ORIGINAL ARTICLE INFECTIOUS DISEASES

Characteristics and outcome of 27 elbow periprosthetic joint infections: results from a 14-year cohort study of 358 elbow prostheses

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Abstract

Elbow arthroplasty is increasingly performed in patients with rheumatic and post-traumatic arthritis. Data on elbow periprosthetic joint infection (PJI) are limited. We investigated the characteristics and outcome of elbow PJI in a 14-year cohort of total elbow arthroplasties in a single centre. Elbow prosthesis, which were implanted between 1994 and 2007 at Schulthess Clinic in Zurich, were retrospectively screened for infection. PJI was defined as periprosthetic purulence, the presence of sinus tract or microbial growth. A Kaplan–Meier survival method and Cox proportional hazard analysis were performed. Of 358 elbow prostheses, PJI was identified in 27 (7.5%). The median patient age (range) was 61 (39–82) years; 63% were females. Seventeen patients (63%) had a rheumatic disorder and ten (37%) had osteoarthritis. Debridement and implant retention was performed in 78%, followed by exchange or removal of the prosthesis (15%) or no surgery (7%).The relapse-free survival (95% CI) was 79% (63–95%) after 1 year and 65% (45–85%) after 2 years. The outcome after 2 years was significantly better when patients were treated according to the algorithm compared to patients who were not (100% vs. 33%, p <0.05). In 21 patients treated with debridement and retention, the cure rate was also higher when the algorithm was followed (100% vs. 11%, p <0.05). The findings of the present study suggest that the treatment algorithm developed for hip and knee PJI can be applied to elbow PJI. With proper patient selection and antimicrobial therapy, debridement and retention of the elbow prosthesis is associated with good treatment outcome.

Keywords: Elbow arthroplasty, microbiology, periprosthetic joint infection, surgical intervention, treatment outcome
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Introduction

Elbow arthroplasty is increasingly used for treatment of post-traumatic arthritis and chronic inflammatory joint disease, such as rheumatic and psoriatic arthropathy [1]. After first successful implantation in the early 1970s [2], elbow prostheses underwent continuous refinements with respect to the implant design and surgical techniques. Currently, aseptic (mechanical) prosthesis loosening, joint instability, ulnar neuropathy and periprosthetic joint infection (PJI) remain a continuous challenge [1,3,4].

Data on elbow PJI are limited because only small case series were published, and non-uniform definitions and variable follow-up periods were used [5–10]. The incidence of elbow PJI is reported to be in the range 3–11%, which is higher than for hip or knee arthroplasties. Moreover, elbow joints have several distinctive differences, such as no weight-bearing function, and hence they seldom develop degenerative arthritis, and have scarce surrounding soft tissue with a higher risk for contiguous infection extending from tissue dehiscence [5].

The optimal surgical and antimicrobial treatment approach for elbow PJI has not yet been determined. Therefore, we investigated the characteristics and outcome of elbow PJI in a 14-year cohort of total elbow arthroplasties in a single centre. We specifically focused on the appropriateness of the

treatment algorithm, which was developed for hip and knee PJI [11]. In this algorithm, the type of surgical procedure (debridement and retention vs. a one or two stage exchange) and the antimicrobial therapy (type of antibiotic and duration) are defined by a combination of clinical, radiological and microbiological criteria.

Patients and Methods

Study population

The Schulthess Clinic is a specialized 160-bed orthopaedic centre and a reference institution for elbow surgery, including primary and revision arthroplasties. A total of approximately 7500 surgical procedures are performed annually. All elbow arthroplasties performed at the Schulthess Clinic, Zurich, Switzerland, are consecutively included in the elbow cohort. For the present study, all elbow prostheses implanted between January 1994 and December 2007 were retrospectively reviewed. All episodes, which fulfilled the predetermined criteria for PJI (below) were included. In patients with suggestive signs or symptoms for elbow PJI, at least one invasive diagnostic attempt to detect the potential pathogen was performed. The Infectious Diseases Service was consulted throughout the study duration. The study protocol was approved by the Institutional Review Board.

Definitions

Elbow PJI was diagnosed, if one or more of the following criteria were fulfilled: (i) visible purulence of a preoperative aspirate or intraoperative periprosthetic tissue (as determined by the surgeon); (ii) presence of a sinus tract communicating with the prosthesis; (iii) microbial growth in a preoperative joint aspirate, intraoperative periprosthetic tissue or sonication fluid of the removed implant; or (iv) synovial fluid with >1700 leukocytes/μL or >65% granulocytes, as determined in previous studies for knee PJI [12]. Similar diagnostic criteria for PJI were used in studies involving various types of joint prostheses [11,13–17]. Acute inflammation in periprosthetic tissue sections was not used as diagnostic criterion in the present study as a result of a high prevalence of underlying rheumatologic joint disorders, which may mimic infection. For low-virulent organisms, such as coagulase-negative staphylococci or Gram-positive anaerobes, growth of the same organism in at least two independent specimens was required.

According to the route of infection, episodes were classified as contiguous, perioperative or haematogenous [18]. Contiguous infection was determined if skin breakdown overlying the elbow prosthesis or preceding open trauma occurred. Perioperative infections were classified into early (within 3 months after surgery) or delayed (3–24 months). A haematogenous infection was diagnosed if blood cultures were positive with a distant source or haematogenous seeding was suspected by acute clinical presentation with fever, pain and redness of the elbow joint in late infections.

Microbiological diagnosis

Aspirated fluid and intraoperative periprosthetic tissue specimens were cultured on aerobic and anaerobic blood agar plates, and incubated at 35°C for 7 days (until July 2006) or for 10 days (after July 2006). In addition, thioglycollate broth was cultured for 10 days. Isolated microorganisms were identified and their antimicrobial susceptibility tested using standard microbiological techniques.

In addition, elbow prostheses explanted after January 2007 were sent for sonication to improve the detection of biofilm bacteria [15]. In brief, the explanted elbow prostheses was aseptically removed in the operating room and transported to the microbiology laboratory in air-tight polyethylene containers (Lock & Lock, Vetrag AG, Stäfa, Switzerland). In the microbiological laboratory, Ringer's solution was added in the containers and the prostheses were processed within 48 h of removal by vortexing (30 s) and sonication (1 min) using an ultrasound bath (BactoSonic, Bandelin GmbH, Berlin, Germany; http://www.bactosonic.info) at a frequency of 40 ± 2 kHz and a power density of 0.22 ± 0.04 W/cm^2. The resulting sonication fluid was vortexed again to homogenously distribute the sonication fluid, which was plated in aliquots of 0.1 mL onto aerobic and anaerobic sheep blood agar plates and 3 mL in 7 mL in thioglycollate broth. Cultures were incubated at 37°C for 7 days and inspected daily for bacterial growth.

Surgical treatment

The approach was individually determined at surgeon's discretion. In the case of PJI, the type of revision was chosen among three potential approaches: (i) debridement and implant retention; (ii) one-stage; or (iii) two-stage exchange of the implant. We retrospectively determined whether the surgeon's decision was in agreement with the treatment algorithm for hip and knee PJI [11]. According to this algorithm, the least invasive surgical treatment should be used, whereas retention of the implant is allowed only if all of the following four conditions were fulfilled: (i) short duration of infection, including early postoperative infection (within 3 months after surgery) or acute haematogenous infection; (ii) short duration of clinical signs (not longer than 21 days); (iii) not severely damaged surrounding soft tissue; and (iv) the availability of antimicrobial agents active against biofilms (e.g. rifampin for staphylococci and quinolones for Gram-neg-

ative rods). If one or more of these conditions were not fulfilled, retention of the implant was considered inappropriate and the implant needed to be exchanged. The exchange could be accomplished in one stage (in the case of intact soft tissue and the absence of difficult-to-treat organisms) or in two stages (in all other situations). Difficult-to-treat organisms included rifampin-resistant staphylococci, enterococci, nutritionally variant streptococci (*Abiotrophia* and *Granulicatella* spp.), quinolone-resistant Gram-negative rods and fungi.

Antimicrobial treatment

As for surgical treatment, we retrospectively determined whether the antimicrobial therapy was in agreement with the treatment algorithm [11]. The appropriateness of the antimicrobial regime was determined according to the type of organism, its susceptibility and the chosen surgical modality [11]. Antimicrobial treatment was considered appropriate, if an initial intravenous treatment was administered for initial 2 weeks, followed by oral treatment. The total duration of antimicrobial treatment was 3 months if the implant was retained or a two-stage exchange with short interval (2 weeks) was performed. In this case, a rifampin-combination regime was required for staphylococcal PJI. In case of two-stage exchange with long interval, antimicrobial treatment was administered for at least 6–8 weeks (rifampin was not required), followed by an antibiotic-free period of at least 2 weeks before reimplantation.

Outcome evaluation

Patients were evaluated regarding signs and symptoms of infection and functional outcome in the orthopaedic outpatient clinic during regularly scheduled visits at 3 months, 6 months, and 1, 2, 5 and 10 years after surgery. Only patients with at least 1 year of follow-up were evaluated in the present study. Follow-up evaluations included clinical examination, laboratory investigations and plain X-ray of the prosthetic elbow (at the discretion of the orthopaedic surgeon). In addition to orthopaedic follow-up, patients with elbow PJI were independently contacted by phone by one of investigators (Y.A.) and specifically interviewed for signs and symptoms of PJI, such as pain, redness or swelling.

Statistical analysis

The probability of relapse-free survival and the 95% CI was estimated using the Kaplan–Meier survival method. Cox proportional hazard analysis was used for comparison of relapse-free survivals of subgroups. Statistical calculations were performed with the SAS software package, version 8.2 (SAS Institute Inc., Cary, NC, USA) and graphic analysis was conducted using ORIGINPRO, version 8 (Origin Lab Corp., Northampton, MA, USA).

Results

Characteristics of 358 patients included in the elbow cohort

Underlying joint disorders were rheumatic disease in 203 episodes (57%) and osteoarthritis in 155 episodes (43%) (Table 1). At the time of implantation, no differences were observed regarding patient age, gender, underlying joint disorder or type of arthroplasty between patients who have developed elbow PJI and those which have not.

Characteristics of 27 patients with elbow PJI

Of 358 cases, 27 (7.5%) developed elbow PJI (median age at the time of infection was 61 years, range 39–82 years, 63% were females). In 24 of 27 cases (88%) a Gschwend–Scheier–Bähler III (GSB III) elbow prosthesis was implanted [19] (Table 2). The median time between the last surgical procedure of the elbow and time of infection was 6 months (range 0.6–162 months). The median time from primary implantation to time of infection was 45 months (range 0.6–183 months).

Microbiology

In the majority (26 of 27 patients), microbial growth was detected preoperatively and/or intraoperatively. In the one patient with negative cultures, sinus tract with purulent discharge was observed and intraoperatively abundant pus around the prosthesis was noted. Table 3 summarizes the causing microorganisms. In five patients, *S. aureus* was found as the cause of haematogenous infection. Microbiological

TABLE 1. Characteristics of 358 elbow prostheses at time of implantation, which were included in the elbow cohort

Characteristics	Value
Median age (range), years	60 (20–83)
Female gender	216 (60%)
Underlying joint disorder	
Rheumatic	203 (57%)
Rheumatoid arthritis	196
Psoriasis arthropathy	7
Osteoarthritis	155 (43%)
Post-traumatic arthritis	92
Primary osteoarthritis	13
Other	49
Type of arthroplasty	
Primary	262 (68%)
Revision[a]	96 (32%)

Values are given as *n* (%), if not indicated otherwise.
[a]Revisions not as a result of infection included a total exchange of the elbow prosthesis ($n = 76$), elongation of the ulnar component ($n = 15$) and partial exchange of the ulnar component ($n = 5$).

diagnosis was made by periprosthetic tissue biopsies in 18 (66%), intraoperative swabs in three (11%), synovial fluid in six (21%) and sonication fluid culture in one (4%).

Treatment strategy

Surgical treatment modalities are summarized in Table 2. In 78% of cases (n = 21), debridement and implant retention was performed; in four cases, the prosthesis was exchanged in one (n = 1) or two stages (n = 2), one prosthesis was resected (no reimplantation) and, in two cases, no surgery was performed (only antibiotics). Both patients with a two-stage exchange had an implant-free interval of 16 and 28 weeks, respectively; both received prolonged antimicrobial therapy for 3 months followed by an antibiotic-free interval prior to reimplantation. The medium duration of antimicrobial therapy was 3 months with a range of 0.5–16 months. Initially, intravenous therapy of at least 2 weeks was administered in 24 of 27 cases (89%). All patients received a combination therapy with rifampin, if staphylococci were isolated and the prosthesis was retained (Table 4).

TABLE 2. Characteristics of 27 episodes of elbow periprosthetic joint infection (PJI)

Characteristics	Number (%) of episodes
Median age (range), years	61 (39–82)
Female	17 (63%)
Underlying joint disorder	
Rheumatic	17 (63%)
Osteoarthritis	10 (37%)
Type of arthroplasty	
Primary	19 (70%)
Revision	8 (30%)
Type of elbow prosthesis	
GSB III	24 (88%)
Coonrad–Morrey	2 (7%)
Discovery	1 (4%)
Manifestation of PJI after last surgery	
Early (<3 months)	14 (48%)
Delayed (3–24 months)	3 (11%)
Late (>24 months)	11 (40%)
Route of infection	
Haematogenous	8 (30%)
Perioperative	16 (59%)
Contiguous[a]	3 (11%)
Surgical treatment	
Debridement with implant retention	21 (78%)
One-stage exchange	1 (4%)
Two-stage exchange[b]	2 (7%)
Resection arthroplasty	1 (4%)
No surgery (antibiotics only)	2 (7%)

GSB, Gschwend–Scheier–Bähler [19].
[a]Skin breakdown was present in the region overlying the prosthesis.
[b]Both patients with a two-stage exchange had an implant-free interval of 16 and 28 weeks, respectively.

TABLE 3. Microbiology of 27 episodes of elbow periprosthetic joint infection

Microbiological characteristics	Number (%) of episodes
Single microorganism	
Staphylococcus aureus[a]	11 (41%)
Coagulase-negative staphylococci[b]	9 (33%)
Streptococcus agalactiae	2 (7%)
Enterobacter cloacae	1 (3.7%)
Corynebacterium pseudodiphtheriticum	1 (3.7%)
Polymicrobial[c]	2 (7%)
No organism	1 (3.7%)

Percentages are rounded and may not add up to 100%.
[a]No methicillin-resistance was observed in *S. aureus*.
[b]*Staphylococcus epidermidis* (n = 6), *Staphylococcus capitis* (n = 2), *Staphylococcus caprae* (n = 1). Methicillin-resistance was observed in eight of 11 (73%) isolates of coagulase-negative staphylococci (including those from polymicrobial infections).
[c]Methicillin-resistant *S. epidermidis* and *E. cloacae* in one episode; methicillin-resistant *S. epidermidis* and *S. aureus* (methicillin-susceptible) in one episode.

Outcome evaluation

At follow-up, 19 (70%) patients were free of infection (median follow-up time 2.7 years, range 1.0–11.3 years) and eight (30%) had a relapse (median time to relapse 0.56 years,

TABLE 4. Intravenous and oral antimicrobial treatment of 27 episodes of elbow periprosthetic joint infection

Intravenous antimicrobial treatment		Oral antimicrobial treatment	
Antibiotic (s)	Number of cases	Antibiotic (s)	Number of cases
Amoxicillin-clavulanate/rifampin	7	Ciprofloxacin/rifampin	14
Flucloxacillin/rifampin	8	Levofloxacin/rifampin	4
Vancomycin/rifampin	6	Linezolid	1
Vancomycin/impenem/rifampin	1	Amoxicillin	2
Imipenem/rifampin	1	Fucidin/rifampin	1
Teicoplanin	1	Ciprofloxacin	1
		Amoxicillin-clavulanate/rifampin	1
No intravenous therapy	3	No oral therapy	3

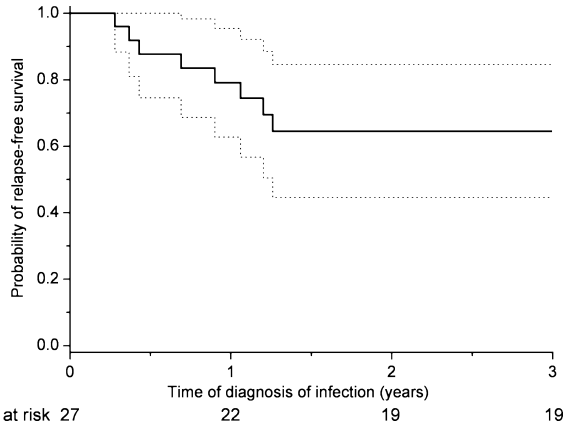

FIG. 1. Relapse-free survival of 27 elbow periprosthetic joint infection. The dotted lines represent the 95% CI. The relapse-free survival (95% CI) was 79% (63–95%) after 1 year and 65% (45–85%) after 2 years.

range 0.1–1.3 years. Fig. 1 shows a relapse-free survival of elbow PJI, which was 79% (95% CI 63–95%) after 1 year and 65% (95% CI 45–85%) after 2 years. Among 21 patients treated with debridement and retention, 13 cases (62%) were free of infection and eight cases (38%) experienced a relapse of the infection. Overall, five of 27 (19%) patients with PJI died; one patient due to infectious endocarditis with secondary haematogenous elbow PJI, two due to sepsis of the hip or knee PJI and two for non-infectious reasons.

Patients without a relapse of infection were interviewed regarding functional outcome in January 2009. The majority of patients (13 of 19; 68%) were satisfied with the function of the elbow prosthesis and did not report any local inflammatory symptoms. Two patients complained about diminished muscle strength and one patient reported persistent joint effusion; all three were without suspicion of elbow PJI.

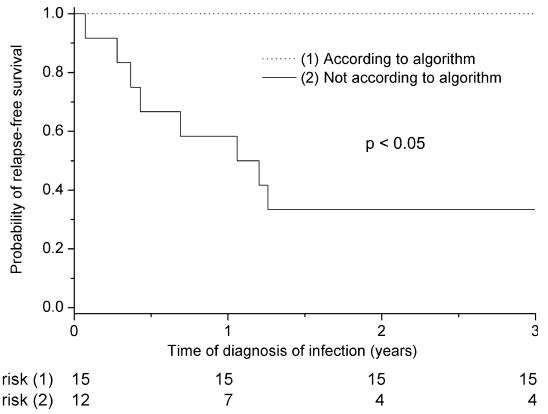

FIG. 2. Relapse-free survival of elbow periprosthetic joint infection stratified if treated (n = 15) or not (n = 12) according to the treatment algorithm. The outcome after 2 years was significantly better when treated according to the algorithm than in patients who were not (100% vs. 33%, p <0.05).

Evaluation of the treatment outcome with respect to the treatment algorithm

If the treatment algorithm was followed (in 15 episodes), the relapse-free survival was 100%. By contrast, if the algorithm was not followed (in 12 episodes), the relapse-free survival was 58% after 1 year and 33% after 2 years (Fig. 2) (p <0.05). In 21 patients treated with debridement and retention, the cure rate was higher when the algorithm was followed (12 of 12 cases; 100%) than in patients where the algorithm was not followed (one of nine; 11%) (p <0.05).

In all eight patients with infection relapse, either antimicrobial therapy or surgical procedure (or both) was not in accordance with the recommended algorithm (Table 5). In patients with an infection relapse, debridement and implant retention was performed instead of two-stage exchange (two patients with delayed, three with late contiguous infection and one patient with early infection but duration of symptoms of more than 3 weeks). Moreover, a shorter then suggested antimicrobial treatment duration was used (2 months instead 3 months) in episodes with debridement and retention or the patient prematurely discontinued the antibiotic therapy.

Discussion

No standard surgical and antimicrobial treatment standard approach exists for elbow PJI. Therefore, we retrospectively investigated elbow PJI in a cohort of 358 elbow arthroplasty during a 14-year-period in a single institution. The infection rate of elbow PJI was 7.5%. This is comparable to the rates reported by Morrey *et al.* [8] (9%), Wolfe *et al.* [9] (7.3%) and Schmidt *et al.* [4] (10.3%), and is higher than that reported by Yamaguchi *et al.* [7] (3.2%) and Gille *et al.*

TABLE 5. Elbow periprosthetic joint infection (PJI) with relapse of infection: differences between recommended and performed antimicrobial and surgical procedure

Number	Type of infection[a]	Infecting organism initially	Infecting organism at relapse	Recommended procedure	Performed procedure
1	Early (2 months)	*Staphylococcus aureus*	*S. aureus*	AB 3 months	AB 2 months
2	Early (1 months)	*Staphylococcus agalactiae*	*S. agalactiae*	AB 3 months	Noncompliance for AB
3	Early, symptoms >3 weeks, soft tissue-compromised	CNS, *Enterobacter cloacae*	*E. cloacae*	2-stage exchange	Debridement and retention
4	Delayed (6 months)	CNS	CNS	3 months	Retention, AB 2 months
5	Delayed (8 months)	*E. cloacae*	Mixed (*E. cloacae*, CNS)	2-stage exchange, AB 3 months	Retention, AB 1 months
6	Late contiguous (8.7 years)	CNS	CNS	2-stage exchange	Retention
7	Late contiguous (9 years)	CNS	Mixed (CNS, *Micrococcus* spp.)	2-stage exchange	Retention
8	Late contiguous (4.2 years)	CNS	CNS	2-stage exchange	Retention, no intravenous therapy

CNS, coagulase-negative staphylococci; AB, antibiotics.
[a]Time (in parenthesis) denotes the duration between elbow implantation and the manifestation of elbow PJI.

(1.9%) [6]. The higher infection rates in elbow arthroplasty compared to hip (<1%) and knee prostheses (<2%) may be due to several reasons. First, the main reason for a hip or knee arthroplasty is the degenerative osteoarthritis, whereas, in elbow arthroplasties, the main underlying disorder is rheumatic or post-traumatic osteoarthritis. Rheumatic disorders are associated with a higher risk for infection as a result of chronic inflammatory progress and immunosuppressive treatment [5,6,20]. Second, the subcutaneous placement and lack of muscle coverage of the elbow prosthesis provides little protection against contiguous infection after bursitis or skin breakdown. Third, soft tissue is more vulnerable and prone to infections in patients with post-traumatic or rheumatologic arthritis than in healthy individuals [4]. And last, multiple reconstructive procedures prior to elbow arthroplasty for posttraumatic osteoarthritis are associated with a higher risk of infection.

In the present study, the most frequently isolated pathogen was *S. aureus* (41%) followed by coagulase-negative staphylococci (33%), which is in accordance with other studies [6,7,9,10]. Interestingly, no *Propionibacterium acnes* was isolated despite the optimized diagnostic procedure. We speculate that lower density of sweat glands at the elbow region compared to shoulder may explain this difference [21,22].

The relapse-free-survival in the present study was 65% at 2 years. All eight relapses occurred within 15 months of antibiotic treatment. Furthermore, the cure rate at 2 years was only 33% when the algorithm was not followed compared to 100% when the treatment was in agreement of the algorithm ($p < 0.05$). This observation is important because the algorithm was developed for treatment of hip and knee PJI and has never been evaluated in patients with elbow PJI. Patients with elbow arthroplasty might represent a unique population as a result of technical challenges in revision surgery and the underlying comorbidity. The results are especially important in patients treated with debridement and retention of the prosthesis, in whom the cure rate was also significantly higher when the algorithm was followed than in patients where the algorithm was not followed (100% vs. 11%, $p < 0.05$).

The algorithm was developed on the basis of studies performed *in vitro*, animal models of foreign body infections [23,24] and clinical studies [25,26]. The cure rate in other studies following the algorithm was 94.3% after knee arthroplasty [27], 83% [28] and 91% [29] after hip arthroplasty, and 100% in a population with different orthopaedic devices [26]. However, when the algorithm was not followed, the cure rates were significantly lower, in the range 57–60% [27,30]. The most common deviations from the proposed algorithm were the improper selection of patients for implant retention (e.g. loose implants in delayed infections) or a lack of use of rifampin-containing regimens in staphylococcal PJI (7–9). Rifampin is an essential factor for the eradication of staphylococcal biofilms when prosthesis retention is attempted or a two-stage exchange with a short interval is used.

A strength of the present study is the systematic analysis of a cohort of 358 elbow arthroplasties in a single centre with four dedicated elbow surgeons using similar surgical techniques and postoperative management. Limitations are the retrospective design and the low number of patients with a relapse of infection, which does not allow risk factor analysis. Nevertheless, the present study suggests a high probability of long-term success if the treatment algorithm is followed. This finding needs to be confirmed in larger cohorts with a longer follow-up period.

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Transparency Declaration

None reported. No conflicts of interests.

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