J Antimicrob Chemother
doi:10.1093/jac/dky354

Journal of Antimicrobial Chemotherapy

Use of gentamicin-impregnated beads or sponges in the treatment of early acute periprosthetic joint infection: a propensity score analysis

Marjan Wouthuyzen-Bakker[1]*, Claudia A. M. Löwik[2], Bas A. S. Knobben[3], Wierd P. Zijlstra[4], Joris J. W. Ploegmakers[2], Glen Mithoe[5], Aziz Al Moujahid[6], Greetje A. Kampinga[1] and Paul C. Jutte[2] on behalf of the Northern Infection Network Joint Arthroplasty (NINJA)

[1]Department of Medical Microbiology and Infection Prevention, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [2]Department of Orthopaedic Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [3]Department of Orthopaedic Surgery, Martini Ziekenhuis, Groningen, The Netherlands; [4]Department of Orthopaedic Surgery, Medisch Centrum Leeuwarden, Leeuwarden, The Netherlands; [5]Department of Medical Microbiology, Certe Medical Diagnostics & Advice, Groningen, The Netherlands; [6]Center for Infectious Diseases Friesland, Izore, Leeuwarden, The Netherlands

*Corresponding author. Tel: +31-50-361-61-61; E-mail: m.wouthuyzen-bakker@umcg.nl

Received 12 July 2018; returned 6 August 2018; revised 7 August 2018; accepted 7 August 2018

Objectives: Early acute periprosthetic joint infections (PJIs) treated with debridement, antibiotics and implant retention (DAIR) have failure rates ranging from 10% to 60%. We determined the efficacy of applying local gentamicin-impregnated beads and/or sponges during debridement in early PJI.

Methods: Patients with early acute PJI, defined as less than 21 days of symptoms and treated with DAIR within 90 days after index surgery, were retrospectively evaluated. Early failure was defined as PJI-related death, the need for implant removal or a second DAIR or antibiotic suppressive therapy owing to persistent signs of infection, all within 60 days after initial debridement. Overall failure was defined as implant removal at any timepoint during follow-up. A 1:1 propensity score matching was performed to correct for confounding factors.

Results: A total of 386 patients were included. Local gentamicin was applied in 293 patients (75.9%) and was withheld in 93 patients (24.1%). Multivariate analysis demonstrated that the use of local gentamicin was independently associated with early failure (OR = 1.97, 95% CI = 1.12–3.48). After propensity matching, early failure was 40.3% in the gentamicin group versus 26.0% in the control group ($P = 0.06$) and overall failure was 5.2% in the gentamicin group versus 2.6% in the control group ($P = 0.40$). These numbers remained when solely analysing the application of gentamicin-impregnated sponges.

Conclusions: Even after propensity score matching, failure rates remained higher if local gentamicin-impregnated beads and/or sponges were administered in early acute PJI. Based on these results, their use should be discouraged.

Introduction

Periprosthetic joint infection (PJI) is a major complication after total joint arthroplasty, occurring in ∼1%–2% of primary arthroplasties and in up to 10% of revision arthroplasties.[1,2] The majority of these infections occur in the early post-surgical period and are treated with debridement, antibiotics and implant retention (DAIR). Successful treatment of early PJI by DAIR depends on multiple host- and implant-related factors, such as the causative microorganism(s) and their susceptibility to antibiotics.[3–18] As treatment success ranges from 40% to 90%, it is crucial to improve surgical techniques and optimize antibiotic treatment to achieve infection control without the need for additional surgeries.[19–25] Indeed, many studies report the importance of exchanging the modular components during debridement and emphasize the need for prescribing antibiotics with high efficacy against biofilms.[3–8,13–15] In addition, applying local antibiotics during surgical debridement may be another option to achieve higher cure rates, by rapidly obtaining sufficient levels of antibiotics at the site of the infection. For this reason, gentamicin-impregnated beads and sponges were introduced many years ago. Gentamicin is eluted from beads over the course of 2–6 weeks and sponges provide a burst release in the first 24 hours and are 'empty' after 3 days.[26–28] Both are able to produce levels of local gentamicin far above the MIC values but, until now, retrospective analyses did not show any benefit in clinical outcome.[29,30] It is well known that retrospective

studies are prone to selection bias, particularly in evaluating treatment strategies, as a more aggressive treatment approach is often applied in severe infections compared with milder clinical courses. By means of a propensity score analysis, this particular type of bias can be addressed. Therefore, we determined the efficacy of gentamicin-impregnated beads and/or sponges in a large cohort of early acute PJI patients by using a propensity score analysis to control for confounding factors.

Methods

Study design

Patients with early acute PJI of the hip, knee, shoulder or elbow and treated with DAIR between January 2006 and December 2016 were retrospectively analysed. Early acute PJI was defined as a PJI that developed within 3 months after the index surgery with less than 21 days of symptoms. Diagnosis of PJI was determined according to the diagnostic criteria defined by the Musculoskeletal Infection Society (MSIS).[31] Patients who did not meet the MSIS criteria were excluded from the analysis, as well as patients who underwent arthroscopic debridement instead of open surgical debridement. Patients were recruited in two general hospitals (Martini Hospital and Medical Center Leeuwarden) and one university hospital (University Medical Center Groningen) in the Netherlands. Informed consent was retrieved when required by the ethics committee of the participating center.

Surgical and antimicrobial treatment

As previously described in this cohort of patients, surgical treatment consisted of a DAIR procedure, in which the wound was opened via the preexisting incision.[17] Haematoma and avital tissue were extensively excised and the wound was thoroughly irrigated using 3–6 L of saline. According to the clinical judgement of the orthopaedic surgeon, mobile components were exchanged and gentamicin-impregnated beads or sponges were inserted into the joint cavity. After obtaining multiple deep tissue biopsies for culture, empirical broad-spectrum intravenous antimicrobial treatment was started and, if necessary, adjusted according to the results of the antibiogram. Intravenous treatment was maintained for at least 2 weeks before switching to an oral regimen that was continued for an additional 10 weeks. Rifampicin was added to the antimicrobial treatment regimen in infections caused by rifampicin-susceptible staphylococci.

Definition of failure

The primary outcome was early treatment failure, defined as one of the following events within 60 days after initial debridement: (i) a second DAIR procedure; (ii) implant removal; (iii) PJI-related death; or (iv) long-term suppressive antimicrobial treatment in the case of persistent clinical signs of infection. In the case of a second DAIR procedure being solely performed for removal of gentamicin-impregnated beads that were placed during the initial debridement, without clinical and biochemical signs of persistent infection, the second debridement was not considered to be a failure. The secondary outcome was overall failure and was defined as the need for implant removal at any timepoint during follow-up.

Statistical analysis

A χ^2 test was used to analyse differences between groups for categorical variables. To correct for bias between the gentamicin group and the control group, a propensity score matching was performed. A propensity score was calculated using a logistic regression model in which the use of local gentamicin was used as the dependent variable and several (pre)operative variables that were statistically different between both groups as covariates. Matching was performed using a caliper of two decimals and identical propensity scores were randomized to perform the matching. In addition, a logistic regression analysis was performed to identify risk factors for early and overall failure. Variables with a difference between both groups, defined as a P value <0.1 in the univariate analysis, were subsequently included in the multivariate analysis. All analyses were two-tailed and P values <0.05 were considered statistically significant. A Kaplan–Meier survival curve with a Cox regression analysis was performed to evaluate failure rate in time. Statistical analysis was performed using SPSS, version 23.0 (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

A total of 386 patients were included in the final analysis, including 86 knees and 296 hips (comprising 99% of the total cohort). Local gentamicin was applied in 293 patients (75.9%) and was withheld in 93 patients (24.1%). In the gentamicin group, gentamicin-impregnated beads were administered in 28 patients (9.6%), gentamicin-impregnated sponges were administered in 184 patients (62.8%) and both were administered in 81 patients (27.6%). The mean number of inserted gentamicin-impregnated beads was 66.4±22.0 and the mean number of inserted gentamicin-impregnated sponges was 2.6±1.0.

Table 1 shows the baseline characteristics of the analysed patients, separated according to insertion of local gentamicin. The gentamicin group had a significantly higher rate of hypertension and chronic renal insufficiency, longer duration of symptoms, a higher rate of fracture as an indication for arthroplasty, higher inflammatory parameters at clinical presentation, a higher rate of pus during debridement and infection that was more often polymicrobial in origin and/or caused by *Staphylococcus aureus*. Additional variables that are known in the literature to be associated with worse outcome, like rheumatoid arthritis, revised or cemented prostheses, not exchanging the modular components and the use of antibiotics with low efficacy against biofilms were similar in both groups (Table 1).[3–8,13–16]

Clinical outcome: gentamicin group versus control group

Table 1 shows the outcomes of both groups before and after propensity matching. Before propensity matching, early failure within 60 days after initial debridement was observed in 43.0% of patients who were treated with local gentamicin versus 23.7% in whom local gentamicin was withheld ($P = 0.001$). For both groups, the majority of failure (>80%) was due to the need for a second debridement because of persistent clinical signs of infection. Implant removal was necessary in 9.2% of the gentamicin group versus 2.2% of the control group ($P = 0.02$). After 1:1 propensity score matching for variables that were significantly different between the gentamicin group and the control group, a total of 77 patients in each group remained eligible for analysis ($n = 154$). Although not statistically significant ($P = 0.06$), early failure within 60 days after initial debridement remained higher in the gentamicin group (40.3% versus 26.0%). Implant removal was necessary in 5.2% of patients in whom local gentamicin was applied compared with 2.6% in whom it was withheld ($P = 0.40$). Figure 1 shows the failure rate in time after propensity score matching. Additional multivariate analysis demonstrated that the use of local

Table 1. Clinical characteristics and outcome in patients receiving or not receiving local gentamicin during debridement

	Total patient group			Propensity matching 1:1		
	local gentamicin[a] ($n = 293$)	control ($n = 93$)	*P*	local gentamicin[a] ($n = 77$)	control ($n = 77$)	*P*
Baseline characteristics						
male	60.4% (177/293)	65.6% (61/93)	0.37	42.9% (33/77)	37.7% (29/77)	0.51
age >80 years	33.1% (97/293)	32.3% (30/93)	0.88	23.4% (18/77)	37.7% (29/77)	0.05
BMI >30 kg/m^2	47.4% (127/268)	37.5% (33/88)	0.10	52.1% (37/71)	37.5% (27/72)	0.08
ASA classification ≥III	41.3% (121/293)	36.6% (34/93)	0.42	28.6% (22/77)	41.6% (32/77)	0.09
Medical history						
hypertension	66.2% (194/293)	48.4% (45/93)	**0.002**	48.1% (37/77)	54.5% (42/77)	0.42
ischaemic heart disease	22.2% (65/293)	12.9% (12/93)	0.05	23.4% (18/77)	15.6% (12/77)	0.22
heart failure	11.3% (33/293)	8.6% (8/93)	0.47	9.1% (7/77)	10.4% (8/77)	0.79
diabetes mellitus	22.2% (65/293)	18.3% (17/93)	0.42	14.3% (11/77)	18.2% (14/77)	0.51
COPD	22.5% (66/293)	16.1% (15/93)	0.19	22.1% (17/77)	18.2% (14/77)	0.55
chronic renal insufficiency	8.2% (24/293)	2.2% (2/93)	**0.04**	2.6% (2/77)	2.6% (2/77)	1.00
liver cirrhosis	1.4% (4/293)	0% (0/93)	0.26	0% (0/77)	0% (0/77)	1.00
rheumatoid arthritis	7.8% (23/293)	5.4% (5/93)	0.45	7.8% (6/77)	6.5% (5/77)	0.75
Medication						
oral anticoagulant	25.3% (74/293)	22.6% (21/93)	0.60	19.5% (15/77)	26.0% (20/77)	0.34
immune-suppressive drugs	11.3% (33/293)	11.8% (11/93)	0.88	7.8% (6/77)	11.7% (9/77)	0.42
Characteristics of infected implant						
hip	78.2% (229/293)	72.0% (67/93)	0.22	80.5% (62/77)	72.7% (56/77)	0.25
knee	20.8% (61/293)	26.9% (25/93)	0.22	19.5% (15/77)	27.3% (21/77)	0.25
indication prosthesis: fracture	37.9% (111/293)	25.8% (24/93)	**0.03**	23.4% (18/77)	26.0% (20/77)	0.71
revision prosthesis	14.3% (42/293)	15.1% (14/93)	0.86	6.5% (5/77)	14.3% (11/77)	0.11
cemented stem	84.6% (248/293)	81.7% (76/93)	0.50	79.2% (61/77)	85.7% (66/77)	0.29
Clinical presentation						
duration of symptoms ≥10 days	30.3% (88/293)	44.1% (41/93)	**0.01**	36.4% (28/77)	37.7% (29/77)	0.87
temperature >38.3°C	19.8% (58/293)	16.1% (15/93)	0.43	19.5% (15/77)	16.9% (13/77)	0.68
redness	44.4% (130/293)	33.3% (31/93)	0.06	46.8% (36/77)	33.8% (26/77)	0.10
wound leakage	87.4% (256/293)	83.9% (78/93)	0.39	85.7% (66/77)	85.7% (66/77)	1.00
pus	22.9% (67/293)	8.6% (8/93)	**0.002**	15.6% (12/77)	10.4% (8/77)	0.34
sepsis	19.5% (57/293)	17.2% (16/93)	0.63	19.5% (15/77)	18.2% (14/77)	0.84
CRP >115 mg/L	35.8% (105/293)	21.5% (20/93)	**0.01**	23.4% (18/77)	22.1% (17/77)	0.85
leucocytes >12 cells/μL	35.8% (105/293)	34.4% (32/93)	0.80	33.8% (26/77)	33.8% (26/77)	1.00
Identified microorganism						
polymicrobial	48.8% (143/293)	35.5% (33/93)	**0.03**	39.0% (30/77)	39.0% (30/77)	1.00
S. aureus	50.2% (147/293)	36.6% (34/93)	**0.02**	33.8% (26/77)	36.4% (28/77)	0.74
Enterococcus species	18.1% (53/293)	18.3% (17/93)	0.97	16.9% (13/77)	19.5% (15/77)	0.68
Gram-negative bacilli	21.2% (62/293)	19.4% (18/93)	0.71	11.7% (9/77)	19.5% (15/77)	0.18
Gentamicin resistance of (one of) the infecting microorganisms	19.5% (57/293)	25.8% (24/93)	0.19	13.0% (10/77)	28.6% (22/77)	**0.02**
Surgical and antibiotic treatment						
exchange modular components	21.8% (64/293)	18.5% (17/92)	0.49	18.2% (14/77)	19.5% (15/77)	0.84
debridement ≥21 days after index arthroplasty	31.4% (92/293)	28.0% (26/93)	0.53	14.3% (11/77)	9.1% (7/77)	0.32
use of rifampicin for staphylococci	83.0% (122/147)	84.8% (28/33)	0.79	73.6% (39/53)	73.7% (42/57)	0.99
use of fluoroquinolones for Gram-negatives	56.5% (35/62)	61.1% (11/18)	0.73	55.6% (5/9)	53.3% (8/15)	0.92
Outcome						
early failure (<60 days)	43.0% (126/293)	23.7% (22/93)	**0.001**	40.3% (31/77)	26.0% (20/77)	0.06
second DAIR owing to uncontrolled infection	84.9% (107/126)	81.8% (18/22)		93.5% (29/31)	80.0% (16/20)	
overall failure (implant removal)	9.2% (27/293)	2.2% (2/93)	**0.02**	5.2% (4/77)	2.6% (2/77)	0.40

Values in bold are statistically significant. ASA, American Society of Anesthesiologists; CRP, C-reactive protein.
[a]Local gentamicin consisted of gentamicin-impregnated beads, sponges or both.

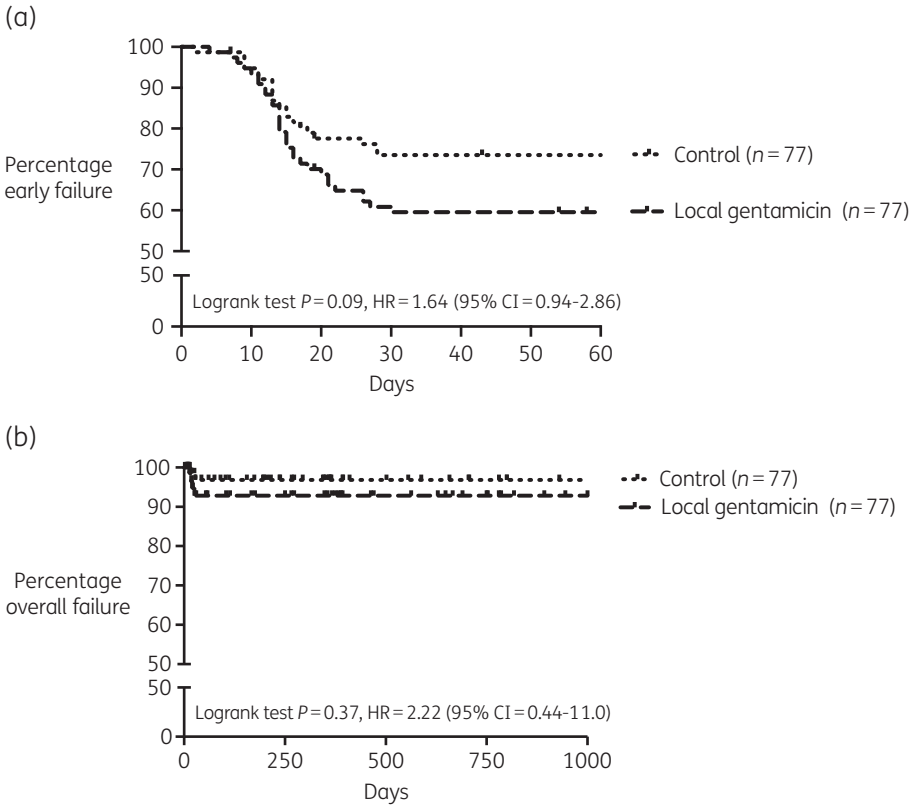

Figure 1. Failure rate of early acute PJI according to the application of local gentamicin-impregnated beads and/or sponges in the propensity matched cohort. Early failure (a) is defined as a second debridement because of persistent clinical signs of infection, implant removal, PJI-related death or the need for suppressive antibiotic therapy. Overall failure (b) is defined as implant removal at any timepoint during follow-up.

gentamicin was independently associated with early failure (OR = 1.97, 95% CI = 1.12–3.48), as well as overall failure (OR = 4.46, 95% CI = 0.99–20.07).

Subgroup analysis

To determine whether certain subgroups may benefit from local gentamicin, we performed several subanalyses. Compared with the control group, the administration of local gentamicin did not show any beneficial effect on early failure in the following groups: old age (>80 years) [23.3% (7/30) versus 52.6% (51/97), $P = 0.005$]; DAIR performed more than 21 days after index surgery [30.8% (8/26) versus 29.3% (27/92), $P = 0.89$]; DAIR performed in patients with more than 10 days of symptoms [24.4% (10/41) versus 50.0% (44/88), $P = 0.006$]; presence of wound leakage [23.1% (18/78) versus 42.6% (109/256), $P = 0.002$]; *S. aureus* infections [41.2% (14/34) versus 49.0% (72/147), $P = 0.41$]; enterococcal infections [29.4% (5/17) versus 39.6% (21/53), $P = 0.45$]; and polymicrobial infections [33.3% (11/33) versus 39.2% (56/143), $P = 0.53$].

Mechanisms for higher failure rate in the gentamicin group

To assess whether the second procedure for the removal of gentamicin-impregnated beads exposed patients to a higher risk of recurrent infection, we compared the outcome in patients who underwent one DAIR ($n = 204$) with patients who underwent one DAIR and an additional lavage for the removal of gentamicin-impregnated beads without signs of persistent infection ($n = 57$). In this analysis, in which failure was defined as the need for implant removal, PJI-related death or the need for suppressive therapy, failure rates were 9.7% and 10.5%, respectively ($P = 0.9$). In addition, since sponges do not need extra surgery for removal, but can remain *in situ*, we performed a subanalysis on solely gentamicin-impregnated sponges. Early failure within 60 days after initial debridement was 38.6% (71/184) in the sponge group versus 23.7% (22/93) in patients without local gentamicin ($P = 0.013$). Removal of the implant was necessary in 2.2% (2/93) in the control group versus 7.1% (13/184) in the sponge group ($P = 0.09$). After performing 1:1 propensity analysis, early failure was 40.4% (21/52) in the sponge group versus 26.0% (20/77) in the control group ($P = 0.09$) and implant removal was necessary in 5.8% (3/52) and 2.6% (2/77) ($P = 0.36$), respectively. We additionally performed a subanalysis in PJI cases with solely gentamicin-intermediate or -susceptible strains ($n = 305$): early failure was 41.5% in the gentamicin group and 26.1% in the control group ($P = 0.02$) and overall failure was 8.1% in the gentamicin group and 1.4% in the control group ($P = 0.05$).

Discussion

By applying a propensity score matching analysis to correct for confounding factors, our study demonstrates an ∼2-fold higher

failure rate with the use of gentamicin-impregnated beads and/or sponges in the treatment of early acute PJI. This failure rate included not only the need for a second surgical debridement owing to persistent clinical signs of infection in the early post-surgical course, but also included the necessity for implant removal during the whole follow-up period. Despite its retrospective design, our data clearly indicate that the application of gentamicin-impregnated beads and/or sponges in a DAIR procedure has no advantage and, therefore, their use should be discouraged.

By providing both dead-space management and by achieving high concentrations of antibiotics at the site of infection, application of gentamicin beads and/or sponges should theoretically lead to higher cure rates in severe orthopaedic infections, like PJIs. However, their application so far does not seem to be beneficial in actual clinical outcome. Few studies have been published on the additional value of gentamicin beads/sponges to systemic antibiotic therapy in PJI. One retrospective study performed by Kuiper *et al.*[29] demonstrated a higher cure rate when using gentamicin-impregnated sponges and a higher failure rate when using gentamicin-impregnated beads, but this association was not found in the multivariate analysis. Only one small randomized controlled trial has been performed (with ∼14 patients in each arm), demonstrating no beneficial effect of gentamicin beads.[32–34] However, in this study the application of local antibiotics was compared with systemic antibiotics, instead of complementary use. Other studies only described the outcome of their routine usage, without the inclusion of a control group.[34–37]

In some studies, including ours, applying gentamicin carriers in orthopaedic infections even appear to do more harm than good. To illustrate, Blaha *et al.*[33] performed a randomized study in a large cohort of chronic osteomyelitis patients and demonstrated a higher recurrence rate when gentamicin-containing polymethylmethacrylate (PMMA) beads were implanted at the site of infection compared with systemic antibiotic treatment alone. In addition, a high recurrence rate (17%) has also been observed in a large observational study performed by Walenkamp *et al.*[34] in patients with chronic osteomyelitis treated with the sole use of gentamicin-impregnated PMMA beads. It has been postulated that the lack of efficacy may be due to reduced activity of gentamicin in an environment with a low pH and low oxygen level, which is the case in the presence of a biofilm.[30] Indeed, Neut *et al.*[35] demonstrated bacterial growth on the majority of removed gentamicin-impregnated beads, suggesting that the beads maintain rather than treat the infection. Although this may partially be explained by the presence of gentamicin-resistant strains, a previous study observed no difference in cure rate between strains with high and low MICs of gentamicin.[36] Our results also showed no difference in outcome when solely analysing PJIs with gentamicin-susceptible strains. We did not find any other potential explanation for the worse outcome in the gentamicin group; according to subanalyses, the additional surgery to remove the gentamicin beads did not seem to expose patients to a higher risk of reinfection and the higher failure rate was also observed in the sole use of gentamicin-impregnated sponges that can remain *in situ*. These sponges form a kind of sludge and may well act as a foreign body just like beads after they have emptied their load.

Future studies should address whether other types of local antibiotic application may be useful in the treatment of acute PJI in patients with a high risk of failure. A promising type appears to be the administration of vancomycin powder, which has been applied as a prevention measure in hip and knee revision arthroplasty and does not necessitate additional surgery for its removal.[38,39] Riesgo *et al.*[39] retrospectively evaluated the infection-free survivorship in acute PJI after implementing a vancomycin povidone-iodine protocol and demonstrated a reduction in failure rate from 37% to 17% in a cohort of 74 cases. Its use and potential benefit should be confirmed and further explored in future studies.

Despite the fact that propensity matching is an important strength of our study, it has limitations as well. Although propensity matching corrects for confounding factors, remaining selection bias cannot be ruled out, since one can only correct for objective variables and not for the clinical judgement of the orthopaedic surgeon who decided to apply local gentamicin. In addition, the matched cohort only included a subselection of patients of the total cohort (40%). However, despite this subselection, the high failure rates remained the same in the matched cohort, which makes it unlikely that the matched analysis was performed in cases with less severe infections. Moreover, subgroup analysis in high-risk groups for failure did not show any benefit from local gentamicin either and the use of local gentamicin was an independent predictor of failure in the multivariate analysis as well.

In conclusion, the use of gentamicin-impregnated beads and/or sponges is associated with higher failure rates in early PJI and, therefore, their use should be discouraged. Future studies should conclude whether other types of local antibiotics can improve treatment outcome.

Funding

This study was carried out as part of our routine work.

Transparency declarations

None to declare.

References

1 Kurtz SM, Ong KL, Lau E *et al*. Prosthetic joint infection risk after TKA in the Medicare population. *Clin Orthop Relat Res* 2010; **468**: 52–6.

2 Kunutsor SK, Whitehouse MR, Blom AW *et al*. Re-infection outcomes following one- and two-stage surgical revision of infected hip prosthesis: a systematic review and meta-analysis. *PLoS One* 2015; **10**: e0139166.

3 Tsang SJ, Ting J, Simpson AHRW *et al*. Outcomes following debridement, antibiotics and implant retention in the management of periprosthetic infections of the hip: a review of cohort studies. *Bone Joint J* 2017; **99**: 1458–66.

4 Zhang C, Yan CH, Chan PK *et al*. Polyethylene insert exchange is crucial in debridement for acute periprosthetic infections following total knee arthroplasty. *J Knee Surg* 2017; **30**: 36–41.

5 Choi HR, von Knoch F, Zurakowski D *et al*. Can implant retention be recommended for treatment of infected TKA? *Clin Orthop Relat Res* 2011; **469**: 961–9.

6 Lora-Tamayo J, Murillo O, Iribarren JA *et al*. A large multicenter study of methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* prosthetic joint infections managed with implant retention. *Clin Infect Dis* 2013; **56**: 182–94.

7 Lora-Tamayo J, Senneville É, Ribera A *et al*. The not-so-good prognosis of streptococcal periprosthetic joint infection managed by implant retention: the results of a large multicenter study. *Clin Infect Dis* 2017; **64**: 1742–52.

8 Rodríguez-Pardo D, Pigrau C, Lora-Tamayo J *et al*. Gram-negative prosthetic joint infection: outcome of a debridement, antibiotics and implant retention approach. A large multicentre study. *Clin Microbiol Infect* 2014; **20**: O911–19.

9 Urish KL, Bullock AG, Kreger AM *et al*. A multicenter study of irrigation and debridement in total knee arthroplasty periprosthetic joint infection: treatment failure is high. *J Arthroplasty* 2018; **33**: 1154–9.

10 Triantafyllopoulos GK, Poultsides LA, Sakellariou VI *et al*. Irrigation and debridement for periprosthetic infections of the hip and factors determining outcome. *Int Orthop* 2015; **39**: 1203–9.

11 Marculescu CE, Berbari EF, Hanssen AD *et al*. Outcome of prosthetic joint infections treated with debridement and retention of components. *Clin Infect Dis* 2006; **142**: 471–8.

12 Buller LT, Sabry FY, Easton RW *et al*. The preoperative prediction of success following irrigation and debridement with polyethylene exchange for hip and knee prosthetic joint infections. *J Arthroplasty* 2012; **27**: 857–64.

13 Tornero E, Morata L, Martínez-Pastor JC *et al*. Importance of selection and duration of antibiotic regimen in prosthetic joint infections treated with debridement and implant retention. *J Antimicrob Chemother* 2016; **71**: 1395–401.

14 El Helou OC, Berbari EF, Lahr BD *et al*. Efficacy and safety of rifampin containing regimen for staphylococcal prosthetic joint infections treated with debridement and retention. *Eur J Clin Microbiol Infect Dis* 2010; **29**: 961–7.

15 Martínez-Pastor JC, Muñoz-Mahamud E, Vilchez F *et al*. Outcome of acute prosthetic joint infections due to gram-negative bacilli treated with open debridement and retention of the prosthesis. *Antimicrob Agents Chemother* 2009; **53**: 4772–7.

16 Tornero E, Morata L, Martínez-Pastor JC *et al*. KLIC-score for predicting early failure in prosthetic joint infections treated with debridement, implant retention and antibiotics. *Clin Microbiol Infect* 2015; **21**: 786.e9–17.

17 Löwik CAM, Jutte PC, Tornero E *et al*. Predicting failure in early acute prosthetic joint infection treated with debridement, antibiotics and implant retention: external validation of the KLIC score. *J Arthroplasty* 2018; **33**: 2582–7.

18 Vilchez F, Martínez-Pastor JC, García-Ramiro S *et al*. Outcome and predictors of treatment failure in early post-surgical prosthetic joint infections due to *Staphylococcus aureus* treated with debridement. *Clin Microbiol Infect* 2011; **17**: 439–44.

19 Sukeik M, Patel S, Haddad FS. Aggressive early débridement for treatment of acutely infected cemented total hip arthroplasty. *Clin Orthop Relat Res* 2012; **470**: 3164–70.

20 Cobo J, Garcia San Miguel L, Euba G *et al*. Early prosthetic joint infection: outcomes with debridement and implant retention followed by antibiotic therapy. *Clin Microbiol Infect* 2011; **17**: 1632–7.

21 Duque AF, Post ZD, Lutz RW *et al*. Is there still a role for irrigation and debridement with liner exchange in acute periprosthetic total knee infection? *J Arthroplasty* 2017; **32**: 1280.

22 Fehring TK, Odum SM, Berend KR *et al*. Failure of irrigation and débridement for early postoperative periprosthetic infection. *Clin Orthop Relat Res* 2013; **471**: 250–7.

23 Bergkvist M, Mukka SS, Johansson L *et al*. Debridement, antibiotics and implant retention in early periprosthetic joint infection. *Hip Int* 2016; **26**: 138–43.

24 Westberg M, Grøgaard B, Snorrason F. Early prosthetic joint infections treated with debridement and implant retention. *Acta Orthop* 2012; **83**: 227–32.

25 Aboltins CA, Dowsey MM, Peel T *et al*. Early prosthetic hip joint infection treated with debridement, prosthesis retention and biofilm-active antibiotics: functional outcomes, quality of life and complications. *Intern Med J* 2013; **43**: 810–5.

26 Kelm J, Anagnostakos K, Regitz T *et al*. MRSA-infections—treatment with intraoperatively produced gentamycin-vancomycin PMMA beads. *Chirurg* 2004; **75**: 988–95.

27 Swieringa AJ, Goosen JH, Jansman FG *et al*. In vivo pharmacokinetics of a gentamicin-loaded collagen sponge in acute periprosthetic infection: serum values in 19 patients. *Acta Orthop* 2008; **79**: 637–42.

28 Moojen DJ, Hentenaar B, Vogely CH *et al*. In vitro release of antibiotics from commercial PMMA beads and articulating hip spacers. *J Arthroplasty* 2008; **23**: 1152–6.

29 Kuiper JW, Vos CJ, Saouti R *et al*. Prosthetic joint-associated infections treated with DAIR (debridement, antibiotics, irrigation, and retention). Analysis of risk factors and local antibiotic carriers in 91 patients. *Acta Orthop* 2013; **84**: 380–6.

30 Barth RE, Vogely HC, Hoepelman AI *et al*. 'To bead or not to bead?' Treatment of osteomyelitis and prosthetic joint-associated infections with gentamicin bead chains. *Int J Antimicrob Agents* 2011; **38**: 371–5.

31 Parvizi J, Zmistowski B, Berbari EF *et al*. New definition for periprosthetic joint infection: from the workgroup of the musculoskeletal infection society. *Clin Orthop Relat Res* 2011; **469**: 2992–4.

32 Nelson CL, Evans RP, Blaha JD *et al*. A comparison of gentamicin-impregnated polymethylmethacrylate bead implantation to conventional parenteral antibiotic therapy in infected total hip and knee arthroplasty. *Clin Orthop Relat Res* 1993; **295**: 96–101.

33 Blaha JD, Calhoun JH, Nelson CL *et al*. Comparison of the clinical efficacy and tolerance of gentamicin PMMA beads on surgical wire versus combined and systemic therapy for osteomyelitis. *Clin Orthop Relat Res* 1993; **295**: 8–12.

34 Walenkamp GH, Kleijn LL, de Leeuw M. Osteomyelitis treated with gentamicin-PMMA beads: 100 patients followed for 1–12 years. *Acta Orthop Scand* 1998; **69**: 518–22.

35 Neut D, van de Belt H, Stokroos I *et al*. Biomaterial-associated infection of gentamicin-loaded PMMA beads in orthopaedic revision surgery. *J Antimicrob Chemother* 2001; **47**: 885–91.

36 Janssen DM, Geurts JA, Jütten LM *et al*. 2-stage revision of 120 deep infected hip and knee prostheses using gentamicin-PMMA beads. *Acta Orthop* 2016; **87**: 324–32.

37 Geurts JA, Janssen DM, Kessels AG *et al*. Good results in postoperative and hematogenous deep infections of 89 stable total hip and knee replacements with retention of prosthesis and local antibiotics. *Acta Orthop* 2013; **84**: 509–16.

38 Otte JE, Politi JR, Chambers B *et al*. Intrawound vancomycin powder reduces early prosthetic joint infections in revision hip and knee arthroplasty. *Surg Technol Int* 2017; **7**: 284–9.

39 Riesgo AM, Park BK, Herrero CP *et al*. Vancomycin povidone-iodine protocol improves survivorship of periprosthetic joint infection treated with irrigation and debridement. *J Arthroplasty* 2018; **33**: 847–50.