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Looking to the Future: Vitamin E Infused Highly Cross-Linked Polyethylene Acetabular Cups

Sarah Sutter Kaufmann, PA-S and Melissa Hango, PA-S

ABSTRACT

Objective: To compare literature investigating the efficacy of vitamin E infused highly cross-linked acetabular cups versus cross-linked polyethylene cups without Vitamin E with the goal of determining whether this intervention can be used to extend the lifespan of implants used in total hip arthroplasty (THA). **Introduction:** THA has become a routine surgical procedure, with an estimated 1 million Americans undergoing either a total hip or knee arthroplasty each year.¹ However, the longevity of implants is variable, ranging from 15-25 years.² Therefore, researchers are working to improve the lifespan of the implants to reduce the need for subsequent THAs in patients that have already undergone one THA. Recent studies have investigated the use of vitamin E in highly cross-linked polyethylene cups to reduce oxidation of the acetabular cup prosthesis without compromising its strength or wear. **Design:** Systematic literature review. **Methods:** Literature search was performed in PubMed utilizing the MeSH terms "Polyethylene," "Vitamin E," and "Arthroplasty, Replacement, Hip." The following limits were used: 5-year follow up post-operatively, human subjects, randomized control trials, use of uncemented cross-linked polyethylene cups, and English. **Results:** Our systematic literature review resulted in three articles that met our inclusion and exclusion criteria. All three studies showed a significant decrease in femoral head penetration in the vitamin E infused acetabular group when compared to use of cups without vitamin E³⁻⁵, and Nebergall et al³ specifically demonstrated non-inferiority of the vitamin E infused liners. **Conclusion:** Vitamin E infused highly cross-linked polyethylene acetabular cups in THA demonstrated significantly lower femoral head penetration rates at 5 years post-operatively; however, in order to extrapolate these findings to clinical practice, these studies must be followed long-term, as the average lifespan of a THA can reach 25 years in select patients.

INTRODUCTION

Total hip arthroplasty (THA), commonly referred to as a "hip replacement" is a surgery in which the femoral acetabulum and femoral head are replaced with an artificial implant. In 2010, it was estimated that over 1 million Americans underwent either a total hip or knee arthroplasty yearly, and that number continues to rise as the "baby boomers" age.¹ THA has over a 100-year operative history, and researchers are constantly working to improve the longevity of the implant so that patients can avoid undergoing subsequent replacements in the future.⁶ In the United States, there are currently four combinations of implant material available: metal-on-polyethylene, ceramic-on-polyethylene, ceramic-on-ceramic, and ceramic-on-metal.⁷ The metal-on-polyethylene is one of the most widely used implants today.⁶ The replacement acetabular component - the "cup" - can be made with ultra-high molecular weight polyethylene, but aseptic loosening has been known to occur due to the wear particles of this material.³ When irradiated beyond the normal sterilization dose, the polyethylene then becomes highly cross-

linked, which has been shown to improve wear rates when compared to ultra-high molecular weight polyethylene. However, this process creates free radicals, which require the material to be melted or annealed post-irradiation to eliminate free radicals, compromising its strength. Vitamin E infusion of the highly-linked polyethylene cup has been proposed as a solution to reduce the risk of oxidation without compromising the strength or wear of the cup.³

Currently, the average lifespan of the hardware is 15-25 years before a second THA is needed.² This becomes important as younger patients who undergo trauma or high levels of activity find themselves in need of a THA. By utilizing Vitamin E infused highly-linked polyethylene cups, it is thought that this will ultimately reduce osteolysis, thus preventing aseptic loosening and increasing the longevity of the implant. The objective of this study is to compare literature investigating the efficacy of vitamin E infused highly cross-linked cups versus cross-linked polyethylene cups without Vitamin E through assessment of femoral head penetration via radiostereometric analysis, with the goal of determining whether Vitamin E can be used to extend the lifespan of the implant.

Case: A 40-year-old male with a history of left hip trauma as an adolescent leading to degenerative joint disease presents to discuss total hip arthroplasty. He is concerned about needing multiple hip replacements over the course of his lifetime and would like to be informed about what materials he should use in order to maximize the longevity and duration of his new hip.

Clinical Question: *In adult patients undergoing a total hip replacement, does using vitamin E highly cross-linked polyethylene acetabular cups reduce femoral head penetration 5 years post-operatively when compared to cross-linked polyethylene cups without vitamin E?*

METHODS

A search of PubMed performed in September 2022 using MeSH terms "Polyethylene," "Vitamin E," and "Arthroplasty, Replacement, Hip" yielded 41 results, 17 of which were clinical trials, and none of which were duplicates. The 17 clinical trials were assessed for eligibility. Exclusion criteria included less than 5-year follow up, use of materials other than uncemented cross-linked polyethylene cups, extremely small sample size, or lack of relevance to the clinical question. Three studies remained (Figure 1).

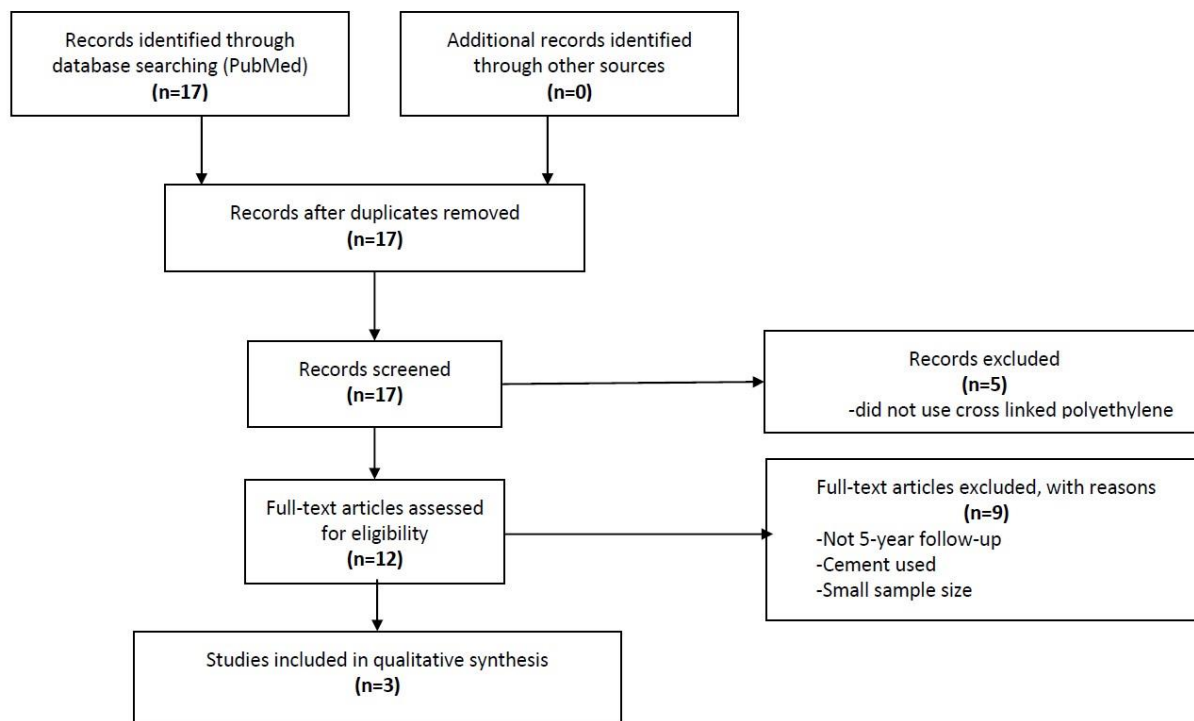


Figure 1: PRISMA Diagram

RESULTS

Study #1

Reduced wear in vitamin E-infused highly cross-linked polyethylene cups: 5-year results of a randomized controlled trial. Rochcongar et al.⁴

Objective

Evaluate whether vitamin E infused highly cross-linked polyethylene acetabular cups continue to show less wear at five years post-operation, as compared to ultra-high molecular weight polyethylene acetabular cups.

Study Design

This single-center, blinded prospective randomized control trial of 62 patients ages 18-75 with a diagnosis of primary or secondary osteoarthritis or osteonecrosis needing primary THA, was carried out at Caen University Hospital in France.⁸ At five-years post-operation, 40 patients were analyzed. Femoral head penetration was measured using radiostereometric analysis with the patient standing on both legs at seven days post-operation as baseline and then at six months, one, two, three and five years post-operation and analyzed using Medis Specials medical imaging software. Femoral head penetration was calculated as the sum of medial, proximal and anterior translation to express a single femoral head penetration measurement.

Clinical scores - including the Harris hip score, Merle d'Aubigne and Postel score - were also measured preoperatively and postoperatively at the same intervals as RSA. The Mann-Whitney U test was used to compare the two groups, and the intention-to-treat principle was applied. This study was designed as a superiority study and a p-value of < 0.05 was considered significant.

Study Results

From one to five years post-surgery the authors found that mean femoral head penetration increased 0.08mm in vitamin E infused HXLPE cups, as compared to 0.2 mm in ultra-high molecular weight polyethylene cups, which was shown to be significantly lower penetration in the vitamin E infused group ($p < 0.001$). Clinical scores improved for both groups when comparing pre-operative values to five-year postoperative values, however there was no statistically significant difference shown between the two groups at five years ($p=0.4$ for HHS scores; $p=0.3$ for MAP scores).

Study Critique

Limitations in this study acknowledged by the authors include relatively small samples size and loss of ten patients to follow-up. In addition, they explain that the vitamin E infused polyethylene cups were manufactured from a different kind of cross-linked polyethylene than the ultra-high molecular weight cross linked polyethylene, so they were unable to completely isolate the impact of the vitamin E infusion on the strength of the polyethylene. Another weakness of this study is that it expresses no intention at this time to perform another analysis in future years i.e. at ten years post-operation.

Study #2

Vitamin E diffused highly cross-linked polyethylene in total hip arthroplasty at five years: a randomised controlled trial using radiostereometric analysis. Nebergall et al.³

Objective

Comparison by radiostereometric analysis of femoral head penetration into vitamin E infused highly cross-linked polyethylene (HXLPE) acetabular cup liners and medium cross-linked polyethylene acetabular cup liners at five years post THA.

Study Design

82 patients between 20-75 years old with osteoarthritis requiring primary THA were randomized to either receive a vitamin E infused HXLPE liner (E1) or a medium cross-linked polyethylene liner (ArComXL) in this blinded study. The other necessary components were the same for all patients: an uncemented highly porous titanium acetabular component (Regenerex), an uncemented femoral stem (Bi-Metric) and a 32 mm ceramic head. All surgeries were done by 6 surgeons at Aalborg University Hospital in Denmark. The measurements for analysis - radiostereometric radiographs with patient supine, plain radiographs and patient-reported outcome measures (PROMs) - were obtained pre-operatively, immediately postoperatively, and at six weeks, one year, three years and five years post-operatively.

Researchers used the Shapiro-Wilk test to determine that the data were not normal, and therefore the Wilcoxon signed rank non-parametric test was used for statistical analysis of differences over time for both RSA and PROMs within each group, and the Mann-Whitney nonparametric test was used for differences between groups. This study was designed as a non-inferiority study.

Study Results

The five-year median proximal femoral head penetration into the E1 liner was -0.04 mm (-0.13 to 0). There was no difference observed by the Wilcoxon signed rank tests between the three- and five-year penetration in the E1 group. The five-year median proximal femoral head penetration into the ArComXL liner was 0.07mm (-0.03 to 0.16), also with no significant differences between the three- and five-year measurements. The Mann-Whitney test was used to show that at both three- and five-years, the median proximal femoral head penetration into the ArComXL liners was significantly greater than penetration into the E1 liners ($p=0.029$ and $p=0.019$ respectively).

Using Wilcoxon signed rank tests, no significant changes in PROMs were seen in either group after the one-year mark, and using Mann-Whitney tests, no differences between groups were seen at any time.

At five-year post-THA, the vitamin E infused HXLPE liners show non-inferiority to the medium cross-linked polyethylene liners in femoral head penetration and PROMs. This study will be continued until 10-year post-operation.

Study Critique

Due to patients being lost to follow up, exclusion because of need for revision, and withdrawal of consent, only 28 patients in the E1 group and 26 patients in the ArComXL group were analyzed for femoral head penetration at five years post-operation.

The researchers acknowledge that one limitation of their study is that the use of ceramic femoral heads may limit how much generalization can be taken from this study, since it is more common for metal femoral heads to be used with polyethylene.

Another limitation that they acknowledge is that there is a limitation to the precision of their measurements because they did not use implanted beads in the polyethylene lining edge, which would have increased their measurement points from five points to nine points. They explain that this limitation in precision is likely why there is negative penetration seen in the E1 group at three and five years. However, the authors do not believe it compromises their findings because the same limited precision measurement techniques and instruments were also used in the ArComXL group, and they expect that the significant differences seen between the two groups would remain even if nine points of measure had been used instead of five.

Study #3

*Wear of Vitamin E-Infused Highly Cross-Linked Polyethylene at Five Years. Shareghi et. al.*⁵

Objective

To evaluate whether vitamin E-infused (E1) highly cross-linked polyethylene liners showed less proximal-distal femoral head penetration than compression-annealed highly cross-linked polyethylene (ArComXL) liners at 5 years.

Study Design

This was a randomized control trial of 63 hips comparing femoral head penetration between 2-years and 5-years post-THA. This study had been previously evaluated 2 years after surgical intervention.⁹ Inclusion criteria comprised of non-inflammatory hip arthritis, age 20-75, and primary osteoarthritis or certain etiologies of secondary osteoarthritis (slight dysplasia, idiopathic femoral head necrosis, Legg-Calve-Perthes disease, and slipped capital femoral epiphysis).⁹ Participants were randomized to receive either an ArComXL or E1 highly cross-linked polyethylene liner. All patients received an uncemented Bio-Metric stem with a 32-mm cobalt-chromium head. Femoral head penetration was measured using radiostereometric analysis at three months, one, two, and five years following the THA. Radiostereometric analysis consists of two x-rays taken simultaneously from different directions, creating a “stereo” image, to allow for more precise visualization of the surgical implant.¹⁰ Femoral head penetration was measured using point motion to evaluate the movement of the center of the femoral head relative to the femoral shaft. Medial or lateral (x-translation), distal or proximal (y-translation) and anterior or posterior (z-translation) movement was measured with total penetration being calculated via the Pythagorean theorem ($\sqrt{x^2 + y^2 + z^2}$). This was used to determine total point motion between 2 and 5 years. Data were presented as the median distance and range from minimum to maximum and mean distance with 95% confidence intervals. The Mann-Whitney U test was used to compare femoral head penetration between both groups, and the Wilcoxon signed-rank test used to compare results within the group over the period of 5 years. Clinical outcomes were also evaluated prospectively using the Harris Hip Score, a self-reported questionnaire completed by patients. This was administered preoperatively and at the 5-year follow-up, noting changes in the Harris Hip score and pain scores.

Study Results

At 5-year follow-up, median proximal femoral head penetration in the E1 group was significantly lower than the ArComXL group ($p < 0.001$). The total 3-dimensional femoral head penetration was also significantly lower in the E1 group than the ArComXL group ($p = 0.004$). Between 2 and 5 years, both the rate of median and mean proximal femoral head penetration was slower in the E1 group than the ArComXL group ($p < 0.001$), and the rate of total 3-dimensional penetration was slower ($p < 0.001$). In both groups, there was a significant increase in proximal and total head penetration from 2 to 5 years, noting that there was indeed some level of wearing in both prostheses. Clinical results showed no significant difference between the groups at 5 years on the Harris Hip Score or corresponding median pain scores.

Study Critique

Strengths of this study include having multiple follow-up evaluations. The benefit of having data from both 2 years and 5 years allowed for more information regarding the rate of change in femoral head penetration per year, and whether or not that rate changed as the years progressed. This may be helpful in future studies when determining the longevity of a THA beyond 5 years.

Limitations of this study include losing 7 patients to follow up at the 5 year analysis, one of which was in the E1 group, and 6 in the ArComXL group; therefore 37 hips were analyzed in the E1 group and only 26 in the ArComXL group. Additionally, the sample size itself is not that large. This study focused primarily on outcomes at 5 years post-surgery; however, further research with a longer duration of followup needs to be conducted in order to better understand the longevity of the vitamin E infused acetabular cups compared to the standard acetabular cups. Currently, the average lifespan of a hip replacement is 15-25 years²; therefore, in order to determine whether vitamin E infused acetabular cups prolong the lifespan of the implant, these studies need to be followed for at least that long.

DISCUSSION

THA is an invasive procedure requiring a lengthy recovery that can be challenging for patients, especially when combined with other comorbidities. The ability to reduce the number of subsequent surgeries a patient may need to undergo would avoid additional stresses to the body, likely improving quality of life. In our analysis of three, five-year follow-up studies, we found that each study demonstrated significant differences between intervention and control groups, showing non-inferiority of vitamin E infused highly crosslinked polyethylene acetabular cups in femoral head penetration as a marker of acetabular wear five years post THA.³⁻⁵

However, these studies do have limitations which should be taken into account by clinicians when making recommendations to their patients. As mentioned previously, the average lifespan of a THA varies, ranging from 15-25 years,² and these studies have only been followed for 5 years. It would be presumptuous to conclude that vitamin E infused highly cross-linked polyethylene acetabular cups demonstrate an improved lifespan of the implant. The short-term data is promising, but the rate of wear could rapidly increase over the next several years.

Additional limitations of these studies include small sample sizes (ranging from 62-82) and loss to follow up, creating an unequal distribution of participants between groups. Furthermore, each study included a wide range of patient ages from 18-75 years of age in order to reach a sufficient statistical power for their studies. Ideally these studies will be repeated with larger sample sizes consisting of more homogeneously-aged study participants to account for differing levels of activity and their impact on wear of the acetabular cup. It should be noted that in Nebergall et al³ and Shareghi et al,⁵ all radiostereometric analyses were performed with the patients in a supine position, while Rochcongar et al⁴ obtained these images with the patient standing. Studies have demonstrated that weight-bearing hip radiographs do influence the joint space width when compared to supine radiographs;¹¹ therefore, this is something to keep in mind when making comparisons between studies. Finally, it is important to consider that although all three studies used a vitamin E infused highly cross-linked polyethylene acetabular

cup, two different materials for the femoral head were used, potentially altering the wear of the acetabular component in the process. Nebergall et al³ used a ceramic femoral head, whereas Rochcongar et al⁸, and Shareghi et al⁹ used a cobalt-chromium femoral head.

CONCLUSION:

Returning to our patient from above, it appears at this time that in adult patients undergoing THA, using vitamin E highly cross-linked polyethylene acetabular cups reduces femoral head penetration at five years post-operatively as compared to cross-linked polyethylene cups without vitamin E. Therefore, we would advise this patient to discuss the availability of vitamin E infused highly cross-linked polyethylene acetabular cups with their surgeon, while also acknowledging that further long-term studies at 10,15, and 20+ years will likely need to be performed in order to determine the true longevity of these components. There is not currently any known risk in using this material and patient satisfaction scores have been comparable to the control groups.

REFERENCES:

1. Maradit Kremers H, Larson DR, Crowson CS, et al. Prevalence of Total Hip and Knee Replacement in the United States. *J Bone Joint Surg Am.* 2015;97(17):1386-1397. doi:10.2106/JBJS.N.01141
2. Evans JT, Evans JP, Walker RW, Blom AW, Whitehouse MR, Sayers A. How long does a hip replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. *Lancet Lond Engl.* 2019;393(10172):647-654. doi:10.1016/S0140-6736(18)31665-9
3. Nebergall AK, Greene ME, Laursen MB, Nielsen PT, Malchau H, Troelsen A. Vitamin E diffused highly cross-linked polyethylene in total hip arthroplasty at five years: a randomised controlled trial using radiostereometric analysis. *Bone Jt J.* 2017;99-B(5):577-584. doi:10.1302/0301-620X.99B5.37521
4. Rochcongar G, Remazeilles M, Bourroux E, et al. Reduced wear in vitamin E-infused highly cross-linked polyethylene cups: 5-year results of a randomized controlled trial. *Acta Orthop.* 2021;92(2):151-155. doi:10.1080/17453674.2020.1852785
5. Shareghi B, Johanson PE, Kärrholm J. Wear of Vitamin E-Infused Highly Cross-Linked Polyethylene at Five Years. *J Bone Joint Surg Am.* 2017;99(17):1447-1452. doi:10.2106/JBJS.16.00691
6. Knight SR, Aujla R, Biswas SP. Total Hip Arthroplasty - over 100 years of operative history. *Orthop Rev.* 2011;3(2):e16. doi:10.4081/or.2011.e16
7. Health C for D and R. General Information about Hip Implants. *FDA.* Published online April 25, 2019. Accessed October 8, 2022. <https://www.fda.gov/medical-devices/metal-metal-hip-implants/general-information-about-hip-implants>
8. Rochcongar G, Buia G, Bourroux E, Dunet J, Chapus V, Hulet C. Creep and Wear in Vitamin E-Infused Highly Cross-Linked Polyethylene Cups for Total Hip Arthroplasty: A Prospective Randomized Controlled Trial. *JBJS.* 2018;100(2):107-114. doi:10.2106/JBJS.16.01379
9. Shareghi B, Johanson PE, Kärrholm J. Femoral Head Penetration of Vitamin E-Infused Highly Cross-Linked Polyethylene Liners: A Randomized Radiostereometric Study of Seventy Hips Followed for Two Years. *J Bone Jt Surg.* 2015;97(16):1366-1371. doi:10.2106/JBJS.N.00595
10. Radiostereometric Analysis (RSA) at HSS. Hospital for Special Surgery. Accessed October 20, 2022. https://www.hss.edu/conditions_radiostereometric-analysis-at-hss.asp
11. Fuchs-Winkelmann S, Peterlein CD, Tibesku CO, Weinstein SL. Comparison of Pelvic Radiographs in Weightbearing and Supine Positions. *Clin Orthop.* 2008;466(4):809-812. doi:10.1007/s11999-008-0124-8

