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Unveiling the link: highly porous tantalum-augmented implants and periprosthetic joint infection in revision total knee arthroplasty—a systematic review and meta-analysis

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Abstract

Background The trend of the literature suggests that tantalum (Ta) may possess antibacterial properties. However, no consensus has been reached on Ta's preventive role in periprosthetic joint infection (PJI) in patients undergoing revision total knee arthroplasty (rTKA).

Question What is the PJI incidence rate after rTKA using Ta-augmented implants for both septic and all-cause revision reasons? Is there a difference in the PJI rate following rTKA performed using Ta-augmented implants compared to non-Ta implants?

Methods Using 5 major databases, the authors searched for studies reporting the rate of PJIs following rTKA using Ta-augmented implants until January 2022. The PJI rates for the Ta group were pooled, compared to the control group, and presented as odds ratios (OR) and 95% confidence intervals (CI) using forest plots.

Results Thirty eligible studies involving 881 knees were included. The overall PJI rate following rTKA using Ta-augmented implants was 8.1% (CI = 6.6%-9.9%). Specifically, in cases of septic revision, the infection rate was 15.7% (95% CI = 11.7%-20.7%). The comparative analysis indicated a similar PJI rate between the Ta- augmented and non-Ta group across 3 studies, which was found to be similar (OR = 0.52, 95% CI = 0.13–2.0, *P* = 0.35).

Conclusion PJI poses a significant risk following both aseptic and septic revision rTKA, even when Ta-augmented implants were administrated. The rate of PJI after rTKA was similar for Ta- augmented implants and non-Ta implants. Further rigorous studies with a high level of evidence are essential to definitively determine the potential impact of Ta derivatives on infection rates following rTKA, particularly in septic revision.

Level of evidence IV.

Keywords Total knee arthroplasty, TKA, Prosthesis-related infections, PJI, Tantalum, Trabecular metal

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Introduction

Periprosthetic joint infection (PJI) is a catastrophic complication following total joint arthroplasty (TJA) and continues to be a challenge for orthopedic surgeons. PJIs occur in approximately 2% of primary total knee arthroplasty (TKA) procedures [1–4]. There is a higher incidence of PJI in revision TKAs (rTKAs), as high as 8% within two years [5]. PJI recurrence is also high in septic cases following two-stage rTJA (7–33%), complicating the situation [6–10].

Trabecular Metal (TM) implants, which consist of a porous carbon structure covered by a porous Tantalum (Ta) covering, are becoming increasingly popular in complex reconstructive procedures in cases of massive bone loss, such as rTKA [11, 12]. Ta possesses high porosity, which facilitates osteointegration, and its elastic properties are similar to trabecular bone, minimizing stress shielding and reducing micromotion due to superior frictional characteristics [13]. Many studies claim that using highly porous Ta is associated with a lower incidence of PJIs in patients undergoing rTJA compared with other materials [14–18]. Based on laboratory studies, pure Ta is less likely to be affected by *Staphylococcus aureus* adhesion than materials frequently used for orthopedic implants, such as titanium alloys [16]. TM has a porous surface resembling dense cancellous bone, which allows vascularized soft tissue to proliferate on the surfaces while maintaining a high level of attachment strength [19, 20]. TM-conditioned media also increased leukocytes'phagocytosis and chemotactic response [17]. However, Ta's innate antimicrobial properties and clinical efficacy remain unclear [20, 21].

"International Consensus Meeting (ICM) 2018"asked members about the efficacy of highly porous Ta in preventing SSIs and PJIs in patients undergoing revision arthroplasty, especially in treating PJI (PJI recurrence) [11, 22]. There has been no consensus on this challenging question, which remains controversial [23]. In this context, we aim to address the following questions through the current systematic review and meta-analysis: 1. What is the incidence of PJI following rTKA using Ta- augmented implants? 2. Is there a difference in the rate of PJI after rTKA performed with Ta- augmented implants compared with the lack thereof? 3. Considering only rTKA for septic reasons, are Ta-augmented implants associated with a reduced risk of postoperative PJI?

Methods

Population (P), Intervention (I), Comparison (C), and Outcome (O)

P: Patients undergoing rTKA

I: Using porous Ta- augmented component(s)

C: Using Non-Ta implants

O: Periprosthetic joint infection (PJI)

Screening and search strategy

Our study was performed under PRISMA guidelines- Preferred Reporting Items for Systematic Reviews and Meta-Analyses [24]. The current review has been registered through"The International Prospective Register of Systematic Reviews"(PROSPERO, registration ID: CRD42021268518, available at https://www.crd.york.ac.uk/PROSPERO). The"Tehran University of Medical Sciences"institutional review board has approved the study (Approval ID: IR.TUMS.MEDICINE.REC.1400.1333).

We searched Medline, Embase, Scopus, Web of Science, and Cochrane Library using a variety of keywords as well as database-specific heading vocabulary until January 2022, including"Tantalum"or"Trabecular metal"AND"Infection "or"PJI"AND"Total knee arthroplasty"or"TKA"or"revision arthroplasty". The search query has been modified per each database's search policy. In addition, a hand search of relevant bibliographies was conducted.

Covidence's online systematic review software was used to import all records (https://www.covidence.org). In 2 steps of title/abstract screening and full-text screening, 2 independent reviewers (P.R and R.M) independently assessed all imported articles for eligibility according to the distinct inclusion/exclusion criteria. A third reviewer (SMJ.M) was consulted to resolve conflicts in this and other sections.

Criteria for inclusion and exclusion

The original studies reporting the incidence of PJI following rTKA using Ta- augmented materials were included in the current study. Our exclusion criteria included 1) studies that excluded PJIs, 2) non-human studies, 3) non-English literature, 4) reviews, congress abstracts, commentaries, and book chapters, and 5) less than 3-month follow-ups for PJI incidence.

Assessment of study quality

The quality of the included studies was assessed using the Newcastle Ottawa Scale (NOS) [25]. Selection, comparability, and outcome assessment were the 3 qualifying domains. The total points ranged from 0 to 9, with higher scores indicating higher quality. Studies with a score of 7 or more are considered high-quality, while those with a score of 4 or less are considered low-quality.

Extraction and collection of data

Two reviewers (P.M. and M.ME) extracted data from eligible retrieved articles and organized them into a predesigned table. The following variables were extracted: primary author's name, year of publication, country, study design, follow-up period, study groups and population, sex, age, indications for revision, re-revision rate, PJI rate, PJI recurrence rate in septic revision cases, and details regarding Ta- augmented materials.

Statistical analysis and data synthesis

Eligible retrieved data were meta-analyzed using Comprehensive Meta-Analysis Software (version 3). The pooled prevalence of PJI following rTKA with Ta was determined. The odds ratio (OR) was used to compare the outcome of the Ta- augmented materials with the control groups. In addition, the incidence of PJI following rTKA to treat PJI was also determined (septic revisions). The funnel plot and Egger test were also used to evaluate publication bias. We applied the I^2 test to identify heterogeneity among eligible studies. We assumed that I^2 values of 25%, 50%, and 75% would result in low, moderate, and high heterogeneity, respectively [26]. Random-effect models were used when the I^2 exceeded 50%.

We performed a leave-one-out meta-analysis (sensitivity analysis) to identify the sources of heterogeneity. We excluded studies containing less than 10 persons as the denominator of prevalence from our analysis. Whenever we are faced with the same authors from the same population presenting more complete results, the former study is also excluded from the analysis. A significant *P*-value was determined to be <0.05.

Results

Search results and demographic features

Figure 1 illustrates the process of identifying articles for inclusion. Our comprehensive search strategy and manual search investigation identified 3633 publications, of which 30 met our eligibility criteria [15, 27–55]. A summary of the key characteristics of the eligible studies is presented in Table 1. A total of 30 rTKA studies included 881 knees and consisted of 4 case series, 2 prospective, and 24 retrospective cohort studies. The mean follow-up period ranged from 17 to 126.5 months.

Quality assessment

Based on quality assessment using NOS, 9 studies (30%) were rated as high quality, 16 (53.3%) as medium quality, and 5 (16.7%) as low quality (Table 2). The mean (SD) NOS score is measured at 5.7 ± 1.8, and the quality of the studies is considered medium to high overall.

PJI rate after all-cause rTKA

Qualitative synthesis

According to 30 studies investigating the infection rate following rTKA using Ta implants, the PJI rate ranges from 0 to 13%. Three eligible case–control articles compared the rate of PJI between the Ta and the control group [27, 35, 38], among which 2 reported recurrences of PJI in septic revision cases. In the Ta- augmented implants and control groups, PJI rates ranged from 0–6.1% and 1.1–10.2%, respectively [27].

A prospective study by Bedard et al. evaluated the limb alignment and stem positioning of 115 patients who underwent revision TKA using uncemented stems (21 Ta cones and 94 without cones). There were no revisions required, but one patient from the non-Ta cone group required arthrodesis after recurrent PJI (PJI: 0 vs. 1.1%, $P > 0.05$). A 9-year follow-up study conducted by Sandiford et al. revealed no significant difference between TM Cones ($n = 14$) and Femoral Head Allografts ($n = 30$) in the management of substantial structural defects of the femur and tibia during rTKA (PJI: 0 vs. 3%, $P > 0.05$). The Ta group did not experience any PJIs. A study by Bohl et al. compared porous Ta metaphyseal cones with traditional hybrid stem fixation ($n = 49$) to address bone defects following rTKA with 3.5 years of follow-up. PJI rates were not significantly different between groups (3 vs. 5% PJI patients, $P > 0.05$). However, considering the study's small population size and low statistical power, it is prudent to interpret the results cautiously.

Quantitative synthesis

Table 3 summarizes the results of the quantitative syntheses. Meta-analysis showed a pooled rate of 8.1% (95% CI =6.6%– 9.9%) after all-cause rTKA with Ta implant (Fig. 2). The studies had low heterogeneity ($I^2 = 0.0$, Q/df =0.6). Egger's test and funnel plots revealed publication bias among the studies (Egger's $P = 0.008$) (Fig. 3).

The rate of PJI between Ta- augmented and non-Ta groups (three comparative studies) was similar (OR =0.52, 95% CI =0.13–2.0, $P = 0.35$) (Fig. 4). The studies had low heterogeneity ($I^2 = 0.0$, Q/df =0.27), and no publication bias was detected (Egger's $P = 0.32$). The NOS assessment indicates that none of these studies is of low quality. The sensitivity analysis indicated no change in the result when one study was omitted ($P > 0.05$).

PJI rate after rTKA in septic cases (re-infection)

Seventeen studies were found to report the recurrence of PJI in septic revision cases [6, 15, 28, 31–33, 36, 42, 46, 50, 53, 56–58], of which 2 studies compared the latter incidence between Ta cones and lack thereof [27, 38]. The rate of PJI after rTKA in septic revisions (re-infection) ranged between 0 to 75%. Re-infection rates have been reported to be 16.6% and 8.3% for the Ta-cones compared to non-Ta, respectively, in the Bohl et al. study and 0 vs. 3.8% in the Bedard et al. study [27].

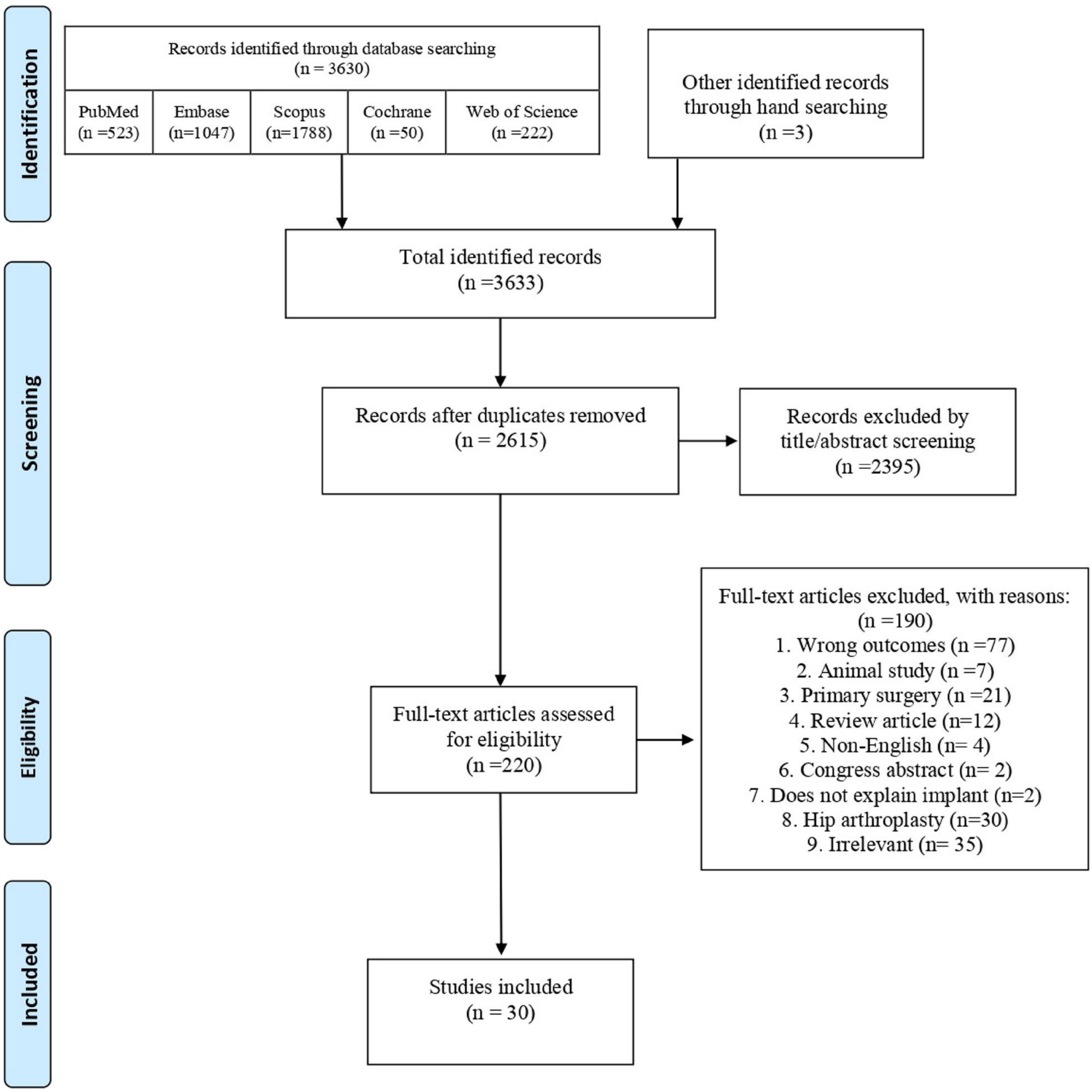

Fig. 1 PRISMA diagram of the screening process

Quantitative synthesis

Meta-analysis of nine studies revealed that the pooled rate of PJI after rTKA with Ta in septic cases (re-infection) was 15.7% (95% CI =11.7%− 20.7%) (Fig. 5) (Table 3). The studies had moderate heterogeneity (I^2= 35.5, Q/df =1.5), and no publication bias was detected (Egger's P= 0.44). Since there were few studies with a comparison group, no analysis was performed to compare the PJI rate after rTKA in septic cases between the Ta- augmented and the non-Ta group.

Summary of representative studies

According to Chalmers et al. [29], PJI indications for rTKA were an independent risk factor for reoperation (HR =4.2, P= 0.002), and Abdelaziz et al. The study also found that it has a significant effect on cone revision following index surgery (P <0.001) [36]. This necessitates paying attention to septic revisions and considering preventive measures to minimize re-infection risk.

In Abdelaziz et al.'s study [36], 72 patients underwent one-stage rTKA for PJI using porous Ta cones

Table 1 Summary of the characteristics and outcomes of the included studies

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
1	Chalmers 2021 [29]	Retrospective cohort	Highly porous metaphyseal tibial cone in revision TKA	178	Aseptic loosening: = 75 (46%) **Chronic PJI = 46 (28%)** Instability = 24 (15%) Peri-prosthetic fracture = 8 (5%) Arthrofibrosis = 5 (3.0%) Suspected metal hypersensitivity = 5 (3.0%)	30 (24–48)	7 (4%)	10 (5.6%)	NA	NA	Porous metaphyseal tibial cones
2	Rajgopal 2021 [34]	Retrospective cohort	TM cones for severe bone loss in primary and revision TKA	**Revision = 48** Total = 62	**Loosening + periprosthetic joint infection + polywear = 38** Periprosthetic fracture = 10	110 (60–156)	3 (5%)	2 (4.2%)	NA	TM cones demonstrated favorable clinical/radiological outcomes and reasonable therapeutic options against severe bone defects during primary/revision TKA	Porous TM cones
3	Erivan 2021 [30]	Retrospective cohort	Tibial cones in revision TKA with a severe proximal tibial bone defect	61	**The second stage after infection = 2** Aseptic loosening = 55 Instability = 3 Rotational problem = 1	Minimum 24-month	5 (8.2%)	4 (6.5%)	NA	The present study of cones used for tibial revision shows excellent results	TM cones
4	Abdelaziz 2020 [36]	Retrospective cohort	Tantalum cones in one-stage knee exchange for PJI	72	**PJI**	49.9 ± 18.8	15 (21%)	8 (11.1%)	8 (11.1%)	The first study reports on outcomes of the 1-stage exchange using Ta cones for knee periprosthetic joint infection with additional severe bone loss. Midterm cone-related and infection-free survival offered good results and provided reasonable functional outcomes	Porous Ta cones

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
5	Abdelaziz 2019 [37]	Retrospective cohort	Hinged knees and Ta cones	32	Aseptic loosening in all cases femoral component = 9 Tibial component = 9 Both components = 7	126.5 (120–142)	8 (25%)	3 (9.4%)	NA	Porous Ta cones in revision TKA exhibited no favorable but reasonable long-term durability. Rotating-hinge designs should be used whenever possible to reduce the risk of aseptic loosening	Ta cones
6	Rajgopal 2019 [55]	Retrospective cohort	Ta TM cones for severe distal femoral bone deficiency (stacked two-cone arrangement)	11 (after excluding primary TKA)	**Septic loosening = 5** Periprosthetic fracture = 3 Aseptic loosening = 3	57	0 (0%)	0 (0%)	NA	The use of stacked cones in selected cases of severe distal femoral deficiency has an acceptable outcome	Ta TM cones
7	Panda 2019 [54]	Retrospective cohort	TKA patients requiring metaphyseal reconstruction for large femoral or tibial defects using porous tantalum cones	59	PJI = 26 Aseptic loosening = 17 Periprosthetic fracture = 7 Component malpositioning = 3 Varus malalignment = 2 Osteolysis = 2 Polyethylene wear = 2	83 (50–95)	3 (5.1%)	2 (3.4%)	NA	TM cones are a practical option for treating severe bone defects during TKA with predictable osteointegration and good long-term clinical outcomes	Porous Ta cones
8	Burastero 2018 [28]	Retrospective cohort	Ta metaphyseal cones	60	**Staged revision for periprosthetic knee infection = 60**	43.5 ± 17.4	2 (3.3%)	2 (3.3%)	2 (3.3%)	Excellent clinical and radiographic mid-term outcomes were achieved with a low complication rate. Ta cones may be considered a safe and effective option in the management of massive bone defects and septic knee revision surgery	Ta cones

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
9	Kukreja 2018 [32]	Case Series	Tibial Ta cones without metallic augments	6	Aseptic = 5 **Two-stage infected revision = 1**	49.2 (18–72)	1 (16.7%)	0 (0%)	0 (0%)	The "Tibial base plate-cone without augments (BCCA)" type of construct may offer a valid long-term advantage over the tibial base plate-augment-cone combination in massive tibial bone defects	Tibial Ta cones without metallic augments
10	Bohl 2018 [27]	Retrospective cohort	Ta metaphyseal cones to manage bone defects	98	NA	42) 24–120)	NA	NA	NA	Metaphyseal cones are not associated with superior outcomes at short-term follow-up. Given the increased cost associated with using cones compared to traditional techniques, this study cannot support the routine use of metaphyseal cones in revision TKA	Ta metaphyseal cones
			Group 1: Ta Cone	49	Aseptic loosening = 16 (33%) **Infection = 12 (25%)** Instability = 12 (25%) Malrotation = 2 (4%) Periprosthetic fracture = 1 (2%) Stiffness = 6 (12%)	40.5 ± 16.4	0 (0%)	3 (6.1%)	2 (16.6%)		
			Group 2: Non-cone	49	Aseptic loosening = 16 (33%) **Infection = 12 (25%)** Instability = 12 (25%) Malrotation = 2 (4%) Periprosthetic fracture = 1 (2%) Stiffness = 6 (12%)	44.3 ± 19.4	2 (4%)	5 (10.2%)	1 (8.3%)		

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
11	Sandiford 2017 [35]	Retrospective cohort	TM cones and femoral head allografts in revision TKA	45	Aseptic loosening = 37 Instability = 2 **Infection = 2** Periprosthetic fracture = 2	87 (60–108)	NA	NA	NA	No significant difference in function, pain, or recurrent revision was observed in comparison with either TM cones or femoral head allografts in the context of severe bone defects following revision TKA	TM cone
			Group 1: TM augments in TKA	15	NA		0 (0%)	0 (0%)	NA		
			Group 2: Femoral head allografts	30	NA	109 (72–144)	2 (6.7%)	1 (3.3%)	NA	There was no significant difference between the groups	
12	Girerd 2016 [31]	Retrospective cohort	TM cones	52 Knees (51 patients)	Aseptic loosening = 22(42%) **Infection = 19 (37%)** Instability = 1(2%) Abnormality of the patella or extensor mechanism = 2(4%) Unexplained pain = 2(4%) Osteolysis and/or polyethylene wear = 3 (6%) Mechanical implant failure = 1(2%) Stiffness = 1(2%) Other = 1(2%)	28 (21–32)	4 (7.8%)	4 (7.8%)	4 (21.1%)	TM cones employed to fill metaphyseal and/or epiphyseal bone defects amid revision TKA provided promising outcomes comprising evidence of osteointegration, direct fixation, and favorable short-term stability even in infected patients	Metaphyseal and/or epiphyseal cone

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
13	Potter 2016 [33]	Retrospective cohort	Ta metaphyseal femoral cones in revision TKA	159 Knees (157 patients)	**Infection = 75** Aseptic loosening = 56 Osteolysis = 26 Implant failure = 16 Instability = 11 Fracture = 1	60 (24–120)	23 (14.4%)	14 (8.8%)	13 (17.3%)	The survivorship in the subgroup with infection was virtually the same as that in the entire cohort, suggesting that failure rates of porous femoral cones do not increase in the infection settings	TM metaphyseal femoral cones
14	Boureau 2015 [39]	Case series	Porous Ta cones (2-cone technique)	7	Aseptic = 4 **Septic revisions = 3**	17 (12–25)	0 (0%)	0 (0%)	NA	Ta cone can be an alternative to allografts or mega-prostheses in case of massive bone defects	Porous Ta cones
15	Bédard 2015 [38]	Prospective cohort	All revisions (N = 115)	115	Aseptic Loosening = 32 **Infection = 29** Instability = 27 Stiffness = 16 Implant breakage = 2 Extensor mechanism rupture = 2 Patella and malrotation = 1	NA	NA	NA	NA	TM cones do not negatively influence the ability to achieve optimal mechanical alignment when using an uncemented stem technique in revision TKA	TM cones
			Group 1: Revisions with TM Cones	21	Aseptic Loosening = 13 **Infection = 3** Instability = 2 Stiffness = 2 Implant Breakage = 1	NA	0 (0%)	0 (0%)	0	NA	NA

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
			Group 1: Revisions without TM cones	94	Aseptic Loosening = 19 **Infection = 26** Instability = 25 Stiffness = 14 Implant breakage = 1 Periprosthetic fracture = 6 Extensor mechanism rupture = 2 Patella and malrotation = 1	NA	0 (0%)	1 (1.06%)	1 (3.8%)	NA	NA
16	Brown 2015 [40]	Retrospective cohort	Revision TKA using TM cones	83	Complex primary = 4 Revision = 79: Aseptic loosening = 30 **Infection = 21** Instability = 16 Stiffness = 6 Periprosthetic fracture = 3 Malalignment = 2 Traumatic arthrotomy and MCL failure = 1	40 (24–84)	10 (12%)	11 (13%)	7 (33.3%)	TM cones represent an attractive option for managing bone loss in complex primary and revision TKA with a high rate of osseointegration	TM cones

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
17	Kamath 2015 [43]	Retrospective cohort	Porous Ta metaphyseal cones	66 cones (63 patients)	**Second-stage reimplantation for deep infection = 26** Aseptic loosening of the tibial component = 15 Severe tibial osteolysis in the presence of a well-fixed tibial component = 10 Fracture of the tibial component = 2 Periprosthetic tibial fracture = 1 Severe global knee instability with associated bone loss = 12	70 (60–106)	3(5%)	7(11%)	NA	Porous Ta tibial cones offer a promising management option for severe tibial bone loss. At the intermediate-term follow-up (5–9 years), porous Ta tibial cones had durable clinical results and radiographic fixation. The biological ingrowth of these implants offers the potential for successful long-term structural support in complex knee reconstructions	Porous Ta tibial cones
18	De Martino 2015 [42]	Retrospective cohort	Ta cones	18	Aseptic loosening = 5 **Second-stage reimplantation for deep infection = 13**	72 (60–96)	2 (11.1%)	2 (11.1%)	2 (15.4%)	Ta cones for reconstructing massive bone defects in revision TKA yielded secure fixation with excellent results at an average follow-up of 6 years. These devices are viable for surgeons to use in situations with severe bone loss	Ta cones

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
19	Derome 2014 [41]	Retrospective cohort	Highly porous TM cone	29	Aseptic loosening/wear = 20 **Second-stage revision after deep infection = 7** Periprosthetic fracture = 2	33 (13–73)	2 (6.9%)	2 (6.9%)	NA	Favorable short-term outcomes and low complication rate	Porous Ta cones
20	Jensen 2014 [45]	Retrospective cohort	TM cone	36	Aseptic loosening = 15 **Deep infection = 15** Knee instability = 5 Severe knee pain without loosening of the implant = 1	40 (12–84)	4 (11.1%)	2 (5.6%)	2 (13.3%)	TM cones can provide an effective treatment regarding surgical efficacy, clinical results, and radiological results. It may be at least as effective as the other options reviewed in the literature	TM cone
21	Villanueva-Martínez 2013 [15]	Retrospective cohort	All patients	21	Aseptic revision = 16 **After sepsis = 5**	36	1 (4.76%)	2 (9.5%)	2 (40%)	In the short term, porous Ta metaphyseal cones provided structural support for large femoral and tibial defects. They also provided the environment for bone graft osseointegration, repair of femoral fractures, and effective interdigitation of cement mantle into the TM cone	Ta cones
22	Rao 2013 [48]	Case series	TM cones with accompanying rotating hinged prosthesis	29 Knees (26 Patients)	Aseptic loosening = 15 (51%) Peri-prosthetic fracture = 4 (14%) **Infection = 9 (31%)**	36 (24 – 49)	2 (7%)	2 (7%)	2 (22.2%)	Ta cones yield satisfactory outcomes, including pain relief and promising functional survival while managing major osteolytic defects	TM cones

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
23	Fosco 2013 [58]	Retrospective cohort	Porous TM cones	11 Knees (10 Patients)	**Deep infection = 4 (36%)** Aseptic loosening = 5(45%) Malrotation of prosthetic components = 1(9%) Failed mega prosthesis tibial component, following a tumor resection = 1(9%)	39.8 (24- 78)	0 (0%)	0 (0%)	0 (0%)	No significant correlation was found between the employed TM cones and subsequent risk of re-infection	Cemented/cementless Ta cones
24	Schmitz 2013 [49]	Retrospective cohort	Porous Ta cones	38	Aseptic loosening of the tibial component = 12 Aseptic loosening of the femoral component = 12 Aseptic loosening of both components = 14	37 (35–42)	2 (5.3%)	0 (0%)	NA	The favorable clinical and radiological outcomes using TM cones in managing relevant bone loss in revision TKA were found	Porous Ta cones
25	Panni 2013 [47]	Retrospective cohort	Ta cone	7 knees (out of 38 knees)	**Second-stage for deep infection = 16** Aseptic loosening = 11 Osteolysis = 7 Pain = 2 Instability = 2	84 (54–144)	0 (0%)	0 (0%)	NA	Ta cones could provide well-functioning and durable revision TKAs	Ta cone

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
26	Lachiewicz 2012 [46]	Retrospective cohort	Ta metaphyseal cones in revision TKA	27 knees (27 patients)	**Infection = 13** Aseptic loosening = 10 Osteolysis/polyethylene wear = 4	42 (24–68.4)	4 (14.8%)	1 (3.7%)	1 (7.7%)	Employing Ta cones for massive structural defects revision TKA represents a promising technique with a low infection rate and component loosening	TM metaphyseal cones
27	Howard 2011 [50]	Retrospective cohort	Ta femoral cones	24	Aseptic loosening of the femoral component = 11 **Second-stage reimplantation for the treatment of deep infection = 7** Severe osteolysis around a well-fixed femoral component = 3 Periprosthetic femoral fracture = 2 Severe knee instability = 1	33 (24–50)	0(0%)	0 (0%)	0 (0%)	During the short-term follow-up, the porous Ta metaphyseal femoral cones effectively provided structural support for the revision of TKA's femoral implants	Porous Ta metaphyseal cones
28	Long 2009 [53]	Retrospective cohort	Porous Ta cones	16	Aseptic loosening = 13 **Infection = 3**	31 (24–38)	2 (12.5%)	2 (12.5%)	2 (66%)	Reconstructive tools achieved good short-term results in complex revisions	Porous Ta tibial cones

Table 1 (continued)

No	Study author and year	Study design	Group(s)	Population (Knees)	Revision indication	Follow-up (months, mean ± SD or range)	Total re-revision rate	Infection rate (PJI)	Subsequent infection (recurrence of PJI)	Conclusion about the effectiveness of tantalum in terms of infection	Tantalum details
29	Meneghini 2008 [51]	Prospective cohort	Porous Ta metaphyseal tibial cones	15	**Deep infection = 5** Aseptic loosening of the tibial component = 4 Severe tibial = 3 Fracture of the tibial component = 2 Severe global knee instability with associated bone loss = 1	34 (24–47)	4 (26%)	2 (13%)	NA	Porous Ta metaphyseal tibial cones may provide adequate structural support for the implants	Porous Ta metaphyseal cones
30	Radnay 2006 [52]	Case series	TM cone	10	NA	NA	1 (10%)	1 (10%)	NA	TM augments with stem fixation, an alternate technique with early clinical and radiographic success for reconstructions with severe bone loss	TM cone

NA not available, *TM* trabecular metal, *Ta* tantalum, *TKA* total knee arthroplasty, *PJI* prosthetic joint infection, *MCL* medial collateral ligament to reconstruct extensive bone loss. 15 patients (21%) underwent re-revision surgery, of whom eight (11.1%) were diagnosed with PJI. Most of the reinfections were caused by new pathogens (6 out of 8), and all had been previously diagnosed with PJI. Failure rates for tibial and femoral cones were not significantly different ($P = 0.6$). However, previous septic revision significantly increased the risk of failure ($P < 0.001$). According to their findings, one-stage rTKA with Ta metaphyseal cones provided satisfactory cone-related and infection-free survival rates with acceptable functional outcomes following PJI with severe bone loss.

Burastero et al. [28] retrospectively evaluated 60 patients who underwent two-staged rTKA for PJI and used 94 Ta cones to manage massive bone defects. After 44 months of follow-up, there was no evidence of loosening or migration of any cones. A total of 2 failures (3.3%) occurred following the recurrence of PJI, but no mechanical failures related to the cone were reported, with a survival rate of 97.8%. This study demonstrated that Ta metaphyseal cones effectively treat metaphyseal defects following two-stage rTKA for PJI.

A retrospective study by Fosco et al. [58] examined 11 knees (12 cones) undergoing rTKA that harbored type 2B/3 Engh bone defects. After 39.8 months of follow-up, there was no evidence of re-infection. A radiological assessment revealed no evidence of aseptic loosening or component migration. In all cases, a lack of re-infection or aseptic loosening supports using Ta metaphyseal cones for rTKA with large amounts of bone defects. In addition, they exclude any possibility that TM cones are related to the recurrence of infection.

In Long et al.'s study [53], PJI recurrence rates in septic revision cases were as high as 67%. A retrospective review of 16 cases of rTKA performed using porous Ta tibial cones for bone defects was conducted with a mean follow-up of 31 months. The study included three cases of staged re-implantation for PJI, of which 2 (67%) experienced recurrent sepsis, which required the removal of an adequately fixed cone. There is no evidence that porous Ta cone use is responsible for the high re-infection rate (2/3) in this complex group of patients. They believe porous cones are a superior alternative to placing large metal augments or large amounts of dead bone.

Martino et al. [42] retrospectively evaluated the clinical outcomes of 18 patients (18 knees) who underwent rTKA with 26 Ta cone applications (13 femoral and 13 tibial). Reoperations due to recurrent PJI (2 out of 13, 15.4%) were recorded after a mean of 6 years in these 2 cones despite good osseointegration. Radiographs taken during the last 6 years showed no evidence of migration or loosening of the implants.

Discussion

The major finding of this study was that the overall rate of postoperative PJI following rTKA with Ta-augmented material was 8.1%. In contrast, the rate of PJI was comparable between Ta-augmented and non-Ta groups ($P > 0.05$). When rTJA was performed as part of a septic revision, the infection rate was 15.7% for rTKAs. The PJI rates after rTKA (8.1%) were similar to those reported in the Divano et al. systematic review of rTKA with Ta cones (7.1%) [59]. The articles also generally agreed that Ta-augmented implants are an effective method of treating bone defects following rTKA for septic and aseptic reasons and have a high survival rate.

Porous Ta coatings possess several advantages, including reduced stress shielding, decreased micromotion, improved osteointegration, and prevention of bone resorption [11]. Though a growing body of literature asserts that Ta has intrinsic antimicrobial characteristics and bioactive properties, there is a lack of consensus. Recent trend literature has raised doubts regarding previously published literature [11, 16, 60, 61].

Several laboratory studies have revealed that the adhesion potency of *S. aureus* to pure Ta is lower than that of orthopedic implant materials, and Ta may inhibit *S. aureus* proliferation [16, 20]. Additionally, high levels of human leukocyte activation and increased releases of cytokines are expected when Ta-conditioned media is incubated [17]. In this regard, activated leukocytes on the surface of TM materials might facilitate local host defense [17]. However, little evidence in vivo supports the intrinsic antimicrobial properties of Ta. [20, 21]. Harrison et al. reported that Ta does not have inherent antibiofilm or antimicrobial properties against *S. epidermidis* and *S. aureus* compared to titanium [21].

Ta cone application during rTKA has been demonstrated to be a feasible option in severe metaphyseal defects, providing an excellent outcome regarding implant stability and survival [62]. However, the definitive indication for septic revision surgery, particularly for extensive bone loss, is unknown. The 2018 International Consensus Meeting on Musculoskeletal Infection has also failed to draw a conclusive conclusion regarding the effectiveness of Ta augments in preventing re-infection following a one-stage exchange procedure [11]. In revision hip arthroplasty clinical settings, Tokarski et al. showed a trend toward a lower infection rate in the Ta cup group than in the Ti cup group (2.9% vs. 5%, $P > 0.05$). Considering only septic revisions, the PJI rate in the Ta group was significantly lower (3.1% vs. 17.5%, $P < 0.05$). In contrast, several studies have not found significant differences between Ta and non-Ta implants [22, 63–66]. The use of cones is widely practiced in rTKA, with reported benefits including reliable osseointegration

Table 2 Quality assessment result based on Newcastle–Ottawa Scale (NOS)

No	Study author and year	Quality assessment (Newcastle–Ottawa Scale)			Score	Overall quality
		Selection	Comparability	Outcome/ exposure		
1	Chalmers 2021	**	*	**	5	Medium
2	Rajgopal 2021	*	*	**	4	Low
3	Erivan 2021	***	*	**	6	Medium
4	Abdelaziz 2020	****	*	***	8	High
5	Abdelaziz 2019	****	*	***	8	High
6	Rajgopal 2019	**		**	4	Low
7	Panda 2019	**		***	5	Medium
8	Burastero 2018	****	*	***	8	High
9	Kukreja 2018	*		**	3	Low
10	Bohl 2018	***	**	***	8	High
11	Sandiford 2017	***	**	**	8	High
12	Girerd 2016	**	**	***	7	High
13	Potter 2016	**	**	*	5	Medium
14	Boureau 2015	*		**	3	Low
15	Bédard 2015	**	**	*	5	Medium
16	Brown 2015	***	**	***	8	High
17	Kamath 2015	***	*	**	6	Medium
18	De Martino 2015	***	*	***	7	High
19	Derome 2014	***		***	6	Medium
20	Jensen 2014	**	*	**	5	Medium
21	Villanueva-Martínez 2013	***	*	**	6	Medium
22	Rao 2013	**	*	***	6	Medium
23	Fosco 2013	**	*	***	6	Medium
24	Schmitz 2013	***		***	6	Medium
25	Panni 2013	*	*	*	3	Medium
26	Lachiewicz 2012	*	*	***	5	Medium
27	Howard 2011	***	*	***	7	High
28	Long 2009	***	*	**	6	Medium
29	Meneghini 2008	***	*	**	6	Medium
30	Radnay 2006			*	1	Low

*indicates the number of stars each study received in each assessment domain

Table 3 Summary of quantitative synthesis

	Pooled effect size	95% CI	*P*-value	Model	I^2 index	Q/df	Publication bias (Egger's *P*-value)	Related figures
PJI rate after rTKA with tantalum	Rate = 8.1%	6.6%–9.9%	-	Fixed effect	0.0	0.6	Yes (0.008*)	(Fig. 2) (Fig. 3)
Comparing the PJI rate between tantalum and none-TA group after rTKA	OR = 0.67	0.10–4.34	0.67	Fixed effect	0.0	0.2	No (0.86)	(Fig. 4)
PJI rate after rTKA in septic cases (re-infection)	Rate = 15.7%	11.7%–20.7%	-	Fixed effect	35.5	1.5	No (0.44)	(Fig. 5)
Comparing the PJI rate between the tantalum and none-Ta group after rTKA in septic cases (re-infection)	Not applicable							

CI confidence interval, *rTKA* Revision total knee arthroplasty, *OR* Odds ratio

[*] Statistically significant *p*-value

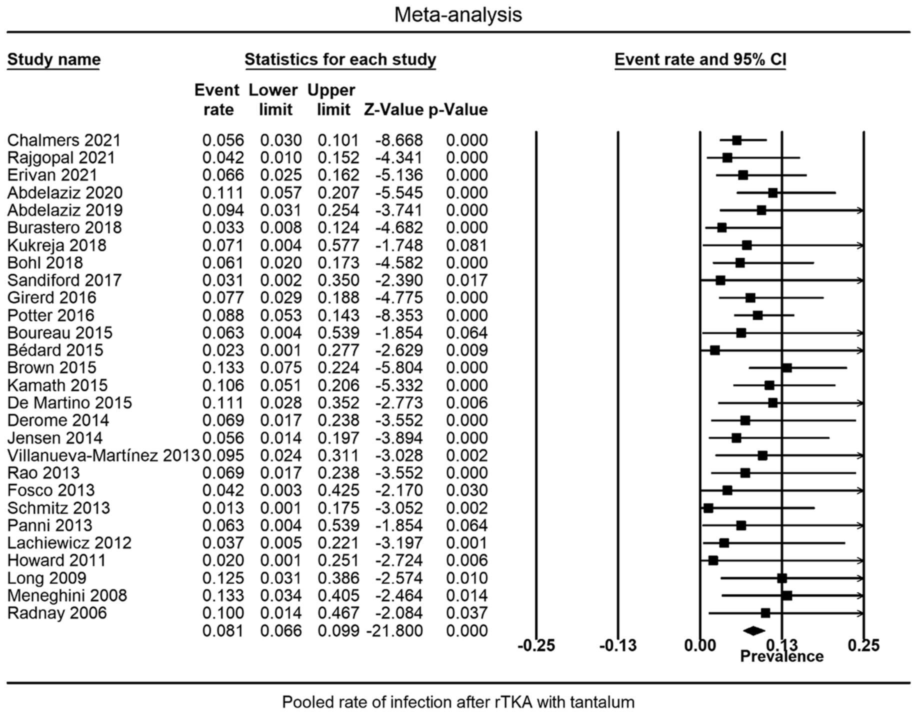

Fig. 2 Meta-analysis of PJI rate after all-cause rTKA using Ta-augmented implant

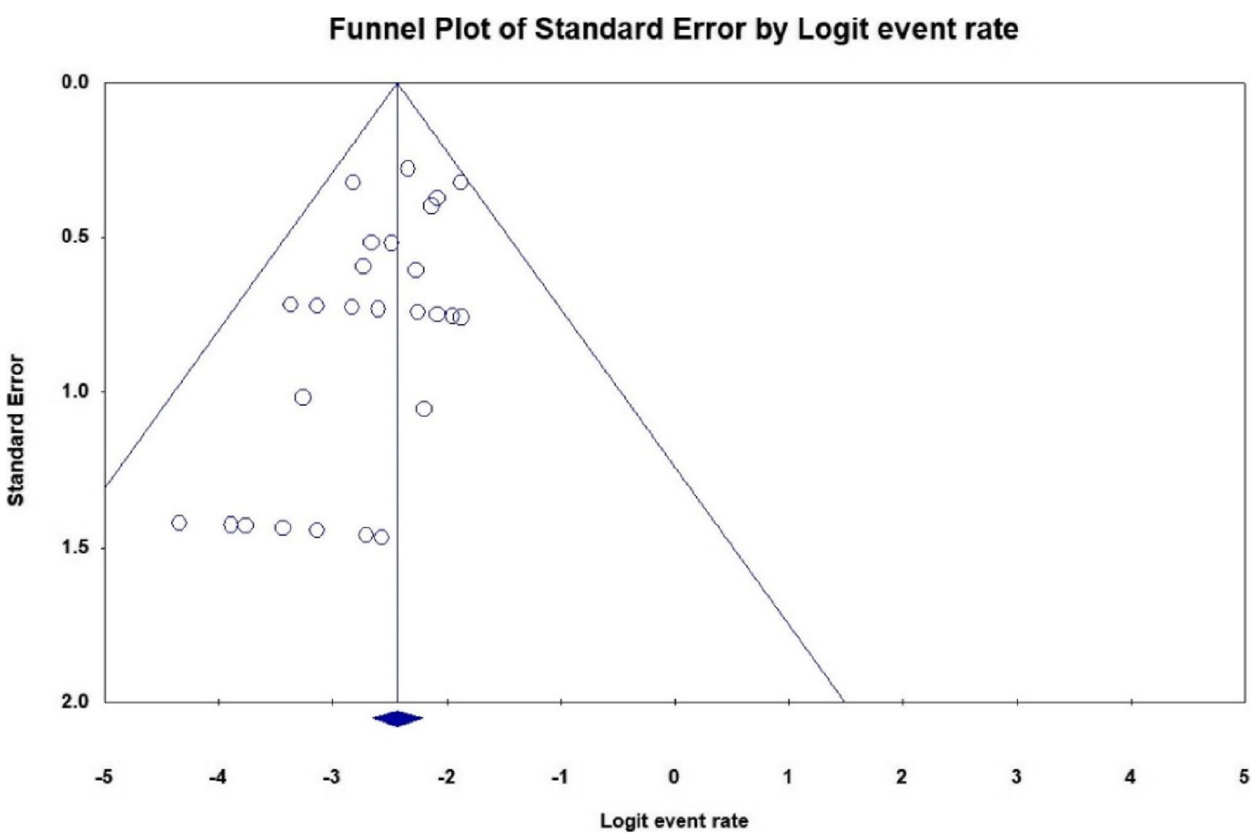

Fig. 3 Funnel plot showing publication bias

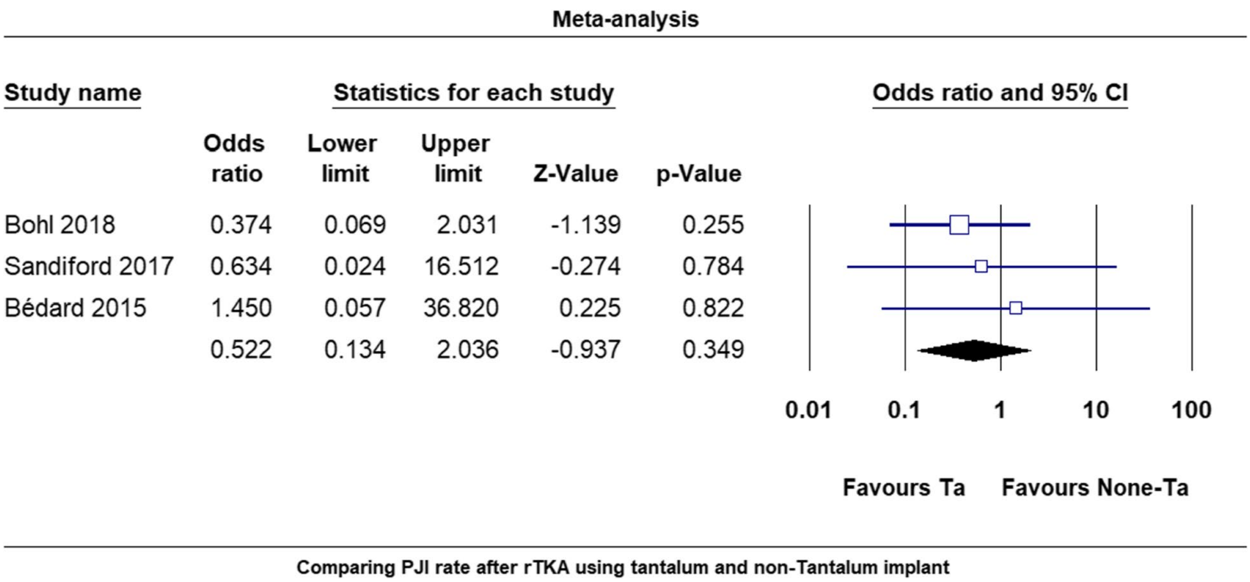

Fig. 4 PJI rate is similar between the Ta- augmented and the non-Ta groups for all-cause rTKA

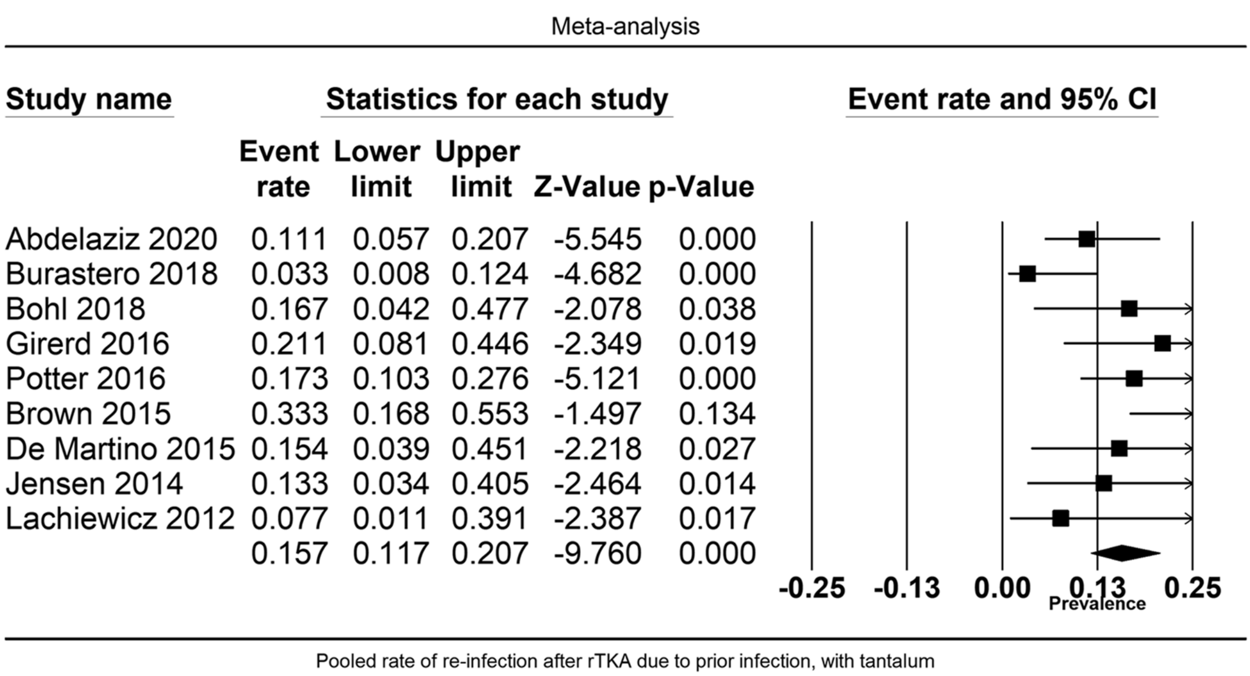

Fig. 5 Pooled rate of infection after rTKA with Ta- augmented in septic revisions (re-infection)

with bone, the ability to fill defects, and effective stress transfer. However, the widespread metaphyseal cone application has been questioned, as it adds complexity to achieve implant stability and poses substantial costs of nearly $4,000 per cone [27, 28].

Despite promising outcomes, some investigations have raised concerns regarding the distinct Ta-related disadvantage. Ta implants require extreme removal efforts when indicated for circumstances such as recalcitrant PJIs in which there may be no bone stock at the end of the procedure. The removal of Ta implants faces a potential challenge, as the literature lacks data regarding extracting porous Ta cones [15, 51].

The current study has several limitations. Since several of the eligible retrieved articles had a moderate level of evidence and quality, and most of them were retrospective studies with small sample sizes, a considerable bias may threaten the study's conclusion. It is recommended that longitudinal randomized clinical trials (RCTs) be conducted to investigate the anti-infection properties of Ta administered in the context of rTKA. However, the overall PJI rate is relatively low, making conducting either an RCT or a prospective cohort study challenging. Moreover, several studies did not distinguish between aseptic and septic reasons for the revision. As another limitation, most studies evaluated only patients suffering from extensive bone loss during revision surgery, and these results should only be interpreted for this complex subset of patients. We also acknowledge the limited number of eligible studies distinguishing reconstruction solely using Ta-coated implants vs. lack thereof. The characteristics of mixed implants may inherently affect the findings for isolating Ta's effects. Hence, the definitive interpretation remains debatable. While our findings suggest that adding Ta is not associated with a higher incidence of prosthetic joint infection (PJI), they do not definitively determine Ta's role in PJI prevention.

Conclusions

PJI following all-cause and septic-cause rTKA is a serious complication and is not uncommon among patients, even those using Ta-coated materials. The rate of PJI after rTKA was similar for Ta-coated materials and lack thereof. The current study confirms that adding Ta does not decrease the risk of PJI following rTKA. Future investigations are warranted to establish the significance of Ta's preventive role in PJI.

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Authors' contributions
"P. Mirghaderi and SMJ. Mortazavi contributed to the study's conception and design. P. Rahimzadeh and R. Mirghaderi did the screening, table design, and first draft of the manuscript. P. Mirghaderi and M. Mirahmadi Eraghi analyzed the data and extracted data. Supervising, editing, and introducing the concept were performed by SMJ. Mortazavi. All authors commented on previous versions of the manuscript and revised them. All authors read and approved the final manuscript."

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Declarations

Ethics approval and consent to participate
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Consent publication
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Competing interests
The authors declare no competing interests.

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