

Article

Titanium-Nitride Coating Does Not Result in a Better Clinical Outcome Compared to Conventional Cobalt-Chromium Total Knee Arthroplasty after a Long-Term Follow-Up: A Propensity Score Matching Analysis

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Abstract: Background: The impact of titanium nitride (TiN) coating on implant components is controversial. TiN coating is proposed as having superior biomechanical properties compared to conventional cobalt-chromium (CoCr) alloy. This study compared long-term clinical data as well as meteoro-sensitivity in patients who underwent total knee arthroplasty (TKA), with either CoCr alloy or TiN coating. Methods: In this retrospective observational study, the clinically approved cemented “low contact stress” (LCS) TKA with conventional CoCr coating, was compared to un-cemented TiN-coated “advanced coated system” (ACS) TKA. Propensity score matching identified comparable patients based on their characteristics in a one-to-one ratio using the nearest-neighbor method. The final cohort comprised 260 knees in each cohort, with a mean follow-up of 10.1 ± 1.0 years for ACS patients and 14.9 ± 3.0 years for the LCS group. Physical examinations, meteoro-sensitivity, and knee scoring were assessed. Results: The clinical and functional Knee Society Score (KSS) (82.6 vs. 70.8; $p < 0.001$ and 61.9 vs. 71.1; $p = 0.011$), the postoperative Visual Analogue Scale (VAS) (2.9 vs. 1.4; $p = 0.002$), and the postoperative Tegner Score (2.6 vs. 2.2; $p = 0.001$) showed significant intergroup differences. The postoperative Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) was similar (79.9 vs. 81.3; $p = 0.453$) between groups. Meteoro-sensitivity of the artificial joint was significantly more prevalent in the ACS patient cohort (56% vs. 23%; $p < 0.001$). Conclusion: This study suggests that TiN coating does not provide improved clinical outcomes in this patient cohort after a long-term follow-up. Interestingly, sensitivity to weather changes were more correlated with un-cemented ACS implants.

Keywords: knee arthroplasty; functional outcome; titanium-nitride; meteoro-sensitivity

1. Introduction

Total knee arthroplasty (TKA) is the golden standard therapy for pain release in end-stage osteoarthritis (OA). Due to increasing rates of OA of the knee joint, there will be an excessive use of knee implants in the future, which could result in a fourfold increase in knee arthroplasty utilization by 2030 [1,2]. In spite of the great enthusiasm and continuously increasing implantation rates, TKA can

fail over time with reported ten-year revision rates of 6.2% [3]. Moreover, sustained knee pain has been described in up to 20% of patients receiving TKA [4]. It is still unclear whether persistent pain after TKA and other clinical symptoms such as stiffness and swelling, which can lead to TKA failure, are influenced by component materials [5].

The most common metal alloys used in orthopedic surgery are cobalt-chromium (CoCr), stainless steel, and titanium-aluminum-vanadium alloys [6]. In the 1980s, titanium-nitride (TiN) was considered as the first ceramic coating for total hip and knee replacements [7]. TiN ceramic coatings are mainly used to enhance CoCr alloy surgical implants with the properties of TiN. A special technique called physical vapor deposition (PVD) is carried out to modify implants with a TiN layer of 3–4 μm . Thus, only the surface of the implant is modified, not the material properties of the substrate or the biomechanical functionality. TiN was designed to improve the wear properties of standard alloy in order to reduce the potential for wear debris-induced osteolysis [8,9]. In vitro testing has revealed very good wear rates against conventional polyethylene as well as an increased resistance to abrasive third-body wear compared with CoCr [10,11]. This is especially important since there is increasing evidence that metal-stimulated lymphocytes may play a role in the pathogenesis of osteolysis [12,13]. Loose metal particles can induce an osteoclastogenic cytokine release that can directly and indirectly promote osteoclast activity and inhibit osteoblast activity [12,13]. Moreover, beneficial properties of TiN include increased surface hardness and a decrease in Co and Cr ions release [7,14]. TiN is expected to exhibit higher corrosion resistance to the corrosive body fluids than the metallic substrate [15]. Synovial fluid from the joint is the first biological fluid into which the debris are released. High levels of Co and Cr ions in the synovial fluid are correlated with a remarkable increase of Co and Cr concentrations in the blood [16,17]. Co and Cr are essential microelements required for normal biological functions, but excessive levels can be harmful [18,19]. Local elevated concentrations cause serious damage that affect the integrity of the synovial tissue of the joint [19]. In vitro studies have suggested that released metallic ions can act as haptens and complex with proteins, thus becoming capable of acting as antigens for circulating lymphocytes [13,20,21]. These metal-protein complexes are considered to induce a cell-mediated delayed-type (type IV) hypersensitivity response via the activation of TH1 lymphocytes [20,22]. TH1 activation releases pro-inflammatory cytokines (i.e., TNF- α , IFN- γ , IL-1, and IL-2), which recruit macrophages to the site of the implant [22,23]. This phenomenon may be the reason of postoperative local inflammatory symptoms like swelling, increased skin temperature, and persistent post-surgical pain in the absence of other clear surgical-related problems [14,24].

The theoretical negative effects of CoCr alloy raise concerns about its clinical use. However, TiN coatings also have disadvantages. A major complication includes failure of coating adhesion. Since TiN is an extremely hard coating, its adhesion resistance on a softer metal is a limitation [7]. New techniques such as a multilayer application have been introduced to improve this issue [7]. Moreover, retrieval studies have shown that TiN coatings of knee replacements undergo wear and degradation during in vivo use, causing damage of the TiN film that led to delamination of the coating [25,26]. There is no clear evidence on the impact of the costly TiN-coated implants in terms of clinical outcomes and implant failures. Reports lacking clinical effects/outcomes and unfavorable results have been published [5,27]. The clinical benefits of TiN on knee implant surfaces should be comprehensively investigated, and long-term clinical data should be collected [14]. Up to date, there is no long-term comparison between CoCr and TiN TKA.

Unclear postoperative pain might be a result of an orthopedic device that is not well tolerated, but many patients with artificial joints believe that their pain is affected by weather. It has already been shown that many patients with rheumatic diseases and two in every three patients with knee, hip, or hand osteoarthritis claim that they feel worse before or during weather changes [28,29]. In general, meteorosensitivity, or meteoropathy or weather pain of an artificial joint describe an association between weather changes (i.e., cold temperatures, air humidity, barometric pressure) and the occurrence of pain or abnormal sensations [28]. Results of studies on the influence of weather conditions and the

frequency of meteorite-sensitivity; however, are scarce and contradictory and so far, no comparison has been made between two different types of prostheses.

Therefore, the purposes of this study are two-fold: (1) to compare long-term clinical data from two groups of patients who underwent TKA, with either a conventional CoCr alloy or TiN coating and (2) to evaluate the frequency of meteorite-sensitivity between these two groups. We hypothesized that TiN-coated TKA would induce more favorable outcomes and that rates of meteorite-sensitivity are equal among the two groups.

2. Materials and Methods

2.1. Sample Size

During 2015 and 2016, all patients who had received the TiN-coated un-cemented Advanced Coated System (ACS) (Implantcast, Buxtehude, Germany) (Figures 1 and 2) TKA between 2004 and 2006 ($n = 669$), were invited to the first author's institution (Department of Orthopaedics and Trauma, Medical University of Graz, Graz, Austria) for a ten-year follow-up examination. From 2004 to 2006, the ACS was the implant of choice for all patients in one of the author's (R.E.) institution (Department of Orthopaedics, LKH Radkersburg, Bad Radkersburg, Austria). Three hundred and one patients were not available because they did not respond ($n = 106$) to our invitation, some had died ($n = 135$) during follow-up, or some had been revised ($n = 60$). Thus, 368 patients (404 knees) were included (response rate = 55%). Revision cases and causes that led to revision were collected during follow-up and were analyzed by a different study group at the authors' institution.



Figure 1. Femoral part of the Advanced Coated System (ACS) total knee prosthesis with the easily identifiable golden color of titanium-nitride (TiN).



Figure 2. Tibial part of the Advanced Coated System (ACS) total knee prosthesis with the easily identifiable golden color of titanium-nitride (TiN).

A similar follow-up of a historic cohort of 236 patients (260 knees) from the first author's institution, receiving CoCr cemented Low Contact Stress System (LCS) (DePuy Synthes, Warsaw, IN, USA) TKA with rotating platform, as earlier described by our group, was used for comparison [30]. This cohort was taken to ensure comparability between two knee systems that are similar with regard to design, geometry, knee kinematics, and implantation technique. ACS and LCS TKA both provide a high degree of anatomical conformity regarding the trochlear groove and patella. The tibia first method with the balancing of the flexion gap was carried out using a medial parapatellar approach in both groups. All the patients had been suffering from severe osteoarthritis of the knee confirmed by radiograph (Kellgren-Lawrence-Score III/IV), persistent pain in at least two knee compartments despite conservative treatment, and reduced knee mobility. Postoperatively, patients followed a standardized rehabilitation protocol consisting of full weight bearing immediately after surgery with the use of crutches and continuous passive motion (CPM) therapy on the first postoperative day. Radiological evaluations were performed routinely according to local hospital standards after 3, 6, 12, and 48 months, and then biennially (Figure 3).



Figure 3. Anteroposterior radiograph of the Advanced Coated System (ACS) total knee prosthesis 12 months after surgery.

To reduce selection bias and to ensure covariate balance, a propensity score matching 1:1 in terms of age and sex was used to match the smaller LCS group, with a subset of the ACS group (Figure 4). Table 1 shows group comparisons before and after matching. The average length between surgery and the time of study was 10.1 ± 1.0 years for the ACS group and 14.9 ± 3.0 years ($p < 0.001$) for LCS patients.

Table 1. Characteristics of the study population. ACS patients were matched to LCS patients for age and sex.

| Patient Characteristics | ACS ($n = 404$) | LCS ($n = 260$) | p | Matched ACS ($n = 260$) | p |
|-------------------------|-------------------|-------------------|--------|---------------------------|-------|
| Age, mean \pm SD | 65.6 ± 8.2 | 65.8 ± 11.3 | 0.775 | 66.5 ± 9.1 | 0.423 |
| Sex (F:M) | 275:129 | 209:51 | <0.001 | 209:51 | 0.999 |

ACS: Advanced Coated System; LCS: Low Contact Stress System; SD: standard deviation.

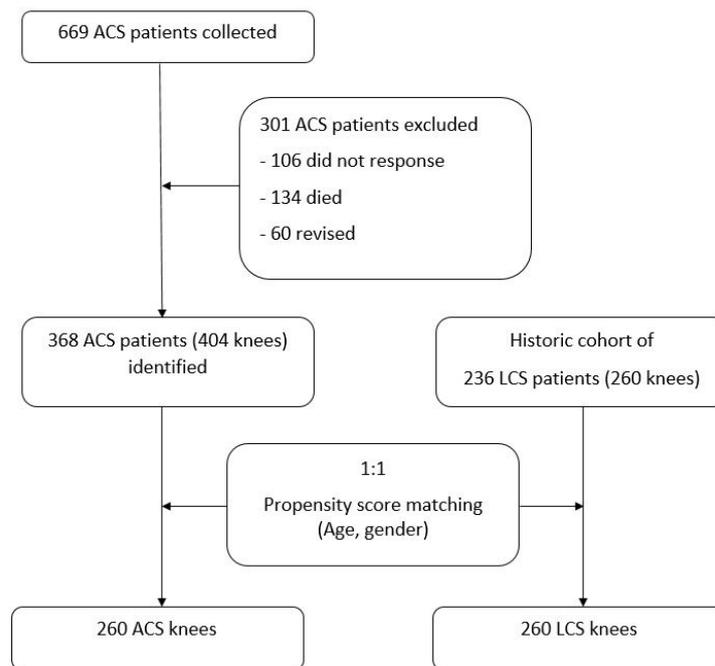


Figure 4. Flow chart of study inclusion.

2.2. Outcome Measurements

Pre- and postoperative activity levels, functions and pain were evaluated using the Tegner Activity level scale [31], the Visual Analogue Scale (VAS), the Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) [32], and the Knee Society Score (KSS) system [33]. Tegner and VAS scores were obtained preoperatively and during the final follow-up. The WOMAC and KSS function and clinical scores were evaluated during the last follow-up. Additionally, the self-reported status of meteorosensitivity (yes/no) was included in the survey for all patients. Meteorosensitivity was defined as weather-related pain of the artificial knee joint.

This study followed accepted ethical, scientific, and medical standards and was conducted in compliance with recognized international standards, including the principles of the Declaration of Helsinki. Informed consent was obtained from all participants. The local ethics committee of the Medical University of Graz (26–527 ex 13/14) approved the study protocol.

2.3. Statistical Methods

The data was analyzed by SPSS Version 23.0 (IBM Corporation, New York, NY, USA). We compared demographic characteristics and clinical scores between the LCS and the ACS groups. The data was tested for normality by using the Kolmogorov–Smirnov test. Statistical analyses were performed using chi-squared tests for comparison of categorical parameters, and t-tests for comparisons of continuous normally distributed parameters. We defined statistical significance at the 5% level ($p \leq 0.05$).

Post hoc power analyses using significance levels set to an alpha of 0.05 were performed to determine whether the sample had sufficient power to detect significant differences. A power > 80% was considered sufficient. We calculated post hoc power according to Hoenig and Heisey [34].

3. Results

The Overall Population

The comparison of Tegner, VAS, WOMAC, and KSS scores for pain and function is summarized (Table 2). Both groups showed a significant ($p < 0.001$) improvement in VAS scores. The Tegner score was however lower for both prostheses at the last follow-up, when compared to preoperative data.

The changes in score (preoperatively to latest postoperatively) demonstrated a significant ($p = 0.003$) group difference in terms of Tegner scores in favour of LCS TKA.

Table 2. Comparison of Meteoro-sensitivity and Clinical Outcome before (except KSS and WOMAC) and after mean final follow-up between ACS and LCS patients.

| | ACS (n = 260) | LCS (n = 260) | p |
|----------------------------------|------------------|------------------|-------------|
| KSS Pain (mean ± SD) | 82.6 ± 15.6 | 70.8 ± 21.9 | $p < 0.001$ |
| KSS Function (mean ± SD) | 61.9 ± 25.4 | 71.1 ± 29.1 | $p = 0.011$ |
| WOMAC (mean ± SD) | 79.9 ± 15.2 | 81.3 ± 14.6 | $p = 0.453$ |
| VAS (mean ± SD) | | | |
| Pre-operative | 7.7 ± 1.2 | 6.9 ± 1.8 | $p < 0.001$ |
| Post-operative | 2.9 ± 2.0 | 1.4 ± 1.8 | $p = 0.002$ |
| Change in VAS | 5.6 ± 2.3 | 4.4 ± 3.3 | $p < 0.001$ |
| TAS (mean ± SD) | | | |
| Pre-operative | 2.9 ± 1.2 | 3.0 ± 1.5 | $p = 0.256$ |
| Post-operative | 2.6 ± 1.1 | 2.2 ± 1.5 | $p = 0.001$ |
| Change in TAS | 0.3 ± 1.4 | 0.6 ± 1.7 | $p = 0.072$ |
| Meteoro-sensitivity (yes) | 150 (58%) | 54 (21%) | $p < 0.001$ |

SD: standard deviation; ACS: Advanced Coated System; LCS: Low Contact Stress System; KSS: knee society score; WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index; VAS: visual analogue scale; TAS: Tegner Activity Scale.

In the ACS group, the latest KSS pain score was significantly higher when compared to the LCS group (82.6 ± 15.6 vs. 70.8 ± 21.9 ; $p < 0.001$), whereas the KSS function score performed significantly worse (61.9 ± 25.4 vs. 71.1 ± 29.1 ; $p = 0.011$). No differences were observed with respect to WOMAC scores at final evaluation.

The comparison between the ACS and LCS groups regarding sensitivities to weather changes revealed that 56% (226/404) of the ACS group described their artificial knee joints as being sensitive to weather changes. When compared with LCS patients, this reflected a significant difference ($p < 0.001$) as only 21% (54/260) of LCS patients considered their prosthetic knee as meteoro-sensitive (Table 2). The magnitude of this difference between both groups reached a *post hoc* power greater than 80%, according to Hoenig and Heisey [34].

4. Discussion

The most important finding of this study was that TiN-coated implants did not show clinical benefits after long-term follow-up, when compared to conventional CoCr TKA. Secondly, meteoro-sensitivity was reported more frequently in un-cemented TiN knees when compared to cemented CoCr TKA. The present study is unique in that it provides a comparison between the two surfaces with the longest follow-up so far.

Several studies have provided data on TiN-coated TKA. Thienpont et al. [35] concluded that TiN components can be used for metal-allergic patients, with essentially equivalent clinical and radiological outcomes when compared to patients without metal allergies receiving conventional implants. Additionally, Van Hove et al. [5] in a five-year double-blind randomized controlled trial, determined no clinical benefits between TiN-coated and CoCr TKA in non-allergic patients. These authors showed no differences in postoperative pain, swelling, skin temperature and knee function. Another study by Mohammed et al. [36] found that survival of TiN-coated TKA was 95.1% after ten years, which is in line with overall ten-years revision rates after TKA, according to arthroplasty registers [37,38].

TiN coating aims to reduce wear debris since the clinical consequences cover a broad spectrum from radiolucencies to massive osteolysis and implant failure [39]. Aseptic loosening is the most

common cause for revision surgery in TKA, and therefore the reduction of debris-induced osteolysis should result in decreased revision rates compared to CoCr TKA [40]. However, registry data reveal ACS revision rates that are slightly higher than LCS, although both provide satisfying mid-term results [37,38].

Revision rates are well suited for comparative analysis; however, a low revision rate of an implant does not automatically represent a good value in patient-based outcome measurement. Beverland et al. reported similar revision rates for compared hip and knee arthroplasties, although the percentage of “very happy” patients was 54% vs. 4% in favor of hip arthroplasty [41]. Ideally, numerous assessment scales should be administered to the patient in order to accurately reflect the patient characteristics [42]. In the present study, a statistically significant difference in favor of LCS TKA in the matched overall patient cohort was observed for the functional component of the KSS. In contrast, LCS patients were significantly worse in terms of the latest KSS pain. Compared to the results of WOMAC, TAS, and VAS, however, KSS differences are clinically not relevant, as these discrepancies could not be observed in the other outcome scores. Furthermore, patients were evaluated by various observers, which could have caused interobserver KSS variations making KSS results questionable [43]. Therefore, the findings indicate that ACS and LCS TKA performed equally.

We also examined if rates of meteoro-sensitivity of the operated knee were equal among our study groups. It was reported by Loth et al. that 18% of their TKA patients rated themselves as sensitive to changes in weather conditions [44]. Interestingly, in this study we observed significant ($p < 0.001$) differences between the two TKA systems. LCS patients displayed almost identical rates of meteoro-sensitivity when compared to the literature. In contrast, ACS patients rated themselves as much more sensitive to weather changes. It is noteworthy that the weather sensitivity differed between the two implants in such a way. Timmermans et al. [45] reported that women reported meteoro-sensitivity more often, but the gender distribution of the two matched-cohorts is identical. The reasons for the high incidence of meteoro-sensitivity in the ACS group is speculative. It is important to consider that not only did the alloy differ between study prostheses, but also the fixation methods differed. Cement was used in all LCS TKA procedures and an un-cemented press-fit technique was performed in the majority (97.6%) of ACS cases. This raises the question whether cement limits the probability of a meteoro-sensitive artificial knee joint. An essential factor in weather-related pain is barometric pressure [46,47]. In animal studies, changes in barometric pressure induces sympathetic activation. Hence, this may directly activate nociceptive fibers and induce vasoconstriction, thus increasing pain [47]. Therefore, we hypothesize that cement may prevent or reduce this activation in artificial joints. Further research in this field is required; however this study is unique in comparing meteoro-sensitivity in two different TKA systems after a long-term observation period.

There are limitations to our study. Firstly, data were collected in a retrospective manner, and results should be interpreted accordingly. We could only determine the differences in functional outcome scores and meteoro-sensitivity between CoCr and TiN TKA, and not necessarily causation. Further confounders have to be considered regarding the comparison between two different surfaces. Although implants with similar design and geometry were used, functional outcome scores are also dependent from the surgeon, the implantation technique, the surgical approach, the pain management and the patients' characteristics [48]. A randomised-controlled study design with the use of the same implant in a CoCr version as well as TiN-coated with identical follow-up time would be beneficial to confirm our findings. Secondly, propensity score matching in terms of BMI and comorbidities could not be performed since data were not available for LCS patients. Thirdly, another limitation is the inconclusive response rate, which although this is a purely observational study, could represent a selection bias. Fourthly, preoperative data concerning clinical and functional components of KSS and WOMAC were unavailable, therefore, we could not determine pre- and post-operative differences in these outcome scores between the ACS and LCS groups. Finally, the cause of the difference in sensitivity in terms of weather change remains unclear and no objective parameters were available.

5. Conclusions

After a long-term observation period, TiN-coated TKA reported similar clinical outcome scores when compared to conventional CoCr TKA. Surprisingly, sensitivity to weather changes were more correlated with un-cemented ACS implants. The authors will continue to use TiN-coated TKA only in patients with a known or suspected metal allergy.

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