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Primary Knee

Titanium Niobium Nitride Mobile-Bearing Unicompartmental Knee Arthroplasty Results in Good to Excellent Clinical and Radiographic Outcomes in Metal Allergy Patients With Medial Knee Osteoarthritis



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ABSTRACT

Background: The main purpose of the present study was to analyze the clinical and radiological outcomes of patients with positive skin patch tests who underwent medial mobile-bearing titanium niobium nitride unicompartmental knee arthroplasty (UKA) during a mid-term follow-up.

Methods: Thirty-seven patients with positive skin patch tests were included in this prospective study. The clinical evaluation consisted of Oxford Knee Score and Knee Society Score (KSS) reports. Each patient was clinically evaluated the day before surgery (T_0) as well as at T_1 (11.9 ± 1.3 months) and during the final follow-up T_2 (67.2 ± 19.1 months). The positioning of the UKA was evaluated during the final follow-up using standardized radiographs (T_2 : 67.2 ± 19.1 months).

Results: Oxford and KSS ranged from a respective mean preoperative value of 23.0 ± 2.7 and 51.5 ± 5.0 to 42.1 ± 1.7 and 87.6 ± 2.2 , respectively, at T_1 ($P < .001$) and to the final values of 45.0 ± 1.9 and 91.9 ± 3.4 , respectively, at T_2 ($P < .001$ both vs T_1 and T_2). At T_2 , the mean femoral angle was $7.0^\circ \pm 4.5^\circ$, mean tibial angle was $3.0^\circ \pm 2.1^\circ$, and mean tibial slope was $5.1^\circ \pm 3.2^\circ$. A significant difference was found between KSS and Oxford with ANOVA for repeated measures over time ($P < .001$). The Oxford and KSS scores showed significant improvements during each follow-up. No complications were found, and not a single patient required a revision surgery during the follow-up period.

Conclusion: The hypoallergenic titanium niobium nitride mobile-bearing UKA showed comparable results to standard CoCr UKA regardless of the gender, age, BMI, and implant size of metal allergy patients with medial knee osteoarthritis. Careful patient selection processes and accurate medical histories played key roles in the choice of hypersensitivity-friendly implants.

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Today, metal hypersensitivity in knee arthroplasty as a cause of premature failure is one of the most controversial issues. Metal

hypersensitivity is a common finding among patients, affecting about 10% to 15% of the general population. Skin hypersensitivity to metals has been reported in 25% of the patients with well-functioning arthroplasties and up to 60% with poorly functioning arthroplasties [1]. Despite this correlation, it remains unclear whether metal hypersensitivity predisposes an early implant failure [2]. The occurrence of early failure of metallic implants or prostheses may be related to the indirect activation of macrophages by metal ions released after contact with host fluids. This phenomenon was named “aseptic lymphocyte-dominated vasculitis-associated lesion” by Willert et al and proposed as a suggestive but not pathognomonic altered response to metals [3,4]. However, it is

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mostly seen in metal-metal bearing total hip arthroplasty. All the metal components that get implanted in a human body have been reported to potentially interact with the biological system, corroding and releasing metal ions from the implant. These ions can form complexes with native proteins, act as allergens and elicit hypersensitivity responses. Implant-related hypersensitivity reactions are generally delayed responses mediated by T cells (type IV hypersensitivity) [5,6]. The metal most responsible for adverse reactions in humans is nickel, which is followed by cobalt and chromium. All of these metals are commonly used in orthopedic implants (Table 1). In particular, the cobalt-chromium alloy (CoCr) is used in most knee prostheses as well as in numerous everyday objects such as jewelry [7].

Metal hypersensitivity can be preoperatively identified by an epicutaneous patch test, but previous researchers have not found any causal relationships between cutaneous hypersensitivity and implant performance or survivorship [8].

In view of the considerable increase in the use of uni-compartmental knee arthroplasty, prostheses of hypoallergenic materials have been developed. These materials provide an excellent alternative to standard cobalt chromium (CoCr) [9]. Ceramic coatings have also been proposed because they are chemically inert and have high hardness and bioactive features. In particular, titanium niobium nitride (TiNbN), deposited by the physical vapor deposition technique, is a thin ceramic coating characterized by an increase in surface resistance to abrasion and corrosion, thus acting on several biological processes with possible long-term improvements in biocompatibility and osteointegration. To date, there are no clinical studies that report the outcomes and survival rates of patients who underwent hypoallergenic TiNbN medial uni-compartmental knee arthroplasty (UKA).

The primary purpose of the present prospective study was to consecutively analyze the clinical and radiological outcomes of patients with positive patch tests undergoing a medial mobile-bearing TiNbN UKA during their mid-term follow-ups. The secondary purpose was to evaluate the subgroups within the sample, especially with regard to age, gender, body mass index (BMI), side, and implant size.

Materials and Methods

All the procedures involving human participants in this study were in accordance with the ethical standards of the institutional and/or national research committee as well as the 1964 Helsinki

declaration and its later amendments or comparable ethical standards. The study was conducted following the STROBE Checklist for Case Series [10]. Informed consent was obtained from all the participants who were included in the study. The appropriate ethical approval was obtained from the local ethics committee. A consecutive series of 456 patients suitable for medial UKA were screened for metal hypersensitivity by using a standardized questionnaire and, in case of suspicion, a patch test. The reactions were scored using the International Contact Dermatitis Research Group criteria [11]. A total of 37 patients (8.1%) with a positive epicutaneous patch test result for metals (nickel, cobalt, and chromium) were included in this study and prospectively monitored. The demographics are summarized in Table 2. All the patients underwent the UKA with the same type of implant—a cemented TiNbN hypoallergenic medial UKA Oxford (Zimmer-Biomet, Warsaw, IN) with a mobile-bearing inlay.

The primary indication for surgery was isolated osteoarthritis (OA) in the medial knee compartment with full cartilage loss (“bone-on-bone articulation”) or avascular necrosis of the femoral condyle. In all the cases, the anterior cruciate, medial collateral, and lateral collateral ligaments were functionally intact, as confirmed by magnetic resonance imaging, and the varus or valgus deformity was manually correctable. There was no evidence of OA in the lateral compartment. Rheumatoid arthritis, fixed varus/valgus deformities, previous osteotomy, and flexion deformities greater than 15° were considered as contraindications, in accordance with the reported Oxford criteria [12].

Surgical Technique

All the operations were carried out by a senior surgeon experienced in UKA (more than 20 years) (N.U.) using a minimally invasive surgical technique. It involved a medial parapatellar approach without the dislocation of the patella by using microplasty instrumentation. Immediate full weight-bearing was post-operatively allowed [13,14].

Clinical Evaluation

All the clinical assessments were performed by an independent clinician who was not involved in the index surgery. The clinical

Table 1
Chemical Composition of the CoCr Oxford Unicompartmental Knee Arthroplasty.

Element	Composition, % (Mass/Mass)	
	Min	Max
Chromium	27.0	30.0
Molybdenum	5.0	7.0
Nickel	-	0.5
Iron	-	0.75
Carbon	-	0.35
Silicon	-	1.0
Manganese	-	1.0
Tungsten	-	0.2
Phosphorous	-	0.02
Sulfur	-	0.01
Nitrogen	-	0.25
Aluminum	-	0.1
Titanium	-	0.1
Boron	-	0.01
Cobalt ^a	balance	balance

^a Approximately equal to the difference of 100% and the sum percentage of the other specified elements.

Table 2
Demographics of Study Population.

Variables	N = 37
Age at T ₀	66.2 ± 6.1
BMI	27.9 ± 3.5
Height (cm)	161.2 ± 4.3
Weight (kg)	72.5 ± 10.0
T ₁ (mo)	11.9 ± 1.3
T ₂ (mo)	67.2 ± 19.1
Gender	
Male	8 (21.6)
Female	29 (78.4)
Side	
Left	17 (45.9)
Right	20 (54.1)
Femoral size	
S	27 (73.0)
M or L	10 (27.0)
Tibial size	
A or B	27 (73.0)
C or D	10 (27.0)
Bearing size (mm)	
3	23 (62.2)
4 or 5 or 6	14 (37.8)

Values are presented as n (%) or mean ± SD.

Table 3
Mean Scores for Different Time Periods.

Score	T ₀	T ₁	T ₂	P Value
Oxford Knee Score	23.0 ± 2.7	42.1 ± 1.7 ^a	45.0 ± 1.9 ^{a,b}	<.0001 ^c
American Knee Score (KSS)	51.5 ± 5.0	87.6 ± 2.2 ^a	91.9 ± 3.4 ^{a,b}	<.0001 ^c

Values are presented as mean ± SD.

^a Statistically significant vs T₀.

^b Statistically significant vs T₁.

^c Statistically significant difference.

evaluation consisted of evaluating each patient's Oxford Knee Score and Knee Society Score. Each patient was clinically evaluated on the day before surgery (T₀), at T₁ (11.9 ± 1.3 months) and on the day of the final follow-up (T₂: 67.2 ± 19.1 months) [15,16].

Radiographic Assessment

The radiograph evaluations were performed blinded by two orthopedic surgeons not involved in the index surgery. The positioning of the UKA was evaluated using radiological analysis during the final follow-up (T₂: 67.2 ± 19.1 months), as specified in the Oxford Partial Knee surgical technique operating manual, using standing anteroposterior and lateral radiographs of the knee. The following parameters were measured according to the manufacturer's manuals [17]: the femoral component varus/valgus, that is, the angle between the femoral component and femoral axis in the coronal plane, for which an angle of 7° was seen as neutral with a range of tolerance of ±10°; the tibial component varus/valgus, that is, the angle formed by the tibial axis and a line drawn along the tibial tray in the coronal plane, for which the range of tolerance was 0° ± 5°; finally, the anteroposterior slope, that is, the angle of a line drawn along the tibial tray and perpendicular to the tibial axis in the lateral view, for which a slope of 7° was seen as optimal with a range of tolerance of ±5° (2–12°) [17].

After extracting the Digital Imaging and Communications (DICOM—Arlington, VA) Medicine data from the Picture Archiving and Communications System (PACS—Carestream, Rochester, NY), it was inserted into the OsiriX imaging software (version 4.1.2 32-bit) (Pixmeo SARL, Geneva, Switzerland) and evaluated by two independent observers who were unaware of the instrumentation used for UKA.

Statistical Analysis

A sample of 30 subjects was determined to be adequate to detect a five-point increase in both the KSS and Oxford scores at the subsequent time points. The sample size was estimated using a one-tailed paired t-test, assuming a standard deviation of 6, significance level of 2.5%, and power of 99% [17,18].

The data were presented as frequencies with respective proportions for categorical variables and as mean and standard deviation for continuous variables. The mean change of Oxford and KSS scores at the three time points (T₀, T₁, and T₂) using a repeated measure analysis with an unstructured covariance matrix of the residuals was assessed. In the case of a deviation from the assumptions of the model, for example, non-normally distributed errors, a nonparametric analysis was performed using the Friedman and Wilcoxon signed-rank test. Further analysis was conducted to assess variations in the score times across gender, age, BMI, surgical side (left vs right), bearing size (3 mm vs 4 mm, 5 mm, and 6 mm), tibial size (A, B vs C, D), and femoral size (S vs M, L). Age and BMI were included in the analysis as dichotomous variables and dichotomized at their average values. A comparison between the score means of different groups in the same period (within time comparison) and those of the same group in different periods

(within-group comparison) using mixed models or nonparametric tests (Wilcoxon signed-rank and Wilcoxon-Mann Whitney tests) was performed. The Bonferroni correction was used for multiple comparisons. Finally, we estimated and tested for correlations among the variables. Either the Pearson or Spearman rank correlation test was selected according to the distribution of the variables. A two-tailed *P*-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using Statistical Analysis Software (SAS Institute Srl, Milan, Italy).

Results

The demographic data of the patients are given in Table 2. The Oxford and KSS mean preoperative values ranged from 23.0 ± 2.7 and 51.5 ± 5.0 to 42.1 ± 1.7 and 87.6 ± 2.2, respectively, at T₁ (*P* < .001) and to final values of 45.0 ± 1.9 and 91.9 ± 3.4, respectively, at T₂ (*P* < .001 both vs T₁ and T₂). At T₂, the mean femoral angle was 7.0° ± 4.5°, mean tibial angle was 3.0° ± 2.1°, and mean tibial slope was 5.1° ± 3.2°. The detailed results have been reported in Table 3.

Several significant correlations were found. In particular, weight was positively correlated with KSS at T₀ and T₂; moreover, the right side was positively correlated with the preoperative Oxford score and tibial angle. Further detailed results are presented in Table 4.

Significant differences were found between KSS and Oxford with ANOVA for repeated measures over time (*P* < .001). The Oxford and KSS scores showed significant improvements at each follow-up. Detailed results are presented in Table 3.

All the analyzed subgroups showed significant improvements across the consecutive time points and between the preoperative value (T₀) and final follow-up (T₂) (*P* < .05). The only differences within the subgroups concerned patients of BMI ≥ 28 and with a KSS score significantly higher at T₀ (*P* = .012), patients operated on the right side with an Oxford score higher at T₀ (*P* = .013), and patients with tibial sizes C and D and an Oxford score higher at T₁ (*P* = .035). The detailed results are presented in Tables 5 and 6.

Table 4
Significant Correlations Between Demographic Variables and Scores.

Variables	Rho	P Value
Oxford T ₀		
Right side	0.38723	.0179 ^a
Oxford T ₁		
Oxford T ₂	−0.39141	.0166 ^a
Tibial size	−0.36091	.0282 ^a
Oxford T ₂		
KSS T ₁	−0.33345	.0437 ^a
KSS T ₀		
KSS T ₂	0.40629	.0126 ^a
Weight	0.43542	.0071 ^a
BMI	0.36961	.0244 ^a
KSS T ₁		
KSS T ₂	0.45228	.0049 ^a
KSS T ₂		
Weight	0.35863	.0293 ^a
Tibial angle T ₂		
Right side	0.39986	.0142 ^a

KSS, Knee Society Score.

^a Statistically significant difference.

Table 5
Clinical Comparisons Between Groups Divided for Gender, Age, and BMI.

Score	Time Period	Groups		Mean Score Comparison Within Time Period	Mean Score Comparison Within Groups (Bonferroni Adjusted <i>P</i> Value)	
		Gender			Gender	
		Male (n = 8)	Female (n = 29)		Male (n = 8)	Female n = 29)
Oxford	T ₀	22.9 ± 3.2	23.1 ± 2.6	0.8361	T ₁ - T ₀ :	<.0001 ^a
	T ₁	41.9 ± 1.3	42.1 ± 1.9	0.7105	T ₂ - T ₀ :	<.0001 ^a
	T ₂	44.9 ± 2.0	45.8 ± 1.9	0.7662	T ₂ - T ₁ :	0.0237 ^a
KSS	T ₀	51.5 ± 4.9	51.5 ± 5.2	0.8965	T ₁ - T ₀ :	0.0234 ^a
	T ₁	88.1 ± 2.9	87.5 ± 2.0	0.2114	T ₂ - T ₀ :	0.0234 ^a
	T ₂	93.5 ± 4.5	91.5 ± 2.9	0.2404	T ₂ - T ₁ :	0.0234 ^a
		Age < 67 y (n = 18)	≥ 67 y (n = 19)	<i>P</i> value	Age < 67 y (n = 18)	≥ 67 y (n = 19)
Oxford	T ₀	22.8 ± 2.6	23.3 ± 2.9	0.5532	T ₁ - T ₀ :	<.0001 ^a
	T ₁	42.2 ± 1.6	42.0 ± 1.9	0.7752	T ₂ - T ₀ :	<.0001 ^a
	T ₂	44.8 ± 1.8	42.3 ± 2.0	0.4958	T ₂ - T ₁ :	0.0022 ^a
KSS	T ₀	51.0 ± 5.4	52.0 ± 4.8	0.3746	T ₁ - T ₀ :	<.0001 ^a
	T ₁	87.8 ± 2.3	87.5 ± 2.1	0.5851	T ₂ - T ₀ :	<.0001 ^a
	T ₂	91.6 ± 3.4	92.3 ± 3.5	0.4160	T ₂ - T ₁ :	0.0002 ^a
		BMI < 28 (n = 20)	≥ 28 (n = 17)	<i>P</i> value	BMI < 28 (n = 20)	≥ 28 (n = 17)
Oxford	T ₀	22.8 ± 2.8	23.4 ± 2.7	0.4665	T ₁ - T ₀ :	<.0001 ^a
	T ₁	42.3 ± 1.7	41.9 ± 1.8	0.5290	T ₂ - T ₀ :	<.0001 ^a
	T ₂	44.7 ± 2.1	45.5 ± 1.6	0.2200	T ₂ - T ₁ :	0.0026 ^a
KSS	T ₀	49.5 ± 3.6	53.9 ± 5.6	0.0118 ^a	T ₁ - T ₀ :	<.0001 ^a
	T ₁	87.6 ± 2.4	87.8 ± 2.0	0.7783	T ₂ - T ₀ :	<.0001 ^a
	T ₂	91.2 ± 3.3	92.8 ± 3.4	0.0604	T ₂ - T ₁ :	0.0001 ^a

KSS, Knee Society Score.

Values are presented as unadjusted mean ± SD.

^a Statistically significant difference.

The only significant difference found was with respect to the surgical side; the patients who underwent surgery on their left reported lower tibial varus/valgus angles than patients operated on the right side ($2.2^\circ \pm 2.0^\circ$ vs $3.8^\circ \pm 2.0^\circ$; $P = .023$). Detailed results are reported in Table 7.

No complications were found. Moreover, none of the patients required revision surgery during the follow-up period.

Discussion

The most important findings of the present study were the following: In the selected cohort of patients with a positive epicutaneous patch test result, hypoallergenic TiNbN medial UKA provided good to excellent results in the medium term without any complications, regardless of age, gender, weight, and implant characteristics. Furthermore, even if the hypoallergenic femoral component presented only one femoral peg, there were no signs of prosthesis subsidence during the follow-ups. The clinical and radiographic measurements during the final follow-up were comparable with those reported in the current literature for both single and double peg [17,19–21] and with other UKA designs as reported in Table 8.

The unicompartmental prostheses used in this study were all coated with TiNbN. A TiN coating was developed for knee implants to improve their biocompatibility and mechanical properties. TiN is applied as a 3–4 μm layer on CoCr implants [22]. In biomechanical studies, it has been shown to provide a 98% reduction of polyethylene wear [23]. Specifically, TiN shows high resistance to adhesive wear and less adhesion to polyethylene. In addition to the TiNbN prostheses, fully ceramic or zirconium prostheses are currently available in the market, which are promoted for the treatment of patients with suspected metal hypersensitivity.

Ceramic arthroplasties have a load to scratch that is five times greater than that of zirconium oxide (ZrOx) and 10 times greater

than CoCr, resulting in less wear of the surface and, consequently, less third-body wear of the polyethylene [24]. Survival rates of 97.4% at 10 years and 94% at 15 years have been reported with these implants [24].

ZrOx causes less polythene wear than CoCr components and shows better resistance to abrasion. Clinical studies have reported a survival rate of 95–98.7% for 5–10 years of follow-ups [25,26].

The literature includes several studies on hypoallergenic TKA, but scientific evidence is still scarce regarding UKA [6,7,27–29].

In a retrospective study, Thienpoint et al. analyzed 40 TiNbN TKA by comparing them with 80 conventional CoCr implants and found no differences in the clinical, radiological, or patient-reported outcomes. Moreover, no patients were revised during the short-term to medium-term follow-ups [30].

A similar study was performed by Postler et al., which involved randomizing patients to receive a coated or a standard TKA and analyzing the clinical scores and blood metal ion levels. The authors reported that the chromium concentrations in the patients' plasma increased from a median of 0.25 to 1.30 $\mu\text{g/L}$ in the standard TKA group and from 0.25 to 0.75 $\mu\text{g/L}$ in the coated TKA group, showing a significant difference. 13 patients (three coated, 10 standard TKA) had chromium concentrations above 2 $\mu\text{g/L}$. The patient-reported outcome measures demonstrated a substantial improvement after TKA and without any differences between the groups [27].

An interesting study was conducted to assess various immunological and clinical parameters by comparing standard vs coated implants over five years of follow-ups. Both coated and uncoated groups reported improved clinical outcomes, but an increased proinflammatory status was found in the peripheral blood, that is, significant elevation of IL-8 and anti-inflammatory IL-10, after the use of a standard uncoated prosthesis [28].

With the rate of complication-related revision surgery at approximately 9%, the significance of metal implant allergy in the outcome of arthroplasty is receiving increasing attention [31]. The

Table 6

Clinical Comparisons Between Groups Divided for Surgical Side and Implant Components Size.

Score	Time Period	Groups		Mean Score Comparison within Time Period	Mean Score Comparison within Groups (Bonferroni Adjusted <i>P</i> value)		
		Surgical Side			Surgical Side		
		Left Side (n = 17)	Right Side (n = 20)			Left Side (n = 17)	Right Side (n = 20)
Oxford	T ₀	21.9 ± 2.4	24.1 ± 2.6	.0130 ^a	T ₁ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₁	42.3 ± 1.1	41.9 ± 2.2	.4996	T ₂ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₂	45.1 ± 2.0	45.0 ± 1.8	.8530	T ₂ -T ₁ :	0.0017 ^a	0.0002 ^a
KSS	T ₀	52.3 ± 4.8	50.8 ± 5.3	.4160	T ₁ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₁	87.8 ± 2.4	87.6 ± 2.0	.6614	T ₂ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₂	31.9 ± 3.3	92.0 ± 3.5	.9509	T ₂ -T ₁ :	0.0003 ^a	<.0001 ^a
		Tibial size A or B (n = 27)	C or D (n = 10)	<i>P</i> value	Tibial size A or B (n = 27) C or D (n = 10)		
Oxford	T ₀	23.3 ± 2.7	22.4 ± 2.9	.3786	T ₁ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₁	42.4 ± 1.5	41.1 ± 2.0	.0347 ^a	T ₂ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₂	44.8 ± 2.0	45.8 ± 1.5	.1453	T ₂ -T ₁ :	0.0005 ^a	<.0001 ^a
KSS	T ₀	51.5 ± 5.4	51.4 ± 4.1	.9040	T ₁ -T ₀ :	<.0001 ^a	0.0059 ^a
	T ₁	87.7 ± 2.0	87.5 ± 2.7	.8607	T ₂ -T ₀ :	<.0001 ^a	0.0020 ^a
	T ₂	91.6 ± 2.9	92.7 ± 4.5	.8629	T ₂ -T ₁ :	<.0001 ^a	0.0059 ^a
		Femoral size S (n = 12)	M or L (n = 13)	<i>P</i> value	Femoral size S (n = 12) M or L (n = 13)		
Oxford	T ₀	23.3 ± 2.7	22.5 ± 2.7	.4565	T ₁ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₁	42.2 ± 1.3	41.9 ± 2.6	.7055	T ₂ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₂	45.0 ± 1.7	45.2 ± 2.4	.7789	T ₂ -T ₁ :	<.0001 ^a	0.0049 ^a
KSS	T ₀	51.5 ± 5.4	51.5 ± 4.2	.8228	T ₁ -T ₀ :	<.0001 ^a	0.0059 ^a
	T ₁	87.7 ± 2.1	87.5 ± 2.4	.9022	T ₂ -T ₀ :	<.0001 ^a	0.0059 ^a
	T ₂	91.8 ± 2.9	92.3 ± 4.6	.7823	T ₂ -T ₁ :	<.0001 ^a	0.0059 ^a
		Bearing size (mm) 3 (n = 23)	4 or 5 or 6 (n = 14)	<i>P</i> value	Bearing size (mm) 3 (n = 23) 4 or 5 or 6 (n = 14)		
Oxford	T ₀	22.6 ± 2.7	23.9 ± 2.6	.1622	T ₁ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₁	42.3 ± 2.0	41.8 ± 1.1	.4277	T ₂ -T ₀ :	<.0001 ^a	<.0001 ^a
	T ₂	45.8 ± 1.8	45.1 ± 2.1	.8267	T ₂ -T ₁ :	0.0004 ^a	0.0007 ^a
KSS	T ₀	52.1 ± 5.2	50.4 ± 4.8	.2763	T ₁ -T ₀ :	<.0001 ^a	0.0004 ^a
	T ₁	88.0 ± 2.0	87.0 ± 2.4	.1392	T ₂ -T ₀ :	<.0001 ^a	0.0004 ^a
	T ₂	92.4 ± 3.6	91.2 ± 2.9	.4477	T ₂ -T ₁ :	<.0001 ^a	0.0007 ^a

KSS, Knee Society Score.

Values are presented as unadjusted mean ± SD.

^a Statistically significant difference.

wording has been changed in the last years from “metal sensitivity” to “metal-related pathology”. In this scenario, about 2.0% of the revision TKAs were attributed to “metal-related pathology”. In

particular, the only solution in the case of arthroplasty failure due to an allergy to metals is to replace the implant with a hypoallergenic one [6].

Table 7

Comparison of the Angles Between the Different Groups.

Group	Tibial Angle (°)		Femoral Angle (°)		Tibial Slope (°)	
	Mean ± SD	<i>P</i> value	Mean ± SD	<i>P</i> value	Mean ± SD	<i>P</i> value
Gender						
Male	2.8 ± 2.5	.6291	8.1 ± 4.1	.4224	4.5 ± 2.1	.5334
Female	3.1 ± 2.0		6.7 ± 4.6		5.3 ± 3.4	
Age (Y)						
<67	3.2 ± 1.9	.6794	6.2 ± 5.0	.2965	5.7 ± 3.6	.3322
≥67	2.9 ± 2.3		7.7 ± 4.0		4.6 ± 2.8	
BMI						
<28	3.3 ± 2.1	.5499	7.0 ± 5.1	.9738	5.7 ± 2.9	.2949
≥28	2.8 ± 2.2		7.0 ± 3.9		4.5 ± 3.6	
Surgical side						
Left side	2.2 ± 2.0	.0225*	5.0 ± 1.2	.6914	5.8 ± 2.7	.2325
Right side	3.8 ± 2.0		4.2 ± 0.9		4.6 ± 3.5	
Tibial size						
A/B	3.2 ± 2.2	.6297	6.7 ± 5.0	.5583	5.4 ± 3.4	.3409
C/D	2.6 ± 1.9		7.7 ± 3.2		4.3 ± 2.5	
Femoral size						
S	3.1 ± 2.3	1.0000	6.8 ± 4.9	.7314	5.3 ± 3.5	.7039
M/L	2.9 ± 1.7		7.4 ± 3.4		4.8 ± 2.3	
Bearing size (mm)						
3	3.3 ± 2.4	.5724	6.9 ± 4.8	.8611	5.6 ± 2.9	.3010
4/5/6	2.6 ± 1.6		7.1 ± 4.1		4.4 ± 3.6	

Table 8

Clinical Studies Investigating the Use of Unicompartmental Knee Arthroplasty for Medial Knee Osteoarthritis.

Author	Year	Journal	UKA	Age (Y)	Follow-Up	Functional Score	Complications/ Revisions
Pronk et al. [38]	2020	KSSTA	66 MB Oxford Phase III 97 FB ZUK	MB 61.4 ± 7.8 FB 61.2 ± 7.7	6,12 and 24 mo	MB: NRS at 24 mo 9.0 FB: NRS at 24 mo 9.0	MB: 1 deep infection. FB: 2 complications: 1 deep infection and in 1 patient, bone cement debris was removed. none
Hauer et al. [39]	2019	Arch Orthop Trauma Surg	35 FB Sigma HP	66.0 ± 8.6	2.3 ± 1.6 y	KSS pain 96.9 ± 5.2 KSS function (mean ± SD) 93.1 ± 12.1 VAS: 2.2 ± 1.4 WOMAC: 27.9 ± 12.9 AKSS-O: 78.8 ± 14.0 OKS: 36.7 ± 5.5 OKS: 40 (33–45) WOMAC: 19 (8–34) Tegner activity score: 2 (2–4)	10 revisions: 9 inlay dislocations 1 lateral OA
Uzun et al. [40]	2019	Knee	146 MB Oxford Phase III	58.8 ± 7.0	7.41 ± 1.54 y	OKS: 40 (33–45) WOMAC: 19 (8–34) Tegner activity score: 2 (2–4)	19.8% rate of revision
Scholes et al. [41]	2019	J Knee Surgery	661 Inlay Repicci II	66 (59–72)	9 (5–13) y	KSKS: 85.6 KSFA: 64.5	6 revisions: 2 cases of tibial tray loosening 1 case of progressive OA, 1 mechanical failure, 1 persistent pain, 1 infection
Yung et al. [42]	2019	J Orthop Surg	94 UKA (Preservation, Miller, ZUK, Journey)	66.3 ± 7.38	4.3 (0.5–15.2) y	Survivorship of 89.1% at 10 y OKS, AKSS and WOMAC patient-reported outcomes significantly improved in comparison with preoperatively KOOS: 84.3 ± 15.9 Satisfaction: 72.4% very satisfied	24 revisions
Bruce et al. [43]	2020	Knee	214 FB all-polyethylene Uniglide	70 (41–87)	5,8,10 and 12 y	MB WOMAC: 86.5 (78.1–93.8) FB WOMAC: 91.7 (75–95.8) WOMAC	16 revisions
Burger et al. [44]	2020	Bone Joint J	802 FB robotic-arm assisted	63.5 ± 9.5	4.9 ± 2.0 y		MB 10 revisions FB 5 revisions
Neufeld et al. [45]	2018	J Arthroplasty	38 MB Oxford Phase III 68 FB Miller-Galante or High Flex Knee System	MB 60.3 (41.4–81.3) FB 64.6 (45.1–84.3)	MB 14.2 (12.9–15.5) y FB 11.5 (10.2–15.1) y		

UKA, unicompartmental knee arthroplasty; FB, fixed-bearing; MB, mobile-bearing; NRS, Numeric Rating Scale; KSS, Knee Society Score; VAS, Visual Analog Scale for Pain; WOMAC, The Western Ontario and McMaster Universities Arthritis Index; AKSS-O, American Knee Society Score; OKS, Oxford Knee Score; KSKS, Knee Society Knee Scores; KSFA, Knee Societal Functional Assessment; KOOS, Knee Injury and Osteoarthritis Outcome Score.

Thakur et al. presented the cases of five patients with persistent pain and hypertrophic synovitis after TKA with a cobalt-chromium component and after revision surgery with zirconium femoral and titanium metal-backed tibial components. All the patients showed dramatic improvements in their clinical conditions [32].

Similar conclusions were drawn by Zondervan et al. They provided a report on about 46 patients who each presented with a painful knee arthroplasty and positive metal lymphocyte transformation test scores. After revision to a hypoallergenic TKA, their pain scores, walking functions, and range of motion improved [33].

In the present study, no adverse events or complications related to metal hypersensitivity were found. The reported good to excellent clinical outcomes during the final follow-ups were attributed to the careful patient selection process and meticulously standardized treatment algorithm. In fact, every patient was asked to fill in a questionnaire regarding their possible allergies, with specific questions on metals and jewelry. On admission, each patient was re-evaluated with further specific questions. In addition, considering that patients are often not aware of any allergies, a careful check was performed to see if the patient was wearing metal materials. After obtaining their accurate medical history, the patient was asked to undress and remain in only their underwear to

inspect them for skin lesions. Such particular attention is required because, unfortunately, a patient's self-reported medical history is not a reliable predictor of metal allergy before implantation [34]: Among 369 women with self-reported histories, screening for pre-existing metal allergies before patch testing showed positive predictive values of ~60% for nickel allergy [34].

In case of a suspected allergy, or in doubtful cases, an epicutaneous patch test is performed; if the result is positive, the UKA or TKA is switched to a hypoallergenic prosthesis. In the absence of a positive patch test, the implants are standard cobalt-chromium prostheses (Fig. 1).

Preoperative evaluation approaches widely vary—from the expert opinions of orthopedic surgeons in Britain who suggest that metal allergy need not be considered prior to surgery [35] to those in Germany who suggest titanium implants for empiric use among patients with high suspicion of metal allergy [18]. Testing before surgery is uncommon in Denmark and Sweden [36]. In the United States, the American Contact Dermatitis Society recommends that only patients with a significant history of metal hypersensitivity reactions should be considered for testing before surgery [6].

This study has a considerable number of limitations. First, the study sample was rather small. However, Owing to the strict

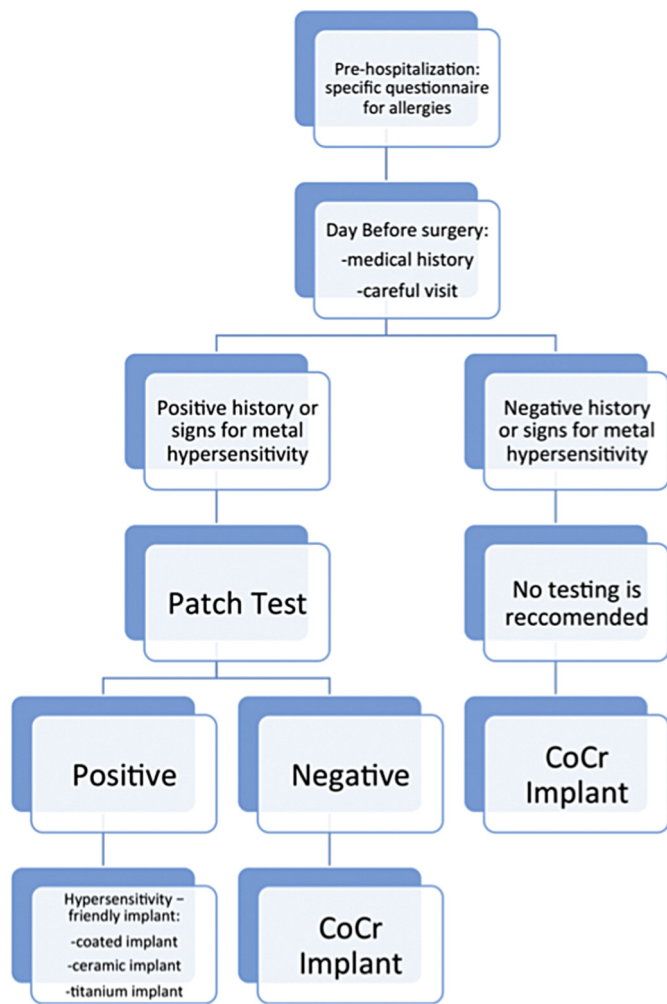


Fig. 1. Preoperative diagnostic algorithm to identify patients with potential metal hypersensitivity.

inclusion criteria, it represented a homogenous and well-sampled cohort. Second, it was a retrospective study of prospectively collected data with potential inherent selection bias. However, this selection bias was limited by the prospective data collection. Third, no control group was reported, but the outcomes were compared with the present literature. Fourth, the results cannot be generalized as only one specific mobile-bearing UKA was used, and finally the femoral flexion angle was not evaluated partly because there has been little knowledge about the sagittal positioning of the femoral components, and much discussion exists about the normal ranges of femoral component flexion and extension angles [37].

However, this study shows an easy and reproducible algorithm for the treatment of patients undergoing knee arthroplasties who are suspected to have hypersensitivity to metals. The patient selection was the key to a successful hypoallergenic UKA.

Conclusions

Hypoallergenic TiNbN mobile-bearing arthroplasty showed comparable outcomes with the standard CoCr prostheses, regardless of gender, age, BMI, and implant size, among metal allergy patients with medial knee OA. The careful patient selection process and accurate medical histories played key roles in the choice of hypersensitivity-friendly implants.

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Appendix

Dataset

Database of Patients Included in the Study.

Lato	Taglie Femore	Taglie Tibia	Inserto	Oxford Pre op	Oxford T1	Oxford T2	Kss Pre	Kss T1	Kss T2	Angolo Tibia T2	Angolo Femore T2	Slope T2	Note
DX	S	A	3	22	42	44	55	88	92	7	2	10	
SX	S	B	3	19	40	45	52	88	90	2	13	8	
SX	M	C	3	18	41	48	56	88	91	0	12	8	
DX	M	C	3	22	39	47	60	88	90	4	7	4	
SX	S	A	3	25	42	44	48	90	88	4	−2	6	
SX	S	A	3	19	44	46	46	84	89	1	11	6	
DX	S	A	3	23	43	45	44	88	91	4	0	8	
DX	S	B	4	28	42	44	48	87	90	4	14	1	
DX	S	B	5	22	42	46	50	88	92	3	10	−3	
SX	S	B	5	23	42	45	53	88	92	0	5	8	
SX	M	A	6	24	42	45	52	86	88	3	11	6	
DX	M	D	3	19	41	45	52	89	100	5	11	4	
SX	S	B	3	19	43	47	50	84	92	0	5	2	
DX	S	C	4	22	41	45	50	84	89	4	6	2	
SX	S	A	4	21	42	46	50	88	92	0	10	6	
DX	L	D	3	25	46	44	52	90	95	1	6	4	
DX	M	C	3	23	39	45	48	88	89	3	10	8	
DX	S	B	4	27	40	44	44	88	88	2	4	8	
SX	S	A	4	24	41	47	46	85	91	3	1	5	
DX	S	B	6	28	41	48	47	86	93	6	11	5	
DX	S	A	3	24	42	45	55	87	90	8	6	3	
DX	S	A	3	26	41	44	58	86	95	5	16	4	
DX	S	A	3	24	45	46	60	89	100	5	6	11	
SX	S	A	3	23	42	44	62	88	94	3	0	10	
DX	S	B	3	22	41	47	58	90	91	4	10	2	
SX	S	B	5	21	42	41	58	91	99	3	12	0	
SX	S	B	4	27	44	42	62	89	93	2	7	5	
DX	M	A	3	27	47	40	47	88	92	4	3	2	
DX	M	D	5	21	41	48	46	82	90	1	3	7	
DX	S	B	3	24	44	43	44	89	89	1	5	8	
DX	S	C	3	28	40	46	48	90	95	0	11	1	
SX	S	A	3	22	43	42	48	91	92	0	2	3	
SX	S	A	4	22	44	47	50	90	92	2	2	10	
SX	S	B	3	23	43	47	52	84	89	4	4	6	
SX	M	C	3	22	42	46	52	90	100	4	7	3	
DX	M	C	4	24	41	44	50	86	88	4	4	2	
SX	S	A	3	20	42	45	52	88	90	7	13	7	

Impianti: ANAL = Anallergico. O = oxford phase III, O TW = oxford microplasty; Taglie Femore: S = Small (Piu Piccola), M = Medium, L = Large; Tibia: AA = Piu Piccola (35MM), A = 38MM, B = 41MM, C = 44MM, D = 47MM, E = 50MM, F = 53MM.

Strobe Statement

Checklist of Items That Should be Included in Reports of Cohort Studies.

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract [1] (b) Provide in the abstract an informative and balanced summary of what was done and what was found [2]
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported [3]
Objectives	3	State specific objectives, including any prespecified hypotheses [4]
Methods		
Study design	4	Present key elements of study design early in the paper [4]
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [4]
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up [4–6] (b) For matched studies, give matching criteria and number of exposed and unexposed [4–6]
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [5,6]
Data sources/measurement	8 ^a	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [4]
Bias	9	Describe any efforts to address potential sources of bias [4]
Study size	10	Explain how the study size was arrived at [4]
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [5,6]
Statistical methods	12	(a) Describe all Statistical methods, including those used to control for confounding [6,7] (b) Describe any methods used to examine subgroups and interactions [6,7] (c) Explain how missing data were addressed [6,7] (d) If applicable, explain how loss to follow-up was addressed [6,7] (e) Describe any sensitivity analyses [6,7]
Results		
Participants	13 ^a	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed [7,8] (b) Give reasons for non-participation at each stage [7,8] (c) Consider use of a flow diagram [7,8]
Descriptive data	14 ^a	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [7,8] (b) Indicate number of participants with missing data for each variable of interest [7,8] (c) Summarize follow-up time (eg, average and total amount) [7,8]
Outcome data	15 ^a	Report numbers of outcome events or summary measures over time [7,8]
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [7,8] (b) Report category boundaries when continuous variables were categorized [7,8] (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period [7,8]
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [7,8]
Discussion		
Key results	18	Summarize key results with reference to study objectives [8]
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [11]
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [8–11]
Generalizability	21	Discuss the generalizability (external validity) of the study results [8–11]
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [11]

An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

^a Give information separately for exposed and unexposed groups.