

HK7: Does the use of antibiotic-impregnated polymethylmethacrylate (PMMA) cement reduce the incidence of infection in patients undergoing aseptic revision arthroplasty?

Mustafa Akkaya, Cheng-Fong Chen, Jean-Yves Jenny, Stergios Lazarinis, Pablo Sanz-Ruiz, Julian Costantini, Khalil Amri, Ismet Gavrankapetanović, Matteo Innocenti

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:

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 [1-3]. 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 [4,5].

Although the literature provides varying rates, one of the most common causes of rTJA is aseptic implant loosening [6,7]. Moreover, despite all the preventive and protective measures, periprosthetic joint infection (PJI) remains a major risk during rTJA performed for aseptic reasons [8,9], with a higher incidence rate (3 to 7.5%) compared to primary PJI [10,11].

The concept of antibiotic-loaded PMMA (AL-PMMA) was first introduced in the literature following a scientific study in 1977 [12] 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 [13-16]. 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 total knee arthroplasty (rTKA) conducted by Bini et al. in 2015 [17]. 114 (10%) of the 1,154 patients underwent re-revision within a mean period of 3.6 years. 30% of these re-revisions were performed for an infection (n: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 [18]. 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 [19,20].

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 [21]. 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 + G, gentamicin 0.5 grams (g)) and the remaining 103 patients received high-dose dual AL-PMMA (COPAL G + C, gentamicin one g + clindamycin one g) [22]. 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 five years [23]. 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 + 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 was used to analyze 2,529 patients who underwent aseptic rTHA and 7,124 patients who underwent aseptic rTKA between 2007 to 2018 in terms of single or dual AL-PMMA use [24]. 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 were 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 [25]. 24-month follow-up results revealed no statistical superiority between single or dual AL-PMMA in terms of PJI in aseptic rTJA.

Conclusion

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 a total of nearly 10,000 patients. There were two recent studies that 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.

References

1. Singh, J.A.; Yu, S.; Chen, L.; Cleveland, J.D. Rates of Total Joint Replacement in the United States: Future Projections to 2020-2040 Using the National Inpatient Sample. *J Rheumatol* **2019**, *46*, 1134-1140, doi:10.3899/jrheum.170990.
2. Sloan, M.; Premkumar, A.; Sheth, N.P. Projected Volume of Primary Total Joint Arthroplasty in the U.S., 2014 to 2030. *J Bone Joint Surg Am* **2018**, *100*, 1455-1460, doi:10.2106/JBJS.17.01617.
3. Shichman, I.; Roof, M.; Askew, N.; Nherera, L.; Rozell, J.C.; Seyler, T.M.; Schwarzkopf, R. Projections and Epidemiology of Primary Hip and Knee Arthroplasty in Medicare Patients to 2040-2060. *JB JS Open Access* **2023**, *8*, doi:10.2106/JBJS.OA.22.00112.
4. Kurtz, S.; Ong, K.; Lau, E.; Mowat, F.; Halpern, M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* **2007**, *89*, 780-785, doi:10.2106/JBJS.F.00222.
5. Shichman, I.; Askew, N.; Habibi, A.; Nherera, L.; Macaulay, W.; Seyler, T.; Schwarzkopf, R. Projections and Epidemiology of Revision Hip and Knee Arthroplasty in the United States to 2040-2060. *Arthroplast Today* **2023**, *21*, 101152, doi:10.1016/j.artd.2023.101152.
6. Jones, C.M.; Acuna, A.J.; Jan, K.; Forlenza, E.M.; Della Valle, C.J. Trends and Epidemiology in Revision Total Hip Arthroplasty: A Large Database Study. *J Arthroplasty* **2025**, doi:10.1016/j.arth.2025.01.011.
7. Jones, C.M.; Acuna, A.J.; Forlenza, E.M.; Serino, J., 3rd; Della Valle, C.J. Trends and Epidemiology in Revision Total Knee Arthroplasty: A Large Database Study. *J Arthroplasty* **2024**, doi:10.1016/j.arth.2024.11.051.
8. Bornes, T.D.; Puri, S.; Neitzke, C.C.; Chandi, S.K.; Gausden, E.B.; Sculco, P.K.; Chalmers, B.P. High Rates of Early Septic Failure, but Low Rates of Aseptic Loosening After Revision Total Knee Arthroplasty With Contemporary Rotating-Hinge Prostheses. *J Arthroplasty* **2025**, *40*, 460-466 e461, doi:10.1016/j.arth.2024.08.013.
9. Rodriguez-Merchan, E.C. Re-revision Total Knee Arthroplasty: Causes, Risk Factors and Results. *Arch Bone Jt Surg* **2024**, *12*, 328-332, doi:10.22038/ABJS.2024.75456.3490.
10. Zingg, M.; Kheir, M.M.; Ziemba-Davis, M.; Meneghini, R.M. Reduced Infection Rate After Aseptic Revision Total Knee Arthroplasty With Extended Oral Antibiotic Protocol. *J Arthroplasty* **2022**, *37*, 905-909, doi:10.1016/j.arth.2022.01.040.
11. Quinlan, N.D.; Werner, B.C.; Brown, T.E.; Browne, J.A. Risk of Prosthetic Joint Infection Increases Following Early Aseptic Revision Surgery of Total Hip and Knee Arthroplasty. *J Arthroplasty* **2020**, *35*, 3661-3667, doi:10.1016/j.arth.2020.06.089.
12. Ger, E.; Dall, D.; Miles, T.; Forder, A. Bone cement and antibiotics. *S Afr Med J* **1977**, *51*, 276-279.
13. Leta, T.H.; Lie, S.A.; Fenstad, A.M.; Lygre, S.H.L.; Lindberg-Larsen, M.; Pedersen, A.B.; A, W.D.; Rolfson, O.; Bulow, E.; van Steenberg, L.N.; et al. Periprosthetic Joint Infection After Total Knee Arthroplasty With or Without Antibiotic Bone Cement. *JAMA Netw Open* **2024**, *7*, e2412898, doi:10.1001/jamanetworkopen.2024.12898.
14. Engesaeter, L.B.; Lie, S.A.; Espehaug, B.; Furnes, O.; Vollset, S.E.; Havelin, L.I. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements

- followed 0-14 years in the Norwegian Arthroplasty Register. *Acta Orthop Scand* **2003**, 74, 644-651, doi:10.1080/00016470310018135.
15. Dunbar, M.J. Antibiotic bone cements: their use in routine primary total joint arthroplasty is justified. *Orthopedics* **2009**, 32, doi:10.3928/01477447-20090728-20.
 16. Bohm, E.; Zhu, N.; Gu, J.; de Guia, N.; Linton, C.; Anderson, T.; Paton, D.; Dunbar, M. Does adding antibiotics to cement reduce the need for early revision in total knee arthroplasty? *Clin Orthop Relat Res* **2014**, 472, 162-168, doi:10.1007/s11999-013-3186-1.
 17. Bini, S.A.; Chan, P.H.; Inacio, M.C.S.; Paxton, E.W.; Khatod, M. Antibiotic cement was associated with half the risk of re-revision in 1,154 aseptic revision total knee arthroplasties. *Acta Orthopaedica* **2015**, 87, 55-59, doi:10.3109/17453674.2015.1103568.
 18. Gandhi, R.; Backstein, D.; Zywielski, M.G. Antibiotic-laden Bone Cement in Primary and Revision Hip and Knee Arthroplasty. *Journal of the American Academy of Orthopaedic Surgeons* **2018**, 26, 727-734, doi:10.5435/jaaos-d-17-00305.
 19. Lewis, G.; Brooks, J.L.; Courtney, H.S.; Li, Y.; Haggard, W.O. An Approach for Determining Antibiotic Loading for a Physician-directed Antibiotic-loaded PMMA Bone Cement Formulation. *Clinical Orthopaedics & Related Research* **2010**, 468, 2092-2100, doi:10.1007/s11999-010-1281-0.
 20. Duey, R.E.; Chong, A.C.; McQueen, D.A.; Womack, J.L.; Song, Z.; Steinberger, T.A.; Wooley, P.H. Mechanical properties and elution characteristics of polymethylmethacrylate bone cement impregnated with antibiotics for various surface area and volume constructs. *Iowa Orthop J* **2012**, 32, 104-115.
 21. Abdelaziz, H.; von Forster, G.; Kuhn, K.D.; Gehrke, T.; Citak, M. Minimum 5 years' follow-up after gentamicin- and clindamycin-loaded PMMA cement in total joint arthroplasty. *J Med Microbiol* **2019**, 68, 475-479, doi:10.1099/jmm.0.000895.
 22. Sanz-Ruiz, P.; Matas-Diez, J.A.; Villanueva-Martinez, M.; Santos-Vaquinha Blanco, A.D.; Vaquero, J. Is Dual Antibiotic-Loaded Bone Cement More Effective and Cost-Efficient Than a Single Antibiotic-Loaded Bone Cement to Reduce the Risk of Prosthetic Joint Infection in Aseptic Revision Knee Arthroplasty? *J Arthroplasty* **2020**, 35, 3724-3729, doi:10.1016/j.arth.2020.06.045.
 23. Bliersch, B.P.; Barthels, M.; Schuster, P.; Fink, B. A Low Rate of Periprosthetic Infections after Aseptic Knee Prosthesis Revision Using Dual-Antibiotic-Impregnated Bone Cement. *Antibiotics (Basel)* **2023**, 12, doi:10.3390/antibiotics12091368.
 24. Bos, P.K.; Spekenbrink-Spooren, A.; Croughs, P.; Bierma-Zeinstra, S.M.A.; Reijman, M.; Van Oldenrijk, J. Risk for re-revision and type of antibiotic-loaded bone cement in hip or knee arthroplasty revisions: report of the Dutch Arthroplasty Register. *Acta Orthop* **2023**, 94, 471-476, doi:10.2340/17453674.2023.18645.
 25. Hamoudi, C.; Hamon, M.; Reiter-Schatz, A.; Debordes, P.A.; Gaudias, J.; Ronde-Oustau, C.; Jenny, J.Y. Cement loaded with high-dose gentamicin and clindamycin does not reduce the risk of subsequent infection after aseptic total hip or knee revision arthroplasty: a preliminary study. *J Orthop Traumatol* **2024**, 25, 37, doi:10.1186/s10195-024-00775-1.