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Hip and Knee

2025 ICM: Use of Antibiotic-Impregnated Polymethyl Methacrylate Cement

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Question 1: Does the use of antibiotic-impregnated polymethyl methacrylate cement reduce the incidence of infection in patients undergoing primary joint arthroplasty?[1]

Response/Recommendation

The evidence among low-level comparative studies is mixed, with some studies suggesting that antibiotic-impregnated cement reduces the risk of infection in patients undergoing primary joint arthroplasty. However, pooling of the available Level 1 evidence, as well as pooled registry data, does not support a reduction in infection risk in primary total joint arthroplasty.

Level of Evidence: Moderate

Delegate Vote: Agree 75.5%, Disagree 18.5%, Abstain 6.0% (Strong Majority, Moderate Consensus)

Rationale

A total of 32 comparative studies were identified and published between 1990 and 2024 across 21 different countries [1–31]. Nearly five million patients were included in total (4,943,801 joints in 4,943,768 patients). Of the studies reporting sex distribution, 37.3% were women. There were six randomized controlled trials (RCTs), one prospective cohort study, 22 retrospective cohort studies, one case-control study, and one economic Markov model analysis. There was one study that was a long-term follow-up of an earlier published RCT [8].

The majority of studies included only total knee arthroplasty (TKA) cases, while six studies included hip arthroplasty cases. Data from four RCTs comparing antibiotic-loaded bone cement (ALBC) versus plain cement in primary TKA revealed no significant difference in infection rates between the ALBC group and the plain cement group.

The evidence among low-level comparative studies was mixed. There were 12 studies that demonstrated no significant difference between ALBC and plain cement in primary hip and knee arthroplasties [3,12,15,18–21,23–25,28,29], while seven studies demonstrated a significant reduction in infection rates with the use of ALBC [10,11,14,16,17,22,31]. Only one study found an increased risk of infection with the use of ALBC [27].

It is worth highlighting the findings from various registries and large database studies as well. A report utilizing data from the United Kingdom's National Joint Registry [17], as well as one from a large national insurance registry in the United States [10], found significant benefits in terms of infection prevention with the use of ALBC. However, three other registry-based studies did not find a difference between ALBC and plain cement [12,19,23]. Importantly, one of these studies combined data from 14 different high-quality national or regional arthroplasty registries, with a sample size of over two million TKA patients [23].

The evidence regarding the economics of antibiotic-impregnated cement is also mixed. Of the two studies evaluating the economics of routine ALBC use, one found that routine antibiotic cement use was not cost-effective [26], while the other found that it was only potentially cost-effective if the antibiotics were added by the surgeon rather than commercially available premixes [27].

Overall, there is a lack of evidence to support the routine use of ALBC in primary total joint arthroplasty. Data for total hip arthroplasty are relatively limited, while there are more studies available on total knee arthroplasty, including some high-quality RCT and registry data. The overall conclusion, whether based on pooling of data or an overall qualitative synthesis of the available literature, does not provide convincing evidence of the efficacy of ALBC in preventing infection in primary total hip and knee arthroplasties. The caveat that must be kept in mind is that with

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the overall rarity of prosthetic joint infection and the very large sample sizes required to answer this question directly (i.e., via RCT); many studies are likely underpowered to definitively answer the question.

Question 2: Does the use of antibiotic-impregnated polymethyl methacrylate cement reduce the incidence of infection in patients undergoing aseptic revision arthroplasty?[2]

Response/Recommendation

Based on available low-level data, the use of antibiotic-impregnated PMMA cement in aseptic revision arthroplasty leads to a clinically relevant reduction in the risk of postoperative infection, regardless of whether a single or dual antibiotic-loaded cement is used.

Level of Evidence: Moderate

Delegate Vote: Agree 73%, Disagree 24.3%, Abstain 2.7% (Strong Majority, Moderate Consensus)

Rationale

Primary total joint arthroplasty (pTJA) has achieved great success in patients who have arthrosis, leading to major improvements in daily quality of life as well as functional abilities. This has rendered pTJA the most commonly performed orthopaedic surgical procedure, with the increasing number of patients undergoing pTJA over time [32–34]. As a result, there has been a marked increase in the number of revision total joint arthroplasties (rTJA), wherein projections for the near future foresee more than a 100% increase in the number of rTJAs performed [35,36].

Although the literature provides varying rates, one of the most common causes of rTJA is aseptic implant loosening [37,38]. Moreover, despite all the preventive and protective measures, periprosthetic joint infection (PJI) remains a major risk during rTJA performed for aseptic reasons [39,40], with a higher incidence rate (3 to 7.5%) compared to primary PJI [41,42].

The concept of antibiotic-loaded polymethyl methacrylate (AL-PMMA) was first introduced in the literature following a scientific study in 1977 [43] and has since been widely studied, particularly for its role in preventing and mitigating the risk of prosthetic and bone infections. It is widely used, particularly in infected rTJA cases. However, the current literature does not provide evidence that clearly supports the use of AL-PPMA for reducing the risk of pTJA PJI or lowering early revision rates [44–47]. Moreover, the impact of using AL-PMMA on the risk of PJI in aseptic rTJA is still a subject of ongoing debate.

The first study that provided important data on this topic is a retrospective study of 1,154 patients undergoing aseptic revision TKA (rTKA) conducted by Bini et al. in 2015 [48]. Overall, 114 (10%) of the 1,154 patients underwent re-revision within a mean period of 3.6 years, and 30% of these re-revisions were performed for an infection (34 of 114). In the study, AL-PMMA was used in 308 of the 1,154 patients undergoing aseptic rTKA, wherein only 12% (n = 14) of these patients required re-revision during follow-up. This study shows that the use of AL-PMMA was linked to a 50% reduction in the risk of all-cause re-revision.

Another relevant study is the AL-PMMA review conducted by Gandhi et al. in 2018 [49]. The study included both pTJA and rTJA cases and reported that the routine use of AL-PMMA in aseptic revision TJA could be regarded as the standard of care, offering advantages in terms of infection rates and all-cause re-revision. In routine practice, aminoglycosides (gentamicin or tobramycin) were preferred for inclusion in cement, whereas vancomycin or daptomycin can also be added in case of clinical requirement, although this may have a negative impact on the strength of cement [50,51].

In a study by Abdelaziz et al., conducted with 32 patients in 2019, a combination of clindamycin and gentamicin was added to PMMA, wherein 18 patients constituted the PJI group and 14 patients constituted the aseptic rTJA group during a 5-year follow-up [52]. At the end of follow-up, none of the patients had required re-revision, and the PMMA loaded with the antibiotic combination had achieved a high level of success in infection prevention and eradication in septic and aseptic rTJA cases. In another study published by Sanz-Ruiz et al. in 2020, the effects of AL-PMMA combinations on PJI were compared in a case series of 246 patients who underwent aseptic rTKA, wherein 143 patients received low-dose single AL-PMMA (PALACOS R plus G, gentamicin 0.5 g (g)), and the remaining 103 patients received high-dose dual AL-PMMA (COPAL G plus C, gentamicin one g plus clindamycin one g) [53]. The patients were evaluated after a minimum follow-up of one year, and it was found that the use of dual AL-PMMA was more effective in PJI prevention in rTKA while also demonstrating a cost-effective profile in all cost calculation models used.

Another recent study on this topic was conducted by Blersch et al. in 2023 with 403 patients who underwent aseptic rTKA with dual AL-PMMA. The patients were retrospectively analyzed with a minimum follow-up of 5 years [54]. There were five patients (1.24%) who were diagnosed with PJI (one acute, four chronic) and underwent re-revision. In conclusion, 98.2% of patients who underwent aseptic rTKA with dual AL-PMMA (Copal G and C) exhibited PJI-free survival throughout the 5-year follow-up.

In an article published by Bos et al. in 2023, data from the Dutch Arthroplasty Register were used to analyze 2,529 patients who underwent aseptic revision total hip arthroplasty (rTHA) and 7,124 patients who underwent aseptic rTKA between 2007 and 2018 in terms of single or dual AL-PMMA use [55]. Among patients who underwent rTHA, single AL-PMMA was used in 1,669 patients, 53 of whom required re-revision for PJI. In addition, dual AL-PMMA was used in 860 patients, wherein 24 patients also required re-revision for PJI. Considering the patients who underwent rTKA, single AL-PMMA was used in 5,270 and dual AL-PMMA in 1,854 patients, 97 and 46 of whom needed re-revision due to PJI, respectively. From the statistical point of view, single or dual AL-PMMA was not found to be superior to one another in rTJA practices.

According to a study by Hamoudi et al. carried out in 2024, 290 patients who underwent aseptic rTJA were evaluated in terms of PJI risk, wherein 145 patients received single and 145 patients received dual AL-PMMA [56]. Overall, 24-month follow-up results revealed no statistical superiority between single and dual AL-PMMA in terms of PJI in aseptic rTJA.

Conclusions

Most of the reviewed studies show that the use of AL-PMMA leads to a statistically and clinically relevant reduction in postoperative PJI risk in patients undergoing aseptic rTJA. This is also supported by a study found in the national registry involving nearly 10,000 patients. There were two recent studies indicated that the use of single and dual AL-PMMA was comparable in terms of their impact on PJI prevention in aseptic rTJA, wherein both led to a decreased risk of PJI. However, all studies have a retrospective design. Therefore, conducting prospective studies on this topic is a scientific necessity. Based on available data, the use of AL-PMMA is recommended to minimize the risk of PJI in aseptic rTJA cases, regardless of whether single or dual AL-PMMA is used.

[2] These authors contributed to Question 2: Mustafa Akkaya, Cheng-Fong Chen, Jean-Yves Jenny, Stergios Lazarinis, Pablo Sanz-Ruiz, Julian Costantini, Khalil Amri, Ismet Gavrankapetanović, Matteo Innocenti

Question 3: Does the use of antibiotic-impregnated polymethyl methacrylate cement reduce the incidence of infection in patients undergoing reimplantation for periprosthetic joint infection?[3]

Response/Recommendation

Unknown. While some studies have reported high success with the use of antibiotic-impregnated polymethyl methacrylate (PMMA) cement in reimplantation, others show limited infection control. In addition, the use of uncemented implants during reimplantation has also demonstrated favorable outcomes.

Level of Evidence: Moderate

Delegate Vote: Agree 73.7%, Disagree 20.5%, Abstain 5.8% (Strong Majority, Moderate Consensus)

Rationale

The use of antibiotic-impregnated polymethyl methacrylate (PMMA) cement in reimplantation for PJI has been proposed as an adjunctive strategy for local antibiotic delivery, aiming to enhance infection eradication while minimizing systemic toxicity [57]. However, the concentration of antibiotics such as vancomycin, gentamicin, tobramycin, or erythromycin in antibiotic-loaded bone cement (ALBC) may not reach and remain at the minimum inhibitory concentration (MIC) and the minimum biofilm eradication concentration (MBEC) over a prolonged period [58]. This raises questions about whether the use of antibiotic-impregnated PMMA cement effectively reduces the incidence of infection in patients undergoing reimplantation for PJI.

To answer the question posed above, a comprehensive systematic review was conducted with inclusion criteria restricted to English-language original articles reporting prospective or retrospective clinical studies on patients who underwent single- or two-stage rTJA for PJI. The review included studies evaluating the use of ALBC or no ALBC in rTKA and cementless or cemented techniques with or without ALBC in revision THA). A comprehensive literature search of the PubMed and Scopus databases yielded 813 abstracts. After the initial screening, 74 studies were selected for full-text review, and 25 were included in the final evaluation. The total number of patients across all included studies was 2,192. There were 15 studies that focused on two-stage revision [59–73], eight studies examined single-stage revision [74–81], and the remaining two studies reported on both single- and two-stage revisions [82,83]. Most two-stage revisions utilized antibiotic cement spacers or beads between stages [59–73,82]. An ALBC was used during reimplantation in 13 studies, covering 990 patients. In contrast, another 14 studies, including two that assessed both ALBC and non-ALBC patients, reported 1,202 patients who did not receive ALBC during reimplantation.

The infection control rate, defined as a successful revision of TJA without recurrence or new infection in patients who received antibiotic-impregnated PMMA cement during reimplantation, ranged from 75 to 100%, with an average follow-up duration from 22.3 months to 10.5 years [67,80]. Hsieh et al. [66] reported on 24 patients who underwent two-stage revision THA for PJI with massive bone loss. They used a cemented polyethylene cup within a metal cage for patients who have acetabular deficiencies and a cemented allograft prosthesis composite for those who have segmental femoral bone loss. Their ALBC protocol during reimplantation involved adding two grams of antibiotics (mostly vancomycin) per 40 grams pack of cement. After a follow-up period of 4.2 years (range, two to seven), no patients experienced recurrent infection. However, two cases of fractures of the cement femoral stem and one case of dislocation occurred, though these complications were unrelated to infection. Another study by Kuo et al. [69] investigated 10 knee and 12 hip PJI cases caused by methicillin-resistant *Staphylococci*. They performed two-stage revisions using one gram of daptomycin per 40 grams pack of bone cement during reimplantation in the second stage. Their treatment protocol achieved a 100% success rate, with no recurrence of infection during a mean follow-up of 33.7 months (range, 24 to 57). However, a study by Leijtens et al. [71] reported an unsatisfactory success rate in 10 patients who had a late infection of a cemented THA treated with two-stage revision while retaining the original well-fixed femoral cement mantle. During the second-stage revision, they implanted a cemented polyethylene cup on the acetabular side and performed a cement-within-cement revision on the femoral side. The ALBC consisted of bone cement mixed with 500 mg of erythromycin and 3,000,000 international units of colistin. After a mean follow-up of 26 months (range, five to 54), the primary microorganism was successfully eradicated in only two patients (20%).

In studies that did not use antibiotic-impregnated PMMA cement during reimplantation, whether in cemented revision THA or TKA or cementless revision THA, the success rate without reinfection ranged from 83 to 100%. The mean follow-up duration for these patients varied between 35 months and 10.4 years [64,68]. There were four studies that reported a 100% success rate with no relapse or new episodes of infection. Born et al. [82] found that all 21 single-stage revision THAs with a cementless stem had no infection failure over a mean follow-up of seven years. Another three studies performed a two-stage revision THA using a cementless prosthesis during the second-stage revision and found no reinfection following surgical intervention [64,72,73]. Similarly, several other studies reported high infection control rates despite not using antibiotic-impregnated PMMA cement [59–61,65,68,74,76,77,80].

While antibiotics in cement may help protect the implant-bone interface during the early postoperative period, infection eradication and successful treatment appear to depend more on meticulous surgical debridement, optimized systemic antibiotic therapy, and the host immune response.

[3] These authors contributed to Question 3: Atthakorn Jarusriwanna, Frank Buttacavoli, Wei Chai MD, Keerati Chareancholvanich, Michael Dunbar, Sérgio Gonçalves, André Grenho, Ianiv Klaber, Aasis Unnanuntana

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