215. Multidrug-Resistant Gram-Negative bacilli Prosthetic Joint Infection: A Worrisome Scenario

Taiana Ribeiro, Medical[1]; Giselle Klautau, Md[2]; Mauro Salles, Md[2] and Infectology Santa Casa-SP; [1]Infectology, Santa Casa de São Paulo, Sao Paulo, Brazil, [2]Santa Casa de São Paulo, Sao Paulo, Brazil

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Background. The spectrum of the microbial etiology of prosthetic joint infections (PJIs) is changing, with a higher occurrence of Gram-negative bacilli (GNB) nowadays. In Latine America, GNB infections are usually caused by strains that produce multiple resistance mechanisms, making antimicrobial treatment increasingly difficult, especially for these biofilm-associated infections. We aimed to demonstrate the higher frequency of PJIs caused by GNB.

Methods. We performed a retrospective observational study with adult patients with a diagnosis of knee and hip PJIs. Patients included were submitted to an exchange of total hip and knee prostheses between September 2010 and December 2016, in two brazilian hospitals. It was included only patients with microbial diagnosis performed using either sonication fluid cultures of retrieved implant and conventional tissue cultures of periprosthetic tissues. The Infectious Disease Society of America (IDSA) definition was used to establish the diagnosis of PJIs. Multidrug-resistant (MDR) organisms were defined as acquired resistance to at least one agent in three or more antimicrobial categories.

Results. Were included 130 adult patients with a median age of 65.5 years, in which 60% were female. Infected hip arthroplasty was more frequent than knee infections (69% vs. 31%) and 61% were classified as late infection according to Zimmerli's classification. One hundred twenty-three microorganisms were isolated on the tissue and sonication fluid culture. Despite the Coagulase-negative *Staphylococci* was the predominant microorganism (35%), Gram-negative bacilli had an expressive frequency of 30% of positivity on culture. Amongst them, 23% showed resistance to carbapenens and 38% were MDR-bacteria. The predominant microorganism was *Pseudomonas* spp., followed by *Enterobacter* spp., *Acinetobacter* spp., *Escherichia coli*, *Stenotrophomonas maltophilia* and *Klebsiella pneumoniae*, *Proteus* spp. and *Serratia marcescens*. There was no statistical difference on the resistance profile of the GNB isolated on tissue and sonicate fluid culture.

Conclusion. We have shown an alarming high frequency of MDR-Gram-negative bacilli PJIs in two Brazilian centers, performing microbial diagnosis using sonication and tissue cultures.

Disclosures. **All authors:** No reported disclosures.

216. Clinical Outcomes of Antipseudomonal vs. Non-Antipseudomonal Therapy in Patients with Osteomyelitis

Jeffrey W. Jansen, PharmD[1] and Ryan P. Moenster, PharmD, FIDSA[1,2]; [1]Pharmacy Services, VA Saint Louis Health Care System, Saint Louis, Missouri, [2]Pharmacy Practice, St. Louis College of Pharmacy, Saint Louis, Missouri

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Background. Osteomyelitis (OM) in diabetics is frequently a polymicrobial infection that rarely involves *Pseudomonas* (4–5% of cases). Bone cultures have a low-positive yield of 34–50% and, as a result, many patients receive antimicrobial regimens which include antipseudomonal (AP) therapy.

Methods. A retrospective cohort analysis of adult Veterans with OM treated with AP compared with non-antipseudomonal (NAP) therapy was conducted. Patients managed by the VA St. Louis outpatient parenteral antimicrobial therapy (OPAT) service from 1/1/2009 to 7/31/2015 were identified and screened for inclusion. Patients with culture negative (CN) or non-pseudomonal superficial swab cultures (SCx) were included. Figure 1 presents the study profile and exclusion criteria. The primary outcome was clinical failure, defined as a composite of: (1) extension of antibiotics beyond 1 week of the planned duration, (2) recurrence of OM at the same anatomical site within 12 months, or (3) any unplanned surgery or amputation at the anatomical site within 12 months of ABx completion.

Results. Overall, 104 patients with 109 OM encounters were included; there were 29 CN encounters and 80 SCx encounters. Table 1 presents baseline demographics. The overall failure rate was 55/109 (50.5%). The results of the analysis are shown in Table 2. While not included in the primary analysis, *Pseudomonas* was isolated from 8/88 (9.1%) swab cultures and 5/33 (15%) deep cultures.

Conclusion. Empiric AP therapy did not improve clinical outcomes in patients with either CN or SCx OM.

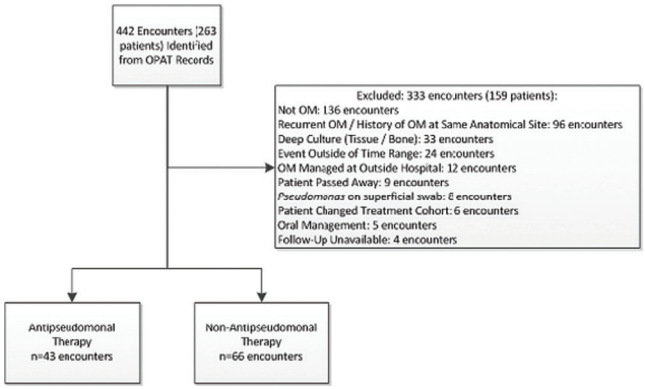
Table 1: Demographics

	AP (n = 43)	NAP (n = 66)	P-value
Age, years (mean ± SD)	62 (±8.60)	62 (±9.60)	0.93
Male	42	64	1.00
White	34	55	0.57
Creatinine clearance, ml/minute (mean ± SD)	65.2 (±27.7)	62.8 (±27.4)	0.65
History of OM	6	14	0.34
Diabetes (DM)	40	55	0.14
Peripheral vascular disease (PVD)	12	26	0.22

Table 2: Analysis

	Clinical Cure (n = 54)	Clinical Failure (n = 55)	P-value
DM	46	49	0.54
PVD	20	18	0.64
History of OM	12	8	0.30
MRSA therapy	33	35	0.77
AP therapy	19	24	0.37
Surgical intervention	30	21	0.07
Clostridium difficile infection	4	4	0.97
MRSA on SCx	8 / 39	7 / 41	0.69
Infection Site			
Lower extremity	46	53	
Upper extremity	3	1	0.52
Other	5	1	
Planned Duration ≥ 6 weeks	51	52	0.98
Microbiology			
CN	15	14	
Monomicrobial	13	9	0.40
Polymicrobial	26	32	

Figure 1. Trial profile.



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217. Predictive Factors for Successful Treatment in Candidial Bone and Joint Infection

Wooyong Jeong, MD[1]; In Young Jung, MD[1]; Heun Choi, MD[1]; Jinnam Kim, MD[2]; Se Ju Lee, MD[2]; Hye Seong, MD[2]; Jung Ju Kim, MD[2]; Nam Su Ku, MD[1,3]; Jun Yong Choi, MD, PhD[1,3]; Young Goo Song, MD, PhD[1,3]; June Myung Kim, MD, PhD[1,3] and Su Jin Jeong, MD/PhD[1,3]; [1]Division of Infectious Disease, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South), [2]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South), [3]AIDS Research Institute, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)

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Background. Candidiasis is a major cause of morbidity and mortality, causing a diverse spectrum of clinical diseases. Candidial bone and joint infection (CBJI) is a rare clinical disease, although it is one associated with significant morbidity. As most prior studies were limited to individual cases and small case series, there were insufficient data on the epidemiology and outcome of CBJI. The aim of this study is to identify the predictive factors for successful treatment in CBJI.

Methods. A retrospective review was performed on 33 patients with Candida confirmed on culture, among patients diagnosed with bone and joint infection between January 2006 and December 2016 at a 2400-bed tertiary hospital in South Korea. Unfavorable outcome was defined as recurrence following completion of treatment or mortality. Clinical characteristics, treatment outcome, and medical records were reviewed.

Results. Of the 33 patients, 15 (45.5%) had unfavorable outcomes; recurrence (n = 9) and mortality (n = 6). Median age was 64.0 years (range, 50.5–71.5 years) and there were 14 (42.4%) males. Seventeen (51.5%) patients had arthritis and 16 (48.5%) osteomyelitis. *Candida albicans* constituted 48.5%, *C. parapsilosis* 24.2%, *C. tropicalis* 6.1%, and *C. glabrata*6.1%. Mechanisms of infection were hematogenous dissemination (57.6%) and direct inoculation (42.4%). There were no significant differences between the favorable outcome group and the unfavorable outcome group for the underlying diseases. The neutrophil percentage in complete blood count at the time of diagnosis showed a difference between the two groups (68.0% vs. 79.6%, P = 0.016). There was a significant difference in neutrophil-lymphocyte ratio (2.2 vs. 4.8, P = 0.023), erythrocyte sedimentation rate (ESR) (40.5 vs. 72.4, P = 0.024) and C-reactive protein (CRP) (15.3 vs. 86.3, P = 0.001) at the end of treatment. The duration of antifungal therapy showed a significant difference (124.9 days vs. 44.3 days, P = 0.041), but there was no

difference in the operation. In the multivariate analysis, CRP at the end of treatment ($P = 0.028$) ws found to be a predictive factor for successful treatment.

Conclusion. CBJI is a rare disease but associated with high treatment failure. Prolonged antifungal treatment is essential for successful treatment of CBJI, and CRP at the end of treatment is a key predictive marker of successful treatment.

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218. The Influence of Obesity on the Infection Risk of Prosthetic Joint Infection in the Geriatric Orthopedic Population

Allina Nocon, MPH[1]; Michael Henry, MD[2]; Celeste Russell, MPH[3]; Geoffrey Westrich, MD[1]; Barry Brause, MD[4] and Andy Miller, MD[5]; [1]Complex Joint Reconstruction Center, Hospital for Special Surgery, New York, New York, [2]Infectious Diseases, Hospital for Special Surgery, New York, New York, [3]Hospital for Special Surgery, New York, New York, New York, [4]Hosp. for Special Surgery, New York, New York, [5]Infectious Disease, Weill Cornell Medical College, New York, New York

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Background. Prosthetic joint infection (PJI) is a dreaded complication of arthroplasty. PJI are more common in the elderly and are associated with a substantial increase in 5-year mortality risk. PJI risk may correlate with increasing body mass index (BMI). However, the effect of BMI on PJI risk in the elderly has not been evaluated, to our knowledge. We sought to evaluate this relationship in a cohort of geriatric arthroplasty patients at an orthopedic specialty hospital.

Methods. A retrospective cohort of hip and knee arthroplasty patients (age >75) from 2009–2014 was identified through administrative hospital data using ICD-9 codes. Patients with a BMI <14 or >60 kg/m^2, height <142 or >200 cm, and weight <36 or >226 kg were excluded. The presence of infection was confirmed via chart review; all PJIs met MSIS criteria. Obesity was defined as having a BMI >30. Univariate analyses were done using χ^2 tests and adjusted models were assessed using logistic regression.

Results. 13,755 geriatric arthroplasty patients (6,408 total hip arthroplasties [THA] and 7,347 total hip arthroplasties [TKA]) were assessed. Mean age and BMI were 82 (±5.4) and 28.1 (±5.3), respectively. In an unadjusted model, obesity was associated with infection in THA ($P = 0.02$), but not TKA ($P = 0.31$). This association remained after adjusting for age, sex, and diabetes. Obesity was associated with an increased risk of infection in THA [OR=1.89 (95% CI 1.12–3.21); $P = 0.02$]. However, as with the unadjusted model, this relationship was not found in TKA ($P = 0.50$).

Conclusion. Obesity increases THR PJI risk in the elderly. However, no such association was found for TKA. Future studies are needed to quantify the compounded risk of obesity in the geriatric arthroplasty patient.

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219. Searching for Bacterial Pathogens in Pediatric Patients with Chronic Recurrent Multifocal Osteomyelitis Using 16S rRNA Quantitative Real-Time PCR

Justin Searns, MD; Infectious Diseases, Children's Hospital Colorado, Aurora, Colorado

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Background. Chronic recurrent multifocal osteomyelitis (CRMO) is a rare auto-inflammatory disease in children that causes relapsing episodes of pain. Patients are treated with anti-inflammatory medications or immune-modulating agents. Increasing evidence suggests that CRMO is mediated by dysregulation of the interleukin-1 pathway, not a bacterial source. However, CRMO is often a diagnosis of exclusion, and patients occasionally receive antimicrobials for possible culture negative infectious osteomyelitis. Few prior studies have utilized molecular diagnostic techniques to identify bacterial pathogens in CRMO bone biopsies.

Methods. Musculoskeletal specimens sent for culture during routine clinical care were banked from patients admitted to Children's Hospital Colorado from 6/2012 to 10/2016. On retrospective chart review, 28 specimens were collected from 16 patients ultimately diagnosed with CRMO. Specimens were processed and extracted prior to molecular testing. All samples underwent quantitative real-time PCR (qPCR) testing using bacterial load assays targeting the bacterial 16S rRNA gene.

Results. Mean age at time of sample collection was 9.2 years. CRMO diagnosis was made by clinical, pathologic, and radiographic findings. All patients had pathology findings consistent with CRMO including lymphoplasmacytic infiltrate, focal necrosis, and/or marrow fibrosis. All patients had MRI findings consistent with CRMO. No patient had bacteria identified on Gram stain; 2/28 samples (7%) had bacterial growth on culture (both were coagulase-negative staphylococcus, felt to be contaminant). None of the 28 specimens met the threshold of bacterial load on qPCR testing to necessitate bacterial sequencing. None of the 16 patients were treated with antimicrobials and there were no readmissions for clinical worsening.

Conclusion. CRMO patients did not have bacteria identified on universal bacterial 16S rRNA testing. This finding further supports that CRMO patients do not require antimicrobial therapy. Future steps to exclude infectious pathogens in CRMO could include next-generation DNA sequencing.

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220. Clinical Experience with Tigecycline in the Treatment of Prosthetic Joint Infections

Allison Lastinger, MD[1]; Matthew Dietz, MD[2]; John Guilfoose, MD[3] and Arif R. Sarwari, MD, MSc, MBA[4]; [1]Internal Medicine, West Virginia University, Morgantown, West Virginia, [2]Orthopedics, West Virginia University, Morgantown, West Virginia, [3]West Virginia University, Morgantown, West Virginia, [4]Medicine, West Virginia University, Morgantown, West Virginia

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Background. As the population in the United States ages, the number of people who will require a joint arthroplasty is expected to rise dramatically. The most serious complication of this surgery is prosthetic joint infection (PJI) which can lead to long-term morbidity and even mortality. Biofilms play a major role in these infections, and studies have suggested that tigecycline may work better than other antimicrobials in the setting of biofilms. In this study, we examined our institution's experience with using tigecycline to treat PJI.

Methods. This was a retrospective review of all adult patients with PJI treated at West Virginia University from January 2008 to March 2016 who received tigecycline for 50% or greater of the treatment course. Demographic data, rationale for tigecycline use, type of surgery, microbiologic data, outcome and complications were assessed. Failure was defined as need to return to the operating room for an infectious complication or persistent drainage from the joint.

Results. In total, 34 patients met inclusion criteria. The median age was 65 years, and 62% of the patients were female. The most common reason for tigecycline use was empiric therapy, but other reasons included antimicrobial allergies and resistant organisms. The antimicrobial was used as frontline therapy in 29 cases (85%), and the mean duration of tigecycline therapy was 38 days. The most common organisms isolated were methicillin resistant Staphylococcus aureus ($n = 7$), coagulase negative Staphylococci ($n = 5$), and Enterococcus species ($n = 4$), but 12 cases (35%) were culture negative. Treatment success was documented for 21 cases (62%); though, there was limited follow-up (2 months or less) in four of the successful cases. Nausea and vomiting was the most common adverse event, occurring in three patients.

Conclusion. Tigecycline is a glycylcycline approved for use in a variety of infections including intra-abdominal and skin soft-tissue infections, but little is known about its use in the treatment of PJI. We found that tigecycline is well tolerated even when given for 6 weeks duration. Twenty-one of the 34 patients (62%) met our definition of successful treatment outcome with tigecycline. More studies are needed to assess tigecycline's use in the treatment of PJI.

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221. Subcutaneous Suppressive Antibiotic Therapy for Bone and Joints Infections: Safety and Outcome in a Cohort of 10 Patients

Tristan Ferry, MD, PhD[1]; Cecile Pouderoux, Resident[2]; Sylvain Goutelle, DPharm, PhD[2]; Sébastien Lustig, MD, PhD[3]; Claire Triffault-Fillit, MD[4]; Fatiha Daoud, MD[4]; Michel-Henri Fessy, MD, PhD[5]; Sabine Cohen, DPharm, PhD[6]; Frederic Laurent, DPharm, PhD[7]; Christian Chidiac, MD, PhD[4]; Florent Valour, MD, PhD[4] and Lyon BJI Study group; [1]Inserm 1111, UCBL1, Hospices Civils de Lyon, Lyon, France, [2]Hospices Civils de Lyon, Lyon, France, [3]Orthopaedic Surgery, Regional Reference Center for Bji, Hospices Civils de Lyon, Lyon, France, [4]ID Department, Regional Reference Center for Bji, Hospices Civils de Lyon, Lyon, France, [5]Hospices Civils de Lyon – Centre Hospitalier Lyon Sud, Pierre-Benite, France, [6]Laboratory of Pharmacology and Toxicology, Hospices Civils de Lyon – Centre Hospitalier Lyon Sud, Pierre-Benite, France, [7]Laboratory of Bacteriology, Regional Reference Center for Bji, Hospices Civils de Lyon, Lyon, France

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Background. Optimal surgical therapy could be sometimes non-feasible, especially in the elderly population. Therefore, a medical therapy with oral prolonged suppressive antibiotic therapy (PSAT) seems to be an option to prevent recurrence and prosthesis loosening. Subcutaneous (SC) administration of injectable intravenous antibiotics as PSAT could be a convenient way when oral treatment is not available to facilitate ambulatory care, even if this practice is considered as an "off-label" practice.

Methods. All patients receiving SC PSAT since 2010 were prospectively enrolled in a cohort study evaluating treatment modalities, efficacy, and safety. Success was defined by the absence of clinical signs of infection at the time of last follow-up.

Results. We included 10 patients (median age of 79 years): seven had PJI and three chronic osteomyelitis. Six had plurimicrobial infections and four had infections due to multidrug-resistant Gram-negative pathogens. Suboptimal surgery was performed in seven patients, and three received only antibiotics. All patients received an induction-phase therapy with conventional antibiotic treatment before SC PSAT. For nine patients, SC injections were delivered by a 50 mlml 30 minute gravity infusion of the antibiotic, using butterfly disposable needle. One patient received direct flash SC administration. The most frequent drug used was ertapenem ($n = 7$; 1–2 g/day), followed by ceftriaxone ($n = 2$; 1 g/day), and ceftazidime ($n = 1$; 2 g/day). The dose was adjusted depending on the results of trough residual blood concentration. Median duration of treatment was 6 months (from 1 to 58 months), corresponding to a total of about 5,000 SC injections. SC PSAT had to be discontinued for side effects in only two patients, including skin necrosis in the patient receiving direct SC infusion (lost to follow-up after treatment discontinuation) and epilepsy under ertapenem therapy (with relapse of the BJI after the treatment discontinuation). One other patient experienced a relapse despite the SC PSAT. Finally, SC PSAT was still ongoing in seven patients with a favorable outcome at the last follow-up.

Conclusion. SC PSAT appears to be a safe and effective alternative therapy when optimal surgical strategy is not feasible and when oral treatment is not available.