Antimicrobial strategies and multidisciplinary care in prosthetic joint infections

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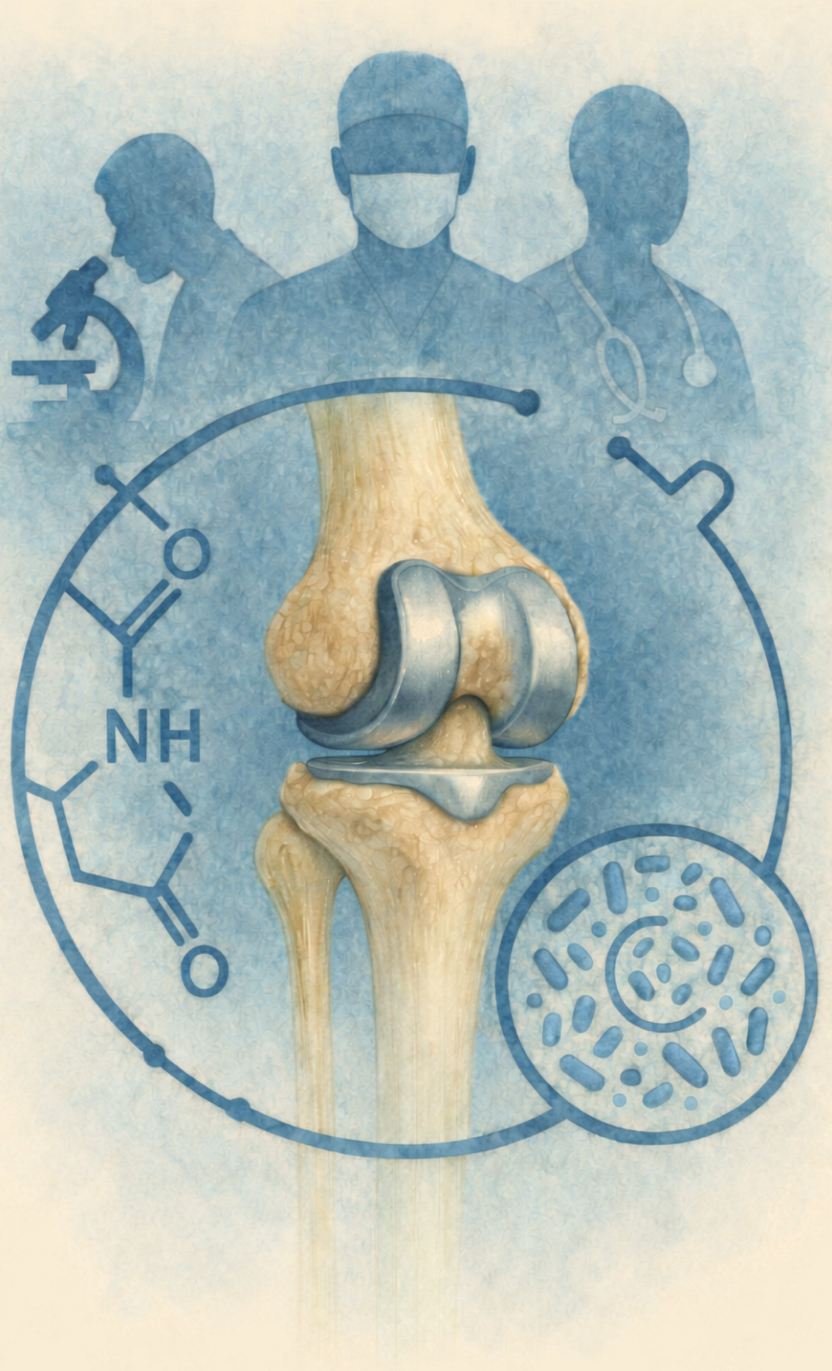
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Part III

Suppressive antimicrobial therapy for prosthetic joint infections

Chapter 5

Global practice variation of suppressive antimicrobial treatment for prosthetic joint infections: A cross-sectional survey study

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Abstract

Objectives To identify global differences in the use of suppressive antimicrobial therapy (SAT) in the management of prosthetic joint infection (PJI).

Methods An online survey was designed to investigate clinician's approach to SAT for PJI, including indications, preferred antimicrobial drugs, dosing, treatment duration and follow-up. The survey was distributed to members of four international (bone and joint) infection societies and study groups.

Results Respondents comprised 330 physicians (204 infectious diseases specialists, 110 orthopedic surgeons, 23 clinical microbiologists) from 43 different countries (Europe, n=134, 41%; Oceania n=112, 34%; North America, n=51, 16%; other, n=33, 10%; total response rate 20%). After debridement, antibiotics and implant retention (DAIR) or one-stage revision, SAT would be initiated often or almost always by 38% of respondents from North America, but only in 6% from Europe and 7% from Oceania. First choices of SAT for staphylococcal PJI were oral cephalosporins (39%) and tetracyclines (31%) in North America; tetracyclines (27%) and anti-staphylococcal penicillins (22%) in Europe; and anti-staphylococcal penicillins (55%) in Oceania. There was no global or regional preferred SAT regimen for Gram-negative PJI. Of all respondents, dosage of SAT was never lowered (n=126, 38%), lowered for specific antibiotics (n=125, 38%) or lowered for all antibiotics (n=79, 24%). SAT was prescribed for a lifelong duration (n=43, 13%), a fixed duration (range 6 months–3 years) (n=104, 32%) or for an undetermined duration (n=154, 47%).

Conclusions Approach to SAT in PJI is highly regional, with no consensus regarding the indication, selection, dose, or duration of SAT between physicians worldwide. This reflects the paucity of data and need for high quality studies to define the optimal use of SAT in the treatment of patients with PJI.

Introduction

Prosthetic joint infection (PJI) is a grievous complication of arthroplasty requiring antibiotics and surgical debridement with- or without or exchange arthroplasty. Following the initial antimicrobial treatment regimen, patients often receive extended antimicrobial therapy, commonly referred to as suppressive antibiotic therapy (SAT). SAT may be started after surgical debridement when risk factors that are associated with a high relapse rate of infection are present, or when surgery is not possible or refused by patients (1). The precise indications for SAT in patients with a PJI are not clear, because the available data on SAT are scarce and of low quality (1-3). The Infectious Diseases Society of America's (IDSA) 2013 guideline on PJI contains recommendations for SAT regimens and dosing, mostly based on expert opinion (4). Moreover, there is no uniform definition of SAT and the optimal treatment duration is unknown (1). The considerable global variation in the use of SAT for PJI belies this lack of data (5-13).

This study aimed to identify international differences for the most common indications and antimicrobial treatment strategies for SAT and to determine discrepancies to guide the direction of further research. For this purpose, we developed a survey on the clinical practice of SAT in PJI, which was distributed across the globe to medical specialists with a special interest in PJI.

Methods

Study and survey design

This was an international cross sectional survey study. A first draft of the survey was constructed by a team of infectious diseases (ID) specialists, clinical microbiologists, orthopaedic surgeons, and clinical epidemiologists specialized in PJI (JLJH, HMJvdL, RJPvdW, JvP, MGJG, MGJdB, HS). From clinical experience and literature review, the team identified unsettled aspects of SAT to be included in the survey. This draft was discussed and amended by the team, leading to a second version, which was reviewed by an international panel of experts (MWB, JSD, DD, LM, DC, AOM, NWCP, AS). This resulted in the final survey consisting of 21 questions on the following topics: organization of care, indication and risk factors; treatment phase before SAT; preferred antimicrobial drug; dosing and treatment duration; follow-up of patients. Respondents were asked to use the definitions of acute and chronic PJI they employ in their daily practice. The survey was in English, voluntary and anonymous. Both the survey design and the collection and management of data were performed

using Formdesk web-based software (Innovero Software Solution B.V., Wassenaar, the Netherlands) hosted at Leiden University Medical Center. The complete survey is available as supplementary data (Suppl. 1).

Ethics approval

A declaration of exemption was issued by the institutional review board of Leiden University Medical Center due to the anonymous and voluntary participation of the survey, reference number nWMODIV2_2024005. By filling in the survey, respondents gave consent to use their data.

Survey distribution

The link to the online survey was sent by email to all members of the European Society of Clinical Microbiology and Infectious Diseases Study Group for Implant-Associated Infections (ESGIAI), the European Bone and Joint infection Society (EBJIS), the Musculoskeletal Infection Society (MSIS) and mailing groups of the Australasian Society of Infectious Diseases (ASID). In addition, all recipients were encouraged to share the survey with colleagues in their network who were involved in PJI care but were member of the above mentioned groups. Recipients were emphatically asked to only fill out the survey if they were actively involved in the treatment of PJI. We estimated that a minimum of 250 respondents would provide reliable results and would be feasible considering the specificity of the topic. The survey was distributed on 12th of March 2024, followed by two reminders by email, and collection of data concluded 12th of April 2024. No financial incentives were offered to the respondents.

Statistical analysis

Returned surveys with less than three questions answered were excluded. Data were summarized using descriptive statistics. Data for categorical variables were presented as proportions or percentages of the number of respondents and stratified per region when feasible and clinically relevant. The estimated response rate was calculated by dividing the reported number of memberships of the respondents by the total number of sent invitation mails to the members of the aforementioned societies. It was assumed that non-member respondents had a similar response rate as members, hence the estimated overall response rate was extrapolated from the member response rate. SPSS Statistics (Version 29.0.0.0, IBM Corporation, Armonk, New York, USA) was used to perform all calculations.

Results

The survey was distributed to all 1483 members of the listed societies and groups. From 42 different countries on 6 six different continents, 330 respondents (223 members of one society, 34 members of two societies, 73 non-members) completed the survey, resulting in an estimated response rate of 20%. A list of the number of respondents per country is provided in Supplementary Table 1. Most respondents (n=291, 88%) completed the full survey. The remaining 39 respondents answered at least 18 of 21 questions (86%). The experience and professional background of the respondents are summarized in Table 1.

Table 1. baseline characteristics of respondents (n=330)

Continent	N (%)
Europe	134 (41)
Oceania	112 (34)
North America	51 (16)
Other[a]	33 (10)
Medical specialty[b]	
Infectious Diseases[c]	204 (63)
Orthopaedic Surgery	110 (33)
Clinical Microbiology	23 (7)
Orthopaedic surgeons per continent	
Europe	50 (37)
Oceania	23 (21)
North America	19 (37)
Other[a]	18 (55)
Years registered as consultant	
in training	9 (3)
<5 years	56 (17)
5-10 years	79 (24)
11-15 years	68 (21)
>15 years	118 (36)
Number of patients with PJI on SAT involved in per year	
1-5	66 (20)
6-10	72 (22)
11-15	50 (15)
>15	141 (43)

Table 1. baseline characteristics of respondents (n=330) *(Continued)*

Member of society[d]	
EBJIS	96 (29)
ASID	96 (29)
MSIS	52 (16)
ESGIAI	47 (14)
non-member	73 (22)
Estimated response rate per society	
EBJIS	19%
ASID	19%
MSIS	21%
ESGIAI	22%

[a]South America, Asia and Africa combined

[b]7 respondents were registered as both ID specialist and microbiologist

[c]9 respondents were internal medicine specialists that for the purpose of this survey were counted as ID specialist

[d]34 respondents were member of two societies

Organization of care

Standard practices regarding consultation, diagnostic strategies and follow-up of patients with SAT are summarized in Table 2. Respondents from Europe (n=90, 67%) were more frequently part of a multidisciplinary team (MDT) for PJI than respondents from other continents (range 24-38%). According 140 respondents (42%), surgeons did not follow-up patients on SAT. In Europe, outpatient clinic follow-up was more commonly conducted solely by surgeons (n=36, 27%) compared to Oceania (n=2, 2%) and North America (n=2, 4%).

Table 2. Organization of care for patients with PJI on SAT

	Total (n=330)	Europe (n=134)	Oceania (n=112)	North America (n=51)	Other continents[a] (n=33)
Consultation other specialty on SAT					
Multidisciplinary team	153 (46)	90 (67)	42 (38)	12 (24)	9 (27)
Other than multidisciplinary team	119 (36)	28 (21)	44 (39)	32 (63)	15 (46)
No	58 (18)	16 (12)	26 (23)	7 (14)	9 (27)
Parameters used for the decision to start SAT					
Inflammatory parameters	220 (67)	85 (63)	79 71)	32 (63)	24 (73)
Imaging	68 (21)	34 (25)	19 (17)	7 (14)	8 (24)
Clinical performance	284 (86)	112 (84)	103 (92)	44 (86)	25 (76)
Follow-up of patients					
Follow-up performed by					
Surgeon and ID specialist and/or GP	144 (44)	50 (38)	54 (48)	28 (55)	11 (33)
Surgeon only	46 (14)	36 (27)	2 (2)	2 (4)	6 (18)
ID specialist only (or together with GP)	133 (41)	44 (33)	53 (48)	20 (39)	16 (49)
GP only	4 (2)	2 (2)	2 (2)	0	0
Frequency of follow-up after 1st year on SAT					
2-4 times a year	232 (70)	92 (69)	75 (67)	36 (71)	29 (88)
Yearly	46 (14)	16 (12)	18 (16)	11 (22)	1 (3)
Once every two years	3 (1)	2 (2)	0	1 (2)	0
Only on patient request	27 (8)	10 (8)	15 (13)	0	2 (6)
Don't know/other	22 (7)	14 (10)	4 (4)	3 (6)	1 (3)

Table 2. Organization of care for patients with PJI on SAT *(Continued)*

	Total (n=330)	Europe (n=134)	Oceania (n=112)	North America (n=51)	Other continents[a] (n=33)
Standard investigations					
Inflammatory parameters	283 (86)	116 (87)	97 (87)	41 (80)	29 (88)
Complete blood count	225 (68)	86 (64)	83 (74)	35 (69)	21 (64)
Kidney function	240 (72)	92 (69)	84 (75)	36 (71)	28 (85)
Liver enzymes	222 (67)	85 (63)	81 (72)	34 (67)	22 (67)
Imaging	89 (27)	43 (32)	22 (36)	12 (24)	12 (36)

[a]South America, Asia and Africa combined

GP: general practitioner

Clinical scenarios and risk factors determining the choice for SAT

Box 1. For the following scenarios, how often would you place the patient on SAT? rarely (=0-25%), sometimes (=26-50%), often (=51-75%), almost always (=76-100%)

1. Acute PJI successfully treated with DAIR without additional risk factors[a] for failure
2. Acute PJI successfully treated with DAIR + ≥ 1 risk factors[a] for failure
3. Chronic PJI treated with DAIR
4. PJI successfully treated with one stage revision
5. PJI with failure of DAIR#
6. PJI with failure of one stage revision[b]
7. PJI treated with antibiotic therapy only (no surgery) but with a draining fistula
8. PJI treated with antibiotic therapy only but no draining fistula present

[a]Those included in figure 2 (e.g. no change of modular component, chemotherapy, megaprosthesis, difficult to treat micro-organisms, etc)
[b]preference for debridement followed by SAT over other surgical options

To investigate the indications for SAT, respondents were asked how often they would place a patient on SAT in eight different clinical scenarios (Box 1). The results from Europe, Oceania and North America are summarized in Figure 1 and supplementary Figure 1. The number of respondents from South America, Asia and Africa were too small to include in this analysis. Most striking was that in patients with acute PJI treated with DAIR or one-stage revision (1SR), nineteen North American (38%) would often or nearly always give SAT as compared to eight European (6%), and seven Oceanian respondents (7%) (figure 1A and supplementary figure 1A). In scenarios 2, 3, 5, 6 and 7, respondents from North America also initiated SAT more frequently compared to European respondents, but a considerable heterogeneity existed within continents for these scenarios (Figure 1B-D and supplementary Figure 1B-C). For patients with PJI who are not treated with surgery, most respondents from Europe, Oceania and North America answered that SAT is indicated, providing patients did not have fistula (SAT initiated 'almost always' or 'often' by 82% of all respondents) (Supplementary Figure 1D).

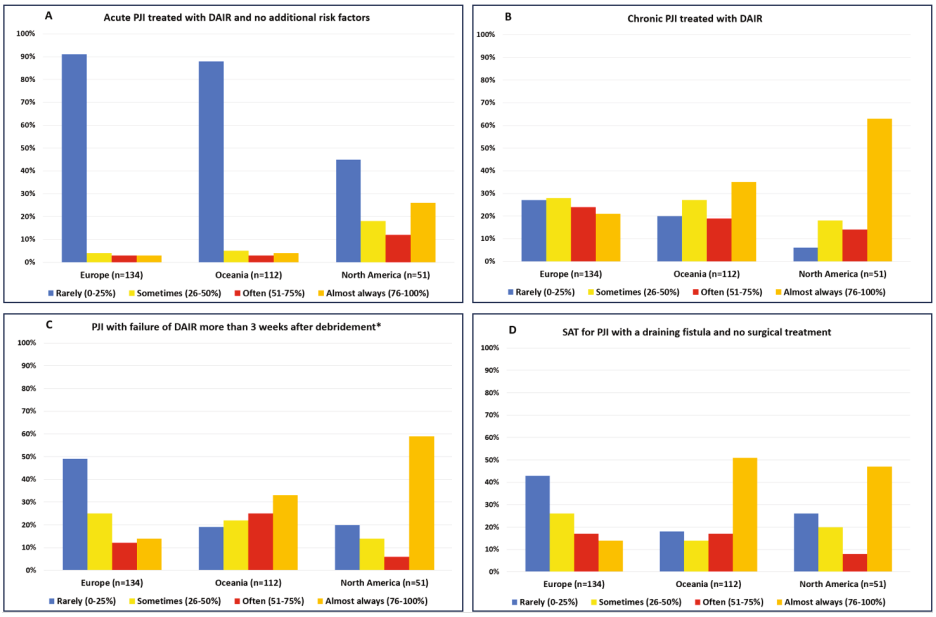

Figure 1. *Clinical scenarios of patient with PJI of which respondents were asked how often they would place patient on SAT stratified per continent. *preference for debridement followed by SAT instead of other surgical options*

The host risk factors for failure considered as an indication for initiating SAT in acute PJI treated with DAIR are summarized in Figure 2. The top five microbiological factors that were reported as indication for SAT were infection with Candida species (n=128, 39%), Pseudomonas species (n=71, 22%), rifampicin-resistant staphylococci (n=70, 21%), methicillin-resistant Staphylococcus aureus (MRSA) (n=61, 18%), and enterococci (n=51, 15%). For 148 respondents (45%), the causative microorganism did not influence the decision to initiate SAT providing an adequate DAIR was performed.

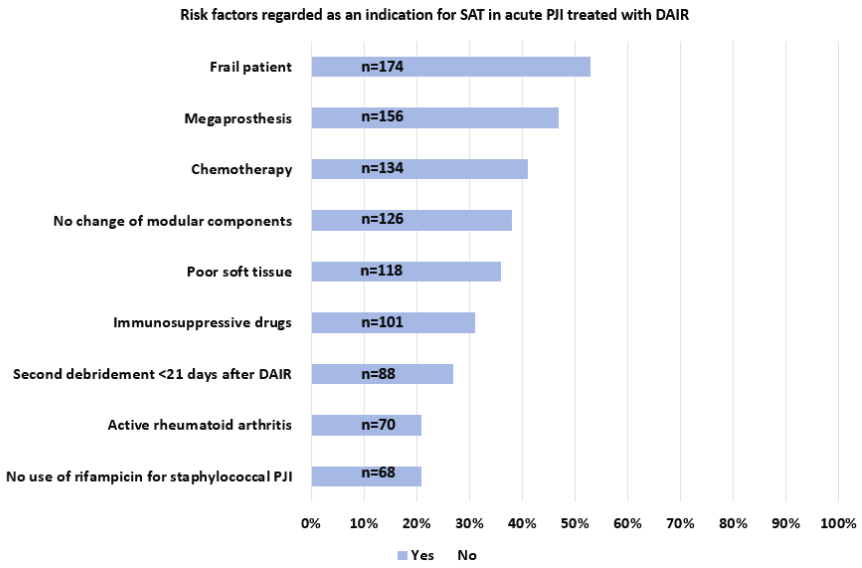

***Figure 2**. Risk factors regarded by >20% of all respondents (n=330) as an indication for SAT in acute PJI treated with DAIR*

Antimicrobial strategy: choice, dose and treatment duration of SAT

Preferred SAT regimens for staphylococcal PJI differed significantly between continents (Figure 3a). Anti-staphylococcal penicillins are rarely used in North America (n=3, 6%) but are preferred in Oceania (n=61, 55%). For streptococcal PJI, most respondents from Europe, Oceania and North America would prescribe a penicillin (Figure 3b). The preferred SAT-regimen for Gram-negative PJI was heterogeneous within and between these three continents (Figure 3c). A detailed overview of all first and second choice SAT regimens, stratified per continent, are provided in supplementary Table 2-4.

With respect to the dosing of SAT, 79 respondents (24%) routinely switch to a lower than therapeutic oral dosage when initiating SAT for PJI, 125 respondents (38%) would consider a lower dose for selected antimicrobials and/or in case of side-effects and 126 respondents (38%) would never lower the dose (Supplementary Table 5). The majority of respondents (n=176, 53%) reported not having a predefined treatment duration, whereas 111 respondents (34%) indicated they stop SAT after 6 months to 3 years in the setting of a good clinical course and normalized inflammatory parameters; only a small proportion (n=43, 13%) indicated they never stop SAT, regardless of the clinical course.

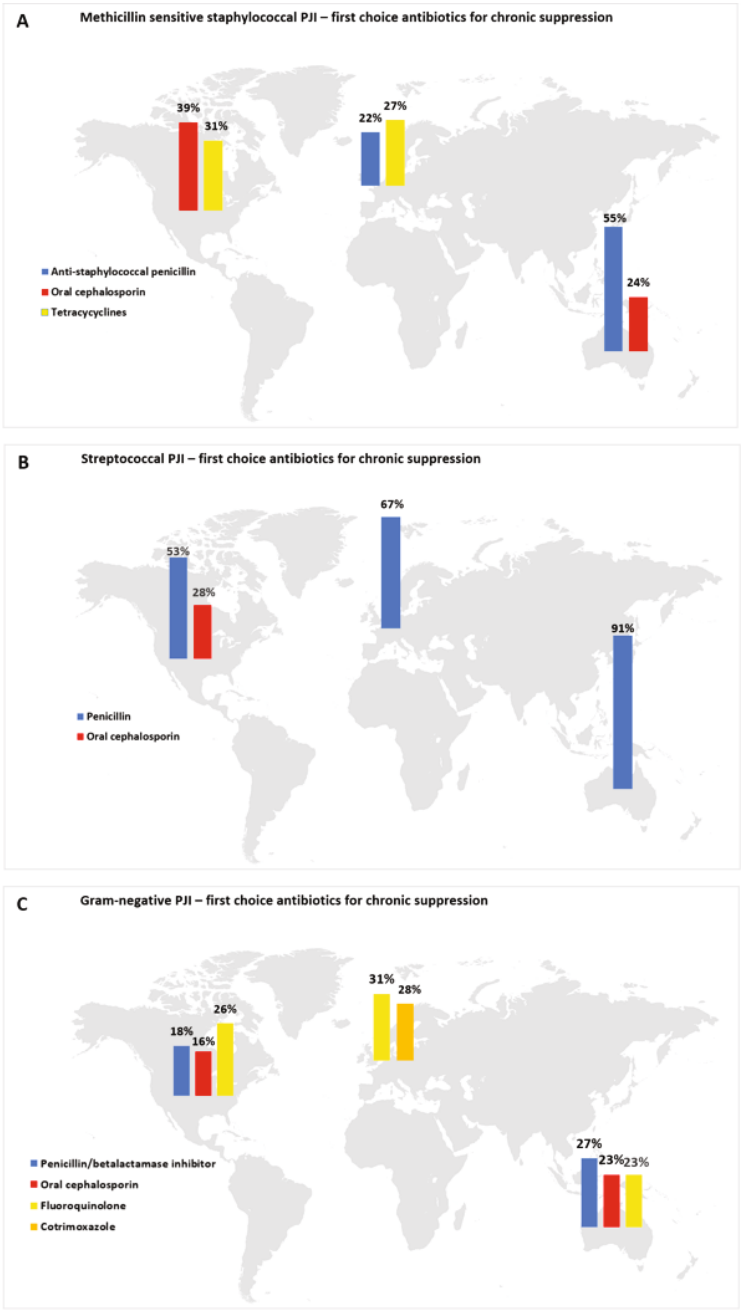

Figure 3. *Antibiotic treatment preferred for suppressive therapy per continent. Percentage of total respondents of the question per continent. Europe: n=134; Oceania: n=112; North America: n=51.*

Discussion

This survey study revealed substantial global variation in the use of SAT in the management of patients with PJI. Variations existed in all aspects of SAT: indications, antimicrobial strategy, dosage and duration of antibiotic treatment and the organization of care.

Organization of care

Respondents from Europe participated more often in an MDT than the rest of the world. Multiple studies reported improved outcomes after installing MDTs and implementation of MDTs for PJI is recommended by several orthopaedic societies and experts (14-16). Possible barriers to the establishment of MDTs are a lack of time, financial support and/or inappropriate infrastructure (17). Nearly all orthopaedic surgeons consulted ID physicians or microbiologists about the antimicrobial treatment even in the absence of a MDT. Remarkably, according to 42% of respondents, the surgeon was not involved in outpatient follow-up.

Indication for SAT

Respondents from North America were more inclined to treat patient with SAT than European respondents. For patients with acute PJI treated with DAIR or 1SR, 38% of North American respondents would likely initiate SAT while this was rarely the case in Europe and Oceania. This difference in management was also demonstrated in a recent retrospective study on SAT following DAIR for acute PJI; In the US 160/184 patients (87%) received SAT and in Europe 7/226 patients (3%) (18). These contrasting approaches are probably based on dissimilarities between American and European guidelines. Interestingly, in the IDSA 2013 guideline committee, only one out of three European panel members would consider SAT in patients after DAIR and rifampicin-based therapy for staphylococcal PJI or fluoroquinolones for Gram-negative PJI, while all six American members considered SAT for all patients after DAIR (4). A recent survey study from the United States (n=413) showed that the majority of ID specialists would initiate SAT for patients after DAIR or 1SR (19). On the other hand, several national guidelines on PJI in Europe do not recommend suppression after DAIR for acute PJI or after 1SR (20, 21). These differences in guideline recommendations probably explain the more frequent use of SAT in the United States compared to Europe.

Overall, large heterogeneity was observed regarding the perceived indications for SAT; in particular in patients with chronic PJI treated with DAIR, patients with failure after DAIR or 1SR and patients with a draining fistula. In a retrospective multicenter

study including patient with PJI and a fistula, most patients received SAT (63/72, 88%) although this did not prevent long-term complications (22). A recent review identified recurrent PJI, severe immunosuppression, *Staphylococcus aureus,* and no exchange of polyethylene liner as factors for which SAT is likely beneficial after DAIR (23). Remarkably, the majority of respondents in our survey, did not regard these risk factors an indication for suppression in acute PJI treated with DAIR. The most important risk factors according to the respondents were frailty and presence of a megaprosthesis. Rifampicin-resistant staphylococci were considered an indication for SAT in acute PJI treated with implant retention by only 21% of respondents, which is in contrast with the IDSA guideline and several studies (4, 7, 23).

Antimicrobial regimens

Substantial diversity was observed between and within Europe, Oceania and North America in the preferred antimicrobials for SAT except for streptococcal PJI. The near absence of the use of oral cephalosporins in Europe is probably due to differences in antimicrobial stewardship and policies. The infrequent use of anti-staphylococcal penicillins by North American respondents could reflect the high MRSA prevalence in community-acquired staphylococcal infections in the US, which is why pharmacies do not stock up on these drugs anymore. Currently, the IDSA 2013 guideline is the only guideline recommending specific antimicrobial regimens, but adherence to those recommendations by respondents was low, likely due to the low quality of available clinical data (4). The effectiveness of tetracyclines, beta-lactams, fluoroquinolones and cotrimoxazole was comparable in the three largest studies on SAT in PJI (combined n=572) with success rates between 59% and 65% (6, 8, 13). To investigate the optimal antibiotics for suppression, large multicenter randomized trials are needed.

Dosage, duration and definition of SAT

One third of respondents would never lower the standard therapeutic dosage for PJI in case of SAT while the majority would do this either routinely or in specific situations. The IDSA recommendations for lower dosages for some antimicrobials are based on expert opinion; studies focusing on the dosing of SAT are scarce (4). Although it is common practice for most physicians world-wide to use a relatively low dosage of antibiotics for SAT, to date there is only one observational study on this approach which reported no difference in failure-free survival between patients with an orthopaedic implant infection treated with low-dosage compared to normal-dosage SAT (24). More data are necessary to inform on the effectivity and risk of antimicrobial resistance development of low dosed SAT.

Most studies mention that chronic SAT is prescribed indefinitely (4, 6-8, 10, 11). In contrast, the vast majority of respondents (>85%) stops or at least considers stopping SAT after a certain amount of time. This observation suggests that most respondents assume that cure can be achieved after a certain duration of SAT. Most relapses in these patients occur in the first two years and limited data suggest similar patient outcomes whether or not SAT is continued beyond this point (6-8, 11, 13, 24).

Definition of SAT

In most European publications, SAT is defined as lifelong antibiotic treatment of 'incurable infections' (patients treated with suboptimal or no surgery) (6-8, 10, 11). Studies from the United States mainly reserve the term SAT for an extended treatment duration after DAIR (13, 25-27). These two 'concepts' of SAT represent two distinct treatment strategies with a different goal and duration aimed at patient categories with variable prognoses. To improve the interpretation of future research, we propose to make a differentiation between these categories by using the following definitions: *Fixed term SAT*: prolonged antimicrobial therapy for a fixed duration of 6-24 months with the main goal of curing the infection.

Indefinite SAT: antimicrobial therapy with an undetermined duration with the main goal to prevent a relapse. In both definitions, SAT is started after the infection is clinically controlled following the standard treatment as established by (inter)national or local guidelines.

Strengths and limitations

To our knowledge, this is the first global survey on SAT for PJI, which revealed a great variation of SAT practices and identified relevant knowledge gaps that need to be prioritized and addressed in clinical research on treatment of PJI. Limitations of the study are the small number of respondents from North America, Asia, South Africa and South America, reducing its generalizability. Furthermore, difference in baseline characteristics between non-responders and responders are unknown, possibly introducing bias. Lastly, it is likely that respondents vary in SAT dose and treatment duration according to the indication for SAT, but we did not survey this specifically. Furthermore, comparing answers between respondents should be done with the notion that we did not ask respondents for their definition of SAT. The response rate was relatively low, but we expected this beforehand because of the specificity of the subject and the request to recipients to only fill out the survey if they were knowledgeable about PJI and had sufficient clinical experience treating patients with SAT.

Summary and conclusions

The global clinical practice of using SAT for patients with PJI is highly heterogeneous and based on expert opinion and observational studies, leaving many clinical questions unanswered. To optimize and harmonize treatment for these patients, future research and guidelines should focus on the indication for SAT and optimal antimicrobial regimens including dosage and duration. A uniform definition of SAT is needed to better compare the outcomes of studies and further improve their clinical value.

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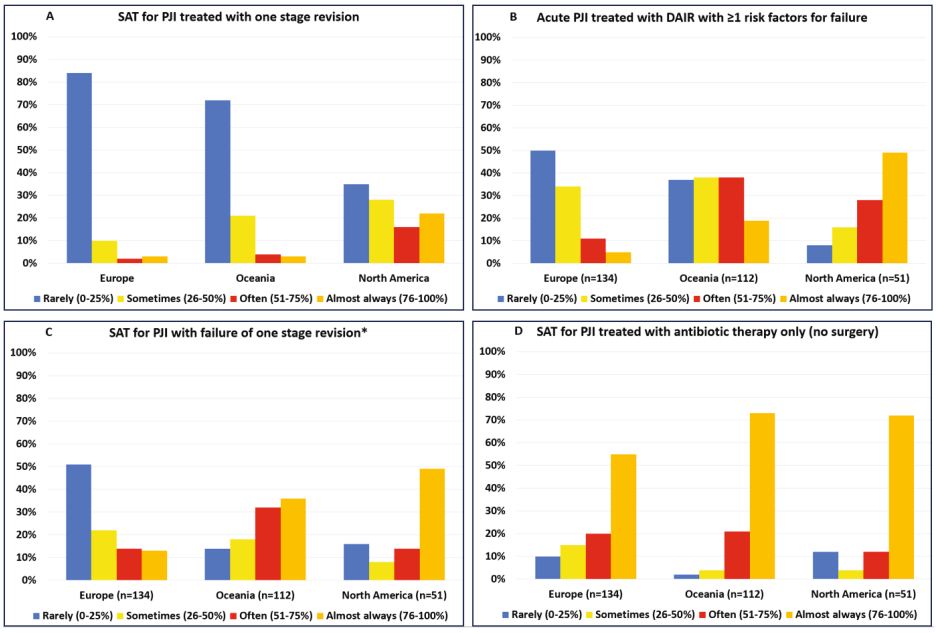
Supplement



Supplementary Figure 1. *Clinical scenarios of patients with PJI of which respondents were asked how often they would place patient on SAT stratified per continent. *preference for debridement followed by SAT instead of other surgical options.*

Supplementary Table 1. Number of respondents per country

Argentina	1
Australia	92
Austria	3
Belgium	3
Bosnia and Herzegovina	1
Brazil	3
Canada	5
China	1
Colombia	1
Croatia	2
Czech Republic	1
Denmark	1
Egypt	1
Finland	2

Supplementary Table 1. Number of respondents per country *(Continued)*

France	5
Germany	6
Greece	5
Hungary	1
India	7
Iran	1
Ireland	3
Italy	8
Korea, republic of	2
Lithuania	3
Netherlands	25
New Zealand	20
Nicaragua	2
Norway	3
Philippines	2
Portugal	7
Romania	1
Singapore	2
Slovenia	1
South Africa	2
Spain	28
Sweden	3
Switzerland	6
Thailand	3
Tunisia	2
Turkey	2
United Kingdom	16
United States	46

Supplementary Table 2. First and second choice SAT for staphylococcal PJI

First choice antibiotic	All respondents	Europe	Oceania	North America	Other continents[a]
	n=330	n=134	n=112	n=51	n=33
Anti staphylococcal penicillins	100 (30)	30 (22)	61 (55)	3 (6)	6 (18)
Oral cephalosporins	61 (18)	6 (5)	27 (24)	21 (41)	7 (21)
Tetracyclines	58 (18)	36 (27)	5 (5)	16 (31)	1 (3)
Cotrimoxazole	26 (8)	17 (13)	4 (4)	2 (4)	3 (9)
Rifampicin/fluoroquinolone	25 (8)	11 (8)	3 (3)	3 (6)	8 (24)
Rifampicin/non-fluoroquinolone	18 (6)	8 (6)	6 (5)	2 (4)	2 (6)
Fluoroquinolone	12 (4)	9 (7)	0	0	3 (9)
Clindamycin	9 (3)	6 (5)	1 (1)	0	2 (6)
Linezolid	0	0	0	0	1 (3)
No preference/per order ID specialist or microbiologist	20 (6)	11 (8)	5 (5)	4 (8)	0
Second choice antibiotic					
Anti staphylococcal penicillins	36 (11)	9 (7)	22 (20)	2 (4)	3 (9)
Oral cephalosporins	73 (22)	7 (5)	48 (43)	15 (29)	3 (9)
Tetracyclines	58 (18)	24 (18)	9 (8)	21 (41)	4 (12)
Cotrimoxazole	51 (16)	30 (22)	10 (9)	3 (6)	8 (24)
Rifampicin/fluoroquinolone	11 (3)	6 (5)	2 (2)	1 (2)	2 (6)
Rifampicin/ non-fluoroquinolone	16 (5)	8 (6)	5 (5)	1 (2)	2 (6)
Fluoroquinolone	6 (2)	3 (2)	1 (1)	1 (2)	1 (3)
Clindamycin	43 (13)	29 (22)	9 (8)	1 (2)	4 (12)
Linezolid	7 (2)	3 (2)	0	0	4 (12)
No preference/per order ID specialist or microbiologist	29 (9)	15 (11)	6 (5)	6 (12)	2 (6)

[a]South America, Asia and Africa combined

Supplementary Table 3. First and second choice SAT for streptococcal PJI

First choice antibiotic	All respondents	Europe	Oceania	North America	Other continents[a]
	n=330	n=134	n=112	n=51	n=33
Penicillins	234 (71)	90 (67)	102 (91)	27 (53)	15 (45)
Oral cephalosporins	30 (9)	7 (5)	4 (4)	14 (28)	5 (15)
Tetracyclines	5 (2)	4 (3)	0	1 (2)	0
Cotrimoxazole	7 (2)	6 (5)	0	0	1 (3)
Rifampicin/fluoroquinolone	9 (3)	4 (3)	0	1 (2)	4 (12)
Rifampicin/non-fluoroquinolone	3 (1)	1 (1)	1 (1)	1 (2)	0
Fluoroquinolone	10 (3)	5 (4)	0	2 (4)	3 (9)
Clindamycin	8 (2)	3 (2)	0	0	5 (15)
No preference/per order ID specialist or microbiologist	24 (7)	14 (11)	5 (5)	5 (10)	0
Second choice antibiotic					
Anti staphylococcal penicillins	32 (10)	10 (8)	2 (2)	13 (26)	7 (21)
Oral cephalosporins	121 (37)	17 (13)	76 (68)	21 (41)	7 (21)
Tetracyclines	25 (8)	15 (11)	2 (2)	6 (12)	2 (6)
Cotrimoxazole	14 (4)	9 (7)	3 (3)	0	2 (6)
Rifampicin/fluoroquinolone	5 (2)	1 (1)	2 (2)	0	2 (6)
Rifampicin/non-fluoroquinolone	5 (2)	3 (2)	1 (1)	1 (2)	0
Fluoroquinolone	13 (4)	6 (5)	3 (3)	0	4 (12)
Clindamycin	62 (19)	48 (36)	10 (9)	1 (2)	3 (9)
Linezolid	4 (1)	1 (1)	0	0	3 (9)
No preference/per order ID specialist or microbiologist	49 (15)	24 (18)	13 (12)	9 (18)	3 (9)

[a]South America, Asia and Africa combined

Supplementary Table 4. First and second choice SAT for gram-negative PJI

First choice antibiotic	All respondents	Europe	Oceania	North America	Other continents[a]
	n=330	n=134	n=112	n=51	n=33
Fluoroquinolone	102 (31)	42 (31)	26 (23)	13 (26)	21 (64)
Cotrimoxazole	67 (20)	38 (28)	18 (16)	6 (12)	5 (15)
Penicillin/beta-lactamase	63 (19)	19 (14)	30 (27)	9 (18)	5 (15)
inhibitor Oral cephalosporins	40 (12)	4 (3)	26 (23)	8 (16)	2 (6)
Tetracyclines	14 (4)	6 (5)	0	8 (16)	0
Fosfomycin	2 (1)	2 (2)	0	0	0
No preference/per order ID specialist or microbiologist	42 (13)	23 (17)	12 (11)	7 (14)	0
Second choice antibiotic					
Fluoroquinolone	62 (19)	30 (22)	18 (16)	9 (18)	5 (15)
Cotrimoxazole	107 (32)	46 (34)	35 (31)	17 (33)	9 (27)
Penicillin/beta-lactamase inhibitor Oral cephalosporins	44 (13)	11 (8)	23 (21)	5 (10)	5 (15)
	36 (11)	9 (7)	18 (16)	4 (8)	5 (15)
Tetracyclines	15 (5)	8 (6)	2 (2)	4 (8)	1 (3)
Fosfomycin	4 (2)	1 (1)	0	0	3 (9)
No preference/per order ID specialist or microbiologist	62 (19)	29 (22)	16 (14)	12 (24)	5 (15)

[a]South America, Asia and Africa combined

Supplementary Table 5. Dosing of SAT

Respondents that lower the dosage of this antimicrobial, n (%)	Total	Europe	Oceania	North America	Other continents[a]
	n=330	n=132	n=112	n=51	n=33
Penicillins	142 (43)	60 (45)	60 (54)	18 (35)	4 (12)
Oral cephalosporins	126 (38)	44 (33)	62 (55)	18 (35)	2 (6)
Tetracyclines	91 (28)	47 (36)	32 (29)	9 (18)	3 (9)
Fluoroquinolones	102 (31)	48 (36)	36 (32)	14 (27)	4 (12)
Cotrimoxazole	124 (38)	58 (44)	42 (38)	17 (33)	7 (21)
Clindamycin	99 (30)	48 (36)	36 (32)	10 (20)	5 (15)
Respondents lowering the dosage of SAT, n (%)					
Never	126 (38)	47 (36)	35 (31)	22 (43)	22 (67)
Always	79 (24)	39 (30)	29 (26)	9 (18)	2 (6)
In selected antibiotics	125 (38)	48 (36)	48 (43)	20 (39)	9 (27)

[a]South America, Asia and Africa combined