International Orthopaedics (SICOT) (2017) 41:1131–1137
DOI 10.1007/s00264-016-3341-x

ORIGINAL PAPER

Chronic periprosthetic hip infection: micro-organisms responsible for infection and re-infection

Nikolai M. Kliushin[1] · **Artem M. Ermakov**[1] · **Tatiana A. Malkova**[1]

Received: 26 September 2016 / Accepted: 7 November 2016 / Published online: 17 November 2016

Abstract
Purpose This study aimed to delineate the infecting micro-organisms identified at the first-time revision for infected THA, analyze pre-operative versus intra-operative findings, as well as intra-operative ones against re-infection micro-organisms.
Material and methods Microbiological laboratory findings were studied in 73 patients (mean age, 51.93 ± 10.9 years) with chronic periprosthetic hip infection pre-operatively and intra-operatively. Forty-three patients had a two-stage revision THA while 30 patients were treated with a modified resection arthroplasty using the Ilizarov apparatus. Re-infection developed in 29 cases. Its microbial species were identified.
Results Pre-operative findings on micro-organisms coincided 50.7 % with the intra-operative ones. Bacterial growth in the intra-operative tests was detected in 72 (98.5 %) cases. Gram-positive single genus infection was identified in 35 patients (48 %); microbe associations were present in 33 patients (45 %). Staphylococcus species prevailed. Gram-negative infection was detected in 5.5 % of cases. One case (1.5 %) did not have any microbe growth. Re-infection happened in 10 cases (23.2 %) in a two-stage revision THA. In the resection arthroplasty group, early re-infection was observed in 63.3 % of cases. Among a total of 29 re-infection cases, staphylococcus species were identified in 19 cases, present either in associations or as single germs.
Conclusion Intra-operative microbiological tests at the first-time revision for infected THR detect a reliable spectrum of micro-organisms to assess microbial resistance to antibiotics, develop treatment protocols, and for prognostic purposes. Preventive measures at primary THR and strategies to fight periprosthetic infection and reinfection should be targeted on staphylococci.

Keywords Total hip arthroplasty · Chronic periprosthetic infection · Microbes · Re-infection

✉ Tatiana A. Malkova
tmalkova@mail.ru

Nikolai M. Kliushin
office@ilizarov.ru

Artem M. Ermakov
ema_cab@mail.ru

[1] Russian Ilizarov Scientific Centre for Restorative Traumatology and Orthopaedics, 6, M. Ulianova st., Kurgan 640014, Russian Federation

Introduction

Periprosthetic joint infection (PJI) that develops after total hip arthroplasty (THA) continues to be a substantial economic and physical burden for patients and the healthcare system [1–4]. The reported incidence of PJI is from 0.2 % to 3 % following primary THR, with the average rate at about 1.6 %. However, the absolute number of infected cases has been increasing as the total number of THRs constantly grows.

Despite that all possible measures are undertaken to avoid re-infection after revision of infected THA, its rates remain rather high and range between four and 33 % [4–7]. Each revision results in a greater bone tissue loss and a shorter period of implant survival. Furthermore, implant removal is an invasive operation. Patients' psycho-emotional suffering and fear of re-infection are also significant factors that should be considered. Therefore, much effort has been undertaken to reduce the burden of infected THA.

Numerous studies have been already published on the outcomes of revision for infected hip and knee arthroplasty

[8–12]. Harvesting material for microbiological study is a very significant part of any THA revision operation that aids to identify infecting micro-organisms and plan antibiotic strategies.

Our study aimed to delineate and analyze the infecting micro-organisms at our bone infection unit pre-operatively and intra-operatively at the first-time revision THR due to chronic infection, early and late re-infection micro-organisms, with the objective to reveal the bacterial spectrum to fight the first-time infected THA and re-infected THA.

Materials and methods

Seventy-three patients were admitted to our bone infection unit for revision due to chronic PJI between 2004 and 2014. There were 46 males and 27 females in the mean age of 51.93 ±10.9 years. Clinical signs of infection were sinuses (89 % of cases), wounds (8 %), hyperemia and swelling (3 %), local rise of temperature, pain or joint function disorders. Infection location was assessed by fistulography findings. At the moment of the revision operation, the infection manifestation time was more than a month in all the cases. Debridement protocol with implant retention was not possible to perform. Revision required debridement and removal of implant components in all cases.

Forty-three patients had a two-stage revision THA with the use of cemented spacers impregnated with antibiotics at stage 1. Thirty patients were treated with a modified resection arthroplasty (MRA) using the Ilizarov apparatus [13]. The indications to MRA were bone defects of grade II to IV (Paprosky), numerous previous operations, soft-tissue deficit, and severe immune deficiency. Several patents of this group rejected revision THA.

In both groups, antibiotics were administered according to susceptibility tests in the maximum dosage starting from the operation day with intravenous infusion for two to three weeks followed by oral antibiotics prescribed for three weeks. Antithrombosis preparations were administered for 35 days.

Microbiological study was conducted in all of them. The findings were studied retrospectively.

Pre-operatively, the object for microbiological study was the discharge from wounds and sinuses. The joint was punctured in case of absent pre-operative sinuses and wounds.

Intra-operatively, the material was collected from the soft tissues prior to approach to the joint. Joint fluid was then collected as well as the material from all the implant component surfaces and cements (five to six tissue samples per patient). Once surgical debridement was completed, the tissues samples from the areas debrided were sent for control in order to evaluate the efficiency of debridement (two to three control tests). Similar microbiological diagnostic tests were performed in all the cases of re-infection.

Identification of microbe genera and species was performed with classical methods (study of their tinctorial, culture, and biochemical properties) as well as with the use of bacterial analyzers (ATB Expression, Bio Merieux, France; Walk Away-40, USA) supplied with microtests and microbiological laboratory software (WHONET 5.6). Sensitivity to antibiotics and quantitative evaluation of microbes in the tissue samples was assessed.

Patients were also examined on the presence of risk factors that may aggravate the condition such as the number of previous surgery on the hip, diabetes, as well as femoral and acetabular defects.

Mean follow-up after treatment was 4.30 ±1.77 years (range, 2–11 years).

Results

Only 37 patients (50.7 %) had a complete correspondence of the pre-operative microbial species to the ones detected in the material taken intra-operatively. According to intra-operative tests, gram-positive single genera were identified in 35 patients (48 %). Staphylococcus species were most common single germs detected in 97 % of all single genus infections. *Staphylococcus aureus* prevailed (74 %). Methicillin-resistent staphylococcus aureus (MRSA) and epidermal staphylococcus (MRSE) were 17 %. Microbe associations (Table 1) were present in 33 patients (45 %). They were two-component in 23 patients (31.5 %). Three-genus infection was detected in ten cases (13.5 %). Staphylococcus species were found in 57 % of mixed infection cases. One patient did not have any bacterial growth. Four cases (5.5 %) of single gram-negative microorganisms were *Acinetobacter baumannii, Burkholderia cepacia, Enterobacter sp., Serratia marcescens.*

Control tests after debridement did not show any microbe growth. However, re-infection developed in a total of 29 patients (25 early and nine late recurrences) (Table 2). Five out 29 patients had both early and late re-infection. Twenty-four cases out of those 29 were affected with staphylococcus species at the index surgery. Staphylococcus infection was identified in 19 out of 24. The same germs of staphylococcus repeated in 16 cases. Microbial associations were identified in 13 patients. Gram-negative bacteria repeated or joined in 11 of them. *Acinetobacter* sp. and *P. aeruginosa* isolates were most common. Complete correspondence of laboratory findings with the ones at index revision surgery was identified in 13 patients with re-infection. All but one were affected with staphylococcus species. *S. aureus* prevailed. Only one patient with single genus gram-negative infection had an early recurrence.

The findings on the risk factors that could have a negative effect on eradication of infection are presented in Table 3.

Table 1 Microbes in associations detected in patients with chronic periprosthetic infection

Family	Genera and species	Absolute number of species	% from the total
Staphylococcaceae	*MRSA, MRSE, MRSH, MRSC*	17	57
	S. aureus	14	
	S. epidermidis	5	
	S. haemolyticus	2	
	S. warneri	2	
	S. auricularis	1	
	S. capitis subspecies	1	
	S. saprophyticus	1	
Enterococcaceae	Enterococcus faecalis	5	11
	Enterococcus faecium	3	
Streptococcaceae		2	2.5
Corynebacteriaceae		1	1
Micrococcaceae		1	1
Enterobacteriaceae	Serratia marcescens	4	20
	Enterobacter sp.	2	
	Citrobacter fzeundii	1	
	Enterobacter species	1	
	Enterobacter cloacae	1	
	Escherichia coli ESBL	1	
	Klebsiella pneumoniae	1	
	Klebsiella pneumoniae ESBL	1	
	Proteus vulgaris	1	
	Proteus mirabilis ESBL	1	
	Yersinia pseudotuberculosis	1	
Pseudomonadaceae	Pseudomonas aeruginosa	4	5
Moraxellaceae	Acinetobacter baumannii	2	2.5
Total			100

In the MRA group, all re-infected cases were debrided with the Ilizarov apparatus on and continued fixation. MRA yielded 93.3 % of final success in fighting infection (28/30 patients) while in the THA group it was 83.8 % (36/43). Two patients with late reinfection were not revised due to associated conditions.

Discussion

It is accepted that a thorough history, physical examination, complete set of radiographs and appropriate laboratory tests including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), synovial fluid leukocyte and neutrophil counts as well as joint aspiration and tissue biopsy are essential in the initial evaluation of suspected infected THA [14, 15]. Aspiration and nuclear imaging are helpful in doubtful cases. ESR or CRP is performed in all patients with a suspected PJI when the diagnosis is not clinically evident. The combination of an abnormal ESR and CRP seems to provide enough evidence in suspected chronic PJI along with clinical signs. Although a number of diagnostic criteria have been proposed by the latest consensus, a gold standard for PJI diagnosis is still lacking [16, 17].

A meticulous study of PJI agents in the material harvested for laboratory culture tests was able to detect the bacteria and the contamination grade at all the stages in our series. Collection of such a material is a very important part of revision in infected THA. However, only intra-operative tests revealed a true spectrum of germs that should be targeted by antibiotic therapy.

As reported, gram-negative bacteria caused infection in 7 % of THA cases, which is similar to our series at index revision [9, 10]. We had one early recurrence in this group but the species could not be detected as the patient received antibiotics prior to second debridement performed early after the index surgery [15, 18]. However, we observed high incidence of gram-negative bacteria in microbial associations in re-infection cases.

It was confirmed by numerous studies that gram-positive bacteria are the main agents that are responsible for 75–88 % of infected cases following primary THA [8, 11, 12, 14, 18]. Gram-positive bacteria were the main causative microorganisms in our patients with chronic PJI that were either

Table 2 Reinfection cases and their microbes

Patients, gender (operation type)	Microbic spectrum			
	Pre-operative	Intra-operative	Re-infection	
			Within a month	Late
1. F (MRA)	Not detected	Not detected	Not detected	
Gram-positive bacteria				
2. M (THA)	S. aureus	S. aureus	S. aureus	
3. M (MRA)	S. aureus, Enterobacter cloacae	S. aureus	S. aureus, Acinetobacter baumannii	
4. M (THA)	S.aureus	S.aureus		S. aureus
5. F (MRA)	S. aureus	S. aureus	S. aureus	S. aureus
6. M (MRA)	S. aureus	S. aureus	S. aureus	
7. F (MRA)	S.aureus	S.aureus	E. coli, K. pneumonicae, P. aeruginosa	
8. M (MRA)	S. aureus	S. aureus	S. aureus	
9. M (MRA)	S. aureus	S. aureus	S. aureus	S. aureus
10. F (MRA)	S. aureus	S. aureus	S. saprophyticus MRSS, Enterococcus faecalis	
11. F (MRA)	S. epidermidis	S. epidermidis	S. epidermidis	
12. M (MRA)	S. aureus MRSA	S. aureus MRSA	S. aureus MRSA, Enterobacter sp.	
13. M (MRA)	S. aureus MRSA, A. baumannii	S. aureus MRSA	S. aureus MRSA	
Microbic associations				
14. M (THA)	Enterobacter species, Escherichia coli, S.aureus	Serratia marcescens, S.aureus		n/a
15. F (THA)	Enterobacter cloacae, Enterococcus faecalis	Enterobacter cloacae, Enterococcus faecalis	Enterobacter species, Acinetobacter baumannii, S. saprophyticus MRSS, Pseudomonas aeruginosa	Enterococcus faecalis
16. M (THA)	Acinetobacter baumannii, Klebsiella pneumoniae ESBL	Acinetobacter baumannii, Klebsiella pneumoniae ESBL	Acinetobacter baumannii, Klebsiella pneumoniae ESBL	
17. M (THA)	S. saprophyticus, S. epidermidis MRSE, Pseudomonas aeruginosa	Pseudomonas aeruginosa, S.aureus,		n/a
18. M (THA)	S. aureus MRSA, Proteus mirabilis ESBL	S.aureus MRSA, Proteus mirabilis ESBL	S. aureus MRSA, Proteus mirabilis ESBL	
19. F (THA)	Klebsiella pneumoniae, Streptococcus sp B-hemilythic	Klebsiella pneumoniae, Enterococcus faecalis, S.aureus MRSA	Klebsiella pneumoniae	S. epidermidis

Table 2 (continued)

Patients, gender (operation type)	Microbic spectrum			
	Pre-operative	Intra-operative	Re-infection	
			Within a month	Late
20. M (THA)	Acinetobacter sp, Pseudomonas stutzeri, S. saprophyticus	S. aureus MRSA, S. aureus		Pseudomonas aeruginosa
21. M (THA)	S. aureus MRSA	S. capitis subspecies, S. aureus MRSA, Pseudomonas aeruginosa	S. aureus MRSA, Pseudomonas aeruginosa	Pseudomonas aeruginosa
22. F (MRA)	S. aureus	S. aureus, S. epidermidis	S. aureus	
23. F (MRA)	S. aureus	S.epidermidis, S. saprophyticus	S. epidermidis, S. saprophyticus	
24. M (MRA)	S. aureus	S. aureus, P. aeruginosa	P. aeruginosa	
25. F (MRA)	S. aureus MRSA	S. aureus, S. aureus MRSA, S. epidermidis MRSE	S. aureus MRSA	
26. M (MRA)	S. aureus MRSA	Serratia marcescens, S. aureus MRSA, Streptococcus Group B	P. aeruginosa, S. aureus, Enterococcus sp., Acinetobacter sp.	
27. M (MRA)	Enterobacter sp. ESBL	S. epidermidis MRSE, S. epidermidis, Enterobacter sp.	S. epidermidis, Enterobacter sp.	
28. M (MRA)	Escherichia coli ESBL, Enterobacter sp. ESBL Gram-negative bacteria	Citrobacter fzeundii, Escherichia coli ESBL	Escherichia coli ESBL	
29. M (THA)	S. warneri	Burkholderiacepacia	Not detected	

F female, *M* male, *THA* total hip arthroplasty, *MRA* modified resection arthroplasty, *ESBL* extended-spectrum β-lactamase

[a] *n/a* indicates that tests were not available in patients with late re-infection due to contraindications to re-implantation at the time of the study due to associated conditions

single genera or mixed with other microbes. Our data confirmed the findings of other studies that the staphylococci were the most common species responsible for primary infection and re-infection [11, 12, 18].

Several studies showed low re-infection rates when a two-stage THA revision was used [19–22], but the most recent studies in the field have shown that even a two-stage THA may not be so successful due to associated medical comorbidities [23–25]. Despite the fact that the implants were removed in our series, the success rate in the two-stage revision THA in fighting infection corresponded to the average reported in the latest literature [22–24].

Current antibacterial preparations are able to fight gram-positive bacteria, including the resistant species such as *S. aureus* (MRSA) and *S. epidermidis* (MRSE). However, the recurrence rate in our series was rather high due to several reasons that provoked re-infection. First, the re-infection cases were mainly caused by resistant strains or associations of microbes [8, 12]. It is also possible that bone debridement failed to remove all the infected tissues and the bacteria could be present as biofilm remnants in the para-articular tissues. Other reasons that should be considered are possible infection of a post-surgical haematoma, previous surgery on the hip, deficit of soft tissues, post-traumatic OA, polymicrobic and resistant infection, prolonged operation time, prolonged wound drainage, poor patient's immune state or age [1, 8, 25]. Therefore, we studied the factors that have a negative effect in fighting

Table 3 Frequency of risk factors in the patients with infection recurrence and without it

Factors	Patients with infection recurrence (n = 29)	Patients without infection recurrence (n = 44)
Age (years)	54.3 ± 11.1	49.57 ± 10.7
Number of previous operations on the hip	3.3 ± 1.66	3.23 ± 1.59
Pre-operative count of leucocytes	8.17 ± 1.85	7.51 ± 0.71
Pre-operative ESR	64.71 ± 19.16	67.44 ± 23.71
Diabetes	25 %	13.3 %
Single gram-positive infection	35.7 %	51.1 %
Polymicrobic infection	60.7 %	42.2 %
Femoral defect (grade III-IV, Paprosky)	28.5 %	28.8 %
Acetabular defect (grade II (B,C)-III Paprosky)	57.1 %	35.5 %

ESR erythrocyte sedimentation rate

infection (Table 1). The combination of these factors was clearly seen in the cases of infection recurrence.

The high rate of acute reinfection in the MRA group might have been due to the haematoma in the residual bone marrow canal of the femur and application of wires and half-pins of the Ilizarov apparatus that was an additional trauma. The main canal of microbe penetration with the use of this technology is wire- and half-pin tracts. Antibiotic therapy and debridement repeated in them within a month resulted only in two late re-infections that were treated with pin-tract sanation measures and antibiotics only. On the contrary, there were seven late re-infections in the THA group. However, our study was not aimed at the comparison of the treatment method groups. We focused on the impacts of infection species and associated factors [8].

Multiple intra-operative bacteriological tests provided a true picture of infecting agents and their sensitivity to design individual protocols of antibiotic therapy. Resistant strains of micro-organisms and *S. aureus* were the main targeted microbes by administration of antibiotics. Nowadays, the most effective antibiotics could be combined in fighting aggressive micro-organisms but there is no uniform approach as to whether to use them alone or combined [14, 18]. Disputes have been held in regard to the duration of antibiotic administration. The standard period of intravenous antibacterial therapy according to susceptibility tests in our hospital is two to three weeks followed by oral administration for three to four weeks. The primary requirement is to achieve maximum high concentrations of effective antibiotics in the bone and para-articular soft tissues that would be able to eradicate the pathogenic micro-organisms [17].

When microbial species were compared, it was obvious that the pre-operative findings on the micro-organisms coincided only 50.7 % with the ones that were obtained after the intra-operative material had been studied. This confirms the findings of several recent studies [26, 27]. Such a disparity in the spectrum of micro-organisms detected could be explained by the fact that the true infection focus is located in the deepness of para-articular structures. Therefore, the infection agents and grade of contamination detected intra-operatively at the first-time surgery for infected THA present reliable findings for assessment of microbial resistance to antibiotics, development of antibacterial treatment protocols, and for prognostic purposes.

There are few studies that reported on the re-infection microorganisms after the revision of infected THA [28, 29]. The bacterial spectrum of re-infection in our series showed that both prophylactic measures at first-time revision for infected THA and therapeutic antibiotic regimes due to re-infection should be focused on targeting staphylococci. However, Acinetobacter sp. and *P. aeruginosa* isolates were frequent species in reinfection cases [29]. Therefore, diagnosis, antimicrobial susceptibility testing, and antibacterial treatment along with a proper choice of a surgical protocol are the most significant issues in the arrest of infection [14, 17].

Conclusion

A thorough study of periprosthetic infection organisms in the material harvested intra-operatively is most essential in revision of infected THA. Prophylactic and therapeutic antibiotic regimes should be focused on targeting staphylococci.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Funding There is no funding source.

Ethical approval The study was approved by the ethic committee of the institution and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and rules of clinical practice in the Russian Federation (ministry of health order # 266, dated 19.06.2003).

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Cordero-Ampuero J, de Dios M (2010) What are the risk factors for infection in hemiarthroplasties and total hip arthroplasties? Clin Orthop Relat Res 468(12):3268–3277. doi:10.1007/s11999-010-1411-8
2. Kurtz SM, Lau E, Schmier J, Ong KL, Zhao K, Parvizi J (2008) Infection burden for hip and knee arthroplasty in the United States. J Arthroplasty 23(7):984–991. doi:10.1016/j.arth.2007.10.017
3. Hernández-Vaquero D, Fernández-Fairen M, Torres A, Menzie AM, Fernández-Carreira JM, Murcia-Mazon A, Guerado E, Merzthal L (2013) Treatment of periprosthetic infections: an economic analysis. Sci World J 2013:821650. doi:10.1155/2013/821650
4. Darwiche H, Barsoum WK, Klika A, Krebs VE, Molloy R (2010) Retrospective analysis of infection rate after early reoperation in total hip arthroplasty. Clin Orthop Relat Res 468(9):2392–2396
5. Sukeik M, Patel S, Haddad FS (2012) Aggressive early debridement for treatment of acutely infected cemented total hip arthroplasty. Clin Orthop Relat Res 70(11):3164–3170
6. Zheng H, Barnett AG, Merollini K, Sutton A, Cooper N, Berendt T, Wilson J, Graves N (2014) Control strategies to prevent total hip replacement-related infections: a systematic review and mixed treatment comparison. BMJ Open 4(3), e003978. doi:10.1136/bmjopen-2013-003978
7. Parvizi J, Saleh KJ, Ragland PS, Pour AE, Mont MA (2008) Efficacy of antibiotic-impregnated cement in total hip replacement. Acta Orthop 79(3):335–341
8. Marculescu CE, Cantey JR (2008) Polymicrobial prosthetic joint infections: risk factors and outcome. Clin Orthop 466(6):1397–1404. doi:10.1007/s11999-008-0230-7
9. Huang R, Hu CC, Adeli B, Mortazavi J, Parvizi J (2012) Culture-negative periprosthetic joint infection does not preclude infection control. Clin Orthop Relat Res 470(10):2717–2723. doi:10.1007/s11999-012-2434-0
10. Malekzadeh D, Osmon DR, Lahr BD, Hanssen AD, Berbari EF (2010) Prior use of antimicrobial therapy is a risk factor for culture-negative prosthetic joint infection. Clin Orthop Relat Res 468(8):2039–2045
11. Holleyman RJ, Baker P, Charlett A, Gould K, Deehan DJ (2015) Microorganisms responsible for periprosthetic knee infections in England and Wales. Knee Surg Sports Traumatol Arthrosc 2015: Apr 1
12. Holleyman RJ, Baker PN, Charlett A, Gould K, Deehan DJ (2016) Analysis of causative microorganism in 248 primary hip arthroplasties revised for infection: a study using the NJR dataset. Hip Int 26(1):82–89. doi:10.5301/hipint.5000313
13. Kliushin NM, Ababkov YV, Ermakov AM, Malkova TA (2016) Modified Girdlestone arthroplasty and hip arthrodesis using the Ilizarov external fixator as a salvage method in the management of severely infected total hip replacement. Indian J Orthop 50(1): 16–24. doi:10.4103/0019-5413.173513
14. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, Rao N, Hanssen A, Wilson WR (2013) Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 56(1):e1–e25. doi:10.1093/cid/cis803
15. Moyad TF, Thornhill T, Estok D (2008) Evaluation and management of the infected total hip and knee. Orthopedics 31(6):581–588, quiz 589–90
16. Parvizi J, Jacovides C, Zmistowski B, Jung KA (2011) Definition of periprosthetic joint infection: is there a consensus? Clin Orthop Relat Res 469(11):3022–3030. doi:10.1007/s11999-011-1971-2
17. Parvizi J, Gehrke T, Chen AF (2013) Proceedings of the International Consensus on periprosthetic joint infection. Bone Joint J 95:1450–1452. doi:10.1302/0301-620X.95B11.33135
18. Sousa R, Pereira A, Massada M, da Silva MV, Lemos R, Costa E, Castro J (2010) Empirical antibiotic therapy in prosthetic joint infections. Acta Orthop Belg 76(2):254–259
19. Gallo J, Smizanský M, Radová L, Potomková J (2009) Comparison of therapeutic strategies for hip and knee prosthetic joint infection. Acta Chir Orthop Traumatol Cech 76(4):302–309, Article in Czech
20. Klouche S, Leonard P, Zeller V, Lhotellier L, Graff W, Leclerc P, Mamoudy P, Sariali E (2012) Infected total hip arthroplasty revision: one- or two-stage procedure? Orthop Traumatol Surg Res 98(2):144–150. doi:10.1016/j.otsr.2011.08.018
21. Gomez MM, Tan TL, Manrique J, Deirmengian GK, Parvizi J (2015) The fate of spacers in the treatment of periprosthetic joint infection. J Bone Joint Surg Am 97(18):1495–1502. doi:10.2106/JBJS.N.00958
22. Berend KR, Lombardi AV Jr, Morris MJ, Bergeson AG, Adams JB, Sneller MA (2013) Two-stage treatment of hip periprosthetic joint infection is associated with a high rate of infection control but high mortality. Clin Orthop Relat Res 471(2):510–518. doi:10.1007/s11999-012-2595-x
23. Winkler T, Trampuz A, Hardt S, Janz V, Kleber C, Perka C (2014) Periprosthetic infection after hip arthroplasty. Orthopade 43(1):70–78. doi:10.1007/s00132-013-2132-y, Article in German
24. Vielgut I, Sadoghi P, Wolf M, Holzer L, Leithner A, Schwantzer G, Poolman R, Frankl B, Glehr M (2015) Two-stage revision of prosthetic hip joint infections using antibiotic-loaded cement spacers: When is the best time to perform the second stage? Int Orthop 39(9):1731–1736. doi:10.1007/s00264-015-2751-5
25. Koenig K, Huddleston JI, Huddleston H, Maloney WJ, Goodman SB (2012) Advanced age and comorbidity increase the risk for adverse events after revision total hip arthroplasty. J Arthroplasty 27(7):1402–1407
26. Holleyman RJ, Deehan DJ, Charlett A, Gould K, Baker PN (2015) Does pre-operative sampling predict intra-operative cultures and antibiotic sensitivities in knee replacements revised for infection?: a study using the NJR dataset. Knee Surg Sports Traumatol Arthrosc 2015:Nov 26.
27. Meermans G, Haddad FS (2010) Is there a role for tissue biopsy in the diagnosis of periprosthetic infection? Clin Orthop Relat Res 468(5):1410–1417. doi:10.1007/s11999-010-1245-4
28. van Diemen MP, Colen S, Dalemans AA, Stuyck J, Mulier M (2013) Two-stage revision of an infected total hip arthroplasty: a follow-up of 136 patients. Hip Int 23(5):445–450. doi:10.5301/hipint.5000049
29. Tikhilov R, Bozhkova S, Denisov A, Labutin D, Shubnyakov I, Razorenov V, Artyukh V, Klitsenko O (2016) Risk factors and prognostic model of hip periprosthetic infection recurrence after surgical treatment using articulating and non-articulating spacers. Int Orthop 40(7):1381–1387. doi:10.1007/s00264-015-3072-4