7ème

Journée Scientifique du CRIOGO

CENTRES DE RÉFÉRENCE POUR LES INFECTIONS OSTÉO-ARTICULAIRES COMPLEXES DU GRAND OUEST
CRIOGO

Antibiothérapie suppressive et IOA

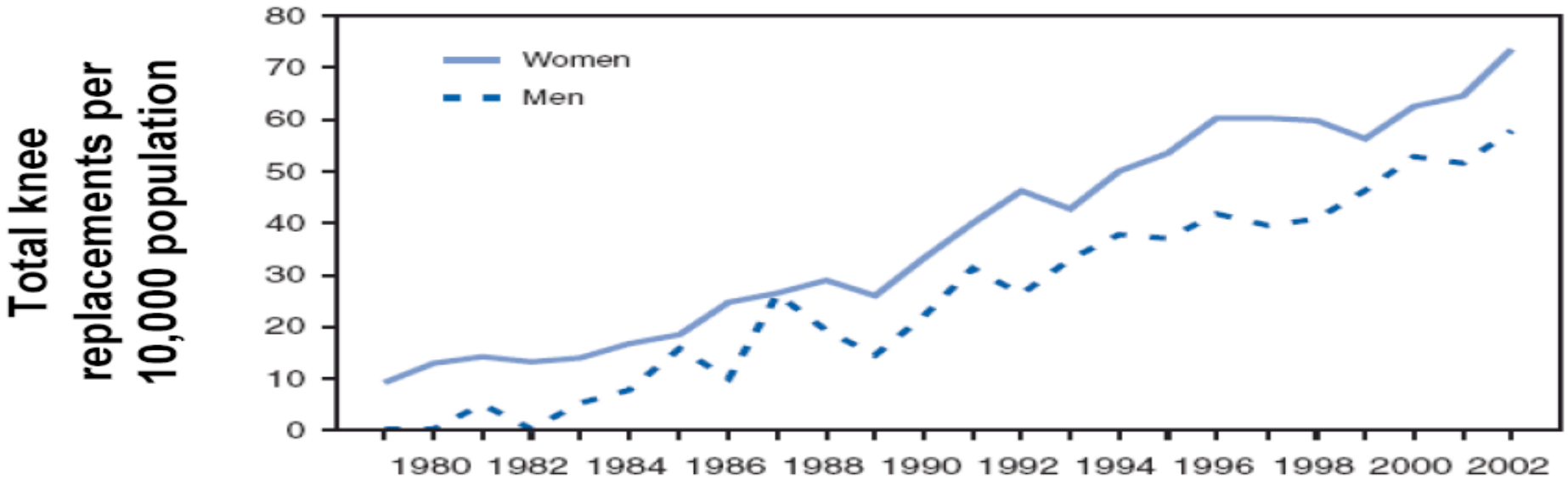
Aurélien Dinh[1], Viriginie Prendki[2]

[1]Maladies infectieuses, HU R. Poincaré, Garches, APHP

[2]Service médecine interne et gériatrie HU Genêve, SW

Contexte

- Augmentation Primo implantations aux USA
- Risque infectieux croissant en cas de reprise de Prothese
- Allongement de durée de vie des patients et des implants



Source: National Center for Health Statistics, www.cdc.gov

Recommandations de pratique clinique

Infections ostéo-articulaires sur matériel

(prothèse, implant, ostéosynthèse)

Texte court

Organisées par
la Société de Pathologie Infectieuse de Langue Française (SPILF)

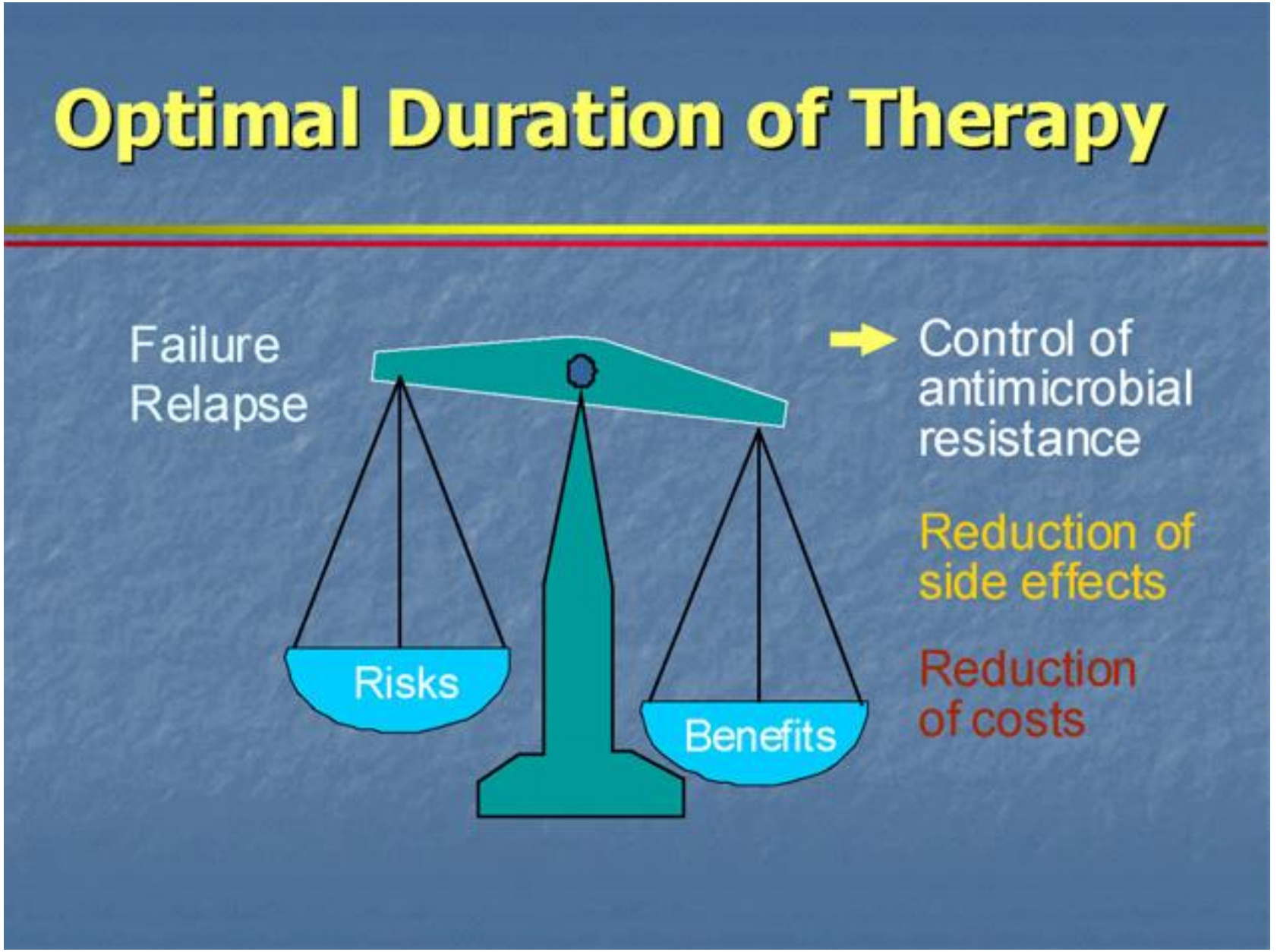
Définition : Antibiothérapie suppressive

Elle consiste à maintenir une antibiothérapie orale pour une durée indéterminée dans le but d'inhiber la multiplication bactérienne autour de la prothèse.

Elle ne s'applique qu'aux situations pour lesquelles la documentation bactérienne est connue et l'infection persiste chez un malade inopérable ayant une prothèse non descellée. Elle ne se conçoit qu'avec des molécules bien supportées et d'administration aisée (voie orale) **(grade C)**.

SPILF 2008

Optimal Duration of Therapy



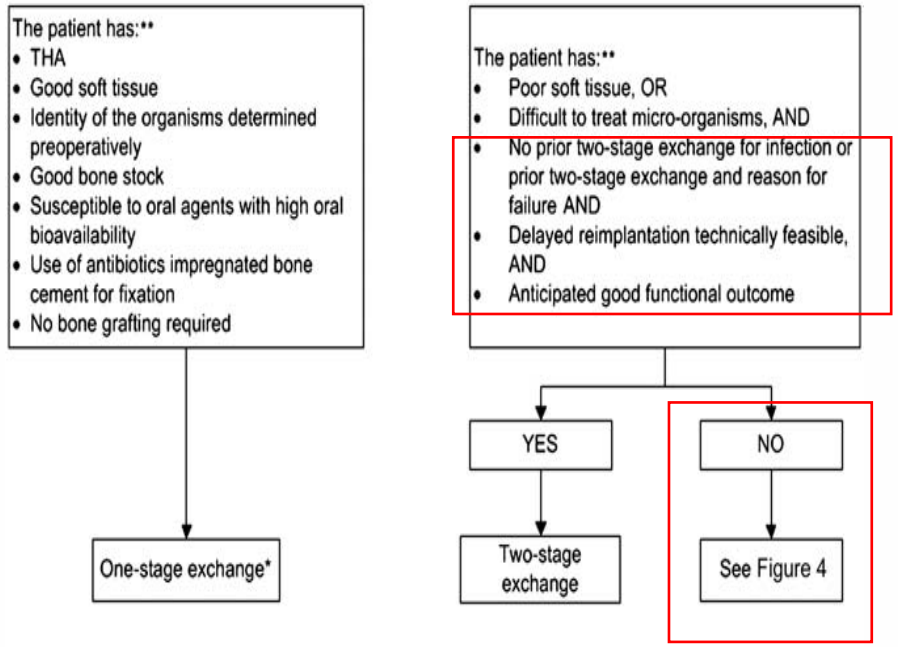
Rubinstein E *et al.* Int J Antimicrob Agents 2007

Clinical Infectious Diseases Advance Access published December 6, 2012

IDSA GUIDELINES

Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America[a]

Douglas R. Osmon,[1] Elie F. Berbari,[1] Anthony R. Berendt,[2] Daniel Lew,[3] Werner Zimmerli,[4] James M. Steckelberg,[1] Nalini Rao,[5,6] Arlen Hanssen,[7] and Walter R. Wilson[1]



CID 2012

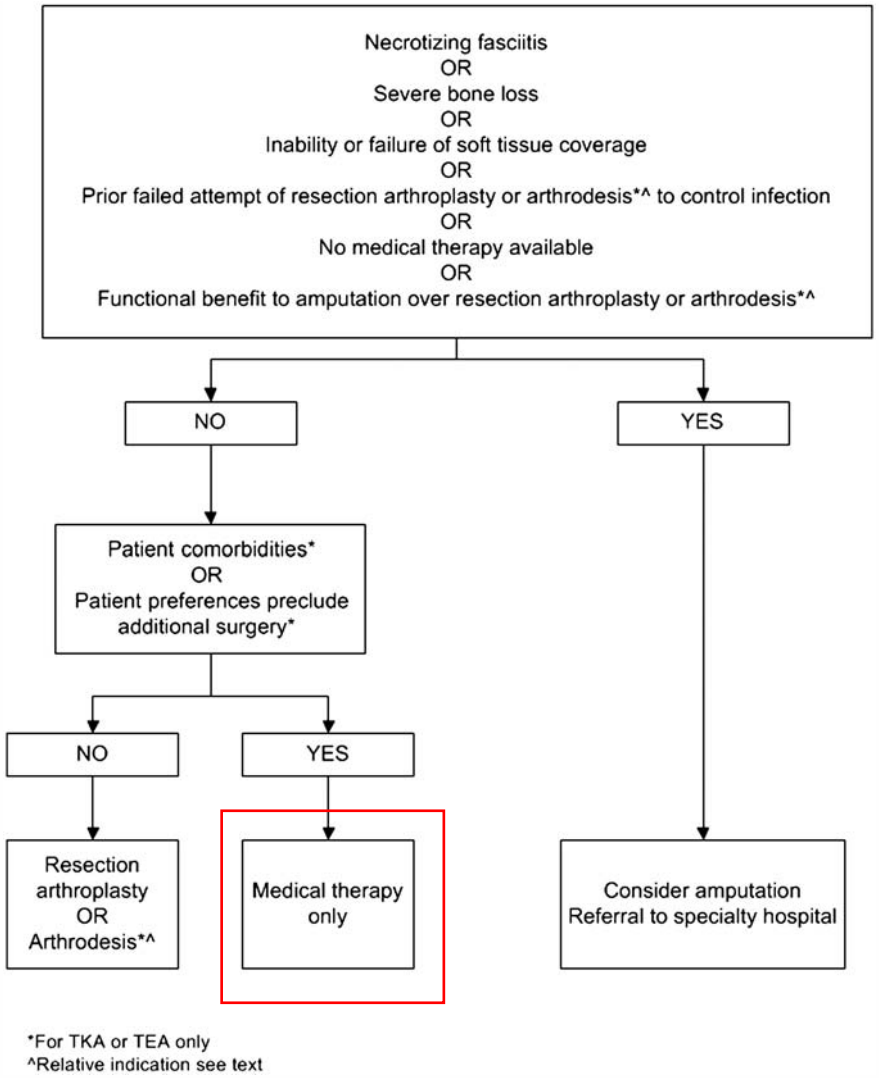


Figure 4. Management of prosthetic joint infection when patients are not a candidate for new prosthesis. Abbreviations: TEA, total elbow arthroplasty; TKA, total knee arthroplasty.

What is the medical treatment for a patient with PJI following debridement and retention of prothesis ?

Staphylococci PJI

- Indefinite chronic oral antimicrobial suppression may follow the above regimen with cephalexin, dicloxacillin, cotrimoxazole, or minocycline based on in vitro susceptibility, allergies, or intolerances (B-III).
- **Rifampin alone** is not recommended for chronic suppression, and rifampin combination therapy is not generally recommended.
  - One member of the panel uses rifampin combination therapy for chronic suppression in selected situations (A. R. B.).
  - The recommendation regarding using suppressive therapy after rifampin treatment was not unanimous (W. Z., D. L.).

PJI Due to Other Organisms

- Indefinite chronic oral antimicrobial suppression may follow the above regimens based on in vitro sensitivities, allergies, and intolerances (B-III).
- Chronic suppression after fluoroquinolone treatment of PJI due to gram-negative bacilli was not unanimously recommended (W. Z., D. L.).

CID 2012

Chronic Oral Antimicrobial Suppression

- The panel could not agree on the use and duration of chronic suppression following the induction course of intravenous antimicrobial therapy in nonstaphylococcal PJI or following the 3- to 6-month course of quinolone or other companion drug/rifampin in staphylococcal PJI treated with debridement and component retention.
  - Some members of the panel (D. L., W. Z.) would never use chronic suppression after rifampin combination therapy;
  - others would recommend the use of chronic suppression in all cases of PJI treated with debridement and component retention, assuming the patient tolerates the medication without difficulty,
  - whereas others would use it selectively in elderly or immunosuppressed patients, patients with a staphylococcal PJI in which rifampin is not utilized, elderly patients with nonstaphylococcal PJI, or patients whose comorbidities would not allow additional surgery or in whom additional surgery may be limb-threatening in case of treatment failure.
- Rifampin alone and linezolid should not be used for indefinite chronic suppression.
- Rifampin combination therapy is also not generally recommended;
- one member of the panel uses rifampin combination therapy for chronic suppression in selected situations (A. R. B.) [62].

Byren I, Bejon P, Atkins BL, et al. One hundred and twelve infected arthroplasties treated with 'DAIR': antibiotic duration and outcome. J Antimicrob Chemother 2009.

Principes généraux

- Clinical and laboratory **monitoring** for efficacy and toxicity is advisable.
- The decision to offer chronic suppressive therapy must take into account the **individual circumstances** of the patient including the ability to use rifampin in the initial phase of treatment, the potential for progressive implant loosening and loss of bone stock, and the hazards of prolonged antibiotic therapy;
- it is therefore generally **reserved for patients** who are unsuitable for, or refuse, further exchange revision, excision arthroplasty, or amputation.

CID 2012

ATB recommandé pour ABS

Microorganism	Preferred Treatment	Alternative Treatment
Staphylococci, oxacillin-susceptible	Cephalexin 500 mg PO tid or qid or Cefadroxil 500 mg PO bid	Dicloxacillin 500 mg PO tid or qid Clindamycin 300 mg PO qid Amoxicillin-clavulanate 500 mg PO tid
Staphylococci, oxacillin-resistant	Cotrimoxazole 1 DS tab PO bid Minocycline or doxycycline100 mg PO bid	
β-hemolytic streptococci	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	Cephalexin 500 mg PO tid or qid
Enterococcus spp, penicillin susceptible	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	
Pseudomonas aeruginosa	Ciprofloxacin 250–500 mg PO bid ????	
Enterobacteriaceae	Cotrimoxazole 1 DS tab PO bid	β-lactam oral therapy based on in vitro susceptibilities
Propionibacterium spp	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	Cephalexin 500 mg PO tid or qid Minocycline or doxycycline 100 mg PO bid

CID 2012

Prolonged Suppressive Antibiotic Therapy for Infected Orthopedic Prostheses

John Segreti, Jeffrey A. Nelson, and Gordon M. Trenholme

From the Rush Medical College, Chicago, Illinois

18 patients/18 infections
Âge moyen 66 ans (31-83 ans)
POA fonctionnelle
PEC : lavage, débridement, 6-8 semaines ATB IV puis ATB orale
EI ATB 22% (pas d'arrêt)
Durée ATB PO (4j-103j).
Succès (définition ?) 14/18 (78%)

Table 1. Characteristics of patients with infected orthopedic prostheses treated with prolonged oral antibiotic therapy.

Patient no./age (y)/sex	Site	Pathogen(s)	Onset of infection	Symptoms	Suppressive antibiotic(s) (dosage)	Duration (mo) of therapy	Antibiotic therapy continued?	Outcome	Complications
1/36/F	R TKA	MSSA	Early	Chronic	Cephalexin (500 mg q.i.d.)	103	Yes	Success	None
2/62/F	L TKA	GBS	Late	Acute	Penicillin (500 mg po q.i.d.)	69	Yes	Success	None
3/63/F	L THA	MSCNS	Early	Chronic	Cefadroxil (500 mg po b.i.d.)	96	Yes	Success	None
4/61/M	R TKA	MSCNS	Early	Chronic	Oxacillin (500 mg po q.i.d.)	51	Yes	Success	None
5/83/F	L TKA	MRCNS	Early	Chronic	Minocycline/rifampin (100 mg b.i.d./600 mg q.d. po)	56	Yes	Success	None
6/65/F	R THA	MRSA	Early	Chronic	Minocycline/rifampin (100 mg/600 mg po q.d.)	69	Yes	Success	Diarrhea
7/76/F	R THA	*Moraxella* species	Late	Acute	Ampicillin (500 mg po q.i.d.)	12	No	Success	None
8/34/M	L TKA	MRCNS	Late	Chronic	Minocycline/rifampin (100 mg/600 mg po q.i.d.)	59	Yes	Success	None
9/73/M	L TKA	MSSA	Late	Acute	Dicloxacillin (500 mg po q.i.d.)	22	No	Failure*	None
10/75/M	R THA	MSSA/*Enterococcus* species	Early	Chronic	Amoxicillin/clavulanate (500 mg po t.i.d.)	103	Yes	Success	None
11/73/M	L TKA	MRSA	Late	Acute	Minocycline/rifampin (100 mg/600 mg po q.d.)	16	No	Success	Diarrhea
12/59/F	R TKA	MSSA	Late	Acute	Dicloxacillin (500 mg po q.i.d.)	28	No	Success	None
13/74/F	R THA	*Streptococcus pneumoniae*	Late	Acute	Penicillin (500 mg po q.i.d.)	49	Yes	Success	None
14/78/M	L TKA	MRCNS	Early	Chronic	Minocycline/rifampin (100 mg/600 mg po q.d.)	50	Yes	Success	None
15/77/M	L TKA	MRCNS/MSCNS	Early	Chronic	TMP-SMZ/rifampin (one DS po q.d./600 mg po q.d.)	71	Yes	Success	None
16/37/M	L THA	MSSA	Early	Chronic	Clindamycin (300 mg po t.i.d.)	4	No	Failure	None
17/81/F	R TKA	MSSA	Late	Acute	Dicloxacillin (500 mg po q.i.d.)	9	No	Failure	Diarrhea
18/77/M	L TKA	MSCNS	Late	Acute	Dicloxacillin (500 mg po q.i.d.)	13	No	Failure	Diarrhea, drug rash

NOTE. GBS = group B streptococci; L = left; MRCNS = methicillin-resistant coagulase-negative staphylococci; MRSA = methicillin-resistant *Staphylococcus aureus;* MSCNS = methicillin-susceptible coagulase-negative staphylococci; MSSA = methicillin-susceptible *S. aureus;* R = right; THA = total hip arthroplasty; TKA = total knee arthroplasty.

Oral antibiotics used as suppressive agents, duration of therapy, and outcome.

DS = double strength; TMP-SMZ = trimethoprim-sulfamethoxazole.
antibiotic therapy was discontinued.

CID 1998

Revue des données

Références	N patients	Stratégie	durée	succès	Taux EI	FDR échec
Nowak et al. Am. J Health Syst Pharm 2015 **Prolonged oral antibiotic suppression in osteomyelitis and associated outcomes in a Veterans population.**	20	Pas de matériel	26 mois ± 14	60%	25%	diabète
Tsukayama DT, et al. Orthopedics. 1991 **Suppressive antibiotic therapy in chronic prosthetic joint infections**	13	DAIR	37,6 mois	30% (10 ablations de prothèses pour infection)	38%	
Barberán J, et al. Am J Med. 2006 **Conservative treatment of staphylococcal prosthetic joint infections in elderly patients**	60	DAIR SA/SCN		65%		Infection chronique Diagnostic tardif R Méthiciline Genou
Rao N, et al. Clin Orthop Relat Res. 2003 **Long-term suppression of infection in total joint arthroplasty**	15	DAIR		86,2%		
Aboltins CA, et al. Clin Microbiol Infect. 2007 **Treatment of staphylococcal prosthetic joint infections with debridement, prosthesis retention and oral rifampicin and fusidic acid.**	20	DAIR	32 mois	90%	10%	
Peel TN, et al. Antimicrob Agents Chemother. 2013. **Outcome of debridement and retention in prosthetic joint infections by methicillin-resistant staphylococci, with special reference to rifampin and fusidic acid combination therapy.**	43	DAIR	33 mois	86%		SARM <4 débridements
Siqueira MB, et al. J Bone Joint Surg Am. 2015 **Chronic Suppression of Periprosthetic Joint Infections with Oral Antibiotics Increases Infection-Free Survivorship.**	92	DAIR	60 mois	68,5%		Pas de chgt des pièces mobiles Germe

Outcome of Prosthetic Joint Infections Treated with Debridement and Retention of Components

C. E. Marculescu,[1] E. F. Berbari,[2] A. D. Hanssen,[3] J. M. Steckelberg,[2] S. W. Harmsen,[4] J. N. Mandrekar,[4] and D. R. Osmon[2]

[1]Division of Infectious Diseases, Medical University of South Carolina, Charleston; and [2]Division of Infectious Disease, Department of Internal Medicine, [3]Department of Orthopedics, and [4]Department of Biostatistics, Mayo Clinic College of Medicine, Rochester, Minnesota

91 patients/99 épisodes
IPOA
DAIR
SA 32% ; SCN 23%
Durée moyenne ATB IV 28 j (1-90)
ATB oral dans 89% des cas durée moyenne 541 jours (5-2673)
Échec 53/99 médiane de suivie 700 j
FDR d'échec : fistule et durée des symptômes >8j

Table 1. Definition of terms for a study of prosthetic joint infection (PJI) treated with debridement and retention of components.

Term	Definition
PJI[a]	Isolation of the same microorganism from ⩾2 cultures of joint aspirates or intraoperative tissue specimens;
	Presence of acute inflammation on histopathologic examination (as determined by the pathologist);
	Sinus tract communicating with the prosthesis;
	Purulence in a joint space (as determined by the surgeon);
	Or culture-negative PJI
Culture-negative PJI	Culture of a joint aspirate or intraoperative specimens negative for aerobic and anaerobic bacteria, in conjunction with purulence surrounding the prosthesis, acute inflammation on histopathologic examination at the time of surgery, or a sinus tract communicating with the prosthesis, with or without prior use of antimicrobials
Treatment failure	Occurrence of a PJI due to the original microorganism at any time after the surgical procedure (relapse of infection);
	Occurrence of a PJI due to a different strain or different microorganism (reinfection) at any time after the surgical procedure;
	Presence of acute inflammation in the periprosthetic tissue on histopathological examination or at any subsequent surgery on the joint;
	Development of a sinus tract;
	Death from prosthesis-related infection;
	Or indeterminate clinical failure
Indeterminate clinical failure	Clinical, laboratory, or radiological findings suggestive of PJI at any time after surgical therapy, as noted in the medical record
Main intravenous or oral antimicrobial agent	Antimicrobial agent used for ⩾50% of the total duration of antimicrobial therapy
Effective antimicrobial therapy	Antimicrobial therapy active against the isolated microorganism causing PJI, according to the in vitro susceptibilities of the microorganism as determined by the clinical microbiology laboratory
Long-term oral antimicrobial suppression	Orally administered antimicrobial therapy of indefinite duration received after completion of intravenous antimicrobial therapy

[a] Based on [2, 6, 17, 38].

Table 3. Demographic factors, comorbidities, symptoms at presentation, and radiologic findings for 99 episodes of prosthetic joint infection (PJI) treated with debridement and retention of prosthesis.

Variable	Value
Age, median years (range)	74 (23–95)
Duration of follow-up, median days (range)	700 (1–2779)
Male sex	52 (52)
PJI of total hip arthroplasty	47 (47)
Rheumatoid arthritis	6 (6)
Diabetes mellitus	17 (17)
Systemic malignancy	21 (21)
HIV infection	0
Sinus tract	15 (15)
Cellulitis	21 (21)
Fever (temperature, ⩾38.4°C)	38 (38)
Bacteremia due to the same microorganism that caused PJI	6 (6)
Infective endocarditis[a]	2 (2)
Available radiographic findings	86 (86)
Radiographic lucencies	13 (13)
Cemented prosthesis	90 (90)

NOTE. Data are no. (%) of episodes, unless otherwise indicated.

[a] Due to *Staphylococcus lugdunensis* (1 episode) or viridans group streptococci (1 episode).

CID 2006

Table 4. Microbiologic findings of 99 episodes of prosthetic joint infection (PJI) occurring in 91 patients, 1995–1999.

Microorganism or infection	No. (%) of episodes	Proportion (%) of episodes treated successfully	Duration of follow-up for successfully treated episodes, median days (range)
Coagulase-negative staphylococci[a]	23 (23)	14/23 (61)	1135 (67–2146)
Staphylococcus aureus[b]	32 (32)	4/32 (12.5)	113.5 (74–1108)
Streptococci[c]	14 (14)	11/14 (78.5)	1277 (671–2110)
Penicillin-susceptible enterococci	3 (3)	2/3 (66.6)	1995 (1598–2392)
Gram-negative bacilli[d]	6 (6)	4/6 (66.6)	1591 (534–1804)
Gram-positive bacilli[e]	1 (1)	0/1 (0)	…
Anaerobic infection[f]	1 (1)	0/1 (0)	…
Polymicrobial infection	8 (8)	4/8 (50)	1904 (1029–2779)
Culture-negative infection[g]	8 (8)	6/8 (75)	1655 (13–2410)
Fungi[h]	1 (1)	0/1 (0)	…
Other	2 (2)	1/2 (50)	139
Total	99 (100)	46/99 (46)	1194 (13–2779)

Table 5. Adverse effects of antimicrobial therapy for 99 episodes of prosthetic joint infection occurring in 91 patients, 1995–1999.

Side effect	No. (%) of episodes
Delayed hypersensitivity reaction	11 (11)
Nephrotoxicity (due to vancomycin)	1 (1)
Hepatotoxicity	0
Ototoxicity or vestibular toxicity	0
Diarrhea	3 (3)
Pseudomembranous colitis	1 (1)
Leukopenia (due to vancomycin)	1 (1)
Skin discoloration (due to minocycline)	1 (1)

Table 6. Univariate assessment of risk factors for treatment failure among patients with prosthetic joint infection treated with debridement and retention of prosthesis.

Variable	Hazard ratio (95% CI)	*P*
Infecting microorganism		
Staphylococcus aureus	5.14 (2.36–11.20)	<.001
Coagulase-negative staphylococci	0.43 (0.12–1.62)	.21
Streptococci	0.80 (0.30–2.12)	.65
Other[a]	1.0 (reference)	
Diabetes mellitus		
Present	1.13 (0.53–2.41)	.75
Absent	1.0 (reference)	
Sinus tract		
Present	2.85 (1.50–5.44)	.002
Absent	1.0 (reference)	
Duration of symptoms		
⩾8 days	1.79 (1.04–3.09)	.04
<8 days	1.0 (reference)	
Joint age		
⩾31 days	0.65 (0.25–1.65)	.36
<31 days	1.0 (reference)	
Rheumatoid arthritis		
Present	1.34 (0.42–4.34)	.61
Absent		
Joint location		
Total knee arthroplasty	1.09 (0.63–1.89)	.75
Total hip arthroplasty	1.0 (reference)	

interval [CI], 36%–71%) and 69% (95% CI, 52%–86%), respectively. A median of 4 additional surgical procedures (range, 1–9) were required to control the infection in the 21 prosthetic joints for which treatment failed. Prostheses that were debrided >2 days after onset of symptoms were associated with a higher probability of treatment failure than were those debrided within 2 days of onset (relative risk, 4.2; 95% CI, 1.6–10.3). These data suggest that debridement and retention of the prosthesis as the initial therapy for PJI due to *S. aureus* is associated with a high cumulative probability of treatment failure and that the probability of treatment failure may be related to the duration of symptoms.

30 patients
DAIR
IPOA à staph
Échec (récidive IPOA) : 21/33
Probabilité d'échec à 1 an (54%) à 2 ans : 69%
Procédures additionnelles : 4 en moyenne

the patient was still receiving iv antistaphylococcal therapy was considered a superinfection.

Reinfection. PJI due to a microorganism other than the original strain of *S. aureus* that occurred after completion of iv antistaphylococcal therapy was considered a reinfection.

Risk factors for treatment failure included rheumatoid arthritis (diagnosed on the basis of the 1987 revised criteria for rheumatoid arthritis [34]); steroid use (≥20 mg of prednisone per day at the time of debridement or any dose of prednisone for >3 months in the year prior to the diagnosis of PJI); evi-

CID 1997

Final treatment outcome. A median of 4 additional surgical procedures (range, 1–9) were required to control the infection in the 21 prosthetic joints for which treatment failed. A median of 2 (range, 1–7) additional surgical procedures were required to control the infection in the 16 TKAs, and 4 (range, 2–9) additional surgical procedures for the 5 THAs. Figure 3 shows the final status of all 33 prostheses at the end of the observation period.

Discussion

In previous studies, treatment of PJI with debridement and retention of the prosthesis was associated with high failure rates [5, 9, 11–20, 22–24]. The overall probability of treatment failure for patients with PJI due to *S. aureus* treated with this

FDR d’échec

- There was no significant association between treatment failure and
  - the patient's age or sex,
  - joint location,
  - prosthesis age,
  - history of rheumatoid arthritis or steroid use,
  - S. *aureus* bacteriemia,
  - evidence of prosthetic loosening, intraoperative purulence,
  - presence of a sinus tract communicating with the prosthesis,
  - number of debridements,
  - duration of iv antimicrobial therapy,
  - or **utilization of chronic suppression**.

Journal of Antimicrobial Chemotherapy (2009) 63, 1264–1271
doi:10.1093/jac/dkp107
Advance Access publication 31 March 2009

JAC

One hundred and twelve infected arthroplasties treated with 'DAIR' (debridement, antibiotics and implant retention): antibiotic duration and outcome

I. Byren[1,2*†], P. Bejon[1,2†], B. L. Atkins[1–3], B. Angus[2], S. Masters[1], P. McLardy-Smith[1], R. Gundle[1] and A. Berendt[1]

Etude rétrospective
120 IPOA
DAIR
Durée moyenne ATB 1,5 an
20 (18%) échecs septiques : 8 échecs sous ATB 12 après l'arrêt

Variable/category	*n*	Number failing	Hazard ratio	95% CI	*P*
Gender					
female	50	10	1		
male	62	10	0.7	0.30–1.73	0.47
Age (years)					
<40	2	0	—		
40–49	2	1	—		
50–59	22	4	1		
60–69	34	5	0.8	0.21–3	0.75
70–79	35	7	1.2	0.35–4.1	0.86
80–89	17	3	1.1	0.26–5.13	0.92
Co-morbidity					
none	45	4	1		
one or more	66	15	2.7	0.91–8.3	0.07
unknown	1	1			
Time from implant to debridement (days)					
<90	77	9	1		
≥90	35	11	3.0	1.2–7.2	0.016
Time from presentation to debridement (days)					
<3	71	9	1		
3–14	25	6	0.77	0.24–2.5	0.67
>14	16	5	0.36	0.12–1.0	0.07
Arthroplasty					
primary implant	86	11	1		
revised implant	26	9	2.6	1.1–6.3	0.031
Surgical debridement					
open debridement	97	12	1		
arthroscopy	15	8	5.4	2.2–13	<0.0005
Joint					
hip	52	7	1		
knee	51	13	0.47	0.19–1.18	0.10
ankle	3	0	—		
shoulder	2	0	—		
elbow	4	0	—		
Surgical findings					
no pus at surgery	54	8	1		
pus at surgery	48	1	1.5	0.59–3.65	0.41
unknown	10	11	—		
Number of debridements					
single procedure	88	14	1		
multiple procedures	24	6	1.8	0.68–4.7	0.24
Microbiology[a]					
MRSA	9	3	2.0	0.59–7	0.26
MSSA	39	10	1.8	0.71–4.4	0.21
CoNS	26	5	1.0	0.36–2.8	0.99
S. aureus	47	13	2.6	0.97–6.9	0.052
Intravenous antibiotics					
<28 days	26	8	1		
≥28 days	86	12	0.41	0.16–0.99	0.050

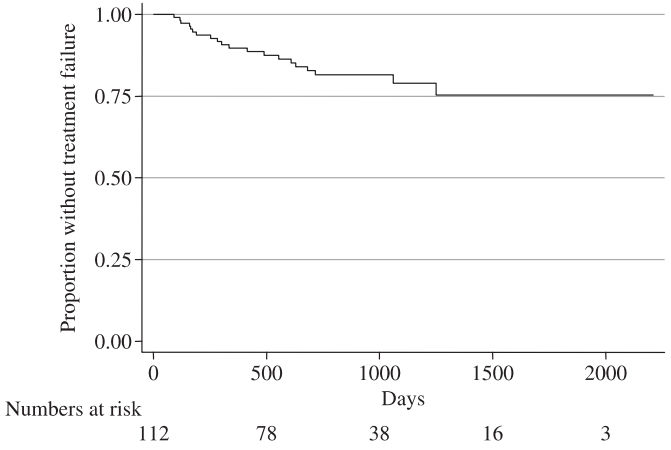


Figure 1. Kaplan–Meier plot of time to treatment failure for all patients, showing all follow-up data available.

Table 2. Multiple Cox regression model of significant factors from univariate analysis

	Hazard ratio	95% CI	*P*
Implant to debridement ≥90 days	1.1	0.31–3.8	0.89
Intravenous antibiotics ≥28 days	0.49	0.18–1.37	0.18
Arthroscopy versus open	4.2	1.5–12.5	0.008
S. aureus	2.9	1.0–8.4	0.050
Revised versus primary arthroplasty	3.1	1.2–8.3	0.008
Presence of co-morbidity	1.81	0.55–5.9	0.32

Goodness of fit: log likelihood = −59.6, $\chi^2 = 17.2$, $P = 0.0006$.

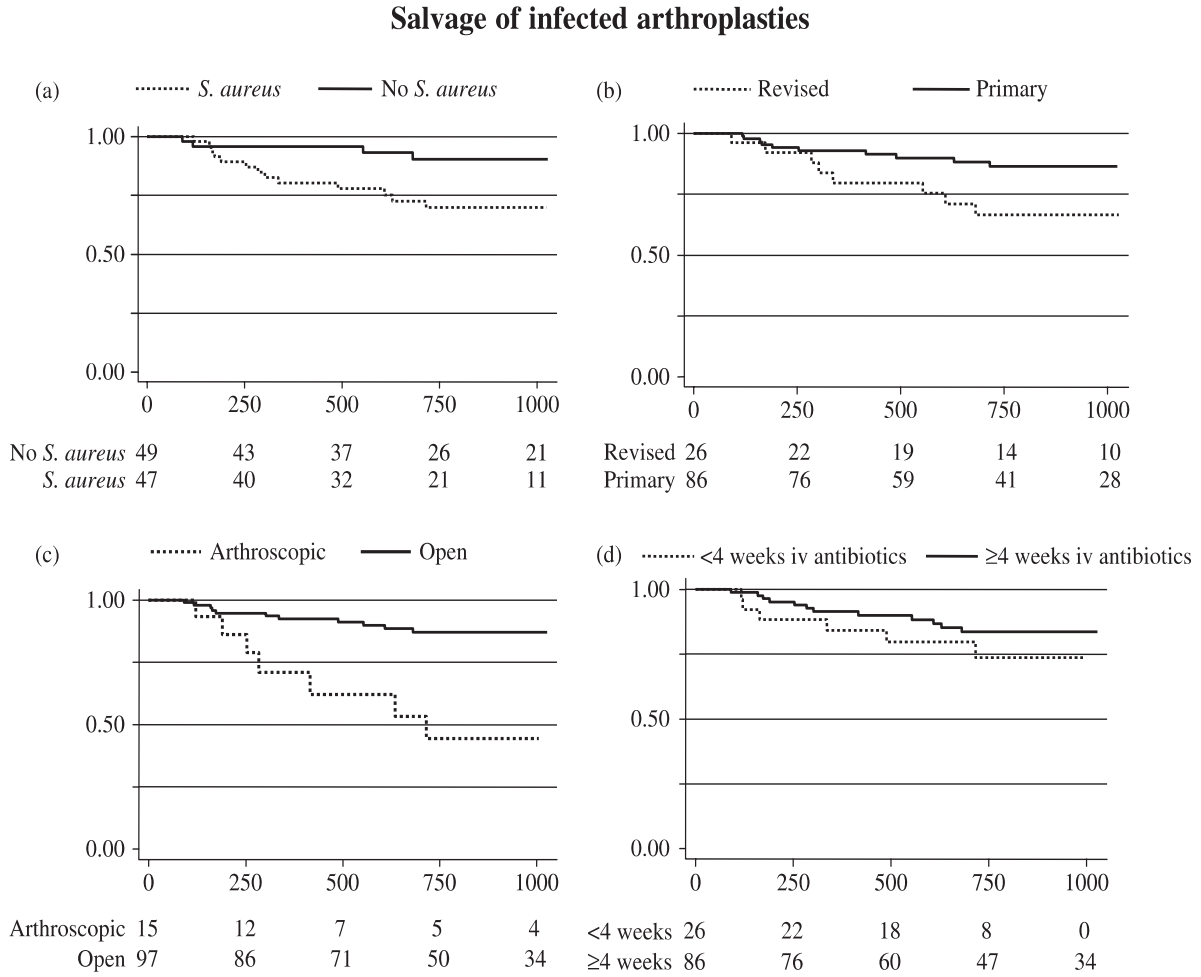


Figure 2. Kaplan–Meier plots for time to failure are shown for (a) the presence or absence of *S. aureus* infection, (b) primary versus previously revised implant, (c) arthroscopic versus open debridement and (d) length of intravenous (iv) antibiotic use. The *x*-axes show days since DAIR and the *y*-axes show the proportion without treatment failure. The numbers at risk at each timepoint are shown beneath each plot.

JAC 2009

L'ATB repousse l'échec mais ne le prévient pas

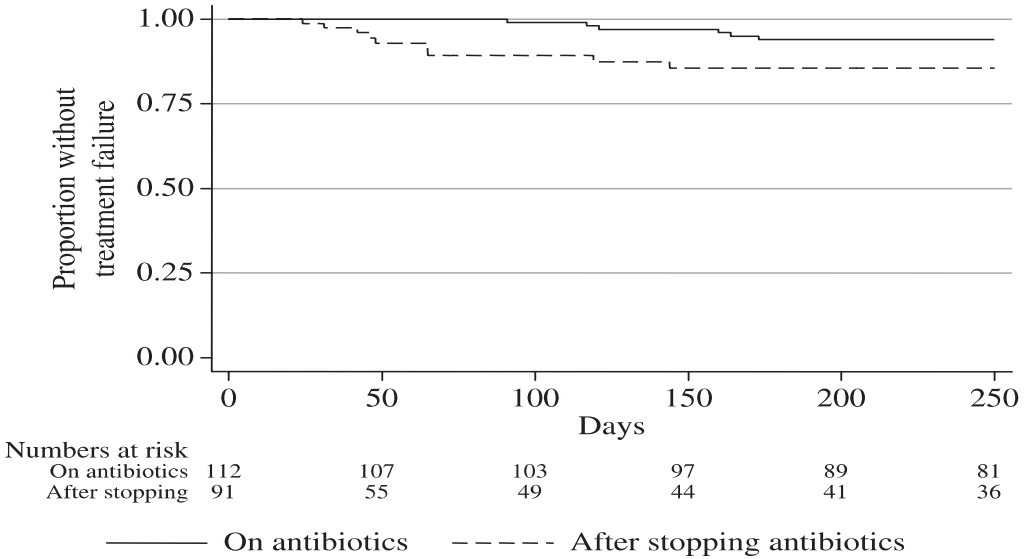


Figure 3. Kaplan–Meier plot of time to treatment failure for patients on oral antibiotics (HR = 1) and patients stopping oral antibiotics (where day of stopping is day 0, HR = 4.3, 95% CI 1.4–12.8, $P = 0.01$).

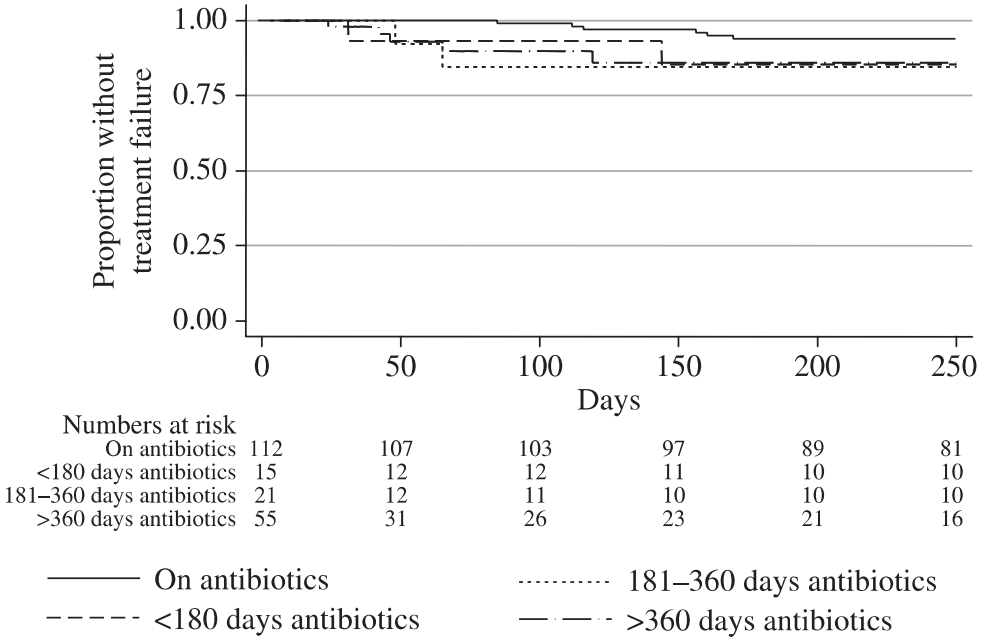


Figure 4. Kaplan–Meier plot of time to treatment failure for patients at the start of the DAIR protocol and patients stopping oral antibiotics (where day of stopping is day 0), divided according to the length of use of oral antibiotics prior to stopping: <180 days oral suppression, HR = 3.7 (95% CI 0.7–18), $P = 0.11$; 181–360 days oral suppression, HR = 9.1 (95% CI 0.9–90), $P = 0.058$; and >360 days oral suppression, HR = 5.1 (95% CI 1.4–19), $P = 0.013$.

JAC 2009

Outcome of patients over 80 years of age on prolonged suppressive antibiotic therapy for at least 6 months for prosthetic joint infection

Virginie Prendki[a,b,c,*], Valérie Zeller[b,c,d], Dorick Passeron[c,d], Nicole Desplaces[c,e], Patrick Mamoudy[c,d], Jérôme Stirnemann[a], Simon Marmor[c,d], Jean-Marc Ziza[b,c]

Baseline characteristics of 38 patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy

Characteristics	
Gender, male, *n* (%)	17 (45)
Age, years, median (range)	84 (80–95)
BMI, kg/m^2, median (range)	26 (15.8–33.3)
Difficulty walking, *n* (%)	17 (45)
Bedsores, *n* (%)	3 (8)
Medical co-morbidity, *n* (%)	36 (95)
Cardiovascular disease,[a] *n* (%)	32 (84)
Chronic renal failure, *n* (%)	7 (18)
Long-term oral corticosteroids, *n* (%)	4 (11)
Malignancy within the last 5 years, *n*	3
Chronic dermatitis, *n*	3
Alzheimer's disease, *n*	1
Insulin-requiring diabetes, *n*	1
Rheumatoid arthritis, *n*	1
Previous PJI, *n* (%)	14 (37)
ASA score of 3, *n* (%)	21 (55)
Site of PJI, *n* (%)	
Hip	24 (63)
Knee	13 (34)
Shoulder	1
Description of the infection, *n* (%)	
Early	15 (39%)
Acute	15 (39%)
Postsurgical	23 (61%)
Physical examination, *n* (%)	
Fever	14 (37)
Sinus tract	9 (24)
Laboratory examination	
Total leukocyte count, $\times 10^9$/l, median (range)	8.820 (5.400–18.950)
CRP, mg/l, median (range)	74 (2–600)
Serum albumin, g/l, median (range)	29 (17–41)

Bacterial pathogens isolated in 38 prosthetic joint infections treated with prolonged suppressive antibiotic therapy

Pathogen	*n* (%)	Event (failure)
Staphylococcus species	20 (53)	11 (6)
Staphylococcus aureus	15 (39)	10 (5)
Methicillin-sensitive	10	5 (3)
Methicillin-resistant	5	5 (2)
Coagulase-negative staphylococci[a]	5	1 (1)
Streptococcus species	7 (18)	1
Streptococcus agalactiae	6 (16)	1
Streptococcus salivarius	1	0
Enterococcus species	2	0
Enterococcus faecalis	2	0
Gram-negative bacilli	5 (13)	1
Enterobacteriaceae[b]	2	0
Campylobacter fetus	3	1
Anaerobic bacteria	4 (11)	2 (1)
Propionibacterium acnes	3	1
Finegoldia magna	1	1 (1)
Bacteraemia[c]	9 (24)	4 (2)
Endocarditis[d]	2 (5)	1 (1)

IJID 2014

Etude rétrospective monocentrique
Patients > 80 ans
IPOA documentée
ATB> 6 mois
38 patients
84 ans (80-95 ans)
24 IPTH
13 IPG
SA 39%
Strepto agalactiae 16%
ATB : penicillines
Durée moyenne de suivi 24 mois
Évènements :

- récidive de l'infection,
- super infection,
- arrêt ATB pour EIG,
- décès en rapport avec l'infection

60% sans événements à 24 mois
6 échecs 9 décès sans rapport avec infection

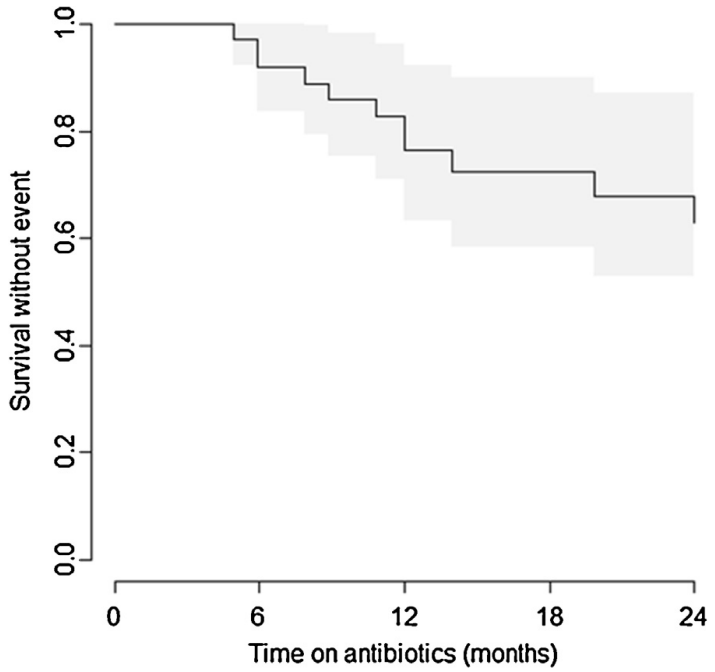


Figure 1. Clinical outcome of 38 patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy. Kaplan–Meier curve showing survival without event (95% confidence interval in grey). Events are defined as failure and unrelated death.

Univariate assessment of risk factors for treatment failure among patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy: qualitative variables

Variables	Total number with characteristic	Number of events (%)	Unadjusted HR (95% CI)	*p*-Value[a]
Age, years				
80–85	22	6 (27%)		
≥85	16	9 (56%)	3.87 (1.29–11.62)	0.016
Gender				
Male	17	5 (29%)		
Female	21	10 (48%)	4.55 (1.23–16.74)	0.023
Joint				
Hip	24	11(46%)		
Knee	13	4 (31%)	0.7 (0.22–2.24)	0.549
Shoulder	1	0	-	
Arthroplasty				
Primary implant	24	12 (50%)		
Revised implant	14	3	0.35 (0.10–1.25)	0.105
Gait disorder				
Absent	17	3 (18%)		0.049
Yes	21	12 (57%)	3.62 (1.002–13.05)	
ASA score				
2	17	4 (24%)		
3	21	11 (52%)	2.57 (0.80–8.26)	0.112
Time free of symptoms, months				
<12	14	4 (29%)		
>12	23	10 (43%)	1.20 (0.37–3.93)	0.760
Sinus tract				
Absent	29	9 (31%)		0.020
Yes	9	6 (67%)	3.74 (1.24–11.35)	
Microbiology				
Other bacteria	18	4 (22%)		
Staphylococcus	20	11 (55%)	7.30 (1.61–33.19)	0.010
Bacteraemia				
Absent	29	10 (34%)		
Yes	9	5 (56%)	1.24 (0.38–3.98)	0.722
Surgery				
No	29	8 (28%)		
Yes	9	7 (78%)	2.11 (0.71–6.26)	0.178
Duration of symptoms				
<30 days	15	5 (33%)		
30–90 days	5	2 (40%)	1.18 (0.22–6.53)	0.850
>90 days	18	8 (44%)	1.52 (0.45–5.08)	0.500

HR, hazard ratio; CI, confidence interval; ASA, American Society of Anesthesiologists.
[a] Log-rank test.

Table 5
Univariate assessment of risk factors for treatment failure among patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy: continuous variables

Variables	Total number with characteristic Median (min–max)	Number of events Median (min–max)	Number without event Median (min–max)	Unadjusted HR (95% CI)	*p*-Value[a]
BMI, kg/m^2	35 25.7 (15.8–44.6)	15 23.3 (15.8–44.6)	20 26.3 (17.3–42.8)	0.94 (0.86–1.03)	0.206
Serum albumin, g/l	19 29 (17–41)	8 22 (17–32)	11 31 (17–41)	0.69 (0.54–0.87)	0.019
CRP, mg/l	38 74 (2–600)	15 70 (2–600)	23 77 (3–421)	0.998 (0.993–1.002)	0.299

HR, hazard ratio; CI, confidence interval; BMI, body mass index; CRP, C-reactive protein.
[a] Log-rank test.

Etude nationale française

Définition de l'antibiothérapie suppressive (ABS)

- ✓ Antibiothérapie prescrite au long cours pour prévenir les complications infectieuses systémiques sans objectif de guérison locale.
- ✓ Efficacité /tolérance de cette stratégie de prise en charge des IPOA mal connues.

Objectifs de l'étude :

Décrire les caractéristiques de l'ABS et l'évolution sous traitement des cas d'infections de prothèse ostéo-articulaire (IPOA)

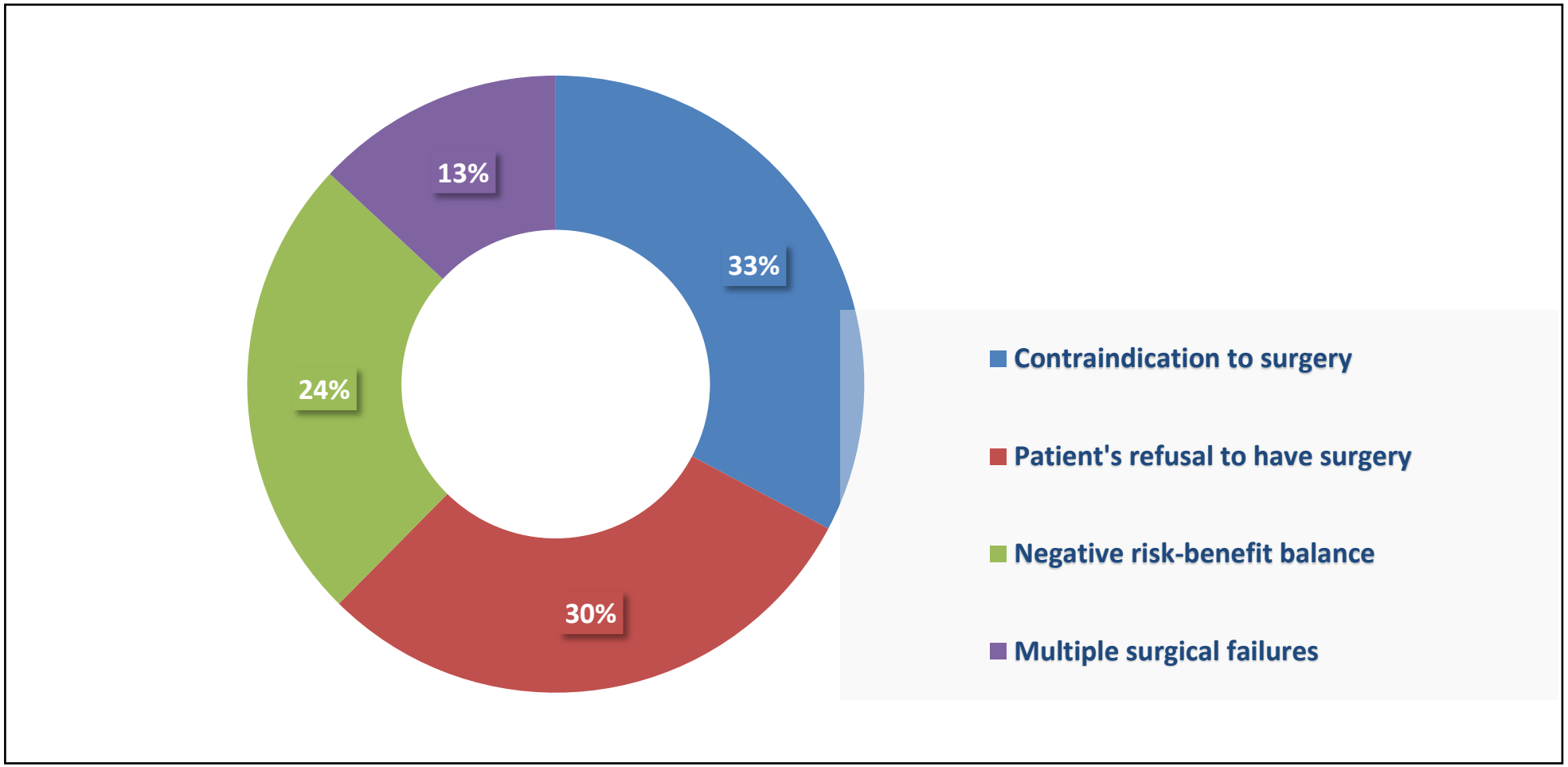
METHODES

- Etude multicentrique rétrospective (transversale) française menée sous l'égide de l'intergroupe SPILF-SFGG.
- **Questionnaire** standardisé, anonymisé et sécurisé envoyé aux participants.
- **Critères d'inclusion** :
  - ✓ Age>75 ans.
  - ✓ IPOA traitée par rétention du matériel infecté et ABS.
- **Définition échec :**
  - ✓ Progression locale de l'infection
  - ✓ Sepsis d'origine ostéo articulaire

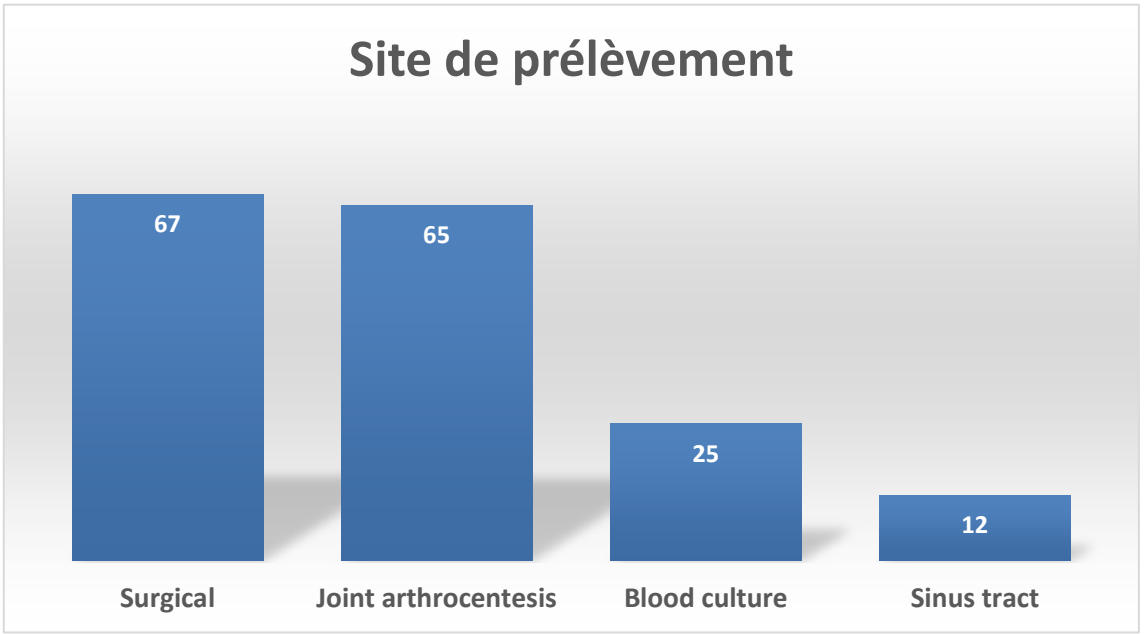
POPULATION

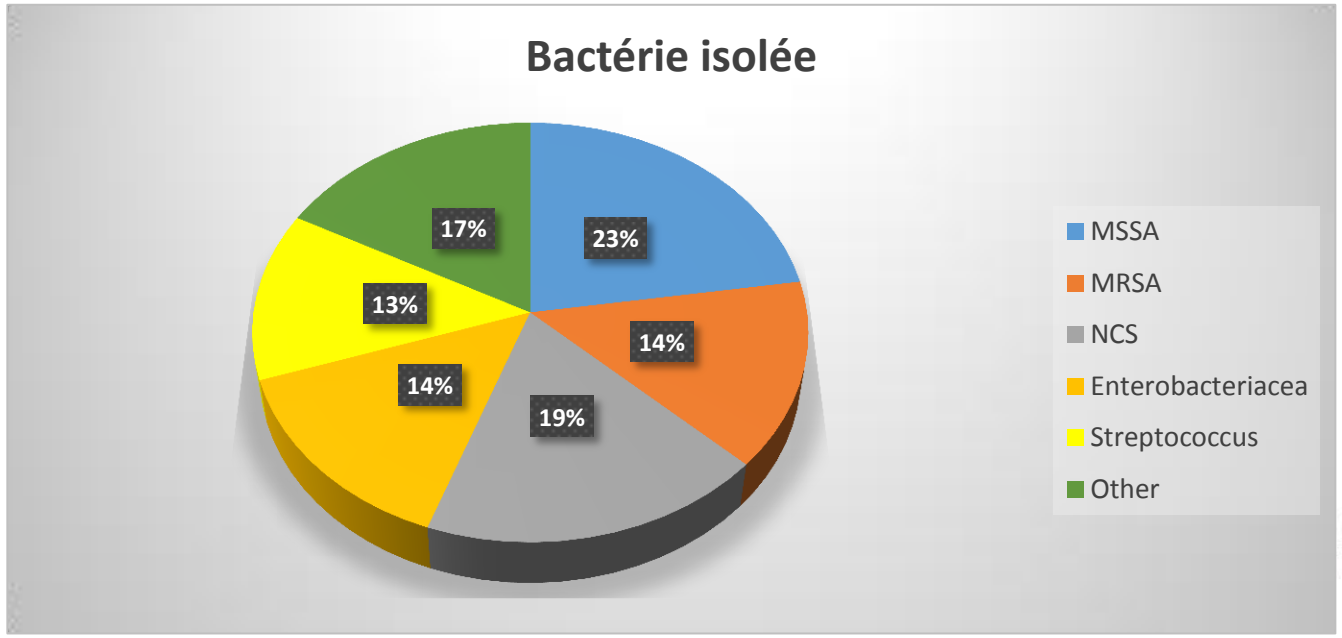
- 136 patients, 72 femmes (52.9%)
- Age médian : 83 ans {IQR 75-97},
- Mode de vie: 95 (69.9%) patients à domicile, 24 (17.6%)en EHPAD, 17 (12.5%)en USLD
- Marche: 44 (32.5%) sans auxilliaire, 70 (51.4%) avec 1 aide,
- 17 (12.6%) étaient grabataire
- 7 avec escarre (5.2%)
- Troubles cognitifs mentionnés: 31 (23%)

INDICATIONS

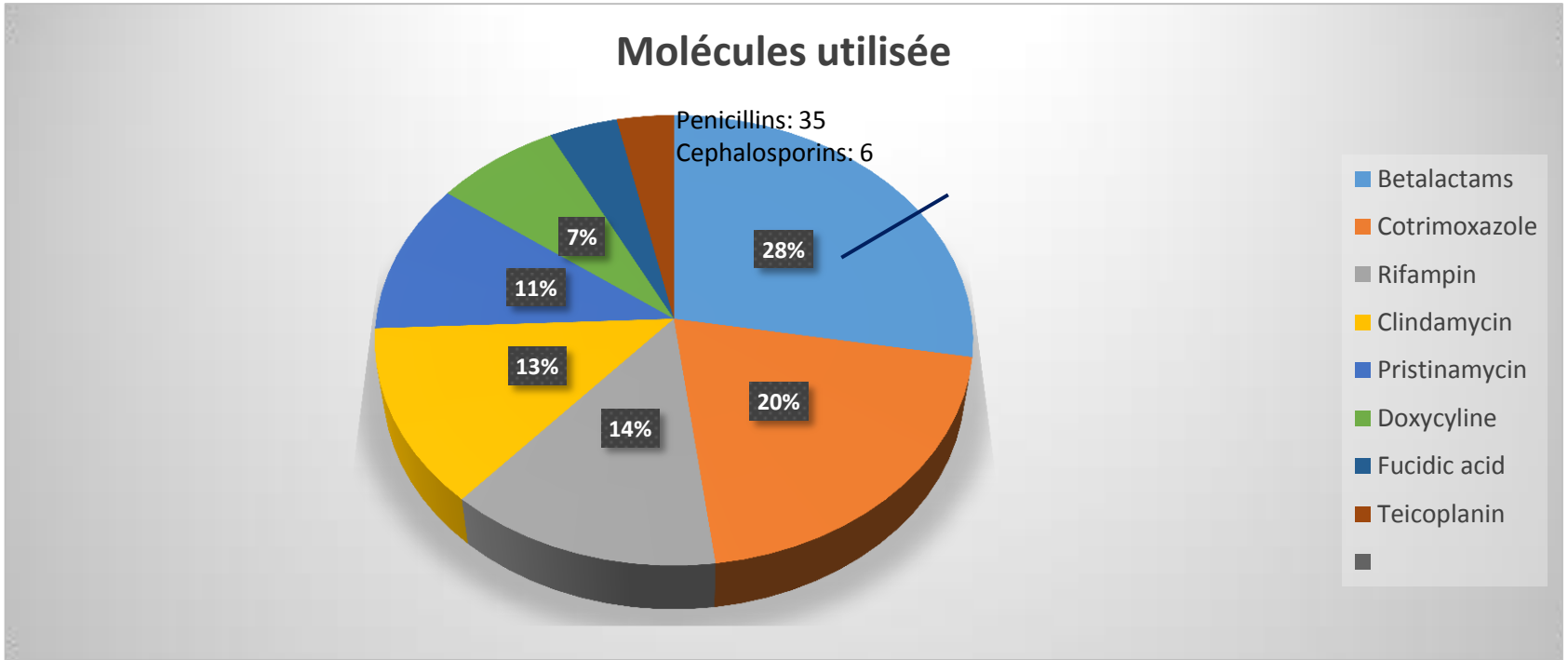


- Site de l’infection : hanche: 81 (59.6%), genou: 53 (39.0%)
- Fistule initiale: 35 (25.7%)
- Documentation bactériologique: 132 cas (97.1%)
- Infection monomicrobienne: 117 cas (86.0%)





- Monothérapie dans 96 cas (70.6%).
- Orale 128 patients / 8 IV
- Durée moyenne : **451 jours** (range 15-3408).
- ABS “palliatif” d’emblée (sans traitement “curatif” préalable) : 41 cas (30.1%).



- Echec : 7 (5,3%)
- Arrêt des ATB: 25 (18.4%):
  - inobservance (9),
  - intolérance médicamenteuse (7),
  - échec septique (5),
  - décès (4)
- Décès: 24 (17.6%) ,
  - 2 liés à l'infection.

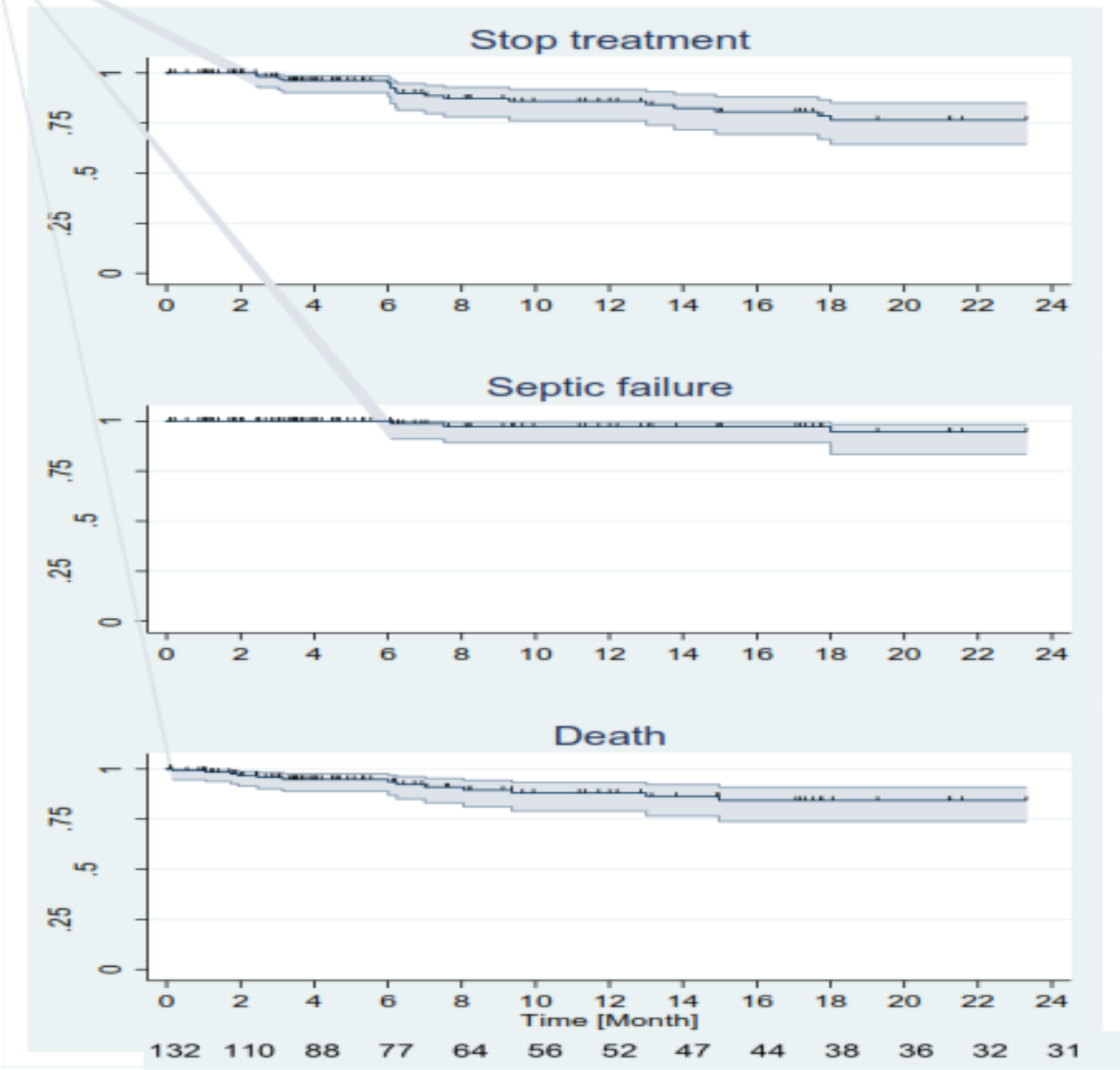


Table 4: Multivariate assessment of risk factors for treatment failure among **all patients treated with PSA (n=136)**

Variable	Adjusted effect	Hazard ratio [95% CI]	*P* value*
Monomicrobial infection	**9.15**	**[1.09-76.63]**	**P=0.041**
Gender	1.82	[0.80-4.18]	P=0.156
Initial intravenous ATB	**0.43**	**[0.20-0.92]**	**P=0.029**
Antibiotic given by another person	**3.39**	**[1.42-8.12]**	**P=0.006**
Bacteremia	**2.73**	**[1.09-6.85]**	**P=0.032**
Score Mc Cabe of 3	**1.67**	**[1.002-2.79]**	**P=0.049**
Intervention of a geriatrician	**2.60**	**[1.05-6.49]**	**P=0.040**

FDR d'échec

Table 4: Multivariate assessment of risk factors for treatment failure among **all patients treated with PSA (n=136)**

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FDR de « succès »

Antibiothérapie suppressive dans les infections sur prothèse ostéo articulaire

2 études rétrospectives	Prendki V. (n = 136)	Meyssonier V. (n = 61)
Inclusion	Infection sur prothèse avec geste chirurgical non optimal	Infection sur prothèse sans geste chirurgical
N centres	27	1
Chirurgie réalisée	79 (58 %)	2 (secondairement)
Age moyen	84 ans	82 ans
Bactérie principale	Staphylocoque doré (37 %)	Streptocoque (24 %), staphylocoque doré (21 %)
ATB les plus fréquents	Bêta-lactamines (28 %), CTM (20 %), clindamycine (13 %)	Bêta-lactamines (62 %), clindamycine (14 %), CTX (11,5 %)
Survie médiane	16 mois	Non précisée
Arrêt de l'antibiothérapie	25 (18 %)	16 (26 %)
Survie avec amelioration de l'IOA	70 % à 2 ans	71 % à 21,5 mois

Prendki V, ECCMID 2016, Abs. O492 ; Meyssonnier V, ECCMID 2016, Abs P0529

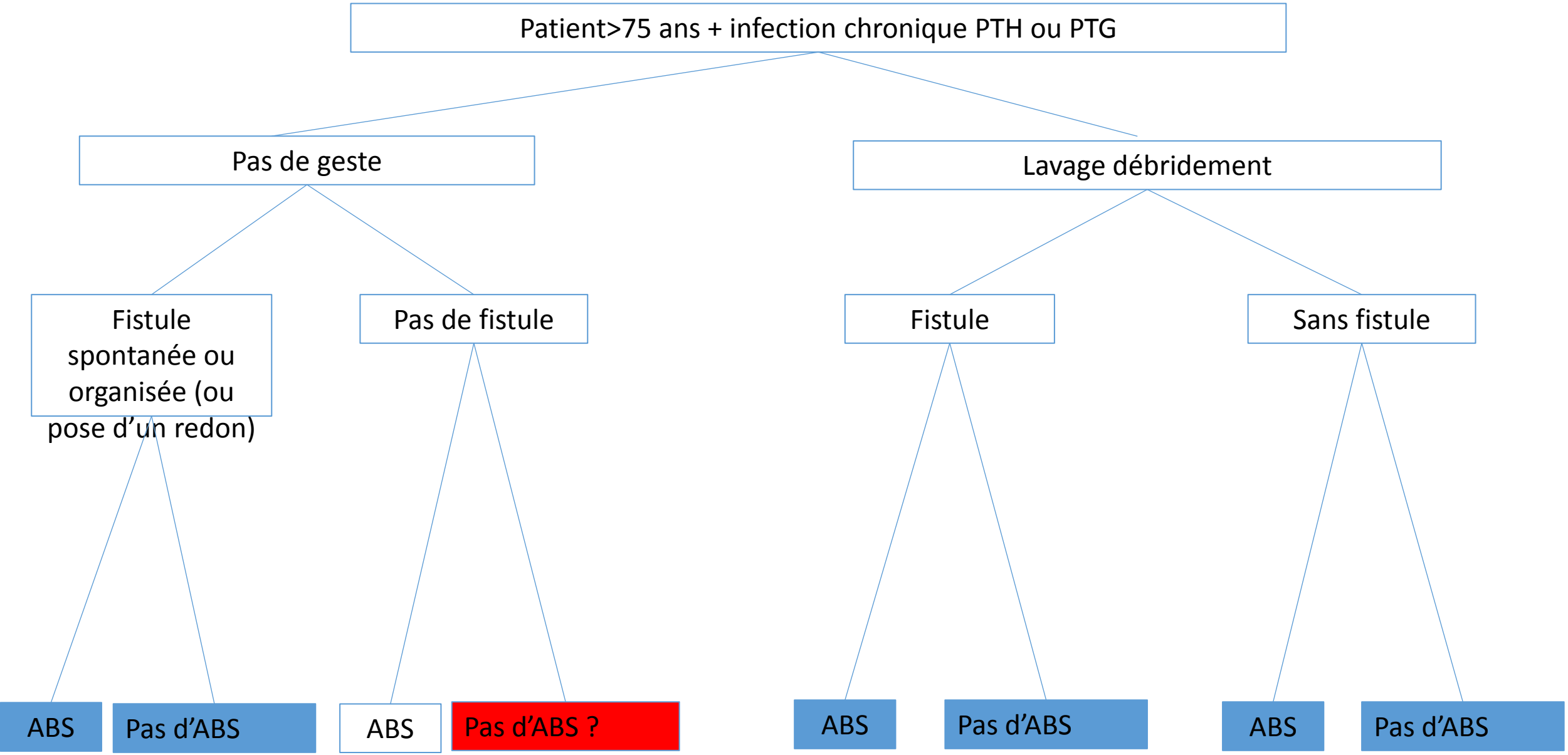
Conclusion

- ABS bien tolérée chez sujet âgé avec peu de décès liés aux IPOA.
- Risque d'échec accru en cas de bactériémie ou de patient fragile (intervention du gériatre, traitement administré par un tiers).
- Facteur protecteur du traitement ATB par voie IV initiale ?
- Peut être proposé en sauvetage chez les sujets fragiles ne pouvant pas avoir le traitement conventionnel (chirurgie).
- Survenue des complications mécaniques non évaluée
- Emergence de résistances
- Situations cliniques et actes chirurgicaux différents
- **Etude prospective nécessaire en réalisant une évaluation gériatrique sytématique et en évaluant les conséquences de cette pratique à long terme**.

Evaluation de l'intérêt de l'antibiothérapie en situation chirurgicale orthopédique non optimale

Observatoire national

SPILF/SFGG


Patient>75 ans + infection chronique PTH ou PTG
Pas de geste
Lavage débridement
Fistule spontanée ou organisée (ou pose d'un redon)
Pas de fistule
Fistule
Sans fistule
ABS
Pas d'ABS
ABS
Pas d'ABS ?
ABS
Pas d'ABS
ABS
Pas d'ABS

Merci de votre attention

Questions

- Emergence de résistance
- Pronostic fonctionnel
- Pronostic en fonction du geste/fistule

Conservative medical therapy of prosthetic joint infections: retrospective analysis of an 8-year experience

G. L. Pavoni[1], M. Giannella[1], M. Falcone[1], L. Scorzolini[2], M. Liberatore[3], B. Carlesimo[4], P. Serra[1] and M. Venditti[1]

ABSTRACT

Successful treatment of prosthetic joint infections often requires multiple surgical interventions and prolonged antimicrobial therapy. However, in certain situations, a surgical approach may not be in the best interest of the patient. A conservative approach was used to treat 34 patients with prosthetic joint infection between 1995 and 2003. Diagnosis of infection was based on clinical–microbiological evidence, confirmed by ^{99}Tc-labelled leukocyte scintigraphy, and involved 12 *Staphylococcus aureus* infections, nine *Staphylococcus epidermidis* infections, two *Enterococcus faecalis* infections, two mixed infections (*S. aureus* plus *Pseudomonas aeruginosa*; *S. epidermidis* plus *E. faecalis*), with the infecting pathogen being unidentified for nine patients. Most infections were treated initially with intravenous or intramuscular teicoplanin ± ciprofloxacin or rifampicin, followed by oral ciprofloxacin or minocycline plus rifampicin. The mean duration of antimicrobial therapy was 41.2 weeks. Overall, only three patients did not respond to therapy, and infection was controlled in the remaining 31 patients. Among these, no relapse was observed in 17 patients during follow-up for 9–57 months; improvement with early (within 6 months of antibiotic discontinuation) or late relapse was observed in seven and three patients, respectively; two patients improved clinically, but continued to receive antibiotic therapy; and two patients whose condition improved initially were lost after a 6-month follow-up following discontinuation of antibiotics. No patient complained of side effects requiring discontinuation of antibiotic therapy. The study confirmed that suppression of infection, with salvage of the infected device in an acceptably functional state, can be achieved in selected cases.

Table 1. Characteristics of 34 cases of prosthetic joint infection

Case	Age, sex	Risk factors	Type of prosthesis	Onset of infection	Bacteria/ diagnostic procedure	Debridement	Initial treatment (weeks)	Subsequent oral treatment (weeks)	Total treatment duration (weeks)	Follow-up (months)	Outcome
1	79, F	AA	Hip	Delayed	MRSA, drainage of sinuses	No	cip (20)	mh + rd (20)	40	19	INR → Surgery for LAL after 9 months
2	50, F	PWC	Hip	Early, (within 1 month)	MRSE + *Enterococcus faecalis*, deep aspiration	Yes	tec + cip + rd (16)	amc + rd (10)	26	9	IER (relapsed after 1 month) → Surgery
3	73, F	AA, PJS	Hip	Early	MSSA, deep aspiration	No	tec + rd + levo (12)	levo + rd (12)	24	27	INR
4	48, F	PJS	Hip	Early	MSSE, drainage of sinuses	Yes	tec + amc + rd (18)	mh + rd (14)	32	40	INR → Surgery for LAL after 18 months
5	60, F	No	Hip	Delayed	MSSA, drainage of sinuses	Yes	cip + rd (24)	No	24	–	INER
6	55, M	DM, PJS	Hip	Early	MRSE, intra-operative culture	Yes	tec + fos (20)	cip + rd (4)	24	36	INR
7	75, F	AA, PJS	Hip	Delayed	Unknown	No	mh + rd (48)	–	48	–	Failure
8	65, F	No	Hip	Delayed	Unknown	Yes	amc + rd (14)	mh + rd (14)	28	12	INR
9	79, F	AA	Hip	Delayed	MRSA + *Pseudomonas aeruginosa*, drainage of sinuses	No	tec + cip (16), tec + levo (12)	–	28	27	INR
10	78, F	AA, PJS	Hip	Late	MRSE, drainage of sinuses	No	tec + rd (12)	mh + rd (30)	42	27	ILR (relapsed after 14 months) → ICST (mh)
11	86, F	AA	Hip	Early (within 1 month)	*Enterococcus faecalis*, drainage of sinuses	No	amc (4)	amc + levo (20), amc (4)	28	–	INER
12	78, F	AA, PJS	Hip	Delayed	MRSA, drainage of sinuses	No	tec + cip + rd (8)	mh + rd (24)	32	17	IER (relapsed after 2 months) → ICST (mh rd)
13	81, F	AA	Hip	Delayed	MRSA, intra-operative culture	Yes	va, cld (4)	mh (64)	68	10	ILR (relapsed after 8 months) → ICST (mh)
14	64, F	DM	Hip	Late	MSSE, intra-operative culture	Yes	va, cld + levo (6)	mh + rd (24), mh (27)	57[a]	–	ICST (mh)
15	56, F	O	Hip	Early	MRSA, drainage of sinuses	Yes	tec + cld (12), tec + fos (12)	sxt + rd (16)	40	34	INR
16	67, F	No	Hip	Delayed	Unknown	No	cip + rd (38)	–	38	57	INR
17	70, F	AA, PJS, PWC	Hip	Late	Unknown	No	tec (4)	mh + rd (38)	42	15	IER (relapsed after 2 months) → Surgery
18	59, F	PJS	Hip	Early (within 1 month)	MRSA, drainage of sinuses	Yes	va + rd + cip (12), tec + levo (8)	mh + rd (4)	24	26	INR
19	67, F	No	Hip	Delayed	MRSA, intra-operative culture	Yes	tec (24)	mh + rd (20)	44	40	ILR (relapsed after 12 months) → ICST (mh)
20	77, F	AA	Hip	Delayed	MRSA, drainage of sinuses	No	tec + rid (8)	mh + rd (76)	84[a]	–	ICST (mh + rd)
21	74, F	AA	Hip	Late	Unknown	No	tec + cip (8)	mh + rd (28)	36	9	INR
22	70, M	AA, ST	Hip	Delayed	MSSE, intra-operative culture	Yes	tec + cip + rd (20) cip + rd (4)	mh + rd (4)	28	11	IER(relapsed after 5 months) → ICST (mh)
23	72, M	AA, PJS	Hip	Late	MRSA, deep aspiration	Yes	tec + moxi (12)	mh + moxi (4), cld (12)	28	17	IER (relapsed after 4 months) → ICST (mh)

Case	Age, sex	Risk factors	Type of prosthesis	Onset of infection	Bacteria/ diagnostic procedure	Debridement	Initial treatment (weeks)	Subsequent oral treatment (weeks)	Total treatment duration (weeks)	Follow-up (months)	Outcome
24	63, F	No	Hip	Delayed	MRSE, drainage of sinuses	No	cip (24)	cld + levo (8)	30	12	INR
25	71, M	AA	Knee	Early (within 1 month)	MSSA, intra-operative culture	Yes	tec + cip + rd (12), tec + moxi + rd (12)	mh (12)	36	–	Failure → Surgery
26	81, F	AA	Knee	Late	Unknown	No	amc + rd (12)	cld (4), mh + rd (24)	40	9	INR
27	73, M	AA	Knee	Early	Unknown	Yes	amc + cn (36)	amc (12)	48	43	INR → Surgery for LAL after 13 months
28	65, F	DM	Knee	Delayed	MSSA, drainage of sinuses	No	tec + cip + rd (8)	cip + rd (20), levo (16)	44	10	INR
29	73, M	AA	Knee	Delayed	MSSE, drainage of sinuses	No	cip + a-cxm + rd (28), tec + cip (8)	cip + rd (56)	92	31	IER (relapsed after 5 months) → Surgery
30	72, F	AA	Knee	Early	MRSE, drainage	No	tec + cip (4), tec + levo (16)	mh + levo (20)	40	9	INR
31	75, M	AA	Knee	Early (within 1 month)	*Enterococcus, faecalis*, deep aspiration	No	amc + genta (4)	amc + rd (48)	52	9	INR
32	60, F	No	Knee	Early	Unknown	No	tec (12)	mh + rd (36)	36	20	INR
33	43, F	ST	Knee	Delayed	MRSE, drainage of sinuses	No	tec + cip (24), tec + rd (12)	mh + rd (24), levo (24), amc + rd (12)	96	–	Failure → Surgery Surgery
34	71, F	AA	Knee	Delayed	Unknown	No	mh + rd (8) tec + cip (6)	mh + cip(16)	30	19	IER (relapsed after 4 months) → Surgery

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- Pavoni GL, Giannella M, Falcone M, Scorzolini L, Liberatore M, Carlesimo B, et al. Conservative medical therapy of prosthetic joint infections: retrospective analysis of an 8-year experience. Clin Microbiol Infect 2004;10:831-7.
- Barberán J, Aguilar L, Carroquino G, Giménez MJ, Sánchez B, Martínez D, Prieto J. Conservative treatment of staphylococcal prosthetic joint infections in elderly patients. Am J Med 2006;119:993.e7-10.

- **Prolonged oral antibiotic suppression in osteomyelitis and associated outcomes in a Veterans population.**
- Nowak MA, et al. Am J Health Syst Pharm. 2015.
- Show full citation
- **Abstract**
- OBJECTIVE: Prolonged oral antimicrobial suppression has been suggested as an alternative treatment for patients with prosthetic joint infections who are unable or unwilling to undergo surgical intervention; however, little data exists for utilizing this approach in patients with chronic osteomyelitis and no artificial hardware.
- METHODS: We retrospectively reviewed the medical records of all patients over a 5-year time frame who were treated with chronic oral antibiotic suppression for osteomyelitis and who had no artificial hardware. Clinical outcomes, risk factors for treatment failure, and adverse drug reactions were evaluated.
- RESULTS: A total of 20 patients were included for evaluation, of which 12 (60%) were able to achieve successful suppression of disease for a mean duration of 778 ± 408 days after discontinuation. Diabetic patients were found to be at higher risk for treatment failure ($p = 0.0281$). We also identified a high rate of adverse events (25%) attributable to suppressive medications. Despite elevated inflammatory markers contributing to the decision to initiate antibiotic suppression in the majority of patients, few were able to achieve normal values throughout suppressive therapy.
- CONCLUSION: Further randomized, controlled studies are needed to determine the utility of antibiotic suppression. However, prolonged oral antibiotic suppression may be a reasonable last-line treatment alternative for chronic osteomyelitis, even in the absence of artificial hardware, for patients who are unwilling or unable to undergo optimal surgical intervention.

- **Suppressive antibiotic therapy in chronic prosthetic joint infections.**
- Tsukayama DT, et al. Orthopedics. 1991.
- Show full citation
- **Abstract**
- Thirteen patients with chronic total joint infections (eight knees, five hips) were treated with suppressive antibiotic therapy and retention of the prosthesis following surgical debridement and 4 to 6 weeks of intravenous antibiotic therapy. These patients faced poor functional outcome after prosthesis removal. After a mean follow up of 37.6 months (range: 24 to 55), only three patients have retained their prostheses. Ten patients required prosthesis removal for recurrent infection a mean of 21.6 months (range: 6 to 48) after starting suppressive therapy. In addition, 38% of patients experienced adverse effects which led to changes in the antibiotic regimen. Suppressive antibiotic therapy in the treatment of chronic prosthesis infections has limited clinical efficacy and is associated with a substantial risk of adverse effects.

- **Conservative treatment of staphylococcal prosthetic joint infections in elderly patients.**
- Barberán J, et al. Am J Med. 2006.
- Show full citation
- **Abstract**
- BACKGROUND: We report the outcome of debridement and prosthesis retention plus long-term levofloxacin/rifampicin treatment of prosthetic joint infections.
- METHODS: Staphylococcal prosthesis joint infections were defined by positive culture of joint aspirate, intraoperative debridement specimens, or sinus tract discharge in the presence of clinical criteria. Patients received long-term oral levofloxacin 500 mg and rifampicin 600 mg once per day. Sixty patients (age 74.6+/-8.4 years) were included.
- RESULTS: Coagulase-negative staphylococci were significantly more frequently isolated in the knee (78.6%; P=.00001). Of the Staphylococcus aureus isolates, 33.3% were methicillin-resistant. Time from arthroplasty to symptoms onset was higher (P=.03) in coagulase-negative staphylococci infections. Global failure was 35% (higher for the knee) and ranged from 16.6% to 69.2% (P=.0045) in patients with symptoms duration of less than 1 month to more than 6 months. A shorter duration of symptoms (P=.001) and time to diagnosis (P=.01) were found in cured patients versus patients showing failure. Among those with S. aureus infections, a higher failure rate was found with methicillin-resistance.
- CONCLUSIONS: Efficacy was higher in patients with shorter duration of symptoms, earlier diagnosis, hip infections, and methicillin susceptibility.

- **Long-term suppression of infection in total joint arthroplasty.**
- Rao N, et al. Clin Orthop Relat Res. 2003.
- Show full citation
- **Abstract**
- Optimal treatment for a chronic infected prosthesis is the removal of infected and necrotic tissue and all the components of the prosthesis with staged revision in conjunction with systemic antibiotics. If this is not possible because of the poor general condition of the patient, because of unacceptable functional results secondary to removal of the prosthesis, or because the patient refuses surgery in an attempt to salvage the infected prosthesis, a reasonable alternative is long-term oral suppressive antibiotic therapy for maintenance of a functioning prosthesis. Prompt recognition with rapid debridement and initiation of antibiotic therapy seems crucial. Our study confirms a favorable outcome of maintenance of functioning prostheses in 86.2% of patients after a mean followup of 5 years. All patients had initial debridement with 4 to 6 weeks of systemic antibiotic therapy. Advanced age did not seem to predict poor outcome. Joint location, duration of symptoms, and the time of onset of infection did not predict success or failure. The overall success rate for Staphylococcus aureus prosthetic joint infection was 69% after a mean followup of 5 years. The ideal regimen and optimal duration of oral suppressive therapy for a favorable outcome is not well-established and needs additional data with prospective multicenter studies.

- **Treatment of staphylococcal prosthetic joint infections with debridement, prosthesis retention and oral rifampicin and fusidic acid.**
- Aboltins CA, et al. Clin Microbiol Infect. 2007.
- Show full citation
- **Abstract**
- There is growing evidence of the efficacy of treating early staphylococcal infections of prosthetic joints with surgical debridement and prosthesis retention, combined with oral antibiotic regimens that include rifampicin in combination with a fluoroquinolone. With rising rates of fluoroquinolone-resistant staphylococci, evidence concerning the efficacy of alternative combinations of antibiotics is required. Twenty patients with staphylococcal prosthetic joint infections who had been treated with surgical debridement and prosthesis retention, and a combination of rifampicin and fusidic acid were analysed. The mean duration of symptoms before initial debridement was 16 (range 2-75) days. The median time of follow-up was 32 (range 6-76) months. Treatment failure occurred in two patients. The cumulative risk of treatment failure after 1 year was 11.76% (95% CI 3.08-39.40%). Two patients had their treatment changed because of nausea. Ten of 11 patients with infections involving methicillin-resistant Staphylococcus aureus had successful outcomes. Debridement without prosthesis removal, in combination with rifampicin and fusidic acid treatment, was effective and should be considered for patients with early staphylococcal prosthetic joint infections, including those with infections involving fluoroquinolone-resistant organisms.

- **Outcome of debridement and retention in prosthetic joint infections by methicillin-resistant staphylococci, with special reference to rifampin and fusidic acid combination therapy.**
- Peel TN, et al. Antimicrob Agents Chemother. 2013.

- **Authors**
- Peel TN[1], Buising KL, Dowsey MM, Aboltins CA, Daffy JR, Stanley PA, Choong PF.
- **Author information**
- [1]Department of Infectious Diseases, St. Vincent's Hospital, Melbourne, Victoria, Australia. tpeel@student.unimelb.edu.au
- **Citation**
- Antimicrob Agents Chemother. 2013 Jan;57(1):350-5. doi: 10.1128/AAC.02061-12. Epub 2012 Oct 31.
- **Abstract**
- The management of prosthetic joint infections remains a clinical challenge, particularly infections due to methicillin-resistant staphylococci. Previously, this infection was considered a contraindication to debridement and retention strategies. This retrospective cohort study examined the treatment and outcomes of patients with arthroplasty infection by methicillin-resistant staphylococci managed by debridement and retention in conjunction with rifampin-fusidic acid combination therapy. Over an 11-year period, there were 43 patients with infection by methicillin-resistant staphylococci managed with debridement and retention. This consisted of close-interval repeated arthrotomies with pulsatile lavage. Rifampin was combined with fusidic acid for the majority of patients (88%). Patients were monitored for a median of 33.5 months (interquartile range, 20 to 54 months). Overall, 9 patients experienced treatment failure, with 12- and 24-month estimates of infection-free survival of 86% (95% confidence interval [CI], 71 to 93%) and 77% (95% CI, 60 to 87%), respectively. The following factors were associated with treatment failure: methicillin-resistant Staphylococcus aureus (MRSA) arthroplasty infection, a single surgical debridement or ≥4 debridements, and the receipt of less than 90 days of antibiotic therapy. Patients with infection by methicillin-resistant coagulase-negative staphylococci (MR-CNS) were less likely to fail treatment. The overall treatment success rate reported in this study is comparable to those of other treatment modalities for prosthetic joint infections by methicillin-resistant staphylococci. Therefore, the debridement and retention of the prosthesis and rifampin-based antibiotic therapy are a valid treatment option for carefully selected patients.
- Patients received a median duration of 341 days (IQR, 199 to 398 days) of oral antibiotic therapy. !!

- Clin Microbiol Infect. 2007 Jun;13(6):586-91. Epub 2007 Feb 28.
- **Treatment of staphylococcal prosthetic joint infections with debridement, prosthesis retention and oral rifampicin and fusidic acid.**
- Aboltins CA1, Page MA, Buising KL, Jenney AW, Daffy JR, Choong PF, Stanley PA.
- **Author information**

- **Abstract**
- There is growing evidence of the efficacy of treating early staphylococcal infections of prosthetic joints with surgical debridement and prosthesis retention, combined with oral antibiotic regimens that include rifampicin in combination with a fluoroquinolone. With rising rates of fluoroquinolone-resistant staphylococci, evidence concerning the efficacy of alternative combinations of antibiotics is required. Twenty patients with staphylococcal prosthetic joint infections who had been treated with surgical debridement and prosthesis retention, and a combination of rifampicin and fusidic acid were analysed. The mean duration of symptoms before initial debridement was 16 (range 2-75) days. The median time of follow-up was 32 (range 6-76) months. Treatment failure occurred in two patients. The cumulative risk of treatment failure after 1 year was 11.76% (95% CI 3.08-39.40%). Two patients had their treatment changed because of nausea. Ten of 11 patients with infections involving methicillin-resistant Staphylococcus aureus had successful outcomes. Debridement without prosthesis removal, in combination with rifampicin and fusidic acid treatment, was effective and should be considered for patients with early staphylococcal prosthetic joint infections, including those with infections involving fluoroquinolone-resistant organisms.

Chronic Oral Antimicrobial Suppression

- If chronic oral suppression is not utilized or discontinued, recent data would suggest that there is a 4-fold increased risk of treatment failure at the time suppression is discontinued, and that this risk of failure is greatest in the 4 months following antimicrobial discontinuation [62].
- However, in this study the majority of patients who had their chronic suppression discontinued did not suffer treatment failure, suggesting that many patients are cured without the use of chronic suppression but that defining that group of patients can be difficult [62].
- Thus if this pathway is chosen, monitoring for treatment failure early after treatment discontinuation is chosen is im- portant. The investigators of this study also pointed out that the vast majority of their study patients received at least 6 months of intravenous or oral antimicrobial therapy.
- Recommending the use of chronic suppression in young patients is particularly controversial and must be done on a case-by-case basis. It is advisable that patients on chronic oral antimicrobial suppression be monitored both for clinical failure and for antimicrobial toxicity

Byren I, Bejon P, Atkins BL, et al. One hundred and twelve infected arthroplasties treated with 'DAIR': antibiotic duration and outcome. J Antimicrob Chemother 2009.

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