

Hypoallergenic unicompartamental knee arthroplasty and return to sport: comparison between Oxidized Zirconium and Titanium Niobium Nitride

Lorenzo Monti¹, Emanuele Franchi¹, Nicola Ursino², Ilaria Mariani³, Katia Corona⁴, Filippo Maria Anghilieri⁵, Riccardo D'Ambrosi²

¹Istituto Clinico Villa Aprica, GSD, Como, Italy; ²IRCCS Istituto Ortopedico Galeazzi, Via Galeazzi 4, 20161, Milan, Italy; ³Institute for Maternal and Child Health – IRCCS “Burlo Garofolo” – Trieste, Italy; ⁴Università degli Studi del Molise, Dipartimento di Medicina e Scienze della Salute Vincenzo, Tiberio, Campobasso, Italy; ⁵Dipartimento di Scienze Biomediche per la Salute, Università degli Studi di Milano, Milan, Italy

Abstract. *Background:* The present study aims to compare the rate of return to sports in patients who underwent surgery for mobile-bearing UKA with either hypoallergenic TiNbN or with oxidized zirconium alloy implants. *Methods:* The records of two consecutive cohorts for a total of 90 hypoallergenic implants were prospectively analysed. The first cohort consisted of 41 consecutive series of medial mobile-bearing hypoallergenic TiNbN UKA, whereas the second cohort consisted of 49 consecutive medial fixed-bearing hypoallergenic Uni Oxinium. The clinical evaluation involved evaluating each patient's University of California, Los Angeles (UCLA) activity scores and the High-Activity Arthroplasty Score (HAAS). Each patient was clinically evaluated on the day before surgery (T_0), then after a minimum follow-up period of 12 months (T_1), and finally after 24 months (T_2). *Results:* The only pre-operative difference between the two groups involved pre-operative BMI with significantly higher BMI in TiNbN Group ($p < 0.001$). Both groups reported significant improvement at each follow-up compared with the previous and also at the final follow up with respect to UCLA and HAAS ($p < 0.05$), except for UCLA in TiNbN between T_1 and T_2 ($p > 0.05$). Moreover, BMI improved significantly at the final follow up, but only in TiNbN group ($p < 0.05$). *Conclusions:* Both TiNbN and Oxinium UKA procedures enabled patients to return to an acceptable level of sports activity with excellent radiographic outcomes after the final follow up regardless of the age, gender, BMI, and bearing type.

Key words: Unicompartamental knee arthroplasty, return to sport, metal allergy, hypoallergenic implants, oxidized zirconium, titanium niobium nitride

Introduction

One of the most debated topics in modern knee arthroplasty is the influence of a metal allergy as a potential cause of implant failure (1-3).

Metal hypersensitivity has been reported in 20% to 25% of patients with well-functioning implants and up to 60% with poorly functioning arthroplasties or loosening prostheses (4). This phenomenon is

speculated to be caused by the indirect activation of macrophages by metal ions released after contact with host fluids; therefore, a loosening prosthesis could release more ions than an intact implant, thus eliciting an allergic reaction (5).

Nickel undoubtedly appears to be the metal most commonly responsible for causing an adverse reaction in humans, followed by Cobalt and Chromium (CoCr) (6). The latter two are generally used in orthopaedic

implants, such as standard knee prosthetic components in the form of CoCr alloy.

On the other hand, titanium, vanadium, tantalum, oxidized zirconium, and alumina are considered relatively biologically inert and have been increasingly considered for the design of modern hypoallergenic implants, providing excellent alternatives to standard CoCr.

For instance, ceramic coatings have been proposed, besides their chemical inertness, for their notable hardness and bioactive features (7-9). Titanium niobium nitride (TiNbN) and oxidized zirconium (Zr) prosthetic components show high surface resistance to abrasion and corrosion, features that enable a long-lasting biomechanical function.

Return to sports activity following knee arthroplasty is of concern to every patient. At present, people are not only able to live longer than in the past, but they also wish to stay active up to and after retiring, having, therefore, higher demands on the surgically treated joint (10,11).

Physical activity, low to moderate in intensity, is safe and increases living standards through higher physical and social mobility and better cardiovascular performance. In addition, some authors have reported several benefits of knee arthroplasty regarding general health and sports performance (12-14).

However, returning to sports activity after unicompartmental knee arthroplasty (UKA) has not been investigated as thoroughly as other outcomes of functional recovery.

The present study aims to compare the rate of return to sports in patients who underwent surgery for UKA with either hypoallergenic TiNbN alloy or with oxidized zirconium alloy implants.

Methods

All the procedures involving human participants in this study were performed in accordance with the ethical standards of the institutional and/or national research committee, as well as the 1964 Helsinki Declaration and its amendments or comparable ethical standards. The study was conducted following the STROBE checklist for cohort studies (15). Informed

consent was obtained from all the participants included in the study. Appropriate ethical approval was obtained from the local ethics committee.

Two consecutive cohorts for a total of 90 patients, with proved metal hypersensitivity, undergoing cemented UKA were included (mean age 66.9 ± 8.35 ; 61 [67.8%] females – 29 [32.2%] males) (16). The first cohort consisted of 41 consecutive series of medial mobile-bearing hypoallergenic Oxford TiNbN UKA with the Oxford Microplasty instrumentation (TiNbN Group/Zimmer-Biomet, Warsaw, Indiana, USA). The second cohort consisted of 49 consecutive medial fixed-bearing hypoallergenic Journey Uni Oxinium UKA (Oxinium Group/Smith & Nephew, Watford, United Kingdom).

The two compared groups were homogeneous for age, gender and clinical parameters (Table 1).

In all patients, the surgery was performed by two of the authors (LM and NU), respectively, who have a vast experience in Oxinium and TiNbN UKA (17).

In both groups, the surgery was performed to treat isolated anteromedial OA or avascular necrosis (AVN) of the medial femoral condyle with bone-on-bone OA. Pre-operative magnetic resonance imaging (MRI) confirmed that both cruciate and collateral ligaments were intact in all the patients. Radiographic inclusion criteria followed those defined by the Oxford group (18). Exclusion criteria for participation in this study were as follows: (1) missing data or radiographs unsuitable for an exact measurement, (2) revision surgery, and (3) previous surgery of the affected knee (except arthroscopy for meniscectomy).

The clinical follow-up was performed by two independent clinicians who were not involved in the index surgery. The clinical evaluation involved evaluating each patient's University of California, Los Angeles (UCLA) activity scores and the High-Activity Arthroplasty Score (HAAS). The UCLA score measures the level of physical activity on a scale from 1 ("no physical activity, depend on other") to 10 ("regular participation in impact sports") and is validated for use in arthroplasty surgery. The HAAS score (scored from 0 to 18, worst to best) was designed to detect subtle variations in the physical function of highly functioning patients. Each patient was clinically evaluated on the day before

Table 1. Characteristics of the patient study population.

	Oxinium n (%)	TiNbN n (%)	p value
N	49	41	
Gender			
Female	28 (57.1)	33 (80.5)	0.033
Male	21 (42.9)	8 (19.5)	
Age	67.31 ± 9.68	66.41 ± 6.50	0.493
Age			
<=65yrs	23 (46.9)	20 (48.8)	1.000
>65yrs	26 (53.1)	21 (51.2)	
Weight	67.65 ± 13.21	73.17 ± 10.82	0.059
Height	1.67 ± 0.09	1.62 ± 0.04	0.008
Pre operative BMI	24.19 (3.35)	27.97 (3.62)	<0.001
Pre operative BMI			
<25	28 (57.1)	14 (34.1)	0.049
>=25	21 (42.9)	27 (65.9)	
Side			
Right	20 (40.8)	23 (56.1)	0.217
Left	29 (59.2)	18 (43.9)	
Length of follow-up			
First follow-up, months (T ₁)	12.04 ± 0.98	12.37 ± 0.70	0.017
Second follow-up, months (T ₂)	37.27 ± 6.54	67.03 ± 18.62	<0.001

SD=Standard deviation; *=statistical significant value (p<0.05)

surgery (T₀), then after a minimum follow-up period of 12 months (T₁), and finally after 24 months (T₂) (19,20).

Positioning of the UKA was evaluated at a minimum two-year follow-up period (T₂), as specified by radiological analysis in the Oxford Partial Knee Surgical Technique operating manual, using standing anteroposterior (AP) and lateral plain radiographs of the knee.

The following parameters were measured according to the manufacturer's manuals (18):

- *Femoral component varus/valgus.* The angle between the femoral component and the femoral axis in the coronal plane; an angle of 7° was seen as neutral, with a range of tolerance of ±10°.
- *Tibial component varus/valgus.* The angle between the tibial axis and a line drawn along the tibial tray in the coronal plane; the range of tolerance was 0° ± 5°.
- *Anteroposterior slope.* The angle between a line drawn along the tibial tray and perpendicular to the tibial axis in the lateral view; a slope of 7° was seen as optimal, with a range of tolerance of ± 5° (2°–12°).

After extracting the Digital Imaging and Communications (DICOM) in Medicine data from Picture Archiving and Communications System (PACS), it was evaluated using OsiriX® imaging software (version 4.1.2 32-bit) by two independent observers, who were unaware of the instrumentation used for implantation (20).

Statistical Analysis

A sample of 82 subjects, 41 for each prosthesis group, was estimated to be adequate to detect a 1.5-point difference in UCLA score between Oxinium and TiNbN UKA, assuming a standard deviation of 2, 5% type I error and 90% power, as well as using a non-parametrical test. Furthermore, this sample was adequate to compare subsequent measurements of UCLA score in the same group, with a 95% power to detect a 1 point mean difference of UCLA score, assuming a standard deviation of 2 and 5% type I error. Additional eight subjects were recruited for the Oxinium prosthesis group to ensure statistical significance, in case of adverse events. Descriptive analyses are presented by absolute number and percentage or mean and standard deviation (SD). Physical activity indices at the same follow-up measurements (i.e., UCLA and HAAS), angles (i.e., femoral angle, tibial angle, and slope) and BMI were compared between Oxinium and TiNbN prosthesis groups using a t-test or a Wilcoxon-Mann Whitney test. A comparison among different follow-up measurements within the same prosthesis group was conducted for physical activity indices and BMI with a repeated measure ANOVA or a Wilcoxon signed ranks test. Bonferroni adjustment was used for multiple comparisons. Furthermore, differences between CoCr and TiNbN

prosthesis in patients with the same gender or similar age or BMI were assessed by applying the previous statistical analysis to the subset identified by gender or similar age or BMI, dichotomised at their rounded average value. Lastly, we studied and tested correlations among physical activity indices, angles, and BMI in each prosthesis group. All tests were two-sided, and p-values less than 0.05 were taken as statistically significant. Statistical analyses were conducted in R version 3.6.3.3.

Results

The only pre-operative difference between the two groups involved pre-operative BMI with significantly higher BMI in the TiNbN Group ($p < 0.001$). Detailed results are reported in Table 1.

Both groups reported significant improvement at each follow-up compared with the previous and at final follow up with respect to UCLA and HAAS ($p < 0.05$), except for UCLA in TiNbN between T_1 and T_2 ($p > 0.05$). Moreover, BMI improved significantly at the final follow up, but only in the TiNbN group ($p < 0.05$).

The only difference between the two groups with respect to HAAS at T_1 and T_2 was the higher value in the TiNbN group ($p < 0.05$). At the final follow-up, a

Table 2. Clinical and radiographic results for all patients, in Oxinium and TiNbN group respectively, at T_0 , T_1 and T_2

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
N	49	41			49	41
Physical activity indexes						
UCLA						
T_0	4.04 ± 0.96	3.68 ± 1.17	0.131	T_0 - T_1	<0.001*	<0.001*
T_1	6.06 ± 1.23	6.15 ± 0.76	0.830	T_0 - T_2	<0.001*	<0.001*
T_2	6.33 ± 1.28	6.34 ± 0.62	0.589	T_1 - T_2	0.005*	0.164
HAAS						
T_0	5.12 ± 1.39	4.51 ± 1.60	0.106	T_0 - T_1	<0.001*	<0.001*
T_1	9.49 ± 2.06	10.34 ± 1.30	0.013*	T_0 - T_2	<0.001*	<0.001*
T_2	10.12 ± 2.17	11.00 ± 0.89	0.004*	T_1 - T_2	<0.001*	0.010*

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
Angles at T₂						
Tibial angle	0.02° ± 3.65	2.83° ± 2.07	<0.001*			
Femoral angle	4.67° ± 2.95	6.90° ± 4.27	0.008*			
Slope	5.76 ± 2.74	4.90 ± 3.10	0.167			
BMI						
T ₀	24.19 ± 3.35	27.97 ± 3.62	<0.001*	T ₀ -T ₂	0.548	<0.001*
T ₂	24.06 ± 3.35	26.84 ± 3.11	<0.001*			

SD=Standard deviation; *=statistical significant value ($p < 0.05$)

UCLA=University of California, Los Angeles activity scores; HAAS=the High-Activity Arthroplasty Score.

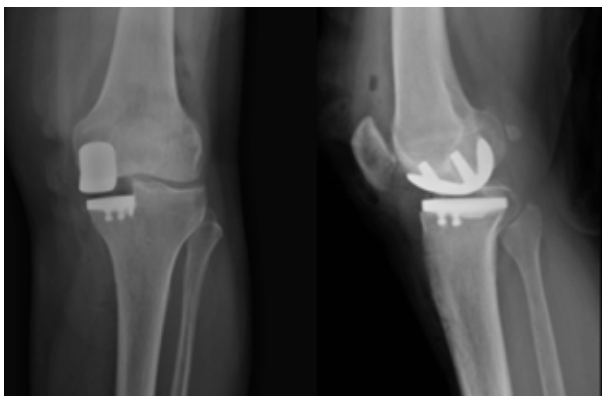


Figure 1. Left knee; Anteroposterior and lateral view of the medial fixed-bearing Oxinium knee arthroplasty.

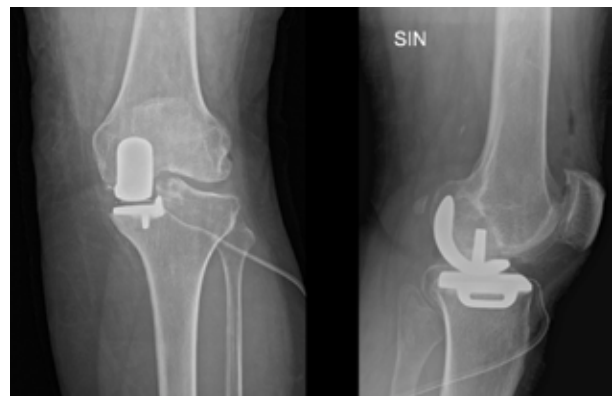


Figure 2. Left knee; Anteroposterior and lateral view of the medial mobile-bearing TiNbN knee arthroplasty.

difference was found also in the tibial and femoral angle ($p < 0.05$). Detailed results are reported in Table 2. Figures 1 and 2 show respectively a fixed-bearing Ox medial knee arthroplasty and mobile-bearing TiNbN medial knee arthroplasty.

Subgroups

All subgroups showed significant improvement at the final follow-up for UCLA and HAAS when compared with the pre-operative value ($p < 0.05$). Only subgroups in the TiNbN Group showed significant

improvement in BMI. Detailed results are reported in Tables 3, 4, 5, 6, 7 and 8.

Correlations

A significant positive correlation was found between BMI and HAAS in TiNbN ($p < 0.05$). Detailed correlations are reported in Table 9.

Complications

No complications or failures were reported in both groups.

Table 3. Clinical and radiographic results for male patients, in Oxinium and TiNbN group respectively, at T₀, T₁ and T₂

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
N	21	8			21	8
Physical activity indexes						
UCLA						
T ₀	4.19 ± 1.08	3.75 ± 1.67	0.576	T ₀ -T ₁	<0.001*	0.044*
T ₁	6.29 ± 1.42	6.12 ± 0.35	0.602	T ₀ -T ₂	<0.001*	0.044*
T ₂	6.62 ± 1.40	6.12 ± 0.35	0.084	T ₁ -T ₂	0.032*	1
HAAS						
T ₀	5.38 ± 1.69	4.38 ± 1.92	0.265	T ₀ -T ₁	<0.001*	0.042*
T ₁	9.95 ± 2.29	10.50 ± 1.07	0.304	T ₀ -T ₂	<0.001*	0.042*
T ₂	10.48 ± 2.25	11.12 ± 0.99	0.236	T ₁ -T ₂	0.028*	1
Angles at T₂						
Tibial angle	-0.24° ± 3.21	2.50° ± 2.07	0.025*			
Femoral angle	4.38° ± 3.34	7.88° ± 3.76	0.027*			
Slope	5.71 ± 2.97	4.12 ± 1.89	0.167			
BMI						
T ₀	25.69 ± 2.11	27.65 ± 2.27	0.045*	T ₀ -T ₂	0.092	0.014*
T ₂	25.16 ± 2.68	26.32 ± 1.42	0.118			

SD=Standard deviation; *=statistical significant value (p<0.05)

UCLA=University of California, Los Angeles activity scores; HAAS=the High-Activity Arthroplasty Score.

Table 4. Clinical and radiographic results for female patients, in Oxinium and TiNbN group respectively, at T₀, T₁ and T₂

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
N	28	33			28	33
Physical activity indexes						
UCLA						
T ₀	3.93 ± 0.86	3.67 ± 1.05	0.302	T ₀ -T ₁	<0.001*	<0.001*
T ₁	5.89 ± 1.07	6.15 ± 0.83	0.406	T ₀ -T ₂	<0.001*	<0.001*
T ₂	6.11 ± 1.17	6.39 ± 0.66	0.391	T ₁ -T ₂	0.197	0.164
HAAS						
T ₀	4.93 ± 1.12	4.55 ± 1.54	0.377	T ₀ -T ₁	<0.001*	<0.001*
T ₁	9.14 ± 1.84	10.30 ± 1.36	0.010*	T ₀ -T ₂	<0.001*	<0.001*
T ₂	9.86 ± 2.10	10.97 ± 0.88	0.007*	T ₁ -T ₂	0.008*	0.025*
Angles at T₂						
Tibial angle	0.21° ± 4.00	2.91° ± 2.10	0.004*			
Femoral angle	4.89° ± 2.67	6.67° ± 4.40	0.096			
Slope	5.79 ± 2.60	5.09 ± 3.33	0.366			

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
BMI						
T ₀	23.06 ± 3.69	28.05 ± 3.91	<0.001*	T ₀ -T ₂	0.414	<0.001*
T ₂	23.23 ± 3.60	26.97 ± 3.40	<0.001*			

SD=Standard deviation; *=statistical significant value ($p < 0.05$)

UCLA=University of California, Los Angeles activity scores; HAAS=the High-Activity Arthroplasty Score.

Table 5. Clinical and radiographic results for young patients (≤ 65 years), in Oxinium and TiNbN group respectively, at T₀, T₁ and T₂

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
N	23	20			23	20
Physical activity indexes						
UCLA						
T ₀	4.48 ± 0.79	3.50 ± 0.69	<0.001*	T ₀ -T ₁	<0.001*	<0.001*
T ₁	6.48 ± 1.31	6.15 ± 0.88	0.247	T ₀ -T ₂	<0.001*	<0.001*
T ₂	6.83 ± 1.30	6.40 ± 0.68	0.038*	T ₁ -T ₂	0.018*	1
HAAS						
T ₀	5.52 ± 1.38	4.25 ± 0.91	0.001*	T ₀ -T ₁	<0.001*	<0.001*
T ₁	9.65 ± 2.33	10.50 ± 1.43	0.176	T ₀ -T ₂	<0.001*	<0.001*
T ₂	10.35 ± 2.19	11.10 ± 0.97	0.179	T ₁ -T ₂	0.011*	0.174
Angles at T₂						
Tibial angle	0.43° ± 3.10	3.05° ± 1.96	0.004*			
Femoral angle	5.48° ± 3.17	6.10° ± 4.71	0.668			
Slope	5.83 ± 3.26	5.30 ± 3.60	0.704			
BMI						
T ₀	24.72 ± 2.84	27.31 ± 3.40	0.019*	T ₀ -T ₂	1	<0.001*
T ₂	24.67 ± 2.92	26.46 ± 3.07	0.075			

SD=Standard deviation; *=statistical significant value ($p < 0.05$)

UCLA=University of California, Los Angeles activity scores; HAAS=the High-Activity Arthroplasty Score.

Table 6. Clinical and radiographic results for older patients (≤ 65 years), in Oxinium and TiNbN group respectively, at T₀, T₁ and T₂

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
N	26	21			26	21
Physical activity indexes						
UCLA						
T ₀	3.65 ± 0.94	3.86 ± 1.49	0.395	T ₀ -T ₁	<0.001*	0.001*
T ₁	5.69 ± 1.05	6.14 ± 0.65	0.139	T ₀ -T ₂	<0.001*	<0.001*

Table 6 (Continued)

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
T ₂	5.88 ± 1.11	6.29 ± 0.56	0.223	T ₁ -T ₂	0.330	0.447
HAAS						
T ₀	4.77 ± 1.34	4.76 ± 2.05	0.663	T ₀ -T ₁	<0.001*	<0.001*
T ₁	9.35 ± 1.83	10.19 ± 1.17	0.029*	T ₀ -T ₂	<0.001*	<0.001*
T ₂	9.92 ± 2.17	10.90 ± 0.83	0.006*	T ₁ -T ₂	0.022*	0.096
Angles at T₂						
Tibial angle	-0.35° ± 4.11	2.62° ± 2.20	0.005*			
Femural angle	3.96° ± 2.60	7.67° ± 3.75	0.001*			
Slope	5.69 ± 2.24	4.52 ± 2.58	0.127			
BMI						
T ₀	23.71 ± 3.74	28.60 ± 3.80	<0.001*	T ₀ -T ₂	0.556	<0.001*
T ₂	23.52 ± 3.66	27.20 ± 3.19	0.001*			

SD=Standard deviation; *=statistical significant value (p<0.05)

UCLA=University of California, Los Angeles activity scores; HAAS=the High-Activity Arthroplasty Score.

Table 7. Clinical and radiographic results for normal weight patients (BMI<25), in Oxinium and TiNbN group respectively, at T₀, T₁ and T₂

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
N	28	14			28	14
Physical activity indexes						
UCLA						
T ₀	3.93 ± 0.81	3.71 ± 0.99	0.269	T ₀ -T ₁	<0.001*	0.004*
T ₁	6.07 ± 0.94	6.29 ± 0.73	0.474	T ₀ -T ₂	<0.001*	0.004*
T ₂	6.29 ± 0.85	6.43 ± 0.65	0.621	T ₁ -T ₂	0.123	1
HAAS						
T ₀	5.18 ± 1.42	3.36 ± 1.28	<0.001*	T ₀ -T ₁	<0.001*	0.003*
T ₁	9.43 ± 1.71	9.79 ± 1.05	0.380	T ₀ -T ₂	<0.001*	0.003*
T ₂	10.07 ± 1.49	10.64 ± 0.74	0.103	T ₁ -T ₂	0.003*	0.174
Angles at T₂						
Tibial angle	-0.46° ± 3.10	2.86° ± 1.96	0.001*			
Femural angle	4.82° ± 2.92	6.00° ± 5.14	0.574			
Slope	5.93 ± 2.62	6.14 ± 2.80	0.608			
BMI						
T ₀	21.83 ± 1.97	23.80 ± 1.20	0.001*	T ₀ -T ₂	0.505	0.012*
T ₂	21.97 ± 1.95	23.45 ± 1.20	0.017*			

SD=Standard deviation; *=statistical significant value (p<0.05)

UCLA=University of California, Los Angeles activity scores; HAAS=the High-Activity Arthroplasty Score.

Table 8. Clinical and radiographic results for overweight patients (BMI \geq 25), in Oxinium and TiNbN group respectively, at T₀, T₁ and T₂

	Groups		Between group comparison <i>p</i> value	Within group time comparison		
	Oxinium <i>Mean ± SD</i>	TiNbN <i>Mean ± SD</i>			Oxinium <i>Adj p value</i>	TiNbN <i>Adj p value</i>
N	21	27			21	27
Physical activity indexes						
UCLA						
T ₀	4.19 ± 1.12	3.67 ± 1.27	0.198	T ₀ -T ₁	<0.001*	<0.001*
T ₁	6.05 ± 1.56	6.07 ± 0.78	0.862	T ₀ -T ₂	<0.001*	<0.001*
T ₂	6.38 ± 1.72	6.30 ± 0.61	0.232	T ₁ -T ₂	0.070	0.267
HAAS						
T ₀	5.05 ± 1.40	5.11 ± 1.42	0.733	T ₀ -T ₁	<0.001*	<0.001*
T ₁	9.57 ± 2.50	10.63 ± 1.33	0.044*	T ₀ -T ₂	<0.001*	<0.001*
T ₂	10.19 ± 2.87	11.19 ± 0.92	0.075	T ₁ -T ₂	0.071	0.096
Angles at T₂						
Tibial angle	0.67° ± 4.28	2.81° ± 2.17	0.043*			
Femoral angle	4.48° ± 3.06	7.37° ± 3.75	0.008*			
Slope	5.52 ± 2.93	4.26 ± 3.11	0.128			
BMI						
T ₀	27.33 ± 1.90	30.13 ± 2.30	<0.001*	T ₀ -T ₂	0.196	<0.001*
T ₂	26.83 ± 2.77	28.60 ± 2.19	0.010*			

SD=Standard deviation; *=statistical significant value (p<0.05)

UCLA=University of California, Los Angeles activity scores; HAAS=the High-Activity Arthroplasty Score.

Table 9. Statistical Significant Correlations

Oxinium N=41			TiNbN N=49		
Variables		<i>Rho</i> (<i>p</i> value)	Variables		<i>Rho</i> (<i>p</i> value)
Tibial angle	Femoral angle	0.36 (0.011*)	BMI T ₀	HAAS T ₀	0.53 (<0.001*)
			BMI T ₂	HAAS T ₀	0.47 (0.002*)
			BMI T ₂	HAAS T ₂	0.31 (0.046*)

Discussion

The main findings of the current study demonstrate that different hypoallergenic UKAs lead to a return to sports activity higher than the pre-operative score in patients with metal allergy and isolated anteromedial OA.

To our knowledge, this is the first study reporting return to sports activity that compares TiNbN or Oxinium UKA.

Metal hypersensitivity has been blamed as a possible cause of impaired postoperative function, hypersensitive skin reactions, persistent pain, or peri-implant osteolysis-induced implant failure, which is a major issue, considering that the number of patients undergoing primary knee arthroplasty is increasing annually between 10% to 48% (21).

There has been a degree of acceptance in some countries that metal related pathology may exist as demonstrated by the Australian Arthroplasty register,

where metal hypersensitivity was reported as the fifth most common cause for revision hip arthroplasty, composing 5.9% of all revisions (21).

When introduced into the biological system, all metals undergo a varying degree of corrosion. The resultant metal ions do not act as a sensitizer in themselves but may form complexes with native serum proteins, yielding a reactive antigen. These implant-degradation complexes are the primary stimulators in component-related metal hypersensitivity reactions. A type-IV cell-mediated mechanism triggers the activation of T-lymphocytes that release inflammatory cytokines, including interferon- γ (IFN γ), tumour necrosis factor- α (TNF- α), interleukin-1 (IL-1), and interleukin-2 (IL-2). This pathway leads to a self-propagating series of macrophage and T-cell activation, with resultant tissue inflammation and degradation (22).

Although metal allergy is a real, well-known pathology, there is still a lack of consensus regarding its clinical impact in daily practice, particularly in the UKA. Recently, Attila et al. compared the functional outcomes and eosinophil counts of UKA patients with and without a history of metal hypersensitivity (23).

Of the total 128 patients, 13 (10.2%) reported a history of metal hypersensitivity prior to the surgery. There was no statistically significant difference between patients with or without a history of metal hypersensitivity with respect to the functional outcomes or eosinophil counts (23).

In contrast, Thomas et al. assessed immunological and clinical parameters in patients who underwent standard and coated total knee arthroplasty (TKA). Five years of follow-up data were obtained from three centres, which used either a standard TKA or the identical implant with multilayer surface zirconium nitride-based coating. Of the 196 patients, 97 had arthroplasty with a coated surface, and 99 were treated by a standard TKA of the same type. The survival rate was 98% for coated and 97% for uncoated implants after five years. Mechanical axis and KSS pain score were comparable. Most serum cytokine levels were comparable, but mean interleukin-8 and interleukin-10 levels were higher in the group with an uncoated implant (24).

In our prospective study, we decided to use different implants: the first with a coating of TiNbN,

and the other composed of Oxidate Zirconium. Hypoallergenic implants can be divided into two types: coated implants and non-allergic implants. CoCr implants coated with a hypersensitivity-friendly thin layer provide the advantage of retaining part of the superior tribological properties of CoCr; yet, the hypersensitivity-friendly layer, after scratching or wear can become damaged, exposing the underlying allergenic alloy. Non-allergenic implants are made of non-CoCr alloys; while reducing the risk of exposure to allergenic metals, they usually show inferior physical properties compared to CoCr alloys (25).

The aim of the development of the Titanium Nitride (TiN) coating of knee implants was to improve their biocompatibility and mechanical properties. TiN is applied as a 3–4 μm layer on CoCr implants. Specifically, TiN showed high resistance to adhesive wear and less adhesion to polyethylene. In addition, while CoCr catalyses polyethylene degradation, TiN is inert. Sealing the CoCr surface, TiN reduces the number of cobalt and chromium ions released, avoiding hypersensitivity reactions (25).

Zirconium is a metal with physical properties resembling those of titanium. Its oxide, named zirconia, is a ceramic material. The coupled zirconium-oxidized zirconium has been used as a hybrid material to produce knee arthroplasty implants. It is composed of a core of solid metal, surrounded by a ceramic zirconium oxide (ZrOx) layer, which cannot be considered as a coating but instead as the surface of the metal alloy. This material couples the superficial wear characteristics of the ceramic zirconia and the strength of the internal metal. ZrOx causes less wear of the polyethylene than CoCr components and shows a better resistance to abrasion. In an *in vitro* study, a reduction of 42% of polyethylene wear was seen (25).

With no nickel, it is safe to be used in metal-sensitive patients. The ZrOx femoral component is usually coupled with a pure titanium tibial baseplate (25).

The first objective of our study was to analyse the return to sports after UKA in patients with metal allergy and isolated medial OA of the knee, as a return to activity following knee arthroplasty is of concern to every patient. It is well known that practising physical activity from low to moderate intensity is safe, increasing standards of living through higher physical and social mobility

and better cardiovascular performance. Furthermore, and from a public health perspective, this reduces costs related to treatments in this population (14). Some authors have even reported the benefits of knee arthroplasty to general health and sports performance (14).

However, returning to sports activity after knee arthroplasty is not as well studied as other aspects of functional recovery. Our data are coherent with current literature, as all groups and subgroups of the two cohorts reported significant improvement with respect to return to sport in two different scales.

Kleeblad et al. analysed patient satisfaction with a return to sports after UKA and their preferred activities. Pre-operatively, 81% participated in sports, which increased to 90% patients after UKA. Satisfaction with a return to sports was recorded in 83%; return to a higher or similar level was reported in 85.4% of the cases (26).

The mean preoperative UCLA score improved from 5.93 ± 2.19 to 6.78 ± 1.92 and HAAS score from 9.13 ± 3.55 to 11.08 ± 2.83 , postoperatively. Regression analyses showed that male sex, preoperative UCLA score and sports participation predicted high activity scores postoperatively (26).

Lo Presti et al. in 2018 surveyed 53 athletic patients who underwent cemented medial UKA to determine not only their subjective and objective evaluation of clinical status with Hospital for Special Surgery (HSS) and visual analogue score (VAS) score but also their sporting and recreational activities at a mean follow up of 48 months. At the last follow up, 48 of 53 patients were engaged in sports and recreational disciplines, resulting in a return to activity rate of 90%. No early failure and no cases of revision were reported. The frequency of activities (sessions per week) and the time session remained constant at the time of the survey. The most common activities after surgery were hiking, cycling, and swimming (27).

The present study bears some limitations that should be considered. The study setting is a high-volume tertiary referral hospital; therefore, our findings may not be generalisable to institutions where UKAs are not performed frequently. Moreover, this study followed patients for only 1–2 years post-surgically; however, patient activity levels may change beyond this period.

Conclusions

Both TiNbN and Oxinium UKA procedures enabled patients to return to an acceptable level of sports activity with excellent radiographic outcomes after the final follow-up regardless of the age, gender, BMI, and bearing type. Considering these findings, it is suggested that a specific hypoallergenic implant (coated or non-allergenic) should be used for the treatment of anteromedial knee OA in young and active patients who are allergic to metals.

Acknowledgements: None

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

Ethical Approval: Permission for the study was obtained from the local ethical committee (a copy of the ethical approval has been submitted)

Consent for Publication: All authors consent to the publication of the manuscript

Funding: None

Competing Interests: None

References

1. Innocenti M, Carulli C, Matassi F, Carossino AM, Brandi ML, Civinini R. Total knee arthroplasty in patients with hypersensitivity to metals. *Int Orthop* 2014; 38: 329-33.
2. Bravo D, Wagner ER, Larson DR, Davis MP, Pagnano MW, Sierra RJ. No Increased Risk of Knee Arthroplasty Failure in Patients With Positive Skin Patch Testing for Metal Hypersensitivity: A Matched Cohort Study. *J Arthroplasty* 2016; 31: 1717-21.
3. Thienpont E, Berger Y. No allergic reaction after TKA in a chrome-cobalt-nickel-sensitive patient: case report and review of the literature. *Knee Surg Sports Traumatol Arthrosc* 2013; 21: 636-40.

4. Bao W, He Y, Fan Y, Liao Y. Metal allergy in total-joint arthroplasty: Case report and literature review. *Medicine (Baltimore)* 2018; 97: e12475.
5. Savarino L, Granchi D, Ciapetti G, et al. Ion release in patients with metal-on-metal hip bearings in total joint replacement: a comparison with metal-on-polyethylene bearings. *J Biomed Mater Res* 2002; 63: 467-74.
6. Baumann CA, Crist BD. Nickel allergy to orthopaedic implants: A review and case series. *J Clin Orthop Trauma* 2020; 11: S596-S603.
7. D'Ambrosi R, Anghileri FM, Corona K, et al. Similar rates of return to sports and BMI reduction regardless of age, gender and preoperative BMI as seen in matched cohort of hypoallergenic and standard Cobalt Chromium medial unicompartmental knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2021. Epub ahead of print.
8. Ragone V, Canciani E, Biffi CA, et al. CoCrMo alloys ions release behavior by TiNbN coating: an in vitro study. *Biomed Microdevices* 2019; 21: 61.
9. Spector BM, Ries MD, Bourne RB, Sauer WS, Long M, Hunter G. Wear performance of ultra-high molecular weight polyethylene on oxidized zirconium total knee femoral components. *J Bone Joint Surg Am* 2001; 83-A: 80-6.
10. Jahnke A, Mende JK, Maier GS, et al. Sports activities before and after medial unicompartmental knee arthroplasty using the new Heidelberg Sports Activity Score. *Int Orthop* 2015; 39: 449-54.
11. Ethgen O, Bruyère O, Richey F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. *J Bone Joint Surg Am* 2004; 86: 963-74.
12. Canovas F, Dagneaux L. Quality of life after total knee arthroplasty. *Orthop Traumatol Surg Res* 2018; 104: S41-S46.
13. Papalia R, Zampogna B, Torre G, et al. Return to sport activity in the elderly patients after unicompartmental knee arthroplasty: a systematic review and meta-analysis. *J Clin Med* 2020; 9: 1756
14. Dagneaux L, Bourlez J, Degeorge B, Canovas F. Return to sport after total or unicompartmental knee arthroplasty: An informative guide for residents to patients. *EFORT Open Rev* 2017; 2: 496-501.
15. Cuschieri S. The STROBE guidelines. *Saudi J Anaesth* 2019; 13: S31-S4.
16. Fransway AF, Zug KA, Belsito DV, et al. North American Contact Dermatitis Group patch test results for 2007-2008. *Dermatitis* 2013; 24: 10-21.
17. Zhang Q, Zhang Q, Guo W, et al. The learning curve for minimally invasive Oxford phase 3 unicompartmental knee arthroplasty: cumulative summation test for learning curve (LC-CUSUM). *J Orthop Surg Res* 2014; 9: 81.
18. Hamilton TW, Pandit HG, Lombardi AV, et al. Radiological Decision Aid to determine suitability for medial unicompartmental knee arthroplasty: development and preliminary validation. *Bone Joint J* 2016; 98-B: 3-10.
19. Monticone M, Capone A, Frigau L, et al. Development of the Italian version of the High-Activity Arthroplasty Score (HAAS-I) following hip and knee total arthroplasty: cross-cultural adaptation, reliability, validity and sensitivity to change. *J Orthop Surg Res* 2018; 13: 81.
20. Calistri A, Di Martino L, Gurzi MD, Bove M, De Smet K, Villani C. Italian version of University of California at Los Angeles (UCLA) Activity Score: cross-cultural adaptation. *J Arthroplasty* 2014; 29: 1733-5.
21. Middleton S, Toms A. Allergy in total knee arthroplasty: a review of the facts. *Bone Joint J* 2016; 98-B: 437-41.
22. Eftekhary N, Shepard N, Wiznia D, Iorio R, Long WJ, Vigdorichik J. Metal Hypersensitivity in Total Joint Arthroplasty. *JBJS Rev* 2018; 6: e1.
23. Atilla HA, Çevik HB, Akdoğan M, Aslan H. Self-reported metal hypersensitivity in patients undergoing unicompartmental knee arthroplasty. *J Clin Orthop Trauma* 2020; 14: 17-21
24. Thomas P, Hisgen P, Kiefer H, et al. Blood cytokine pattern and clinical outcome in knee arthroplasty patients: comparative analysis 5 years after standard versus "hypoallergenic" surface coated prosthesis implantation. *Acta Orthop* 2018; 89: 646-51.
25. Saccomanno MF, Sircana G, Masci G, et al. Allergy in total knee replacement surgery: Is it a real problem? *World J Orthop* 2019; 10: 63-70.
26. Kleebblad LJ, Strickland SM, Nwachukwu BU, Kerkhoffs GMMJ, Pearle AD. Satisfaction with return to sports after unicompartmental knee arthroplasty and what type of sports are patients doing. *Knee* 2020; 27: 509-17.
27. Lo Presti M, Costa GG, Cialdella S, et al. Return to Sports after Unicompartmental Knee Arthroplasty: Reality or Utopia? A 48-Month Follow-Up Prospective Study. *J Knee Surg* 2019; 32: 186-91.

Correspondence:

Received: 11 December 2021

Accepted: 8 February 2022

Dr. Riccardo D'Ambrosi, MD

IRCCS Istituto Ortopedico Galeazzi, Via Galeazzi 4, 20161, Milan, Italy

riccardo.dambrosi@hotmail.it

00393397066151