The John Charnley Award

Highly Crosslinked Polyethylene in Total Hip Arthroplasty Decreases Long-term Wear: A Double-blind Randomized Trial

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Abstract

Background The use of highly crosslinked polyethylene (HXLPE) is now commonplace for total hip arthroplasty. Hip simulator studies and short-term in vivo measurements suggest that the wear rate of some types of HXLPE is significantly less than conventional ultrahigh-molecular-weight polyethylene (UHMWPE). However, there are few long-term data to support its use.

Questions/purposes The aim of this study was to measure the long-term steady-state wear of HXLPE compared with

UHMWPE liners in a prospective, double-blind, randomized controlled trial using radiostereometric analysis.

Methods Fifty-four patients were randomized to receive hip arthroplasties with either UHMWPE liners or HXLPE liners. Complete followup was available on 39 of these patients (72%). All patients received the same cemented stem and an uncemented acetabular component. Three-dimensional penetration of the head into the socket was determined at 10 years using a radiostereometric analysis system, which has an in vivo accuracy of <0.1 mm. Oxford Hip Scores were compared between the groups.

Results At 10 years there was significantly less wear of HXLPE (0.003 mm/year; 95% confidence interval [CI], ± 0.010 ; SD 0.023; range, -0.057 to 0.074) compared with UHMWPE (0.030 mm/year; 95% CI, ± 0.012 ; $p < 0.001$; SD 0.027; range, -0.001 to 0.164). The volumetric penetration from 1 to 10 years for the UHMWPE group was 98 mm^3 (95% CI, $\pm 46 \text{ mm}^3$; SD 102 mm^3 ; range, -4 to 430 mm^3) compared with 14 mm^3 (95% CI, $\pm 40 \text{ mm}^3$; SD 91 mm^3 ; range, -189 to 242 mm^3) for the HXLPE group ($p = 0.01$).

Conclusions This study demonstrates that HXLPE has little detectable steady-state in vivo wear. This may result in fewer reoperations from loosening; however, careful clinical followup into the second decade still needs to be performed.

Level of Evidence Level I, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

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Introduction

Primary hip arthroplasty is a common operation with 80,314 performed in the United Kingdom last year [32] and

over 300,000 in the United States [1]. In an aging population, revision hip arthroplasty represents an increasing healthcare and financial burden with revision hip arthroplasty projected to increase by 137% by 2030 [24].

Aseptic loosening continues to be the predominant mode of failure of hip arthroplasty with over 50% of the revisions being performed for this reason alone [42]. Particulate debris generated by wear of the liner in implants with metal-on-polyethylene bearing surfaces is one of the main stimulators of periprosthetic osteolysis and eventual aseptic loosening [8, 17, 20, 29]. Manufacturers have, in response, attempted to modify bearing surface materials to reduce the amount of wear. Conventional ultrahigh-molecular-weight polyethylene (UHMWPE) used to produce liners can be treated with gamma and electron beam radiation to increase the degree of crosslinking within the material. The resulting highly crosslinked polyethylene (HXLPE) has been shown in vitro to have greater wear resistance compared with UHMWPE and has the potential to improve implant longevity.

In vitro studies, conducted in hip simulators, suggest that the wear characteristics of HXLPE are superior to UHMWPE. However, there are limited long-term in vivo data to corroborate these findings. Furthermore, there is sometimes poor correlation between laboratory wear studies and wear measured in vivo. Hylamer (DePuy DuPont Orthopaedics, Wilmington, DE, USA), for example, was shown to have low in vitro wear but exhibited catastrophic wear and failure in vivo [16, 33]. Additionally, although the wear volume in HXLPE has been shown to be less in vitro than conventional UHMWPE [18, 19], some studies have suggested that it generates smaller particulate debris [10] that are more biologically active in stimulating osteolysis in vitro [31], whereas recent evidence suggests fewer small particles are generated with HXLPE [4]. We previously evaluated the results of a randomized trial comparing UHMWPE with HXLPE at 2 [14], 3 [15], and 7 years [41]. Other groups have reported the wear of highly crosslinked polyethylene at 10 years; however, these studies have typically been limited by small cohort sizes [38] and the inclusion of more than one acetabular component type within the trial design [21].

We therefore report the results at 10 years followup of a prospective, double-blind, randomized controlled trial comparing the in vivo wear rates of HXLPE with conventional UHMWPE acetabular liners in THA using radiostereometric analysis.

Patients and Methods

This study presents the minimum 10-year followup of a double-blind, randomized controlled trial. Fifty-four

patients with hip osteoarthritis were recruited from the routine inpatient waiting list in 2001–2002. The study had the required ethical approval and informed consent for participation was obtained from all patients. Patients with an American Society of Anesthesiologists score of ≥ 3 were excluded from the study.

At 10 years, seven patients (13%) had been lost to followup (two had died, one had moved away, one had a periprosthetic fracture, and three withdrew from the study early, a total of three from the HXLPE group and four from the UHMWPE group). Eight patients (11.1%) had radiographs that were inadequate for analysis. There were no revision operations during the period of study. This left 20 patients in the HXLPE group and 19 in the UHMWPE group. We have previously reported the baseline demographics of this cohort, which were not significantly different between the groups ($p = 0.31$) [41].

A cemented, collarless, polished, tapered femoral component (CPT; Zimmer, Warsaw, IN, USA) with a 28-mm bearing surface and an uncemented acetabular component (Trilogy; Zimmer) were used. At the time of surgery, the patients were randomized to receive either a conventional UHMWPE acetabular liner (Zimmer) ($n = 27$) or a HXLPE liner (Longevity; Zimmer) ($n = 27$). Our randomization methods have been previously reported [11]; patients were stratified by sex and age (< 55 and ≥ 55 years). Randomization occurred at the baseline preoperative assessment, within 4 weeks of the operative intervention. The CONSORT flow diagram is shown (Fig. 1).

The manufacturing and sterilization process for the UHMWPE and HXLPE used in this study have been previously reported in our earlier publications [41].

There was no difference in appearance between the polyethylene liners. Surgeons, researchers, and patients were blinded to the polyethylene type. Two surgeons (PM-S, DWM) performed all operations in both groups over a period of 6 months. Each operation was performed through a modified lateral (Hardinge) approach with the patient in the lateral position. The femoral components were implanted using a low-viscosity, antibiotic-loaded cement (CMW3-G; DePuy, Leeds, UK). Patients in both groups underwent similar wound drainage and postoperative rehabilitation [41]. There were no significant differences in the baseline demographics and Oxford Hip Scores between the groups (Table 1).

Radiostereometric Analysis

Our radiostereometric analysis system has been described previously and has an in vivo accuracy of < 0.1 mm [2] with a high repeatability and precision [13, 22]. It uses

Fig. 1 CONSORT 2010 flow diagram depicts the passage of patients through the randomized controlled trial with details on enrollment, intervention allocation, followup, and analysis.

Table 1. Clinical details and outcome scores for the HXLPE and UHMWPE groups

Variable	HXLPE	UHMWPE
Age (years), mean (range)	68 (52–76)	67 (51–76)
Weight (kg), mean (range)	79 (49–117)	82 (75–108)
Sex (male:female)	11:9	9:10
Oxford Hip Score, mean (range)*		
Preoperative	12 (4–30)	10 (2–32)
1 year postoperatively	46.7 (39–48)	47.1 (42–48)
10 years postoperatively	39.5 (13–48)	42.0 (24–48)

* Possible scores range from 0 to 48; HXLPE = highly crosslinked polyethylene; UHMWPE = ultrahigh-molecular-weight polyethylene.

“off-the-shelf” implants and therefore does not require the manufacture of implants with attached markers. Stereora-diographs were taken with the patient bearing weight

equally on each leg. Measurements were made immediately after surgery and at 3, 6, and 12 months and 2, 3, 5, 7, and 10 years postoperatively. The steady-state rate of femoral head penetration was determined by fitting a regression line to the total penetration data at 1, 2, 3, 5, 7, and 10 years. The gradient of this line was taken to be the wear rate in millimeters per year. The direction and magnitude of the penetration vectors were also projected onto the coronal and sagittal planes. Volumetric wear was calculated from the three-dimensional penetration measured from 1 to 10 years with attention to the magnitude and direction of wear as well as cup geometry, inclination, and version. Cup inclination and version were used to transform global coordinate measurements to an acetabular coordinate system, where it was then possible to consider the direction of penetration relative to the open face of the cup. Volumetric penetration (primarily wear from 1 to 10 years) was then calculated using the formula described

by Wu et al. [43]. The penetration data were normally distributed in both groups.

Oxford Hip Scores

The Oxford Hip Score is a patient-reported outcome measurement validated for use in THA [7, 44]. It is a 12-question score with a range from 0 (worst) to 48 (best). Oxford Hip Scores were completed by the patients in the preoperative assessment clinics and subsequently in outpatient clinics.

Statistical Analysis

Before the study, a sample size calculation was performed with use of an Altman nomogram [3]. The endpoint chosen for the sample size calculation was wear rate. On the basis of the work of Oonishi et al. [34], a rate of penetration of 0.2 mm over 2 years was assumed for the UHMWPE liner. We expected a wear rate of ≤ 0.1 mm over 2 years for the HXLPE [40]. A SD of 0.1 mm was chosen on the basis of our previous radiostereometric analysis studies [2]. The power calculation indicated that a total of 20 patients would be needed for each group ($\alpha = 0.05$, $\beta = 0.9$, $2n = 40$). The study was constructed as a superiority study.

The penetration data were examined for distribution with use of frequency histograms. The data were found to be normally distributed, and thus parametric statistical tests were used. A paired-samples t-test was used to determine whether significant penetration had occurred between 1 and 10 years postoperatively. A two-sample t-test was used to detect significant differences between the groups. A one-sample t-test was used to determine whether the wear rate was significantly different from zero. All statistical analyses were performed with use of SPSS software (Version 20.0; SPSS, Chicago, IL, USA). A p value of < 0.05 was considered to be significant for all statistical tests.

Results

Linear Wear

At 10 years the mean total penetration was 0.33 mm (CI, ± 0.10 ; SD 0.207) for the HXLPE group and 0.61 mm (95% confidence interval [CI], ± 0.10 ; SD 0.214) for the UHMWPE group ($p = 0.005$; Fig. 2). As previously reported [14, 15], the penetration during the first year was greater than that in subsequent years (Fig. 2). After the first year, the relationship between penetration and time was virtually linear in both groups (UHMWPE $R^2 = 0.96$, HXLPE $R^2 = 0.60$). Between 1 and 10 years, HXLPE

Fig. 2 Line graph shows the mean total linear penetration (with vertical bars representing the 95% CIs) over 10 years for both HXLPE and UHMWPE.

Fig. 3 Linear regression between 1 and 10 years shows steady-state wear rate (with 95% CIs) for both HXLPE and UHMWPE.

(0.003 mm/year; 95% CI, ± 0.010 ; SD 0.023; range, -0.057 to 0.074) had 10 times less steady-state wear than UHMWPE (0.030 mm/year; 95% CI, ± 0.012 ; SD 0.027; range, -0.001 to 0.164 ; $p < 0.001$; Fig. 3). Wear rates exceeded the osteolysis threshold (0.1 mm/year) suggested by Dumbleton et al. [8] in two of the patients in the conventional UHMWPE group and none of the HXLPE group (Fig. 4); with the numbers available, this difference was not significant. The direction of wear between 1 and 10 years was in a superior and lateral direction for both groups. In the UHMWPE group, there was wear of 0.059 mm/year superiorly (95% CI, ± 0.033 ; SD 0.073; $p = 0.002$) and 0.049 mm/year laterally (95% CI, ± 0.024 ; SD 0.053). In the HXLPE group, there was no significant wear in the coronal or sagittal planes (superiorly 0.009 mm/year; 95% CI, ± 0.029 ; SD 0.066; $p = 0.26$; laterally 0.003 mm/year; 95% CI, ± 0.027 ; SD 0.062;

Fig. 4 Graph shows individual patient-level wear rates from 1 to 10 years in both the HXLPE and UHMWPE groups. The osteolysis threshold of 0.1 mm/year is shown.

$p = 0.10$). There was no significant AP steady-state wear in either group (HXLPE $p = 0.24$, UHMWPE $p = 0.16$).

Volumetric Wear

The volumetric wear between 1 and 10 years was lower in the HXLPE group ($p = 0.01$). In the UHMWPE group, volumetric wear between 1 and 10 years was 98 mm^3 (95% CI, $\pm 46 \text{ mm}^3$; SD 91 mm^3 ; range, -4 to 430 mm^3) and in the HXLPE group 14 mm^3 (95% CI, $\pm 40 \text{ mm}^3$; SD 102 mm^3 ; range, -189 to 242 mm^3).

There was no significant difference between the groups in terms of volumetric penetration, which was primarily a function of creep. The volumetric penetration in the first year was 196 mm^3 (95% CI, $\pm 49 \text{ mm}^3$; SD 54 mm^3 ; range, 98 – 305 mm^3) for the UHMWPE group and 178 mm^3 (95% CI, $\pm 43 \text{ mm}^3$; SD 49 mm^3 ; range, 91 – 276 mm^3) for the HXLPE group ($p = 0.28$).

Oxford Hip Scores

There were no significant differences between the groups in terms of Oxford Hip Scores. At 10 years the mean Oxford Hip Score in the HXLPE group was 39.5 (range, 13–48) compared with 42.0 (range, 24–48) in the UHMWPE group ($p = 0.42$).

Discussion

Highly crosslinked polyethylene is now the most commonly used polyethylene in THA [32]. Although the long-term wear characteristics have been reported, there is a

paucity of high-quality long-term randomized trials in this area with only two others of which we are aware that report data to 10 years [21, 38]. We report the long-term results of a double-blind, randomized controlled trial comparing UHMWPE and HXLPE. These long-term results show that steady-state wear of HXLPE is lower than that of conventional UHMWPE by an order of magnitude. During the study period, the wear rate remained constant, suggesting that it is likely to continue to do so over the longer term.

A limitation of this study (and all other radiographic wear measurement techniques) is that we cannot determine why the penetration occurs. For example, creep could be distortion of the liner or cold flow into the liner screw holes, and wear may be on the articular surface and/or on the backside. Backside wear was implicated in the high rates of retroacetabular osteolysis observed with Hylamer (DePuy DuPont Orthopaedics) liners [39]. Although finite element analysis estimates rates of backside wear to be minimal compared with the articular surface [26], retrieval studies have shown backside volumetric change to occur at only 2.8% of the rate of articular surface wear [23] and that retroacetabular osteolysis does not correlate to backside wear [45]. A further limitation is that the study involved relatively small numbers and that 28% of the cohort was lost to followup or had radiographs that were inadequate and therefore excluded from analysis; offsetting this, perhaps, is that the loss to followup was distributed equally between the arms (Fig. 1). We cannot therefore accurately estimate the chance of a rare event such as the wear rate of HXLPE being above the osteolysis threshold.

The generation of osteolytic debris as a result of liner wear is one of the primary causes of aseptic loosening. The success of efforts to increase the crosslinking in liners to improve wear characteristics is supported by studies such as ours. The osteolytic debris threshold for polyethylene wear has been estimated at 0.1 to 0.2 mm/year [8, 36]. In our study, none of the HXLPE liners had wear above 0.1 mm/year, whereas two of the UHMWPE liners did. This is an anecdotal observation, however, because our study was not powered to measure the difference in the proportions of patients in each group reaching this threshold. It has been suggested that the threshold should be lower for HXLPE than UHMWPE because the particles generated are smaller and likely to be more biologically active [10, 31]. However, it has been shown in vitro that the biological activity of HXLPE particles is the same or less compared with conventional UHMWPE particles [9, 12]. Even if the biological activity of HXLPE particles was greater than that of UHMWPE, this likely would be offset by the markedly lower wear rate [37]. These observations are supported by clinical studies showing reduced volumes of osteolysis with HXLPE [28], and a recent meta-analysis estimates the odds ratio for osteolysis to be 0.131 in first-

generation HXLPE liners compared with conventional UHMWPE [25]. Because of the low wear rates observed in both groups combined with the limitations of using radiographs (where CT would be more appropriate), we could not effectively evaluate osteolysis in this relatively small study cohort.

For osteolysis and subsequent revision, the volume of wear debris is more important than the wear rate [35]. We believe this is the only study that has accurately assessed volumetric wear in vivo given that we are not aware of any other similar publications in this area. The volumetric wear was calculated from measurements of wear rate and direction and the orientation of the acetabular component as well as information about cup geometry. We are aware of only one other randomized controlled trial using radiostereometric analysis (RSA) that compares wear rates of HXLPE with conventional UHMWPE liners at 10-year followup [21]. This study used implants with a high failure rate that are no longer in use. The RSA radiographs were taken with the patient supine. One patient had “aberrant” wear data and had to be excluded, perhaps as a result of this. Data from this study that showed rapid HXLPE wear between 5 and 7 years have previously been presented but never published. Their report, at 10 years, shows lower wear rates for the HXLPE group. There have been a number of comparative studies of HXLPE versus UHMWPE liners using plain radiographs rather than RSA [5, 30]. These are about an order of magnitude less accurate than RSA and not accurate enough to determine if individual cases are below an osteolysis threshold. Meta-analysis of 28 such studies has shown reduced femoral head penetration and 87% lower risk of osteolysis with HXLPE [25] at early and intermediate followup. However, with regard to whether HXLPE results in reduced revision rates, the one meta-analysis of which we are aware that evaluated this endpoint found no difference in the proportion of patients undergoing revision in those who received HXLPE and those who received UHMWPE [27]. That said, osteolysis resulting from wear is only one of many potential causes of revision; thus, controlling for polyethylene type alone is very difficult. No revision procedures were performed for any cause in our study.

The Oxford Hip Scores measured in this study were no different between the study groups. This is not surprising because pain is likely to be a late complication of wear and osteolysis. This finding has been replicated in other studies comparing bearing material in THA [5, 6].

The evidence base behind new implants is increasingly important as the burden of hip arthroplasty increases [24] and medical devices in general are exposed to more media scrutiny in the wake of problems with metal-on-metal hips. This study demonstrates that HXLPE shows reduced in vivo linear and volumetric wear at 10 years postimplantation.

This supports in vitro studies and meta-analyses of in vivo studies indicating that wear in THAs using HXLPE is less than in THAs using conventional UHMWPE. Given the number of revisions undertaken for aseptic loosening, this seems likely to improve the longevity of implants using HXLPE liners. However, there is no evidence as yet that these findings will result in lower revision rates or improved functional outcomes.

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