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ORIGINAL ARTICLE

No Clinical or Radiographic Differences Between Cemented Cobalt–Chromium and Titanium–Niobium Nitride Mobile-Bearing Unicompartmental Knee Arthroplasty

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Abstract

Purpose This study aimed to compare the clinical and radiographic outcomes of patients with positive patch tests undergoing a medial mobile-bearing titanium–niobium nitride (TiNbN) unicompartmental knee arthroplasty (UKA) to patients undergoing standard UKA (cobalt–chromium [CoCr] implants).

Methods Two successive groups of patients, amounting to a total of 246 individuals, who received Oxford (Zimmer-Biomet, Warsaw, Indiana, USA) UKA were included. The first group was composed of a series of 203 consecutive standard CoCr UKAs (Standard Group), while the second group comprised 43 consecutive hypoallergenic TiNbN UKAs (HA group). The patients of the second group had a positive epicutaneous patch test result for metals. Each patient was evaluated using the Oxford Knee Score (OKS) and Knee Society Score (KSS) a day prior to the surgery (T_0) and at two consecutive follow-ups, namely T_1 (minimum follow-up of 12 months) and T_2 (minimum follow-up of 34 months). Radiographic measurements were performed at the final follow-up (T_2).

Results No statistical differences were noted between the two groups regarding demographic data ($p > 0.05$). No clinical or radiographic differences were found between the HA and standard groups at any follow-up ($p > 0.05$). A statistically significant improvement was found at any follow-up for both OKS and KSS ($p < 0.05$).

Conclusions No clinical or radiographic differences between the hypoallergenic and standard cobalt–chromium groups at any follow-up were found, with a clinically significant improvement being experienced by both groups during the entire follow-up.

Level of evidence Level II—comparative prospective study.

Keywords Oxford mobile-bearing unicompartmental knee arthroplasty · Metal allergy · Knee osteoarthritis

Introduction

Medial unicompartmental knee arthroplasty (UKA) is a safe and reliable option for the treatment of symptomatic end-stage anteromedial osteoarthritis of the knee. Compared to total knee arthroplasty (TKA), medial UKA tends to offer superior functional outcomes, a better range of movement and more physiological knee kinematics [1, 2]. Moreover, patients have a lower rate of morbidity and mortality [1]. Despite the high success rate of knee prosthetic surgery [1, 2], a considerable number of failures, ranging from 10 to 20%, still requires revision, along with the main causes for UKAs which include biomechanical failure and infection [3–8]. In recent years, it has been observed that metal hypersensitivity (MHS) may be another cause of failure after UKA [9].

MHS after arthroplasty is an uncommon condition in which the body immunologically reacts to the metals used in UKA implants [9–11]. Skin hypersensitivity to metals, such as nickel, cobalt and chromium, in the general population has been estimated to range from 1 to 13% [12–15].

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Since UKA is made of several metals, patients could develop a post-operative allergic reaction to these implants, especially those with allergies. Patients with MHS might present pain and effusions, as well as skin abnormalities [16–18] on the operated joint; however, MHS is still a diagnosis of exclusion since current studies report an absence of accuracy in the methods mentioned above [10, 13–15].

Although MHS is a rare condition, the number of UKA patients who test positive for MHS has increased over the last 20 years. The percentage has been estimated up to 25%, which is in contrast with the percentage in the general population that ranges from 10 to 15% [11, 19–21]. Furthermore, in patients with painful arthroplasties, the risk of MHS may be as high as 60% [4]. However, the relationship between MHS and UKA is currently unclear [11, 20, 22, 23].

Due to an increase in the use of UKA, different prostheses with hypoallergenic features should be developed. A substitute to the standard cobalt–chromium (CoCr), titanium–niobium nitride (TiNbN), has been developed and used in recent years [23, 24]. TiNbN has a high surface resistance to abrasion and corrosion and is composed of a fine ceramic coating. These features result in possible long-term improvements in several biological processes such as biocompatibility and osteointegration [23, 24]. However, there are no clinical studies that compare the clinical and radiographic outcomes of patients who underwent hypoallergenic TiNbN to those who underwent standard UKA.

Therefore, the main aim of this study was to compare the clinical and radiographic outcomes of patients with proven metal allergy who undergo hypoallergenic TiNbN UKA and to compare these results to those of a group of patients with standard UKAs (regular cobalt–chromium implants). It was hypothesised that TiNbN implants lead to excellent outcomes comparable to standard UKAs.

Materials and Methods

The study was performed according to the STROBE checklist for group studies [25].

All patients signed an informed consent document before being enrolled in the study. Ethical approval was obtained from the local ethical committee.

Two cohorts of patients who had undergone cemented medial mobile-bearing UKA between January 2015 and December 2017 were included in this study. The first group involved 203 consecutive UKA cobalt–chromium medial mobile-bearing with the Oxford (Zimmer-Biomet, Warsaw, IN, USA) Microplasty instrumentation (Standard Group). The second group was composed of 43 consecutive UKA TiNbN (HA group), with a single femoral peg, using the Microplasty instrumentation in patients with proven positive patch test for metals.

Patients were carefully selected, and the standardised treatment algorithm was meticulously performed in order to decide who should undergo the patch test as previously published [11]. Adverse reactions to metals were recorded according to the International Contact Dermatitis Research Group (ICDRG) criteria [26].

A standardised epicutaneous patch test method was performed to identify allergic contact sensitisation in patients with suspected metal allergy due to the high reliability [27].

A total of 43 patients resulted positive to the metal patch test and were included in this study.

All surgeries were performed by one of the authors (NU) who has considerable experience in knee arthroplasty [28].

In both groups, the indication for surgery was the isolated anteromedial OA or avascular necrosis (AVN) of the medial femoral condyle. Pre-operative clinical examination and magnetic resonance imaging (MRI) ensured ligament integrity. For radiographic inclusion, the Oxford Group criteria were followed [29]. The main exclusion criteria for participation in this study were missing data or radiographs that were unsuitable for obtaining an exact measurement, revision surgery or previous surgery of the affected knee (except arthroscopy for meniscectomy).

Clinical Evaluation

All patients were evaluated by two independent surgeons who were not involved in the index surgery. The clinical evaluation included the examination of each patient's OKS and KSS. Each patient was evaluated on the day before surgery (T_0) and at two consecutive follow-ups, namely T_1 (minimum follow-up of 12 months) and T_2 (minimum follow-up of 34 months) [30–32].

Radiographic Evaluation

The UKA's position was assessed only at the final follow-up (T_2) according to the Oxford Partial Knee Surgical Technique operating manual.

In accordance with the manufacturer's manual, the following parameters were evaluated [29, 33]:

- Femoral component varus/valgus. The angle between the femoral component and the femoral axis in the coronal plane.
- Tibial component varus/valgus. The angle between the tibial axis and a line drawn along the tibial tray in the coronal plane.
- Anteroposterior slope. The angle between a line drawn along the tibial tray and perpendicular to the tibial axis in the lateral view.

Statistical Analysis

A sample of 240 subjects, including 40 hypoallergenic and 200 standard patients, was considered sufficient to observe a five-point group difference in both KSS and OKS score. The assumptions included a standard deviation of 10 for both groups, a 5% two-tailed alpha, an 80% power and the employment of a Wilcoxon–Mann–Whitney test. We also assumed a group disproportion of 5% due to hypersensitivity to metals. Three additional subjects were recruited in both groups to ensure statistical significance in case of unexpected events.

This sample was also adequate to detect a difference of two points at subsequent time points in both KSS and OKS score in non-allergic patients and a five-point difference in both KSS and OKS score in allergic patients, assuming a standard deviation (SD) of 10, a 5% two-tailed alpha, an 80% power and the employment of a Wilcoxon signed-rank test as above [30, 31].

The normal distribution of variables was tested with the Shapiro–Wilk test and pre- and postoperative scores compared to the paired *t* test (parametric data) or the Wilcoxon-rank sum test (non-parametric distribution). The two cohorts (hypoallergenic and standard groups) were compared by employing an independent-samples *t* test for continuous variables and chi-square analyses for categorical variables to report differences between the two cohorts. A difference of $p < 0.05$ was statistically significant. To identify interacting factors and correlations, multivariate analyses (Spearman and Pearson/Point biserial analysis) were utilised. All statistical analyses were performed using an IBM SPSS® statistics software (Version 25.0; Chicago, IL, USA).

Results

A total of 281 patients completed the study, out of which 246 patients satisfied all inclusion and exclusion criteria (43 in the HA group and 203 in the Standard group). Out of the 35 patients excluded, 28 reported previous knee surgery (25 anterior cruciate ligament reconstructions, 1 multi-ligaments reconstruction and 2 tibial osteotomies), while seven patients had radiographic data, which was unfavourable to achieve an exact measurement.

In the HA group, all patients completed the follow-up, while in the standard group, all patients completed T_1 but only 200 patients could complete the entire follow-up due to failure of the arthroplasty. In all the three failed cases, a mobilisation of the tibial component was reported. No statistical differences were found among the groups regarding demographic data ($p > 0.05$). Table 1 shows the detailed results.

Comparison Between the HA Group and Standard Group

No clinical or radiographic variances were seen between the HA and standard groups at any follow-up ($p > 0.05$). Table 2 shows the detailed results.

Hypoallergenic Group

A significant difference was found at T_0, T_1 and T_2, as well as between T_1 and T_2 for both OKS and KSS ($p < 0.05$). Please refer to Table 2 for detailed results.

Table 1 Demographic data for the study groups

	Hypoallergenic Mean ± std (min, max)	Standard Mean ± std (min, max)	*p* value	Test
Age at surgery	67.43 ± 6.35 (54; 78), *n* = 43	70.13 ± 8.35 (44; 89), *n* = 203	0.122	MWU
First follow-up time (T_1)	12.94 ± 0.94 (12; 15), *n* = 43	13.30 ± 1.29 (12; 16), *n* = 203	0. 241	MWU
Last follow-up time (T_2)	69.79 ± 17.49 (34; 95), *n* = 43	67.13 ± 16.20 (34; 95), *n* = 200	0.994	MWU
Gender	26 female 17 male	122 female 81 male	0.964	Fisher
Side	24 right 19 left	105 right 98 left	0.626	Fisher
Weight	72.11 ± 9.40 (54; 95), *n* = 43	75.50 ± 13.88 (50; 116), *n* = 203	0.001	MWU
Height	161.30 ± 10.04 (155; 170), *n* = 43	165.22 ± 9.87 (145; 188), *n* = 203	0.001	MWU
Body mass index	27.70 ± 3.35 (22; 33), *n* = 43	27.66 ± 4.23 (19; 39), *n* = 203	0.969	MWU

MWU Mann–Whitney *U* test, T_1 first follow-up, T_2 last follow-up

Table 2 Diagnosis and pre- and postoperative scores of the 246 patients available for personal

	Hypoallergenic	Standard	*p* value
Oxford Knee Score T_0	23.06 ± 2.70 (18; 28) $n = 43$	22.89 ± 2.64 (16; 28) $n = 203$	0.977
Oxford Knee Score T_1	42.06 ± 1.62 (39; 47)[a] $n = 43$	42.09 ± 2.87 (20; 48)[a] $n = 203$	0.897
Oxford Knee Score T_2	45.04 ± 1.76 (40; 48)[a,b] $n = 43$	44.64 ± 1.93 (40; 48)[a,b] $n = 200$	0.929
KSS T_0	51.25 ± 4.85 (44; 62) $n = 43$	50.80 ± 4.61 (44; 62) $n = 203$	0.997
KSS T_1	87.65 ± 2.03 (82; 91)[a] $n = 43$	86.76 ± 5.46 (44; 91)[a] $n = 203$	0.995
KSS T_2	91.95 ± 3.44 (88; 100)[a,b] $n = 43$	91.39 ± 6.84 (9; 100)[a,b] $n = 200$	0.814
Tibial angle T_2	3.06 ± 2.05 (0; 8) $n = 43$	2.84 ± 2.46 (−6; 9) $n = 200$	0.948
Femoral angle at T_2	7.18 ± 4.56 (−2; 16) $n = 43$	7.06 ± 5.13 (−6; 20) $n = 200$	0.529
Tibial slope at T_2	4.97 ± 3.34 (−3; 11) $n = 43$	5.46 ± 3.13 (−6; 16) $n = 200$	0.064

Follow-up. Values are given as mean ± SD [95% confidence interval] or (minimum; maximum)

[a]Statistical significant difference versus t_0

[b]Statistical significant difference versus T_1

Standard Group

A significant difference was found at T_0, T_1 and T_2, as well as between T_1 and T_2 for both OKS and KSS ($p < 0.05$). Detailed results are reported in Table 2.

Complications/Failure

In the standard group, three (1.47%) patients reported a revision with TKA due to the mobilisation of the tibial component.

Discussion

The main results of the present research illustrate that no clinical or radiographic variances were seen between hypoallergenic and standard CoCr Oxford UKAs at any time points. These results should be considered extremely encouraging, considering the increasing number of successful reports on UKA; in the current literature, Oxford UKA shows a 91% survival rate at 20 years [34].

The possibility of being able to guarantee similar results to patients with metal allergies further increases the interest in this surgery, and therefore, the hypoallergenic UKA should be considered as the ideal treatment in selected sensitive patients with anteromedial knee OA.

Our data significantly contribute to recent interest. The failure of implant continues to occur in a fair percentage of cases, and among them, hypersensitivity to the metal is increasingly becoming a factor. However, even today, the nature and causative mechanism of the relationship between MHS and prosthesis failure remain undefined.

Despite the evidence in the literature of significant incidences of both intolerance to metals and the need for replanting prostheses, our research supports the view that the relation between metal hypersensitivity and revision is presumably not clear and demonstrated.

In light of the significant data of Desai et al., it could be hypothesised that the materials contained within the implant were responsible for hypersensitive reactions [5]. Once the patients underwent the patch test, their bodies reacted to chromium, cobalt and nickel. These are precisely the materials used in our standard group, and the clinical and radiological results are shown to be the same in the HA group, which suggests that the reaction is probably related to other mechanisms and not specifically to a particular material.

Contact with substances that could give rise to hypersensitive reactions was also hypothesised for those who used the coating. The study of Beyer et al., which divided the patients into two cohorts and subjected them to TKA with the coated and uncoated implant variant, presented the same outcomes in both groups at four years' follow-up: the OKS score increased in a comparable manner in both groups, which is in accordance with our study's results [35].

The role of the coating of a prosthetic implant was also analysed by Thomas et al. who compared almost 200 patients undergoing knee arthroplasty to a 5-year follow-up, focusing not only on the clinical outcomes but also on the serum cytokine levels. Based on their analysis,

proinflammatory cytokines, such as Interleukin-8 and Iinterleukin-10, had higher average values in patients with uncoated prostheses, which suggests their possible role in implant failure processes [36].

On the other hand, data differed at several times. It is well known that after excluding various causes of implant failure, with infection topping the list, metal hypersensitivity must always be taken into consideration as a reason for failure. The results of Thakur et al.'s study are confirmed by the fact that after revision with other materials, all patients experienced improvement [16]. Similar results were achieved by Zondervan et al.'s study in which patients with hypersensitivity experienced a significant benefit after a revision with a hypoallergenic component [37].

Hence, the questions arise: how should we proceed? Does preoperative testing make sense to identify the patients who might develop hypersensitivity reactions? Currently, there are no indications for preoperative tests to detect patients with metal hypersensitivity, while only the postoperative test is recommended to patients who develop certain clinical characteristics [38]. This finding seems to have already been encouraged by the study of Frigerio et al. which explained how preoperative tests may not be so useful in light of the discrepancy between the pre- and postoperative results [39].

Important clarifications were provided by Münch et al.'s study in which the patch test did not seem to be the key tool to reveal the patients who would then develop hypersensitivity, but an association between the number of revisions and metal allergy was found [40].

In this respect, the difference between allergy and hypersensitivity should imperatively be clarified given that these terms are often mistakenly used as synonyms. As suggested by Middleton et al., the diagnosis of allergy can be formulated by justifying several specific criteria, whereas the reported 'hypersensitivity' does not justify the use of specific components [41].

Although the results of the study of Walker et al. seem promising in terms of outcomes, we do not believe that an anamnestic questionnaire could represent the most suitable tool to select patients who deserve a particular component in the prosthetic implant [42]. In accordance with the topics covered by Saccomanno et al., we consider that the employment of hypersensitivity screening should be promoted only when a patient's clinical history suggests that it is necessary [43]. Should such a condition be ascertained, it is advisable to think of specific 'hypersensitivity-friendly' implants.

Based on the results obtained from our work and the comparison with the literature, our summary recommendations are as follows: it is certainly important to be able to recognise the signs and symptoms of an implant failure and subsequently trace the ones that can direct us to a hypersensitivity reaction. Moreover, we believe that only patients with a history of metal allergies should be traced and treated properly with specific components in knee arthroplasty**.**

The present study presented several limitations. First, it analyses results for only 24 months after the surgery; however, clinical outcomes may change over this span of time. Besides, the HA group was relatively small although a power analysis was performed to ensure that the sample size was suitable.

Conclusions

The current study showed no clinical or radiographic differences between the hypoallergenic and standard cobalt–chromium groups at any follow-up, with a clinically significant improvement being experienced by both groups over the entire follow-up. In light of these findings, we believe that a specific hypoallergenic implant should be used for the treatment of anteromedial knee OA in selected patients who are clearly allergic to metals.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s43465-021-00486-3.

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Availability of data and materials Raw data have been submitted as supplementary material to the Journal.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Permission for the study was obtained from the local ethical committee.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish All authors consent to the publication of the manuscript.

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