent organisms at each revision were coagulase negative Staphylococcus (36%) and ***Staphylococcus aureus*** (19%). Fungus was cultured from 3% of revisions and 21% of infections were polymicrobial.

Conclusion: Patients undergoing multiple revisions for PJI are highly likely to experience a change in organisms and sensitivities with each subsequent revision. It is important to administer empirical antibiotics at each subsequent revision, appreciating known drug resistance from previous cultures. Our results do not support routine use of empirical antifungals.

[FP H4] CLINICAL OUTCOME AND MICROBIOLOGICAL ANALYSIS OF UNEXPECTED POSITIVE INTRAOPERATIVE CULTURES IN PRESUMED ASEPTIC KNEE AND HIP REVISION ARTHROPLASTY – A TEN YEAR RETROSPECTIVE ANALYSIS WITH A MINIMUM FOLLOW-UP OF TWO YEARS

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Aims: The aim of this study was to assess the incidence the microbiological spectrum and clinical outcome of hip and knee revision arthroplasties with unexpected-positive-intraoperative-cultures (UPIC) at a single center with minimum follow up of 2 years.

Methods: We retrospectively analyzed our prospectively maintained institutional arthroplasty registry. Between 2011 and 2020 we performed presumably aseptic rTHA (n=939) and rTKA (n= 1,058). Clinical outcome, re-revision rates and causes as well as the microbiological spectrum were evaluated.

Results: In total, 219/939 (23.3%) rTHA and 114/ 1,058 (10.8%) rTKA had a UPIC (p<0.001). Single positive intraoperative cultures were found in 173/219 (78.9%) in rTHA and 99/114 (86.8%) in rTKA, whereas 46/219 (21.0%) rTHA and 15/114 (13.2%) rTKA had positive results in ≥2 intraoperative cultures. A total of 390 microorganisms were found among the 333 cases. ***Staphylococcus epidermidis*** 30.9%, CoNS (21.9%), ***Cutibacterium acnes*** 21.1%, and Bacillus spp. 7.3% were the most common microorganisms. Overall, detected microorganisms showed high sensitivity to daptomycin (96.6%), vancomycin (97.3%) and linezolid (98.0%).

After a minimum follow up of 2 years (rTHA 1,470 (735; 3,738) days; rTKA 1,474 (749; 4,055) days). During the 2-year follow-up, 8 patients died and 5 were lost to follow-up. There were 54/219 (24.7%) re-revision in rTHa and 20/114 (17.5%) in rTKA. Overall, there were 23 (10.5%) septic re-rTHA and 9 (7.9%) septic re-rTKA as well as 31 (14.2%) aseptic re-rTHA and 11 (9.6%) aseptic re-rTKA.

Patients with previous septic revisions bevor UPIC procedure showed a significant higher risk for septic re-revision (p<0.05). Moreover, there were less septic re-revisions after single culture positive UPIC (rTHA: 16/173 (9.2%); rTKA 6/99 (6.1%)) compared to ≥2 positive intraoperative cultures UPIC (rTHA: 7/46 (15.2%); rTKA 3/15 (20.0%)).

The most common reason for re-revision in the rTHA-group was aseptic loosening of the cup (34.2%) or of the stem (23.3%), dislocation (18.3%) and periprosthetic-fractures (7.8%). In the rTKA-group it was aseptic loosening (40.4%), instability (24.6%) and secondary patella resurfacing (7.9%). There was a higher septic re-revision rate in consecutive revisions than in planned revisions 17.3% vs. 8.5% in the rTHA-group and 14.3% vs. 7.5% in the rTKA-group, p<0.001.

Conclusion: UPICs are common in rTJA. The rate was higher in hips which may partly explained by the easier pre op joint aspiration in the knee. UPIC may lead to an increase in subsequent re-revisions.

[FP H5] DOES IMPROVEMENT IN PREANALYTICS LEAD TO INCREASED CULTURE YIELD IN PATIENTS WITH PERIPROSTHETIC INFECTIONS?

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Aims: The microbiological detection of microorganisms plays a crucial role in the diagnosis as well as in the targeted systemic and local antibiotic therapy of periprosthetic infections (PJI). Despite extensive efforts to improve the sensitivity of current culture methods, the rate of culture-negative infections is approximately 10-20% of all PJI. This study investigates an preanalytical algorithm (culture collection and direct processing in the OR) to potentially increasing culture yield in patients with PJI.

Methods: Patients undergoing staged revision arthroplasty for PJI in our hospital between October 2021 and 2022 were included in this prospective pilot study. Intraoperatively twenty tissue samples were collected and distributed among 4 groups. Tissue samples were prepared according to standard without medium and in thioglycolate medium at 3 different temperatures (room temperature, 4°C, 37° for 24h before transport to microbiology) directly in the OR. The removed implants were sonicated. Cultures were investigated on days 1, 3, 7, 12, 14 for possible growth. All grown organism, the number of positive samples and the time to positivity were recorded and compared.

Results: 71 patients were included (age, gender). Compared to the standard procedure the thioglycolate broth at 37°C was significantly more often culture-negative (p=0.031). No significant differences in the frequency of culture-negative samples were detected in the other groups.
8.4% (6/71) patients were culture negative in the standard culture but positive in the thioglycolate samples. In contrast, 7% (5/71) were culture negative in the thioglycolate samples but had bacterial detection in the standard approach. In 4.7% (3/63) of the patients, only the sonication showed growth, whereas 25.4% (16/63) had no growth in sonication fluid but in one of the cultures.
For S. caprae, there was a significantly different distribution (p=0.026) with more frequent detection in the group with thioglycolate at 37°C.
The standard procedure (p=0.005) and sonication (p=0.023) showed a shorter time to positivity of the culture compared to the thioglycolate approach at 4°C.

Conclusions: No general differences could be shown between the standard preparation and the thioglycolate preparation; in particular, storage at different temperatures does not seem to result in any difference. For individual cases (8% in this study), bacterial growth was detected in the thioglycolate group that would have been culture-negative otherwise. There might be organism dependent differences in growth in different media.

[FP H6] IS AN ISOLATED POSITIVE SONICATION FLUID CULTURE IN REVISION ARTHROPLASTIES CLINICALLY RELEVANT?

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Aim: The aim of this study was to investigate the clinical relevance of an isolated positive sonication fluid culture (SFC) in patients who underwent revision surgery of a prosthetic joint. We hypothesized that cases with a positive SFC have a higher rate of infection and prosthesis failure during follow-up compared to controls with a negative SFC.

Method: This retrospective multicentre observational study was performed within the European Study Group of Implant-Associated Infections (ESGIAI). All patients who underwent revision surgery of a prosthetic joint between 2013 and 2019 and had a minimum follow-up of 1 year were included. Patients with positive tissue cultures or synovial fluid cultures were excluded from the study.

Results: 95 cases (positive SFC) and 201 controls (negative SFC) were included. There was no difference in infection and prosthesis failure during follow-up between both groups. When solely analysing patients that were not treated with antibiotics, 16% of the cases had an infection during follow-up versus 5% of the controls (P 0.046).

Conclusions: Withholding antimicrobial treatment in patients with an isolated positive SFC is associated with a higher reinfection rate. Antimicrobial treatment should be considered in isolated positive SFC, especially in case of high virulent pathogens.

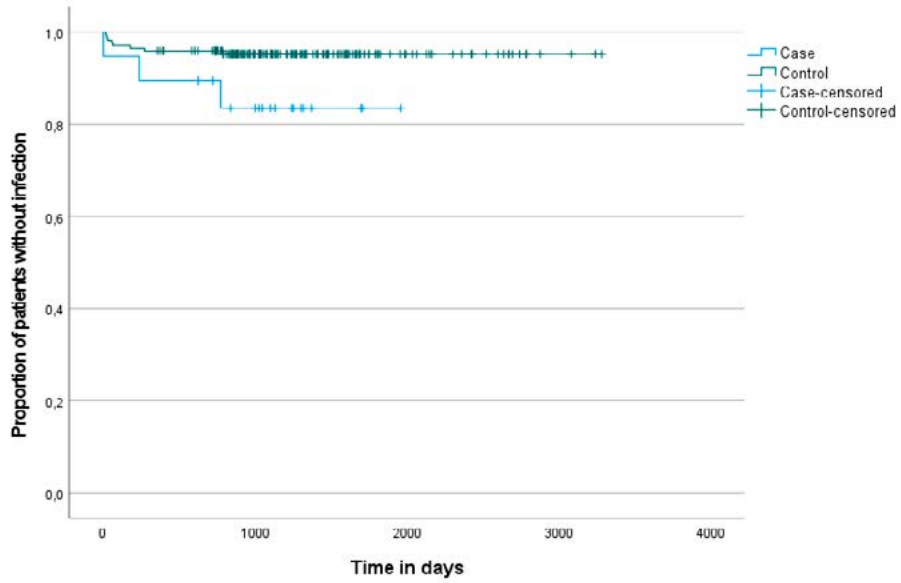

Figure 1. Survival distribution (Kaplan-Meier) plot including cases (n=19) and controls (n=171) not treated with antimicrobial therapy.

[FP H7] MOLECULAR EPIDEMIOLOGY OF COMMUNITY ONSET METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS CAUSING SKIN AND MUSCULOSKELETAL INFECTIONS: AN ALARMING ANTIMICROBIAL RESISTANCE SCENARIO

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Aim: Community-associated methicillin-resistant ***Staphylococcus aureus*** (CA-MRSA) is commonly associated with serious cases of community-onset skin and musculoskeletal infections (Co-SMSI). Molecular epidemiology analysis of CA-MRSA recovered from skin and soft tissues specimens is lacking in Latin American region, especially in Brazil. This study aimed at identifying phenotypic and genotypic features of MRSA isolates recovered from patients presenting Co-SMSI.

Methods: Consecutive MRSA isolates recovered from Co-SMSI episodes of patients admitted between March 2022 and January 2023 in a Brazilian teaching hospital were tested for antimicrobial resistance, characterized as their genotypic features and two-months prospective clinical characteristics of the patients were evaluated. Identification was carried out by automated method and through MALDI-TOF MS. Antimicrobial susceptibility was tested by disk diffusion, broth microdilution and E-test strips for the minimal inhibitory concentration (MIC) evaluation, according to recommendations of the Brazilian Committee on Antimicrobial Susceptibility Testing (BrCAST) and European Committee on Antimicrobial Susceptibility Testing (EUCAST). Gene ***mec***A characterization and Sccmec typing were performed by multiplex polymerase chain reaction (PCR) assay, and gene ***luk***F detection by single PCR.

Results: Overall, 49 ***S. aureus*** isolates were obtained from the 64 specimens recovered from 18 patients, among which 25 (51%) were described by phenotypic methods as MRSA, although ***mec***A gene was identified in only 18 of these samples. ***Scc***mec was untypable in 11 isolates, ***Scc***mec type II in four isolates and 2 were classified as ***Scc***mec type IVa . ***Luk***F gene was identified in five isolates. Antimicrobial resistance profile showed that all isolates were susceptible to linezolid and vancomycin with MIC=1 and MIC=2 in 66.7% and 33.3%, respectively. ***S. aureus*** isolates were also highly susceptible to sulfamethoxazole/Trimethoprim (94.5%). Susceptibility to quinolones was worryingly low, with 50% of isolates showing full resistance ciprofloxacin while the other 50% were sensitivity if increased exposure, and for Levofloxacin 55.6% were resistant and 44.4% showed sensitivity if increased exposure. Isolates were susceptible to gentamicin and tetracycline in 16.6% and 22.2%, respectively. Resistance to rifampicin occurred in a single isolate. Mortality rate evaluated within 1 month of the initial medical evaluation was 13.4%.

Conclusions: Our results evidenced that CA-MRSA isolates causing Co-SMSI demonstrate an alarming pattern of multidrug resistance, including β-lactam and quinolones antibiotics, which have been commonly prescribed as empirical therapy for patients with skin, soft tissue and musculoskeletal infections.

[FP I1] BONY SEQUESTRUM IN CHRONIC OSTEOMYELITIS: CHARACTERISTIC ON 18F-FDG-PET-CT IMAGES

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Aim: The localization of sequestrum in chronic osteomyelitis (COM) is crucial in preoperative planning. The identification of sequestrum on plain X-ray could be difficult. CT and MRI were reported to show the sequestrum. We aimed to analyze the sequestrum characteristics on 18F-FDG-PET-CT images.

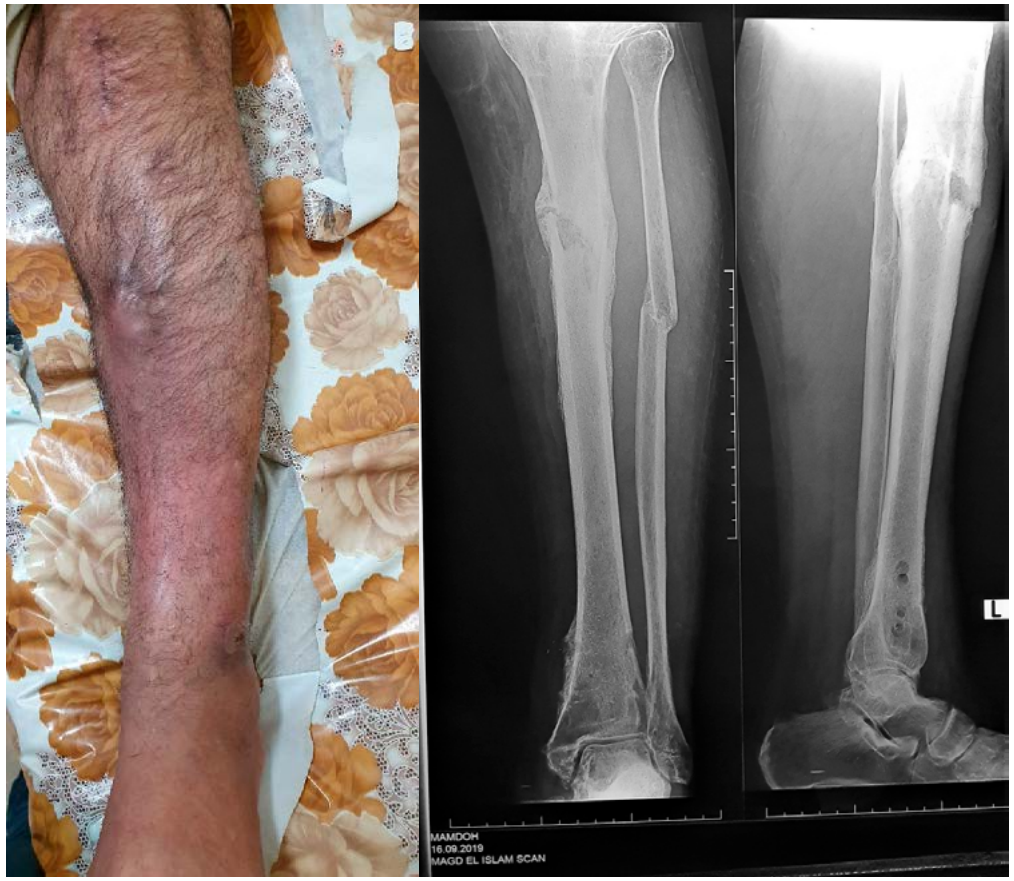
Methods: A prospective study included all patients diagnosed with long-bone chronic osteomyelitis. All patients had preoperative 18F-FDG-PET-CT. Images were analyzed using RadiAnt DICOM Viewer. Axial cuts were used to measure the Standard Uptake Ratio (SUV)max in the Region of Interest (ROI) in the sequestrum, the surrounding area, and the normal bone in the same cut. Surgical debridement was done as standard; samples were taken for microbiology and histopathology, and the intraoperative finding was documented.

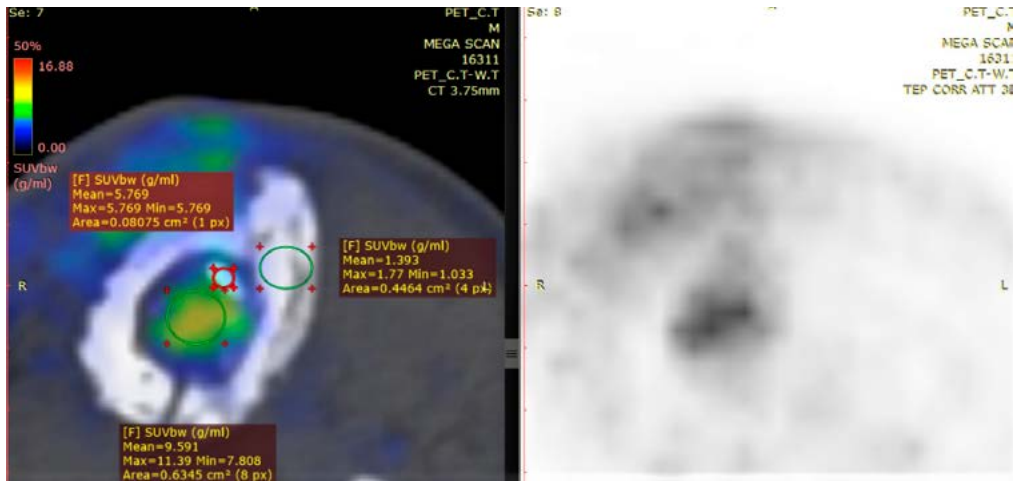
Results: Nineteen patients (17 males/2 females) were operated on in one center between October/2021 and Jan/2023 at a mean age of 32±18. There were 10 tibias, 7 femurs, one ulna, and one fibula. Ten had postoperative COM, six open fractures, and three hematogenous OM. They all showed sequestrum on PET-CT; the dead bone appeared void, surrounded by a halo of increased uptake. There was a trend of lower uptake in the sequestrum compared to the halo around. The mean SUVmax at the sequestrum was 4.18±3.16, compared to the surrounding halo, 7.08±5.81. The normal bone has a mean SUVmax of 1.61±1.42. Sequestrum was removed successfully in all cases.

Conclusion: 18F-FDG-PET-CT can precisely localize the sequestrum preoperatively, it has a lower uptake than tissues around it. This would facilitate planning and improve the quality of debridement.

Patient number 126

A male patient, 60 years old, had a closed fracture left tibia on 04 Feb 2019, operated on by closed nailing after two days. Signs of inflammation and infection started 3 months after surgery, with sinus draining pus at the fracture site. Suppressive antibiotics were used till Union was achieved. The nail was removed in August 2019. However, the infection persisted. After referral to our center, PET-CT showed a bony sequestrum; surgery was done to remove it with proper debridement.





[FP I2] NOVEL DIAGNOSIS MARKER OF PERIPROSTHETIC JOINT INFECTION: A SYSTEMATIC REVIEW

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Background: The identification of novel biomarker which is highly specific and sensitive for periprosthetic joint (PJI) have the potential to improve diagnostic accuracy and ultimately improve patient outcomes. Thus, the aim of this systemic review is to identify and evaluate novel biomarkers for the preoperative diagnostics of PJI.

Methods: MEDLINE, EMBASE, PubMed and Cochrane Library databases identified from 1st of January 2018 to 30th of September. 2022. We used "periprosthetic joint infection" OR "prosthetic joint infection" OR "periprosthetic infection" as the diagnosis of interest and the target index applied AND "marker". To focus on novel biomarkers already used biomarkers of the established PJI diagnostic criteria of MSIS, ICM and EBJIS were not included in the analysis. These three criteria were considered the reference standard during quality assessment.

Results: A total of 19 studies were included. In these, fourteen different novel biomarkers were analyzed. Fifteen studies (79%) had prospective designs and the other four (22%) were retrospective studies. Six studies (33%) included only periprosthetic knee infections and thirteen (67%) included periprosthetic knee and hip infections. Proteins were analyzed in most cases (nine studies), followed by molecules (three studies), exosome (two studies) as well as DNA (two studies), interleukin (one study) and lysosome (one study). One novel and promising marker that had been frequently analyzed is calprotectin.

Conclusion: No marker demonstrated higher sensitivity and specificity than already known parameters used for standardized treatment based on established PJI definitions. Further studies are needed to elucidate the benefit and usefulness of implementing new biomarkers in diagnostic PJI settings.

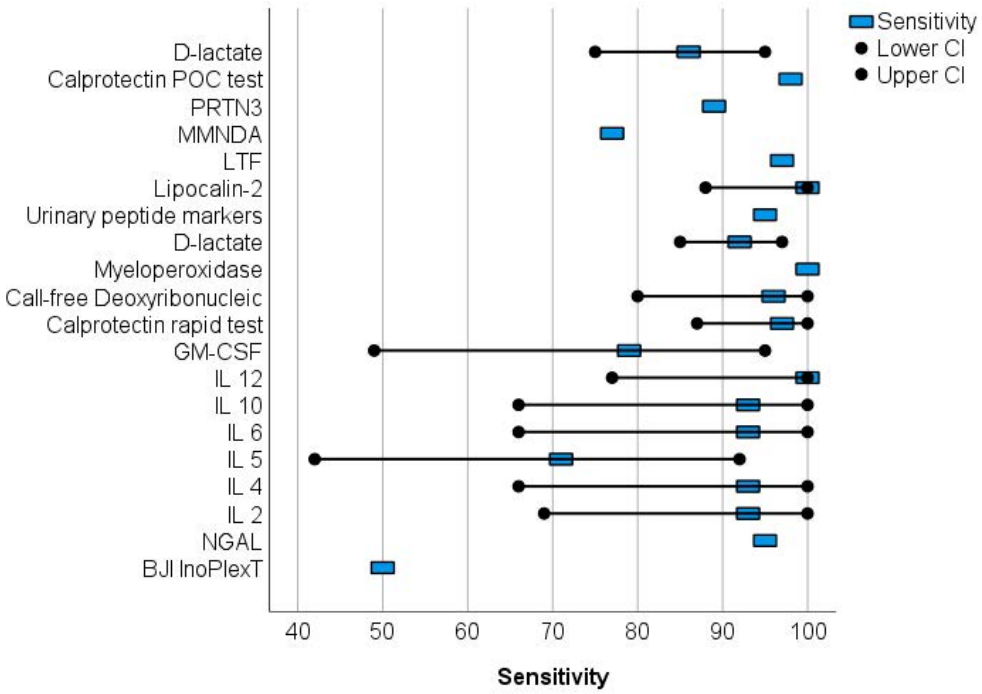

Figure 1: The forest plots of the sensitivity for novel diagnosis marker of periprosthetic joint infection.

[FP I3] CALPROTECTIN: AN IMPORTANT SYNOVIAL MARKER FOR THE DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION

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Background: The diagnosis of periprosthetic joint infection (PJI) remains a challenge in clinical practice and the analysis of synovial fluid (SF) is a useful diagnostic tool. Recently, two synovial biomarkers (leukocyte esterase (LE) strip test, alpha-defensin (AD)) have been introduced into the MSIS (MusculoSkeletal Infection Society) algorithm for the diagnosis of PJI. AD, although promising with high sensitivity and specificity, remains expensive. Calprotectin is another protein released upon activation of articular neutrophils. The determination of calprotectin and joint CRP is feasible in a routine laboratory practice with low cost.

Purpose: Our objective was to evaluate different synovial biomarkers (calprotectin, LE, CRP) for the diagnosis of PJI.

Methods: In this monocentric study, we collected SF from hip, knee, ankle and shoulder joints of 42 patients who underwent revision or puncture for diagnostic purposes. Exclusion criteria included a joint surgery in the previous 3 months and a diagnosis of a systemic inflammatory disease. PJI was diagnosed in a multidisciplinary consultation meeting (RCP) of the Reference Centers for Osteoarticular Infections of the Great West (CRIOGO). SF was analysed for LE, CRP and calprotectin. The cut-off values used were 50 mg/L for calprotectin, 8.8 mg/L for CRP and 125 WBC/µL for LE. The overall sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for these different synovial markers.

Results: Of the 42 patients included, 28 were considered as infected and 14 uninfected. The statistical parameters are presented in Table 1.

Conclusion: The present study shows that the synovial calprotectin assay has an excellent sensitivity and a 100% NPV for the diagnosis of PJI, suggesting that a result < 50 mg/L could exclude PJI. This promising study suggests that calprotectin should be included with synovial CRP in a new decision algorithm for the diagnosis of PJI.

	Sensitivity	Specificity	PPV	NPV
LE	88,90%	86,70%	92,30%	81,25%
CRP	81,50%	93,30%	95,70%	73,70%
Caprotectin	100,00%	73,30%	87,10%	100%

Fig. 1: Sensitivity, specificity, PPV and NPV of leukocyte esterase strip test, C-reactive protein and calprotectin
Abbreviations: PPV, positive predictive value; NPV, negative predictive value; LE, Leukocyte esterase; CRP, C-reactive protein

[FP I4] EVALUATION OF AN UPGRADED SYNOVIAL CALPROTECTIN LATERAL FLOW ASSAY IN UNCLEAR CASES OF HIP AND KNEE PROSTHETIC JOINT INFECTIONS

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Aim: Synovial calprotectin point-of-care test (POC) has shown promising clinical value in diagnosing periprosthetic joint infections (PJIs). However, limited data are available in unclear cases. Moreover, cut-off values for calprotectin lateral flow assay (LFA) and enzyme-linked immunosorbent assay (ELISA) need to be adapted. The aim of this study was to evaluate the performance of an upgraded and more sensitive version of a synovial calprotectin LFA along with ELISA immunoassay in patients with septic, aseptic, and unclear cases.

Methods: Overall, 206 prospectively collected periprosthetic synovial fluid samples from 169 patients (106f/63m; 38 hip/131 knee) who underwent revision surgeries were retrospectively evaluated for calprotectin concentration. The following groups were analyzed: unexpected negative cultures (UNC; 32/206), unexpected positive cultures (UPC; 28/206), and unclear cases (65/206) with conflicting clinical results. In addition, we added a true aseptic (40/206), and true septic (41/206) control groups according to the international consensus meeting (ICM) 2018 PJI classification. Calprotectin concentration was determined by a rapid quantitative LFA (n=206) (Lyfstone®, Norway), and compared to calprotectin ELISA immunoassay (171/206). For the determination of a new calprotectin cut-off value, analysis of the area under the curve (AUC) followed by Youden's J statistic were performed using the calproctectin values from clear septic and aseptic cases. Sensitivity and specificity for calprotectin were calculated. All statistical analyses were performed using IBM-SPSS® version 25 (Armonk, NY, USA).

Results: An absolute calprotectin value of 43 mg/ml, and 40.15 mg/ml was determined to be the optimal cut-off for PJI diagnosis using the new version of the LFA and ELISA, respectively. With this cut-off, the sensitivity and specificity of synovial calprotectin concentration for PJI were 88.1% (95% CI 77.8 to 94.7) and 76.6% (95% CI 61.9 to 87.7) for LFA, and 97.06% (95% CI 89.8 to 99.64) and 93.6% (95% CI 82.5 to 98.66) for ELISA, respectively. Of the evaluated groups, UNC 30/32 (93.8%) ***vs*** 26/27 (96.3%), UPC 6/28 (21.4%) ***vs*** 4/21 (19%), and unclear samples 45/65 (69.2%) ***vs*** 30/56 (53.6%) displayed a high likelihood of infection by using LFA, and ELISA, respectively.

Conclusion: The upgraded version of the calprotectin quantitative LFA with a new suggested cut-off for infected samples showed additional clinical value in identifying cases at high risk of infection in unclear PJI revisions. Additionally, calprotectin ELISA immunoassay had a better performance than LFA. Further large sample-size validation studies are warranted.

[FP I5] INFERIOR DIAGNOSTIC PERFORMANCE OF SERUM ALBUMIN-GLOBULIN-RATIO IN PERIPROSTHETIC JOINT INFECTION

Markus Luger[1], Reinhard Windhager[1], Irene Sigmund[1]

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Aim: Serum parameters continue to be a focus of research in diagnosing periprosthetic joint infections (PJI). Several workgroups have recently proposed serum Albumin-Globulin-Ratio (AGR) as a potential new biomarker. Due to controversies in the literature, its usability in clinical practice remains uncertain. The aim of this study was to assess the value of serum AGR in diagnosing PJI preoperatively, especially in comparison with the well-established marker C-reactive Protein (CRP).

Method: From January 2015 to June 2022, patients with indicated revision hip (rTHA) and knee (rTKA) arthroplasty were included in this retrospective cohort study of prospectively collected data. A standardized diagnostic workup was performed using the 2021 European Bone and Joint Infection Society (EBJIS) definition of PJI, excluding CRP. Diagnostic accuracies of serum AGR and CRP were calculated by receiver operating characteristic curve (ROC) analysis. A z-test was used to compare the area under the curves (AUC).

Results: A total of 275 patients with rTHA and rTKA were included, 144 joints (52.4%) were identified as septic. Decreased AGR and elevated CRP were strongly associated with PJI, optimal diagnostic thresholds were calculated with 1.253 and 9.4 mg/L, respectively. Sensitivities were 62.5% (95%-confidence interval: 54.3–70.0) and 73.6% (65.8–80.1), and specificities 84.7% (77.5–89.9) and 87.8% (80.9–92.4), respectively. CRP showed a significantly higher AUC than AGR (0.807 (0.761–0.853) and 0.736 (0.686–0.786); $p<0.0001$).

Subgroup analysis of acute versus chronic infections yielded significantly higher diagnostic accuracies in acute PJI for both parameters ($p<0.0001$). Similar results were observed when focusing on the causative microorganism; a better diagnostic performance was observed in high-virulence PJI compared to low-virulence PJI ($p\leq0.005$). Furthermore, higher AUCs were calculated in knee PJI compared with hip PJI, with a significant difference for AGR ($p=0.043$).

Conclusions: Due to its limited diagnostic accuracy, serum AGR cannot be recommended as an additional marker for diagnosing PJI. Serum parameters are generally unspecific and can be influenced by comorbidities and other foci of infection. Additionally, parameters may remain within normal levels in low-grade PJI. Evaluating AGR, further possible pitfalls must be considered, for example an increased latency until bottom values are reached and the impact of malnutrition.

[FP I6] PLASMA FIBRINOGEN IS A PROMISING FIRST-LINE SCREENING BIOMARKER FOR THE DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION AND TIMING OF REIMPLANTATION: A MULTICENTER RETROSPECTIVE STUDY

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Aim: The diagnosis of periprosthetic joint infection (PJI) remains a clinical dilemma, since presentations of PJI usually greatly overlap with aseptic failure (AF). The aim of this study is to evaluate the values of plasma fibrinogen, individually or in combination with CRP, ESR and WBC, for distinguishing PJI from AF.

Method: We retrospectively enrolled 357 cases who underwent revision hip or knee arthroplasties in the Third Affiliated Hospital of Southern Medical University, Sun Yat-sen Memorial Hospital and the First Affiliated Hospital of Sun Yat-sen University from January 2013 to December 2021, including 197 AF, 116 PJI and 44 reimplantation. The diagnostic capacity of preoperative fibrinogen, CRP, ESR and WBC as well as their combinations for differentiating PJI from AF were assessed by ROC curves. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated according to the optimal cutoff value based on the Youden index. All biomarkers were further investigated for their potential ability to predict optimal timing of reimplantation as well as their diagnostic capacity in the subgroups of the knee and hip PJI. Furthermore, the correlations among fibrinogen, CRP and ESR in the patients with PJI and AF were analyzed to further evaluate the potential capacity of fibrinogen in the diagnosis of PJI.

Results: The levels of fibrinogen, CRP, ESR and WBC were significantly higher in PJI group than in AF group. ROC analyses showed that the AUCs of fibrinogen, CRP, ESR and WBC were 0.879, 0.903, 0.879 and 0.685, respectively. The optimal threshold of fibrinogen is 4.04 g/L (74.1% sensitivity, 85.6% specificity, 76.1% PPV, 85.0% NPV and 81.8% accuracy). Combining fibrinogen with CRP and/or ESR (AUC: 0.903~0.914) yielded almost equivalent diagnostic efficiency compared with the combination of CRP and ESR (AUC: 0.910). Besides, fibrinogen yielded AUCs of 0.869 (cutoff: 3.44 g/L) and 0.887 (cutoff: 4.12 g/L) in the hip and knee subgroups, with higher specificity and PPV of 93.1% and 96.1% in the knee PJI. Intriguingly, as for the cases with CRP < 10mg/L and ESR ≧ 30 mm/h, the specificity and NPV of fibrinogen for diagnosing PJI were 92.2% and 83.9%.

Conclusions: Plasma fibrinogen is considered as a potential first-line screening marker for PJI detection and timing of reimplantation. As for the patients with an increased ESR but normal CRP, a low fibrinogen level (below 4.04 g/L) is more likely to rule out PJI.

[FP I7] SYNOVIAL FLUID VISCOSITY WITH SYNOVIAL FLUID CELL COUNT: A HIGHLY SENSITIVE AND SPECIFIC DIAGNOSTIC TOOLS OF PROSTHETIC JOINT INFECTIONS

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Aim: Prosthetic joint infection (PJI) represents the second most frequent complication of total joint arthroplasty (TJA) with up to 20% of low-grade PJI treated as aseptic failure. Sensitive diagnostic criteria have been provided by EBJIS. However, to date there is no single test to reliably diagnose all PJIs. Studies of Mazzuco et al. and Fu et al. suggest that synovial fluid (SF) viscosity could be considered as an important marker for PJI. The primary aim of our study was to determine if SF viscosity is a more reliable diagnostic criterion of PJI than the SF cell count with differential (CCD), and the combined diagnostic value of SF viscosity and CCD.

Method: We prospectively analysed the viscosity of SF samples obtained during TJA of hip and knee revisions. We sampled 2.5-5mL of SF for viscosity and CCD. Intraoperatively, 1mL of the sample was analysed for the CCD. The remaining SF was centrifuged for 4min at 7000rpm. The viscosity of the supernatant was determined on Ostwald viscometer as the time required to pass the viscometer at 20°C. During each surgery at least 5 microbiological and multiple histopathological samples were harvested, and explant sonication was performed. The diagnosis was based on EBJIS definition. The viscosity threshold for detecting PJI was set at 65 seconds.

Results: Between December 2020 and January 2023, we analysed 65 knee and 47 hip TJA revision procedures. There were 55 septic and 57 aseptic diagnoses. As a diagnostic marker of PJI, SF viscosity achieved 82.5% sensitivity and 100% specificity, with area under the receiver operating characteristic curve (AUC) of 0.832 (95% CI 0.739, 0.925). The specificity and sensitivity of SF CCD were 98.2% and 78.2%, respectively, with AUC of 0.921 (95% CI 0.869, 0.974). Of the 10 cases incorrectly diagnosed as aseptic based on SF viscosity, 2 were acute traumas and 8 metalloses. The SF CCD in all these cases was <0.5. Of the 12 cases incorrectly diagnosed as aseptic based on SF CCD, 6 cases were culture negative, 4 ***C. acnes*** and 2 ***S. epidemidis*** isolates in microbiology. Taken together, SF viscosity and CCD achieved a combined AUC of 0.953 (95% CI 0.919, 0.987).

Conclusions: Our study is the first to report that SF viscosity is more sensitive but slightly less specific for PJI than SF CCD. The study demonstrates diagnostic value of combining SF viscosity with CCD in decision making in TJA revision surgery.

[FP J1] THE PREDICTIVE VALUE AND RELIABILITY OF ULTRASOUND-GUIDED BIOPSIES FOR DIAGNOSING PERIPROSTHETIC SHOULDER INFECTIONS

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Aim: Diagnosis of periprosthetic shoulder infections (PSI) is difficult as they are mostly caused by low-virulent bacteria and patients do not show typical infection signs, such as elevated blood markers, wound leakage, or red and swollen skin. Ultrasound-guided biopsies for culture may therefore be an alternative for mini-open biopsies as less costly and invasive method. The aim of this study was to determine the diagnostic value and reliability of ultrasound-guided biopsies for cultures alone and in combination polymerase chain reaction (PCR), and/or synovial markers for preoperative diagnosis of PSI in patients undergoing revision shoulder surgery.

Method: A prospective explorative diagnostic cohort study was performed including patients undergoing revision shoulder replacement surgery. A shoulder puncture was taken preoperatively before incision to collect synovial fluid for interleukin-6 (IL-6), calprotectin, WBC, polymorphonuclear cells determination. Prior to revision surgery, six ultrasound-guided synovial tissue biopsies were collected for culture and two additional for PCR analysis. Six routine care tissue biopsies were taken during revision surgery and served as reference standard.
Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV; primary outcome measure), and accuracy were calculated for ultrasound-guided biopsies, and synovial markers, and combinations of these.

Results: Fifty-five patients were included. In 24 patients, routine tissue cultures were positive for infection. Cultures from ultrasound-guided biopsies diagnosed an infection in 7 of these patients, yielding a sensitivity, specificity, PPV, NPV, and accuracy of 29.2%, 93.5%, 77.8%, 63.0%, and 65.6%, respectively.

Ultrasound-guided biopsies in combination with synovial WBC increased the NPV to 76.7% and accuracy to 73.8%. When synovial WBC and calprotectin were combined with ultrasound-guided biopsies, it resulted in a better diagnostic value: sensitivity 69.2%, specificity 80.0%, PPV 69.2%, NPV 80.0%, and accuracy 75.8%. Ultrasound-guided biopsies in combination with calprotectin and ESR yielded a sensitivity of 50.0%, specificity of 93.8%, PPV of 80.0%, NPV of 78.9%, and accuracy of 79.2%.

Synovial fluid was obtained in 42 patients. Sensitivities of WBC, PMN, IL-6, and calprotectin were between 25.0% and 35.7%, specificities between 89.5% and 95.0%, PPVs between 60.0% and 83.3%, NPVs between 65.4% and 69.4%, and accuracies between 64.5% and 70.6%.

Conclusions: In this prospective study we showed that ultrasound-guided biopsies for cultures alone and in combination with PCR and/or synovial markers are not reliable enough to use in clinical practice for the preoperative diagnosis of low grade PSI.

[FP J2] THE VALUE OF PREOPERATIVE ULTRASOUND-DETERMINED FLUID FILM AND JOINT ASPIRATION PRIOR TO REVISION TOTAL HIP ARTHROPLASTY FOR THE DIAGNOSIS OF PERIPROSTHETIC HIP JOINT INFECTION

Jennyfer A Mitterer[1], Bernhard J.H. Frank[1], Matthias Guger[2], Lukas Schoefberger[1], Sebastian Simon[3], Stephanie Huber[1], Maximilian Autherith[1], Jochen Hofstätter[1]

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Background: Data regarding the diagnostic value of ultrasound (US)-determined fluid film and joint aspiration prior to revision total hip arthroplasty (THA) for suspected periprosthetic joint infections (PJIs) is limited. This study aimed to analyse (1) the value of US-determined fluid film, (2) characterisation of the pre- and intraoperative microbiological spectrum and resistance patterns and (3) the concordance between preoperative synovial fluid and intraoperative culture results.

Methods: We analysed 366 US-examinations from 340 patients prior to revision THA. Selected cases were categorized into clearly infected, non-infected and inconclusive, according to the International Consensus Meeting (ICM) 2018 Criteria. If US-determined fluid film was <1mm, no aspiration was performed based on our institutional standard protocol. Patients were grouped into no-aspiration (144/366;[39.3%]), dry-tap (21/366;[5.7%]) and a successful-tap (201/366;[54.9%]). The microbiological spectrum and antibiotic resistance patterns were determined and differences were compared between pre- and intraoperative results.

Results: The absence of US-determined fluid film showed no correlation with the presence of hip PJI. Overall, 29.9% cases of the no-aspiration-group had a confirmed PJI. Discrepancies were found in 43.2% between successful taps and intraoperative cultures. The most prevalent microorganisms in preoperative synovial fluid were Staphylococcus epidermidis (20.9%), Staphylococcus aureus (20.9%) and Enterococcus faecalis (9.3%). The most prevalent microorganisms in intraoperative cultures were Staphylococcus epidermidis, Cutibacterium acnes and other coagulase-negative Staphylococci (14.2%). Additional microorganisms were identified in 43.8% intraoperatively. ***Staphylococcus aureu***s was more often detected preoperatively (20.9% vs. 5.8%;P=0.003), and ***Cutibacterium acnes*** intraoperatively (2.3% vs. 14.4%;P=0.01). There were no differences between the antibiotic resistance patterns of pre- and intraoperative concordant microorganisms.

Conclusion: Absence of US-determined fluid film cannot rule out the presence of hip PJI. US-guided joint aspirations is a well-established technique. However, the preoperative analysis of synovial fluid shows high discrepancies especially in Cutibacterium acnes and other rare gram-positive microorganisms compared to intraoperative cultures.

[FP J3] GENOME-BASED ANALYSIS OF VIRULENCE FACTORS OF THE GENUS CUTIBACTERIUM ISOLATED FROM IMPLANT-ASSOCIATED INFECTIONS IN SLOVENIA

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Aim: The aim of our study was to analyze putative genes for virulence factors of ***Cutibacterium*** isolates obtained from implant-associated infections.

Methods: We analyzed 64 isolates of ***Cutibacterium*** spp (***C. acnes*** (53/64), ***C. avidum*** (6/64), ***C. granulosum*** (4/64), ***C. namnetense*** (1/64)) using NextSeq 550 (Illumina) and performed genomic analysis of 24 genes associated with virulence factors (VFs) of ***C. acnes*** previously reported in the literature (1,2). Most isolates were obtained from implant-associated infections (IAI) between 2012-2021 at the Institute of Microbiology and Immunology, Faculty of Medicine, Ljubljana. Additionally, we included the first ***C. namnetense*** isolated in our laboratory from surgical site infection.

Results: ***C. acnes*** and ***C. namnetense*** have the highest number of VFs among those examined (Table 1). The VFs ***gntK*** (shikimate kinase) and ***hyIIBII*** (hyaluronate lyase) are absent in phylotype IA1 (sequence types (ST) A, C, D according to the SLST scheme) and ***deoR*** (porphyrin) is present only in the group of ST D1. The phylotypes II and IB show a similar distribution of VFs, with the presence of the VFs ***rcsB*** (compound for biofilm formation) and ***HyIIA*** (hyaluronate lyase), which are absent in other ***C. acnes*** phylotypes and other ***Cutibacterium*** spp.

In phylotypes IA1 and IB, the sequence of genes encoding VFs ***DsA1*** and ***DsA2*** does not have 100% genomic coverage, possibly indicating homologs between species. The isolates of ***C. acnes*** and ***C. namnetense*** possess all three CAMP (1,2,4) factors, which are not detected in other ***Cutibacterium*** spp. However, further analysis revealed species-specific CAMP factors in ***C. avidum*** and ***C. granulosum***. Both species also have similar other genes for VFs, mainly encoding heat shock proteins and lipases, while VFs related to biofilm production are mostly absent (***rcsB, ytpA***).

Conclusion: We found several differences in the distribution of VFs among ***Cutibacterium*** spp. isolated from IAI.

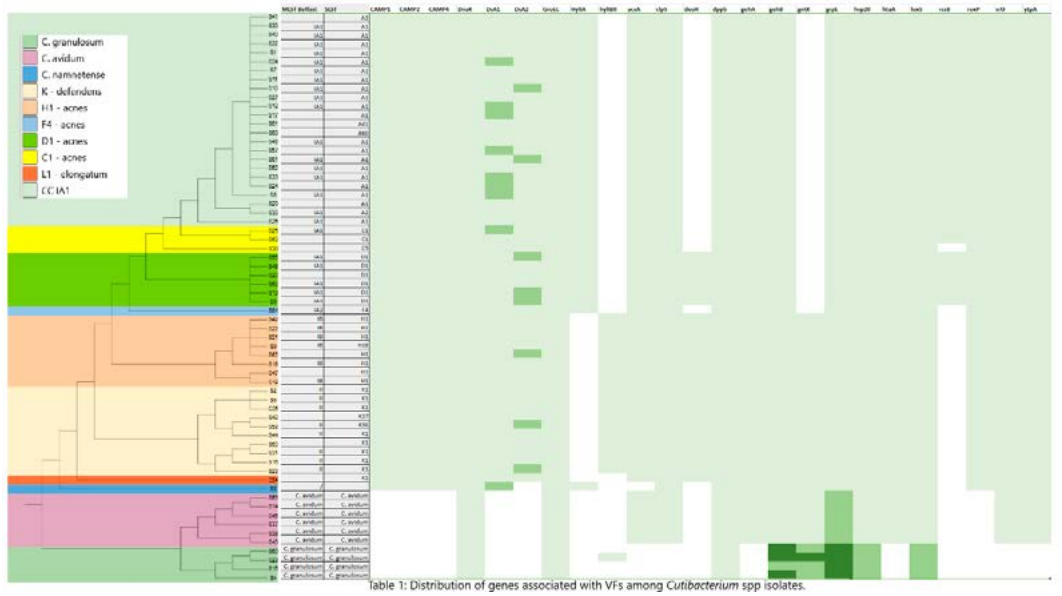

Table 1: Distribution of genes associated with VFs among *Cutibacterium* spp isolates.

Literature:
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[FP J4] IMPROVING THE DIAGNOSIS OF BONE AND JOINT INFECTIONS: EVALUATION OF 16S RDNA TARGETED META-GENOMICS

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Aim: While 16S rRNA PCR - Sanger sequencing has paved the way for the diagnosis of culture-negative bacterial infections, it does not provide the composition of polymicrobial infections. We aimed to evaluate the performance of the Nanopore-based 16S rRNA metagenomic approach using partial-length amplification of the gene, and to explore its feasibility and suitability as a routine diagnostic tool for bone and joint infections (BJI) in a clinical laboratory.

Method: Sixty-two clinical samples from patients with BJI were sequenced on MinION* using the in-house partial amplification of the 16S rRNA gene. BJI were defined based on the ICM Philly 2018 and EBJIS 2021 criteria. Among the 62 samples, 16 (26%) were culture-positive, including 6 polymicrobial infections, and 46 (74%) were culture-negative from mono- and polymicrobial infections based on Sanger-sequencing. Contamination, background noise definition, bacterial identification, and time-effectiveness issues were addressed.

Results: Results were obtained within one day. Setting a threshold at 1% of total reads overcame the background noise issue and eased interpretation of clinical samples. The partial 16S rRNA metagenomics approach had a greater sensitivity compared both to the culture method and the Sanger sequencing. All the 16 culture-positive samples were confirmed with the metagenomic sequencing. Bacterial DNA was detected in 32 culture-negative samples (70%), with pathogens consistent with BJI. The 14 Nanopore negative samples included 7 negative results confirmed after implementation of other molecular techniques and 7 false-negative MinION results : 3 ***Kingella kingae*** infections detected after targeted-PCR only, 2 ***Staphylococcus aureus*** infections and 2 ***Pseudomonas aeruginosa*** infections sterile on agar plate media and detected only after implementation of blood culture media, advocating for the very low inoculum.

Conclusions: The results discriminated polymicrobial samples, and gave accurate bacterial identifications compared to Sanger-based results. They confirmed that Nanopore technology is user-friendly as well as cost- and time-effective. They also indicated that 16S rRNA targeted metagenomics is a suitable approach to be implemented for routine diagnosis of culture-negative samples in clinical laboratories.

* Oxford Nanopore Technologies

[FP J5] WHAT IS THE AGREEMENT BETWEEN PRINCIPLES AND PRACTICE OF ANTI-BIOTIC STEWARDSHIP IN THE MANAGEMENT OF DIABETIC FOOT INFECTIONS?

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Background and aim: In 2019, specific diagnostic and antibiotic treatment recommendations for diabetic foot infection (DFI) and osteomyelitis (DFO) were introduced in our institution. They include principles on numbers of biopsies to obtain for microbiological/histopathological examinations, labeling anatomic localization, and antibiotic treatment (ABT) duration based on the aforementioned findings. ABT should be stopped after complete resection of infected bone. In case of incomplete resection, treatment is continued for 4–6 weeks. Two years after the introduction of these recommendations, we investigated the degree of implementation for hospitalized patients.

Method: Adult patients with DFI/DFO undergoing surgical intervention from 01/2019–12/2021 were reviewed retrospectively. Diagnostic procedures were assigned to each episode when performed ≤30 days before surgical invention. Chi-square and Mann-Whitney-U tests were performed where appropriate.

Results: We included 80 patients with 117 hospital episodes and 163 surgical interventions (mean 1.5 episodes and 2 interventions per patient). The mean age was 69.6 (SD 11.5) years, 75% were male. Vascular examination and MRI were performed in 70.9% and 74.4% of episodes, respectively. Impaired perfusion and DFO were confirmed in 34.9% and 56.3%, respectively. Blood cultures were sampled in 34.2%, bacteremia detected in 7.7% with ***S. aureus*** being the most common microorganism. Biopsies were obtained in 71.8% of operations, in 90.5% of those 3–5 samples. These were sent for histological examination in 63.2% of the interventions. In 43.6% the anatomic location was labeled 'proximal to the resection margin'.

Preoperative antibiotics were administered in 41.9% of the episodes because of concomitant soft-tissue infections. The most commonly used compound was amoxicillin/clavulanate (74.4%). ABT duration varied significantly when there were signs of DFO in preoperative MRI (p=0.015). The mean duration of antibiotic therapy was 9 (IQR 5–15) days in surgically cured episodes and 40.5 (IQR 15–42) days in cases with resection margins in non-healthy bone (p<0.0001). The results were similar when analyzing treatment duration with respect to osteomyelitis in histology: 13 (IQR 8-42) versus 29 (IQR 13-42) days, respectively (p=0.026).

Conclusions: The adherence to recommendations in terms of biopsy sampling was excellent, moderate for sending samples to histology and poor for labeling the anatomic location. The adherence to ABT duration was good but can be improved by shortening treatment duration for surgically cured cases. Results of preoperative MRI appear to be influential on the decision-making for treatment duration.

[FP J6] TO SONICATE OR NOT TO SONICATE?

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Aim: To evaluate whether sonication of implant material and subsequent culturing add clinical relevance to culturing of tissue biopsies for improved antibiotic treatment in treatment of bone and joint infection.

Method: A retrospective examination of patients' charts and microbiological analyses in patients who had explanted material (plates, screws, k-wires and prostheses) send for sonication between December 2020 and April 2022.

Results: 77/143 (54 %) patients had complete agreement between the cultures from tissue biopsies and sonication fluid. 66/143 (46 %) patients had partial or no agreement between the cultures from tissue biopsies and sonication fluid.

Of the 66 patients, 31 (47 %) had a culture positive sonication fluid and tissue biopsies that were positive with one or more bacterial isolates. 26/66 (39 %) patients had a culture positive sonication fluid and tissue biopsies that were negative. 9/66 (14 %) patients had negative sonication fluid and positive tissue biopsies.

Of the 26 patients with culture positive sonication fluid and culture negative tissue biopsies, virulent bacteria were found in 5 (19 %) patients, making the diagnosis and treatment of infection straight forward. The remaining 21 (81 %) patients had ***C. acnes, S. epidermidis*** and CoNS in the sonication fluid, which made the diagnosis less evident but none the less gave the clinician a relevant treatment option.

Conclusion: In this study a high concordance was found between cultures from tissue biopsies and sonication fluid. Additionally, in a small group of patients with culture negative tissue biopsy, the culture of sonication fluid was essential to the identification infections agent. This indicates that culture of sonication fluid is an important diagnostic tool in bone and joint infection, especially in the absence of positive tissue cultures.

[FP J7] DOES HIGH BACTERIAL LOAD IN SONICATION OF MOBILE PARTS PREDICT FAILURE AFTER DAIR IN PROSTHETIC JOINT INFECTIONS?

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Aim: One of the surgical therapeutic options for periprosthetic joint infection (PJI) includes debridement, antibiotics, and implant retention (DAIR). Prognostically favorable criteria for DAIR include short duration of symptoms, stable implant, pathogen susceptible to a 'biofilm-active' antimicrobial agent, and intact soft-tissue conditions. Despite this, there is a proportion of failures after DAIR, possibly because the duration of infection is underestimated. With the hypothesis that the duration of infection correlates with the bacterial load, and hence, the bacterial load is associated with failure after DAIR, we aimed to investigate the association of bacterial load in the sonication fluid of mobile parts and clinical outcome after DAIR.

Method: From our PJI cohort (2010-2021), patients with DAIR (both palliative and curative approaches) were reviewed retrospectively. Patients with hip, knee or shoulder arthroplasties fulfilling infection definition, available sonication results, and ≥2 years follow-up were included. Sonication results were categorized in ≤ or >1000 cfu/mL. Univariate analysis was performed to identify predictors for DAIR failure.

Results: Out of 209 PJIs, we identified 96 patients (100 PJIs, 47.8%) with DAIR. In 67 (69.8%) patients with 71 PJIs, there was a follow-up of ≥2 years. The mean age was 72.7 (SD 12.99) years, 50% were male. The infection affected 36 hips (50.7%), 32 knees (45.1%) and 3 shoulders (4.2%). At follow-up, there were 29 (40.8%) cured and 42 (59.2%) failed cases. When comparing failed and cured cases, we found no difference in comorbidities and previously defined risk factors for PJI, ASA score, Charlson score, anatomic location, no. of previous surgeries, pathogenesis of infection or laboratory values. The proportion of patients with high bacterial load on mobile parts (i.e. >1000 cfu/mL) was significantly higher in the failed DAIR group than it was in the cured group (61.9% vs 20.7%, p<0.001).

Conclusions: In this study, a high bacterial load in sonication fluid of mobile parts was associated with failure after DAIR in patients with PJI. Sonication may help to differentiate acute hematogenous seeding to the implant and late reactivation of a previously silent implant-associated infection.

[BP1] PREVENTION OF PROSTHETIC JOINT INFECTION USING ELECTRICAL FIELDS. PROOF OF CONCEPT IN AN EXPERIMENTAL IN VIVO MODEL

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Aim: To provide proof of concept in an in vivo animal model for the prevention of prosthetic joint infection prevention using electric fields along with conventional antibiotic prophylaxis.

Method: First, we standardized the animal model to simulate implant contamination during the surgical procedure. We then implanted cobalt-chrome prostheses adapted to both knees of two New Zealand White rabbits, under standard aseptic measures and antibiotic prophylaxis with cefazolin. Prior to implantation, we immersed the prostheses in a 0.3 McFarland inoculum of ***S. aureus*** (ATCC 25923) for 30 seconds. In the first animal (control), the joint was directly closed after washing with saline. In the second animal (case), both prostheses were treated with electric current pulses for 30 seconds, washed with saline, and the joint was closed. After 72 hours, both animals were reoperated for the collection of periprosthetic tissue and bone samples, and prosthesis removal. In all samples, we performed quantitative cultures prior to vortexing and sonication, as well as prolonged cultures of the sonication broth. We confirmed the absence of contamination by identification with MALDI-TOF (VITEK-MS) and automated antibiotic susceptibility testing of the isolated colonies (VITEK-2).

Results: In the "control" animal, we isolated ***S. aureus*** in all studied samples. The bacterial count expressed as log10 (cfu/cm2) in the prostheses of the right and left legs was 9.38 and 8.86, respectively. The bacterial count expressed as log10 (cfu/mL) in bone and periprosthetic tissue biopsies was 2.70 and 2.72 in the right leg and 3.24 and 3.87 in the left leg, respectively. In the "case" animal, where an electric field was applied to the implant after placement in addition to cefazolin prophylaxis, all samples (prosthesis, bone, and periprosthetic tissue) were negative, and no isolation of the inoculated strain of ***S. aureus*** was obtained after incubation of the sonication broth for 14 days.

Conclusions: This in vivo model suggests the potential effectiveness of applying an electric field to a prosthetic implant in combination with cefazolin for the prevention of PJI development, after exposure of the implant to an inoculum of ***S. aureus*** (ATCC 25923). Our findings need to be confirmed using a larger sample size.

[BP2] IMPLANT RETENTION IN A RABBIT MODEL OF DELAYED FRACTURE-RELATED INFECTION: SUCCESSFUL ERADICATION BUT IMPAIRED BONE BONE HEALING COMPARED TO EARLY INFECTION

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Aim: The time to onset of symptoms after fracture fixation is still commonly used to classify fracture-related infections (FRI). Early infections (<2 weeks) can often be treated with debridement, systemic antibiotics, irrigation, and implant preservation (DAIR). Late infections (>10 weeks) typically require implant removal as mature, antibiotic-tolerant biofilms have formed. However, the recommendations for delayed infections (2-10 weeks) are not clearly defined. Here, infection healing and bone healing in early and delayed FRI is investigated in a rabbit model with a standardized DAIR procedure.

Method: ***Staphylococcus aureus*** was inoculated into 17 rabbits after plate osteosynthesis in a humerus osteotomy. The infection developed either one week (early group, n=6) or four weeks (delayed group, n=6) before a standardized DAIR procedure and microbiological analysis were performed. Systemic antibiotics were administered for six weeks (two weeks: Nafcillin+Rifampin, four weeks: Levofloxacin+Rifampin). A control group (n=5) also underwent a revision operation (debridement and irrigation) after four weeks, but received no antibiotic treatment. Rabbits were euthanized seven weeks after the revision operation. Bone healing was assessed using a modified radiographic union score for tibial fractures (mRUST). After euthanasia, a quantitative microbiological examination of the entire humerus, adjacent soft tissues, and implants was performed.

Results: All animals were infected at the time of revision surgery, with the bacterial load in the early group (especially in soft tissues) being greater than in the delayed group and control group. This indicates infiltration of bacteria into areas that are more difficult to reach after four weeks of debridement. The infection was eradicated in all animals in both the early and delayed groups at euthanasia, but not in the control group (CFU median (IQR): 2.1×10^7 (1.3×10^7-2.6×10^7). The osteotomy healed in the early group, while bone healing was significantly impaired in both the delayed group and control group (mRUST median (IQR): early group: 16 (14-16), delayed group: 7.5 (6-10), control: 7 (5.5-9); early ***vs.*** delayed: p=0.0411, early ***vs.*** control p=0.0065).

Conclusion: The maturation of the infection between the first and fourth week does not affect the success of infection eradication in this rabbit FRI model. However, bone healing appears to be impaired with increasing duration of infection.

[BP3] MAY LOCAL VANCOMYCIN INCORPORATED INTO BONE SUBSTITUTE INCREASE PLASMA CONCENTRATIONS OF VANCOMYCIN IN PATIENTS WITH OSTEOMYELITIS AND INFLUENCE THE NEED TO PERFORM MORE FREQUENT DOSAGE ADJUSTMENTS?

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Aim: The use of bone substitutes such as calcium sulfate (CaSO4) and hydroxyapatite with local antibiotics are crucial in the treatment of osteomyelitis. They allow the treatment of the dead space and locally provide large concentrations of antibiotics. However, it is unknown whether use of local vancomycin may elute and influence on vancomycin plasma levels.The aim of this study is to assess whether the addition of vancomycin to CaSO4 with hydroxyapatite may increase vancomycin plasma concentrations in in patients with osteomyelitis and therefore alter dosage adjustments.

Method: The present study investigates the vancomycin plasma concentrations at 72-94 h post-surgery after the application of local vancomycin within CaSO4 (660mg vancomycin/10cc) and hydroxyapatite bone substitute in patients treated with empiric intravenous vancomycin and surgically treated for osteomyelitis.

Vancomycin plasma concentrations were analyzed in twelve patients with osteomyelitis surgically treated with local release of vancomycin by CaSO4 and hydroxyapatite and undergoing therapeutic drug monitoring (TDM) of their vancomycin plasma concentrations as it is routinely done in our hospital. From 2019 to 2022, demographic data, microbiology, type of osteomyelitis, amount of local vancomycin applied, alteration of renal function, and vancomycin levels were retrospectively analyzed.

Results: Twelve patients were included: 9(75%) were men. Median (range) demographic and clinical data: age: 51(26-67) years; body mass index: 27.7(18-46.4) kg/m2;baseline serum creatinine: 0.85 (0.7-1.24)mg/dl and 5(41.7%) with and glomerular filtration rate < 90ml/min(CPD-EPI,ml/min). Most frequently isolated microorganisms were Staphylococci (58%). Seven (54%) patients were classified as Cierny-Mader Osteomyelitis type III, 3(23%) as type IV and 2(23%) as type I.
Treatment data: initial dose of vancomycin: 1g/8h in 9(75.0%) and 1g/12h in 3(25%) patients, total daily dose/body weight: 35.3(15.9-46.2) mg/kg. Pharmacokinetic data:days of iv vancomycin treatment until first TDM measurement: 3(3-4) days; minimum and maximum vancomycin plasma concentrations: 9.4(3-17.3) mg/L and 19.6(11.3-33.4) mg/L, respectively; patients with therapeutic concentrations: 6(50%); infratherapeutic: 4(33.3%) and supratherapeutic/potentially toxic: 2(16.7%). These 2 patients were young, had a baseline conserved renal function and were receiving the higher dose of 1g/8h.

Conclusions: Vancomycin incorporated into the bone substitute appears not to increase blood concentrations of the glycopeptide in patients with osteomyelitis treated surgically and with intravenous vancomycin.However, 2 of the 12 patients presented supratherapeutic and potentially nephrotoxic vancomycin concentrations in the first TDM measurement, even though they were young and without renal impairment and needed and unexpected dose reduction. These results suggest the need to confirm the safety of local vancomycin in further larger clinical studies.

[BP4] TOWARDS PREOPERATIVE DIAGNOSIS OF INFECTED NONUNION OF FEMUR OR TIBIA WITH TARGETED PROTEOMICS IN BLOOD PLASMA

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Aim: Differentiation of infected (INF) nonunion from aseptic (AS) nonunion is crucial for the choice of intra- and postoperative treatment. Preoperative diagnosis of infected nonunion is challenging, especially in case of low-grade infection lacking clinical signs of infection. Standard blood markers such as C-reactive protein or leucocyte count do not aid in preoperative diagnosis. Proteomic profiling has shown promising results for differentiation of numerous chronic disease states, and in this study was applied to preoperative blood samples of patients with nonunion in an attempt to identify potential biomarkers.

Method: This prospective multicenter study enrolled patients undergoing revision surgery of femur or tibia nonunion. Patients with implant removal after regular fracture healing (HEAL) were included as a control-group. Preoperative blood samples, intraoperative tissue samples, sonication of osteosynthesis material and 1-year-follow-up questionnaire were taken. Nonunion patients were grouped into INF or AS after assessing bacterial culture and histopathology of retrieved samples. Diagnosis of infection followed the fracture related infection consensus group criteria, with additional consideration of healing one year after revision surgery. Targeted proteomics was used to investigate a predefined panel of 45 cytokines in preoperative blood samples. Statistical differences were calculated with Kruskal Wallis and Dunn´s post hoc test. Cytokines with less than 80% of samples being above the lower limit of detection range (LLDR) were excluded for this study.

Results: We recruited 62 AS, 43 INF and 32 HEAL patients. Patients in the two nonunion groups (INF and AS) did not differ concerning smoking, diabetes or initial open or closed fracture. Thirty-two cytokines were above LLDR in >80% of patients. INF patients showed a significant difference in expression of 8 cytokines compared to AS, with greatest differences observed for Macrophage Colony Stimulating Factor 1 (MCSF-1) and Hepatocyte Growth Factor (HGF) (p<0.01). In comparing AS with HEAL patients, 9 cytokines displayed significant differences, including interleukin (IL)-6, Vascular Endothelial Growth Factor A (VEGFA), Matrix Metalloproteinase 1 (MMP-1). Comparison of INF with HEAL patients revealed significantly different expression of 20 cytokines, including. IL-6, IL-18, VEGFA or MMP-1.

Conclusions: Our study revealed differences in plasma cytokine profile of blood samples from INF and AS patients. Although no single biomarker is sufficient to differentiate these patients preoperatively in isolation, future multivariant analysis of this cytokine data in combination with clinical characteristics may provide valuable diagnostic insights.
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[BP5] DAIR TO STOP: SUPPRESSIVE ANTIBIOTIC TREATMENT AFTER 12 WEEKS OF THERAPY IS NOT BENEFICIAL FOR ACUTE PERIPROSTHETIC JOINT INFECTIONS

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Aim: Debridement, antibiotics, and implant retention (DAIR) is a viable treatment option for acute periprosthetic joint infections (PJI). The landmark DATIPO trial of Bernard et al. concluded that six weeks is not non-inferior to 12-week antibiotic therapy for DAIR. However, it is unknown if suppressive antibiotic treatment (SAT) would improve patient outcomes. Therefore, our study aims to evaluate the utility of SAT after 12 weeks of therapy.

Method: We performed a retrospective study of patients with acute hip or knee PJI managed with DAIR at five institutions; in the U.S. (n=1), Netherlands (n=3), and Spain (n=1) from 2005-2020. We analyzed the effect of SAT using a Cox model among patients after 12 weeks of antibiotic treatment. The primary covariate of interest was whether the patient was on antibiotics after week 12, which was coded as a time-varying covariate. We decided a-priori to control for the clinically important risk factors such as age, sex, type of infection, modular exchange, joint, and presence of bacteremia and ***Staphylococcus aureus***. We excluded patients who died, had treatment failure, or were lost to follow-up before 12 weeks. We defined treatment failure as infection recurrence (same or different organism), unexpected reoperation, or death due to infection.

Results: There were 504 patients included in the study. The majority were female (58%, n=292), with a mean age of 70 years ago (SD 11). Hips and knees were equally proportioned. Primary arthroplasties represented 69% of the total cohort (n=349). Treatment failure was 11.9% in the total cohort (n=60). There was no statistically significant association between SAT after 12 weeks and treatment failure (HR 1.25, p=0.45, 95% CI 0.70-2.24). This finding was consistent across different subgroups, including hip or knee joints, early or late acute infections, cohort, and a subgroup of knee joints after 180 days (Table 1).

Conclusions: SAT after 12 weeks of antibiotic treatment for acute PJI managed with DAIR does not appear to improve patient outcomes.

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

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

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

[BP6] BIOFILM OF CUTIBACTERIUM ACNES: TARGET OF DIFFERENT ACTIVE SUBSTANCES

Ruffier d'Epenoux Louise[1], Erwan Fayoux[1], Joelle Veziers[2], Marie-Ange Dagnelie[3], Amir Khamari[3], Brigitte Deno[3], Stephane Corvec[1]

[1]Nantes University Hospital, Bacteriology, Nantes, France
[2]Nantes University, Regenerative Medicine and Skeleton U1229, Nantes, France
[3]Nantes University, Incit U1302, Nantes, France

Background: Although described as a commensal bacterium with low pathogenicity, Cutibacterium acnes involvement has been reported in many clinical entities: infections associated with devices, such as shoulder prosthetic joint infections, osteosynthesis, breast implants or cerebrospinal fluid shunts. Various studies show that C. acnes grows as a biofilm, contributing to its persistence by allowing its escape from the action of the immune system and antibiotics.

Purpose: Our aim was to assess the activity of different active substances (erythromycin, clindamycin, doxycycline and Myrtacine®) on eight different well-characterized C. acnes strains after growth in biofilm mode.

Methods: Eight susceptible strains of C. acnes were selected for this study, including two reference strains (ATCC6919 and ATCC11827) and six clinical strains. All C. acnes strains were studied using two different methods to study the biofilm production at different time points: the BioFilm Ring Test® technique (early stages of adhesion) and the Crystal Violet (CV) method (mature biofilm). In a second step, the impact of different active substances (erythromycin, clindamycin, doxycycline and Myrtacine®) was studied. For the CV technique, two types of tests were performed: preventive tests (addition of active substances and bacteria at the same time) and curative challenge tests (addition of active substances on a biofilm already formed after 48h). Transmission electron microscopy was performed to investigate the morphology modifications.

Results: C. acnes isolates from phylotypes IA_1 and IA_2, seem to produce more mature biofilm in the first stages of adhesion than other phylotypes. Curative assays were performed to evaluate the efficacy of antibiotics and Myrtacine® on mature biofilm. Significant efficacy of Myrtacine® at 0.03% was observed for C. acnes strains. Moreover, the combination of Myrtacine® and doxycycline appears to decrease the total biofilm biomass. The effect of doxycycline as a preventive measure was minimal. On the contrary, a similar use of Myrtacine® as early as 0.001% showed significant efficacy with a significant decrease in total biofilm biomass for all C. acnes strains. Transmission electron microscopy revealed a significantly decreased biofilm growth in treated bacteria with Myrtacine® compared to untreated bacteria. Moreover, the total number of bacteria decreased as the concentration of Myrtacine® increased suggesting also an antimicrobial effect.

Conclusion: These results confirm the difference in biofilm producing ability depending on C. acnes phylotypes. These results suggest that Myrtacine® may be a promising alternative antibacterial and anti-biofilm agent like peroxide de benzoyle to prevent shoulder prosthetic joint infection involving planktonic and biofilm C. acnes.

[BP7] SEPSIS IN PERIPROSTHETIC JOINT INFECTIONS - EPIDEMIOLOGY, RISK FACTORS, AND OUTCOMES

Susanne Bärtl[1], David Lovasz[2], Jing Li[2], Volker Alt[1], Markus Rupp[1]

[1]Regensburg University Medical Center, Department of Trauma Surgery, Regensburg, Germany
[2]University Medical Center Regensburg, Department of Cardiothoracic Surgery, Regensburg, Germany

Aim: Sepsis is a life-threatening complication of periprosthetic joint infections (PJI) that requires early and effective therapy. This study aims to investigate the epidemiology, associated risk factors, and outcome of sepsis in the context of periprosthetic joint infections (PJI).

Method: This single-center retrospective cohort study included patients treated for PJI from 2017 to 2020. Patients were classified based on the criteria of the European Bone and Joint Infection Society. The presence of sepsis was determined using the SOFA score and SIRS criteria. The cohort with PJI and sepsis (sepsis) was compared to patients with PJI without sepsis (non-sepsis). Risk factors considered were patient characteristics, affected joints, surgical therapy, microbiological findings, preexisting medical conditions, clinical symptoms, and symptom duration. Outcome parameters were mortality, length of hospital stay, and length of stay in the intensive care unit.

Results: A total of 109 patients with PJI were identified, of whom 45 patients (41.3%) met the criteria for sepsis. Patients with sepsis had more severe preexisting diseases compared with the non-sepsis cohort (Charlson Comorbidity Index 3.8 vs. 2.8; $p \leq 0.001$). An increased odds ratio (OR) for a septic course was found for the comorbidities pneumonia (8.2; $p=0.001$), myocardial infarction (2.0; $p=0.02$), atrial fibrillation (3.3; $p=0.01$), diabetes mellitus (1.2; $p=0.04$), endocarditis (5.5; $p=0.01$), and renal disease (2.0; $p \leq 0.001$). Infection with ***Staphylococcus aureus*** (sepsis 20 vs. non-sepsis 10; $p=0.002$), ***Streptococcus dysgalactiae*** (sepsis 7 vs. non-sepsis 2; $p=0.002$) and ***Candida albicans*** (sepsis 5 vs. non-sepsis 0; $p=0.01$) were more prevalent in patients with sepsis. In the sepsis cohort, further infectious foci were present in addition to PJI in 57.8% of patients, compared to 18.8% in the non-sepsis cohort. The presence of sepsis was associated with a longer hospital stay (sepsis 68 days vs. non-sepsis 38 days; $p=0.001$) and longer intensive care unit stay (sepsis 12 days vs. non-sepsis 2 days; $p=0.001$). In-hospital mortality was ten times higher in the sepsis cohort compared to non-septic patients (sepsis 11/42 vs. non-sepsis 2/64; OR 10.3; $p=0.01$).

Conclusions: In a relevant proportion of patients, PJI can lead to a septic course of disease associated with increased mortality. Particularly in patients with preexisting diseases, increased attention is required, and comprehensive screening for other foci of infection seems mandatory. In addition to highly virulent pathogens such as staphylococci and streptococci, fungal infections should be considered as causative pathogens in septic patients with PJI.

[BP8] MENTAL HEALTH AND EXPERIENCED PHYSICAL & PSYCHOLOGICAL IMPAIRMENT IN PATIENTS WITH MUSCULOSKELETAL INFECTIONS

Katinka Wetzel[1], Annabell Mueller[2], Mandy Mathys[3], Mario Morgenstern[1], Martin Clauss[1]

[1]University Hospital Basel, Universitätsspital Basel, Center for Musculoskeletal Infections, Dept. of Orthopaedic and Trauma Surgery, Basel, Switzerland
[2]University Hospital Basel, Quality Management & Value Based Healthcare, Basel, Switzerland
[3]University Hospital Basel, Basel, Switzerland

Aim: Musculoskeletal infection is a serious complication, however literature is lacking prospective data on its impact on mental health. The study aimed to assess mental health in patients with musculoskeletal infections and how they experience the possible mental and physical impairment.

Method: All patients treated in our unit for musculoskeletal infections between July 2000 and March 2022 were prospectively included. To assess specific patient reported outcomes the following questionnaires were used: World-Health-Organization Quality-Of-Life (WHOQOL)-BREF and the Veterans-RAND-12Item Health Survey (VR-12) for mental & physical health; Patient-Health-Questionnaire (PHQ-8) for depression symptoms; Generalized-Anxiety-Disorder-Scale-7 (GAD-7) for anxiety symptoms and Somatic-Symptom-Disorder-B Criteria Scale (SSD-12) for experience of mental & physical impairment. The surveys were conducted at baseline, 6 and 12-weeks and 1-year.

Results: In total 199 patients were included (31 fracture-related infections, 80 prosthetic joint infections, 40 diabetic foot syndromes and 48 other musculoskeletal infections).
Physical health was significantly worse 6 weeks after treatment compared to baseline (WHOQOL p=.002; VR-12 p<.001), but significantly better at 3-months (p<.001; p=.006) and 12-months (p=.003; p<.001). Mental health was significantly worse at 3-months (WHOQOL p=.002), but at final follow-up significantly better (VR-12 p=.046). Social relationships (domain of WHOQOL) were perceived significantly worse 6 weeks and 12 months after treatment initiation (p=.003; p=.007), as were environmental factors.

At baseline moderate to severe depression symptoms (PHQ-8≥10) and moderate to severe anxiety symptoms (GAD-7≥10) were observed in 14.6%, respectively 10.6% of all patients. At 12-months these were 7.4% and 3%.

Over the course of treatment, only patients with DFS showed a significant change in experienced psychological or physical impairment, which was perceived significantly less compared 6 weeks to 12 months (p=.042).

Conclusions: Patients with musculoskeletal infections suffer from a considerable impact on their mental health. The greatest impairment in physical health was seen 6 weeks after beginning of treatment. The psychological well-being was worse at 3-months. Environmental factors, such as mobility, activities of daily living and dependence on medication or medical treatment were worst at 3-months. Also increasingly worse social relationships over the course of treatment was observed.
Further studies are needed to identify psychological impairment and related factors, as well as to determine how patients cope with their disease and treatment. This could serve as a foundation to implement treatment algorithms in order to improve patient related outcome and quality of life.

[BP9] EXTENDED ANTIMICROBIAL PROPHYLAXIS DOES NOT IMPROVE OUTCOME OF UNEXPECTED PJI: A RANDOMIZED CONTROLLED TRAIL

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[1]Sint Maartenskliniek, Internal Medicine - Infectious Diseases, Nijmegen, Netherlands
[2]Sint Maartenskliniek/Radboudumc, Internal Medicine/Infectious Disease, Ubbergen/Nijmegen, Netherlands
[3]Radboud Umc, Radboud Umc, Orthopedics, Heilig Landstichting, Netherlands
[4]Sint Maartenskliniek, Sint Maarenskliniek, Orthopedics, Nijmegen, Netherlands

Aim: In 10% of the presumed aseptic hip or knee revisions, a low-grade infection is unexpectedly diagnosed based on the tissue samples taken during revision. Extended antimicrobial prophylaxis can possibly reduce the failure rate in cases of unexpected PJI, because the prophylaxis can be considered as early empiric treatment. In this randomized controlled study we analysed whether extended antimicrobial prophylaxis compared to a single dose is beneficial to improve the outcome of treatment in unexpected PJI in revision arthroplasty.

Method: This study was nested in a randomized clinical trial comparing single-dose cefazolin with prolonged prophylaxis (15 doses of cefazolin over 5 days) for revision arthroplasty of the hip or knee. For this analysis, patients were included if an unsuspected PJI (defined as ≥2 positive intraoperative tissue samples with the same microorganism) was diagnosed. PJI treatment consisted of 12 weeks of a rifampicin-based regimen in Staphylococcal PJI, without removal of the prosthesis. We examined Infection characteristics and success of treatment after one year, defined as the absence of signs or treatment for PJI during follow-up.

Results: After randomization of 662 patients, 68 unexpected PJI were diagnosed. In 5 cases no antimicrobial treatment was started. The success rate after one year follow-up for those who received PJI treatment was 96% (28/29) in the single dose group and 91% (31/34) in the extended prophylaxis group (p=1.00). The most frequently identified pathogens in unexpected PJI were ***Cutibacterium acnes*** (n=50) and ***Staphylococcus epidermidis*** (n=14). The causatives were susceptible for the cefazolin prophylaxis in 61 of the 63 cases. The interval between the stopped prophylaxis and the re-start of antimicrobial treatment was on average 10 days (SD 4) for the single dose and 5 days (SD 4) for the extended group. The mean duration of antimicrobial treatment was 83 days (SD 12) and did not differ between both groups (p=0.16).

Conclusions: This is the first randomized controlled trial in which extended prophylaxis showed no benefit on the prosthesis survival for patients with an unexpected PJI after assumed aseptic revision of the hip or knee prosthesis. The results imply that extended prophylaxis should not be given as part of early empiric therapy.

[BP10] DEVELOPMENT AND VALIDATION OF A SYNTHETIC SYNOVIAL FLUID MODEL AS DIAGNOSTIC TOOL FOR BIOFILM-RELATED PROSTHETIC JOINT INFECTIONS

Amber De Bleeckere[1], Stien Vandendriessche[2], Anne-Sophie Messiaen[2], Aurélie Crabbé[1], Jerina Boelens[2], Tom Coenye[1]

[1]Ghent University, Laboratory of Pharmaceutical Microbiology, Ghent, Belgium
[2]Ghent University Hospital, Department of Medical Microbiology, Ghent, Belgium

Aim: There is growing evidence that bacteria encountered in periprosthetic joint infections (PJI) form surface-attached biofilms on prostheses, as well as biofilm aggregates embedded in synovial fluid and tissues. However, models allowing the investigation of these biofilms and the assessment of their antimicrobial susceptibility in physiologically relevant conditions are currently lacking. To address this, we developed a synthetic synovial fluid (SSF) model and we validated this model in terms of growth, aggregate formation and antimicrobial susceptibility testing, using multiple PJI isolates.

Methods: 17 PJI isolates were included, belonging to ***Staphylococcus aureus,*** coagulase negative staphylococci, ***Cutibacterium acnes, Pseudomonas aeruginosa,*** enterococci, streptococci, ***Candida*** species and Enterobacterales. Growth and aggregate formation in SSF, under microaerophilic or anaerobic conditions, were evaluated using light microscopy. The biofilm preventing concentration (BPC) and minimum biofilm inhibitory concentration (MBIC) of relevant antibiotics (doxycyclin, rifampicin and oxacillin) were determined for the staphylococcal strains (n=8). To this end, a high throughput approach was developed, using a fluorescent viability resazurin staining. BPC and MBIC values were compared to the minimum inhibitory concentration (MIC) obtained with conventional methods.

Results: The SSF model allowed all isolates to grow well under microaerophilic or anaerobic conditions. When cultured in SSF, all isolates formed biofilm aggregates, varying in size and shape along different species. A susceptibility testing method based on measuring resazurin-derived fluorescence was successfully developed, allowing high throughput determination of the BPC and the MBIC in SSF. For all staphylococci cultured in SSF a reduced susceptibility to the tested antibiotics was observed when compared to susceptibility data obtained in general medium. For rifampicin and doxycyclin the BPC was consistently higher than the MIC (two- to fourfold dilution difference for rifampicin and four- to sixfold dilution difference for doxycyclin). For oxacillin the MIC equaled the BPC for two isolates, while for the other isolates the BPC was higher than the MIC (two- to fourfold dilution difference). Expectedly, the MBIC was higher than the BPC and differences with the MIC were even more pronounced for all antibiotics tested (differences of six- to fourteenfold dilutions were observed).

Conclusion: Our data indicate that the ***in vitro*** SSF model could provide more insight in how PJI-related pathogens form biofilms in physiologically relevant conditions. The BPC and MBIC were consistently and substantially higher than MIC. This model could be a valuable addition to evaluate the antimicrobial susceptibility in biofilms in a PJI context.

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Industry

Industry Symposium A

ZIMMER BIOMET Institute®

Thursday, 12 October, 12:45 – 13:45
Room: San Francisco, 3rd floor

Title: Let's Talk About Infection - Orthopaedic Implants and Biofilm

Agenda

12:45 **Welcome and Introduction**
Speaker: N. Kanakaris

12:50 **Biofilms and implants: the big challenge**
Speaker: H. Hughes

13:00 **Innovations in combatting biofilm**
Speaker: I. Khan

13:10 **Surgical treatment options for the eradication of musculoskeletal biofilm infection**
Speaker: R. Morgan-Jones

13:20 **Biofilm prevention with a new coating technology - early experience in trauma**
Speaker: N. Kanakaris

13:35 **Questions & Answers**

Harriet Hughes	University Hospital of Wales, United Kingdom
Nikolaos Kanakaris	Leeds General Infirmary, United Kingdom
Rhidian Morgan-Jones	Cardiff Knee Clinic, United Kingdom
Imran Khan	Zimmer Biomet, United Kingdom

Heraeus Medical

Thursday, 12 October, 12:45 – 13:45
Room: Sydney, 2nd floor

Title: Re-infections and the role of bone cement. Rethinking local antibiotic strategies

Agenda

Re-Infection Basics

Re-infections from the infectiological perspective
Speaker: Marjan Wouthuyzen

Re-infections from the surgical perspective
Speaker: Volker Alt

Prevention of re-infection and the role of local antibiotics

Why antibiotic combinations and which combinations work
Speaker: Marjan Wouthuyzen-Bakker

Clinical experiences with dual antibiotic-loaded bone cement
Speaker: Volker Alt

Volker Alt — University Hospital Regensburg, Germany
Marjan Wouthuyzen-Bakker — University of Groningen, The Netherlands

Industry Symposium C

INFECTOPHARM
Knowledge is Health

Thursday, 12 October, 17:25 – 18:25
Room: San Francisco, 3rd floor

Title: Interdisciplinary infection management of severe bone & joint infections including prosthetic joint infections (PJI)

Chair/Speaker: A. Trampuz

Agenda

17:25 **Systemic antibiotic therapy in patients with bone & joint infections with consideration of IV Fosformycin**
Speaker: S.Tedeschi (Bologna)

17:40 **Evidence-based treatment concepts for PJI in clinical practice**
Speaker: A. Trampuz (Berlin)

17:55 **Dream or reality? Successful infection management in endoprosthetics with consideration of IV Fosfomycin**
Speaker: S. Frieler (Bochum)

18:10 **Overall discussion and Closing remarks**
Speaker: A. Trampuz and all

Andrej Trampuz	University Charité, Berlin, Germany
Sara Tedeschi	University Bologna, Italy
Sven Frieler	University Hospital Bochum, Germany

Industry Symposium D

BIOMÉRIEUX

Thursday, 12 October, 17:25 – 18:25
Room: Sydney, 2nd floor

IMPACT OF SYNDROMIC MULTIPLEX TESTING ON THE DIAGNOSIS OF JOINT INFECTIONS - Value for Patient Management

Chair: Dr Marjan Wouthuyzen-Bakker
(University of Groningen | RUG, The Netherlands)

Agenda

Implementation of the JI panel and perceived medical value: the srgical point of view
Speaker: Assoc Prof Dr Richard Lass (Medical University of Vienna, Austria)

Improved dignostic yield and performances, and faster time to result for detection of pathogens in joint infections
Speaker: Prof. Dr. Holger Rohde (University of Hamburg, Germany)

The value of fast ID for the management f native joint infections in young children: time to oral treatment only?
Speaker: Dr. Jesús Saavedra-Lozano
(Hospital General Universitario Gregorio Marañón, Madrid, Spain)

Industry Symposium E

Biocomposites®

Friday, 13 October, 12:35 – 13:35
Room: San Francisco, 3rd floor

Title: Local antibiotic delivery - a convincing concept for osteomyelitis, bone and soft tissue infection management

Agenda

A clinical perspective of Calcium sulphate use in orthopaedic patients
Speaker: PD Dr. med. Yvonne Achermann
(Leitende Ärztin Infektiologie und Innere Medizin, Spital Zollikerberg, Switzerland)

STIMULAN® as a suitable carrier of antibiotics: A retrospective cohort study of 137 cases
Speaker: Mr Rob Morley
(Consultant Podiatric Surgeon, Derbyshire Community Health Services NHS FT, Independent Health Group, United Kingdom)

Industry Symposium F

BONESUPPORT™

Friday, 13 October, 12:35 – 13:35
Room: Sydney, 2nd floor

Titel: Grow Your Limb Salvage Repertoire - Delivering patient-friendly surgery with CERAMENT® G and CERAMENT® V

Agenda

Welcome and introduction
Speaker: Prof. Martin McNally

New evidence on the clinical use of CERAMENT G
Speaker: Prof. Martin McNally

Case presentation
Speaker: Dr. Daniel Pérez-Prieto

Case presentation
Speaker: Dr. Claes Olsen

Panel discussion and questions from the audience
Speaker: All

Tips & tricks for using CERAMENT G and CERAMENT V in the operating room
Speaker: Mr Jamie Ferguson

Summary and take-home messages
Speaker: Prof. Martin McNally

Panel

Prof. Martin McNally, Honorary Consultant in Limb Reconstruction Surgery, Oxford Bone Infection Unit, Nuffield Orthopaedic Centre, UK

Mr. Jamie Ferguson, Consultant in Limb Reconstruction Surgery and Trauma, Oxford Bone Infection Unit, Nuffield Orthopaedic Centre, UK

Mr. Alex Ramsden, Consultant Plastic and Reconstructive Surgeon, Oxford Bone Infection Unit, Nuffield Orthopaedic Centre, UK

Dr. Matt Scarborough, Consultant, Infectious Diseases, Microbiology and General Medicine, Oxford Bone Infection Unit, Nuffield Orthopaedic Centre, UK

Case Presenters

Dr. Daniel Pérez-Prieto, Orthopaedic Surgeon, Hospital del Mar / Hospital de l'Esperança, Barcelona, Spain

Dr. Claes Olsen, MD Specialist, Department of Orthopaedic Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden

Exhibitor directory

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Biocomposites Ltd
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Booth 10

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BONESUPPORT AB
www.bonesupport.com
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Our products are used when bone defects cannot heal by themselves, for example in trauma, fracture-related infection, chronic osteomyelitis and diabetic foot osteomyelitis.

Heraeus Medical GmbH
www.heraeus.com
Booth 2

Heraeus Medical stands for delivering value to the patient, the healthcare professional and the healthcare system through innovation and evidence based medicine in Implant Fixation, Infection Management and regenerative treatments for bone, cartilage and soft tissue. Over the years the company built up extensive experience in the field of therapeutic support for PJI with local antibiotics and is a reliable and committed partner in all aspects that deal with the management of musculoskeletal infections.

Gold Partners

Company	Booth

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Booth 4

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Booth 3

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Exhibitor directory

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Booth 14

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curasan
www.curasan.com
Booth 16

curasan develops and manufactures biomaterials in the field of bone and tissue regeneration. As an industry pioneer, curasan has more than 30 years of innovation experience, represented by a strong portfolio for orthopedic surgery based on proven technologies and great brands like CERASORB® or CERACELL®.

G-21
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Booth 8

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Inbiome
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Booth 9

Inbiome is dedicated to creating groundbreaking molecular technology that enhances people's well-being and extends their lifespan. Our cutting-edge Molecular Culture® technology provides a rapid and reliable solution by offering meticulously standardized assays, which are CE/IVD marked, enabling the detection of any bacteria in clinical samples within a matter of hours. Our diverse range of assays surpasses mere identification, enabling the detection of single bacteria as well as complex microbiota. We possess the capability to identify bacteria down to the species level. We collaborate closely with esteemed universities and hospitals to explore emerging areas of bacterial diagnostics and advance preventive and predictive healthcare in relation to the microbiome. Presently, our assay portfolio encompasses two key offerings: Molecular Culture® and Molecular Culture® Microbiota.

Bronze Partners

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Tecres
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Booth 12

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Smith+Nephew	**Smith+Nephew** www.smith-nephew.com/en/	Booth 6

Exhibitor overview

1	BONESUPPORT	BONESUPPORT
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3	Zimmer Biomet	ZIMMER BIOMET Moving You Forward.
4	InfectoPharm	INFECTOPHARM Knowledge is Health
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7	Nuvaisive	NUVASIVE Specialized Orthopedics
8	G-21	G21
9	Inbiome	inbiome.
10	Biocomposites	Biocomposites
11	OSARTIS Gmbh	OSARTIS
12	Tecres	TECRES
13	bioMérieux	BIOMÉRIEUX
14	Bonalive Biomaterials	bonalive
15A	FORTE	FORTE
15B	RESORBA	RESORBA BIOSURGICALS
16	curasan	curasan Regenerative Medicine
17	ECTB	ECTB
18	Axonlab	Axonlab
19	Shionogi	SHIONOGI
20	Dendris	Dendris MOLECULAR DIAGNOSIS
21	Medacta	Medacta International

Floor plan

Exhibition floor plan, 2nd floor

Notes

Notes

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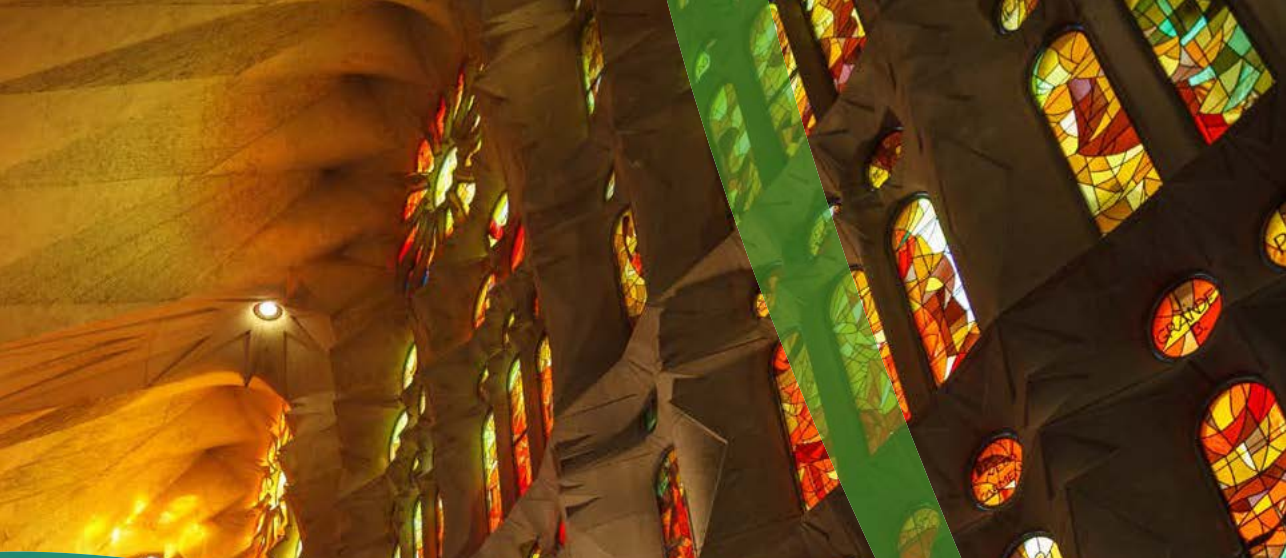

See you next year!

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