

**Title: Lateral osteophytes do not represent a contraindication to medial unicompartmental knee arthroplasty: A fifteen year follow up.**

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**Acknowledgements:** The authors would like to thank L. Skinner, B.E. Marks, J. Brown and J. Ferris for their assistance with this study. TWH has been supported by the NIHR Biomedical Research Centre, based at Oxford University Hospitals Trust, Oxford. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. Financial support has been received from Zimmer Biomet.

**Conflicts of interest:** The author or one or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article. In addition, benefits have been or will be directed to a research fund, foundation, educational institution, or other non- profit organisation with which one or more of the authors are associated.

**Title:** Lateral osteophytes do not represent a contraindication to medial unicompartmental knee arthroplasty: A fifteen year follow up.

### **Abstract**

**Purpose:** Lateral osteophytes have been reported to be associated with lateral compartment disease and as such it is unclear whether medial unicompartmental knee arthroplasty should be performed if these are present.

**Methods:** Using the OARSI classification system, 0 (no osteophyte) to 3 (large osteophyte), radiographs from a series of cemented meniscal-bearing unicompartmental knee arthroplasty implanted in the setting of full thickness lateral cartilage where lateral osteophytes were not considered a contraindication were identified and factors associated with the presence and size of lateral osteophytes, and their impact on clinical outcomes and implant survival were assessed.

**Results:** Pre-operative radiographs from 458 knees (392 patients), independently followed-up for a mean 10.5 years (range 5.3-16.6) were assessed. Lateral osteophytes were present in 62% of knees with 18% scored as Grade 3. Inter-observer reliability was good ( $\kappa=0.70$ ). The presence and size of lateral osteophytes was associated with younger age at joint replacement ( $p=0.01$ ) and increasing BMI ( $p=0.01$ ). No association was seen with gender, pre-operative status, assessed using the Oxford Knee Score (OKS), American Knee Society (AKSS) Objective or Functional Score, and Tegner activity score, or size of medial tibial lesion. Subgroup analysis of Grade 3 Osteophytes, revealed that these were associated with a greater degree of macroscopic ACL damage.

At ten years there was no difference in function, survival or mechanism of failure between groups (*n.s.*). Subgroup analysis of Grade 3 osteophytes, found no significant difference in functional outcome at 10 years or implant survival at 15 years.

**Conclusion:** The presence of lateral osteophytes is not a contraindication to medial meniscal-bearing unicompartmental knee arthroplasty. The clinical relevance of this study is that it highlights the importance of an appropriate preoperative assessment of the lateral

28 compartment as in the setting of full thickness cartilage at operation lateral osteophytes do not  
29 compromise long term functional outcome or implant survival.

30 **Level of Evidence:** Level IV

31 **Keywords:** meniscal-bearing unicompartmental knee arthroplasty, implant survival, functional  
32 outcome, osteophytes, patient selection

## Introduction

Osteophytes are pathognomonic of osteoarthritis, however it is currently unclear whether they represent localised compartmental damage or are a general manifestation of intra-articular disease [14]. This is of particular clinical relevance in patients considering unicompartmental knee arthroplasty (UKA) presenting with bone-on-bone arthritis in, typically, the medial compartment and osteophytes in the lateral compartment, as it is unclear as to whether, in this scenario, osteophytes represent a contraindication to medial UKA [15, 22].

Osteophytes are common and in population based studies have reported to be present in over 50% of knees [3]. In animal studies their presence has been associated with local cartilage damage, as well as induced joint instability [9, 27]. In clinical studies their presence has been associated with increasing age, female gender and metabolic syndrome [7, 8, 13, 24].

To our knowledge whether the presence of lateral osteophytes affects outcomes following medial UKA has not previously been investigated. Previous work, based on MRI data, from the osteoarthritis initiative (OAI) found that, whilst there was no difference in the cartilage thickness or volume between knees with or without osteophytes (all grades), the incidence of full thickness cartilage defects on the tibial side increased from under 2% in knees without lateral osteophytes to 10% in knees with large (Grade 3) osteophytes [3].

Furthermore it is known that the cytokines interleukin-6 (IL-6) and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) which are associated with osteophyte formation, are also associated with knee cartilage loss, and progression of arthritis [16, 25]. As a significant number of patients presenting with anteromedial arthritis have lateral osteophytes, and the commonest reason for failure of medial UKA is progression of arthritis in the retained lateral compartment, occurring in around 2.5% of cases, it is important to establish whether it is safe to perform a UKA in these cases [18].

The null hypothesis is that in knees with full thickness cartilage in the weight bearing portion of the lateral compartment at the time of operation lateral osteophytes do not influence long term function or implant survival following medial UKA. This study investigates whether presence and severity of lateral osteophytes represent a contraindication to medial UKA by

61    assessing the ten-year functional outcomes and fifteen-year implant survival in a series of  
62    patients treated with medial meniscal-bearing UKA where the presence of lateral osteophytes  
63    was not considered a contraindication to this procedure.

## Materials and Methods

Our prospective database of consecutive cemented Phase 3 Oxford medial UKAs performed via a minimally invasive approach by two surgeons (DWM and CAFD) between June 1998 and March 2009 was searched to identify knees with available pre-operative radiographs. In this series UKA was performed for the recommended indications as described by Goodfellow *et al.* with lateral osteophytes not considered a contraindication [5, 19, 20].

Lateral osteophytes were assessed using the Osteoarthritis Research Society International (OARSI) Classification system by an assessor blinded to the outcome of treatment. The OARSI classification system is an atlas-based grading system ranging from Grade 0 (no osteophyte) to Grade 3 (large osteophyte) [1]. The lateral compartment was scored based on the largest osteophytes observed, be that on the tibia or femur. Inter and intra-observer reliability was assessed on 20% of randomly chosen radiographs

All patients were assessed and followed up independently by a senior physiotherapist blinded to radiographic scoring. Assessments were performed pre-operatively and at one, five, seven, ten, twelve and fifteen years post-operatively. At the time of surgery a detailed intra-operative record of the status of each of the compartments within the knee was made and the presence of full thickness cartilage in the weight bearing portion of the lateral compartment confirmed. The size and depth of anteromedial tibial defect as defined previously was measured and classified as: focal ( $\leq 2 \text{ cm}^2$ ) full thickness cartilage loss (FTCL), extensive ( $> 2 \text{ cm}^2$ ) FTCL, bone loss  $\leq 5 \text{ mm}$  or bone loss  $> 5 \text{ mm}$  [23]. The macroscopic status of the ACL was classified as, normal, or having synovial damage or longitudinal splits [4]. Functional outcomes were assessed using the: Oxford Knee Score (OKS), American Knee Society Score Objective (AKSS-O), and Functional (AKSS-F), and the Tegner Activity Score [12, 17, 26].

All patients were contacted in the previous 18 months to ascertain the current functional status of their knee and incidence of re-operations. Where patients had died information about the status of their knee, and the presence of further operations was obtained via primary and secondary care records as well as via patient's relatives where appropriate. Data was extracted from our prospective database on 1<sup>st</sup> September 2014.

This study was approved by the local ethics committee chair person (Oxfordshire Research Ethics Committee C) who confirmed that the clinical and radiological follow up of these patients formed part of routine assessment and therefore does not need formal ethical approval. Consent was taken from all patients for involvement in this study including consent to use data from medical records and radiographs.

## **Statistical analysis**

A power calculation was performed using the minimally clinically important difference reported for OKS [2]. Using the Altman nomogram for a power of 80% at a significance level of 0.05 and using a standard deviation of 8, a sample size of 80 patients is required to detect a clinically important difference between groups.

We performed a primary analysis comparing outcomes in those knees with no lateral osteophytes (OARSI Grade 0), to those knees with lateral osteophytes (OARSI Grades 1 to 3). Subgroup analysis was used to compare the outcomes of those in those knees with no lateral osteophytes and those with OARSI Grade 3 osteophytes.

To compare baseline demographic and functional differences at baseline, 10- years and improvement from baseline a Mann-Whitney U, non-parametric test was performed. To assess for differences in gender, size of medial tibial lesion and ACL macroscopic status a Chi-Squared test was performed. To assess the influence of location of osteophytes on functional performance at baseline, 10 years and improvement from baseline a Kruskal Wallis, non-parametric test was performed.

To detect differences in survival between groups a Mantel-Cox test was performed for implant-related re-operations, which included any re-operations in which components were changed, in which the meniscal bearings were replaced for dislocation, and any re-operations in which new components were inserted. Life-table analysis was performed. Confidence intervals (CI) were calculated using the method described by Peto *et al.* [21].



118 All analyses were performed using SPSS Version 22 (IBM Corporation, Armonk, New York).

119 Statistical significance was set at  $p < 0.05$ .

120

## Results

Radiographs of 458 knees (392 patients) were identified consisting of 326 unilateral procedures and 66 sequential staged bilateral procedures. Inter ( $\kappa=0.70$ ) and intra-observer ( $\kappa=0.70$ ) reliability was good.

Lateral osteophytes were identified in 62% (285) of knees. Of these, Grade one osteophytes were seen in 48% (137 knees), Grade two in 34% (98 knees) and Grade three in 18% (50 knees). Where lateral osteophytes were present they were seen on the tibia only in 47% (134 knees), femur only in 16% (46 knees) and both the tibia and femur in 37% (105 knees).

Baseline demographics are outlined in Table 1. Lateral osteophytes were associated with younger age at joint replacement ( $p=0.01$ ) and higher BMI ( $p=0.01$ ). There was no association seen between the presence and location of lateral osteophytes and pre-operative function as assessed by OKS (*n.s.*), AKSS-O (*n.s.*) or Tegner activity score (*n.s.*), however AKSS-F was found to be lower in knees with both lateral tibial and femoral osteophytes compared to knees with no osteophytes ( $p=0.02$ ) and compared to knees with lateral tibial osteophytes only ( $p<0.01$ ).

Overall there was no association seen between the size of the medial tibial lesion in those knees without lateral osteophytes and those knees with lateral osteophytes (Grade 1-3; *n.s.*) or those knees with Grade 3 lateral osteophytes (*n.s.*). Figure 1. Similarly there was no association seen between the macroscopic status of the ACL in those knees with and without lateral osteophytes (Grade 1-3; (*n.s.*) however subgroup analysis revealed those knees with Grade 3 lateral osteophytes were significantly more likely to have a greater degree of macroscopic damage of the ACL than those without osteophytes ( $p=0.04$ ). Figure 2.

All patients were followed up for a minimum of five years with the exception of those who underwent revision (8 prior to 5 years), died (19) or withdrew from the study due to poor health (1). No patients were lost to follow up. In the patients who died or withdrew from the study at any time point, all due to medical co-morbidities not associated with their knee, we are not aware of any revisions. The mean follow up was 10.3 years (range 5.3 to 16.6) with 198 knees having a minimum 10 year follow.

The mean OKS by year following UKA for each of the three groups is displayed in Figure 3. At ten years no significant difference in absolute or improvement from baseline OKS (*n.s.*), AKSS-O (*n.s.*), AKSS-F (*n.s.*) or Tegner activity score (*n.s.*) was detected between groups or on subgroup analysis of knees with large lateral osteophytes (Grade 3). Table 2.

At 10 years no difference in functional outcome was seen between groups based on location of lateral osteophytes as assessed by OKS (*n.s.*), AKSS-F (*n.s.*) or Tegner activity score (*n.s.*) however AKSS-O was found to be significantly lower in knees with lateral femoral osteophytes compared to other groups (no osteophytes ( $p=0.01$ ), lateral tibial osteophytes only ( $p<0.01$ ), both lateral tibial and femoral osteophytes ( $p<0.01$ )). Overall, no difference in improvement from baseline across all functional scores was seen between groups.

Overall there were 20 implant related reoperations. In knees without lateral osteophytes there were five reoperations (3%) at a mean of 6.3 years (range 0.8 to 11.4 years), two of which were for progression of arthritis in the lateral compartment (1%). In knees with lateral osteophytes (Grade 1-3) there were 15 reoperations (5%) at a mean of 6.2 years (range 0.7 to 14.7 years), six of which were for progression of arthritis in the lateral compartment (2%). In knees with Grade 3 lateral osteophytes there was one reoperation (2%) at a mean of 4.6 years for progression of arthritis in the retained lateral compartment (2%). No difference was seen in the timing or mechanism of failure between groups.

When implant-related re-operations are considered failures the fifteen-year survival rate is 94% (95% Confidence Interval [CI], 82 to 100) in those patients without lateral osteophytes, 88% (95% CI, 76 to 100) in those patients with lateral osteophytes (Grade 1 – 3) and 98% (95% CI, 83 to 100) in those knees with Grade 3 lateral osteophytes. Figure 4. Overall no significant difference in survival existed between knee without lateral osteophytes and those with lateral osteophytes (Grade 1 – 3; *n.s.*) or between knees without lateral osteophytes and those with Grade 3 lateral osteophytes (*n.s.*). No difference in implant survival was seen based on the location of lateral osteophytes (*n.s.*).

## Discussion

The most important finding of this study is that it has demonstrated that the presence of lateral osteophytes does not affect long term functional outcomes or implant survival, and as such should not represent a contraindication to meniscal-bearing UKA. We found that in around two thirds of knees lateral osteophytes were observed, and that 18% of these were large Grade 3 osteophytes. Increasing incidence and size of lateral osteophytes was associated with younger age at joint replacement and increased BMI, with those knees that had Grade 3 osteophytes also having a higher grade of macroscopic ACL damage at the time of operation, compared to those without osteophytes.

At ten years no difference in functional outcome assessed by the OKS and AKSS Objective and Functional Scores, or in activity level assessed by the Tegner activity Score was found between knees without lateral osteophytes and knees with lateral osteophytes (Grade 1 – 3) or on subgroup analysis of those knees with large (Grade 3) osteophytes. At fifteen years no difference in implant survival, or failure mechanism, was detected between groups. In knees with Grade 3 lateral osteophytes there was only one failure with the fifteen year survival calculated as 98% (95% confidence interval, 83 to 100%). Whilst, due to the small number of knees (50) in this group caution must be taken with interpretation of this results, this finding provides further support that lateral osteophytes should not be seen as a contraindication to medial UKA in the setting of full thickness lateral cartilage at baseline.

Assessing whether location of osteophytes influences outcomes at ten year no difference in OKS, AKSS-F or Tegner Activity Score was seen between groups. Whilst the AKSS-O was found to be lower in knees with lateral femoral osteophytes compared to other groups the small number of knees in this subgroup with ten year functional results limits the strength of this finding. As no difference in improvement from baseline to ten years was seen between this, and other groups and no difference in implant survival was observed at 15 years this group does not appear to have worse outcomes and as such, whilst further studies are warranted, the current evidence does not support restricting UKA in these cases.

The results of this study suggest that the presence of lateral osteophytes represents a general manifestation of disease, rather than a compartment specific indicator of damage. In this series it was interesting to note that younger age at joint replacement and increased BMI were both associated with an increasing size and incidence of lateral osteophytes. The reasons for this association are unclear however metabolic syndrome (body mass index (BMI)  $\geq 30 \text{ kg/m}^2$  with two out of three of: hypertension, insulin resistance or dyslipidemia) has been reported to be associated with increased osteophyte formation secondary to increased pro-inflammatory cytokine activity [24]. Cytokine levels within the arthritic knee have previously been correlated with pain scores and as such it may be an increased pre-inflammatory cytokine burden, as opposed to the presence of lateral osteophytes, which we have demonstrated to be asymptomatic following UKA, that leads patients to seek surgery sooner rather than later [11]. In addition to lateral osteophytes intra-articular pro-inflammatory cytokines may result in notch osteophyte formation which may explain the increasing macroscopic ACL damage seen to be associated with the presence of large Grade 3 lateral osteophytes in this study.

In this study all patients satisfied the indications for meniscal-bearing medial UKA and had antero-medial OA with (a) medial bone-on-bone arthritis (b) functionally normal ACL (c) functionally normal MCL (d) full thickness lateral cartilage and (e) patellofemoral joint without lateral grooving and bone loss. In this situation lateral osteophytes do not compromise the outcome and therefore they should not be considered to be a contraindication and can be ignored. The clinical relevance of this study is that it highlights the importance of ensuring that when performing UKR knees meet these five criteria and in particular an appropriate preoperative assessment of the lateral compartment is performed. The key to assessment of the lateral compartment is determining whether or not there is full thickness lateral cartilage. As the status of lateral compartment, in particular the cartilage thickness, is difficult to assess intra-operatively, it is important that this is performed pre-operatively. The best way to assess the thickness of the lateral cartilage preoperatively is with valgus Stress radiographs. This approach has been adopted in a radiographic Decision Aid, which these and other views and reported a 95% accuracy in identifying suitability for UKA, with a 98.9% implant survival seen

at 5 years in an independent population [6]. Whilst some surgeons use MRI to assess the lateral compartment this has been demonstrated to have a high false-positive rate at detecting lateral compartment disease, resulting in patients being unnecessarily contraindicated for UKA [10]. Furthermore, the use of MRI adds additional cost and time to the workup for joint replacement without delivering additional benefits in terms of patient selection.

The strengths of this study are that it represents a large series of patients undergoing UKA, with standardised patient selection and surgical management, and comprehensive, independent, long term follow up. Limitations of the study are that the results represent those seen at a high-volume centre and further correlation of these results is required. Additionally, all patients did not have valgus Stress radiographs pre-operatively and therefore did not have a formal pre-operative assessment of the lateral compartment. However, if the other radiographic criteria for antero-medial OA are satisfied valgus Stress radiograph are not always essential. During the validation of the Decision Aid it was demonstrated that if valgus Stress radiograph were not performed the accuracy in identifying suitability for medial UKA was reduced by 5%, as provided knees met all other radiological criteria the lateral compartment was acceptable in the majority of cases.

The clinical relevance of this study is that it highlights the importance of an appropriate preoperative assessment of the lateral compartment as in the setting of full thickness cartilage at operation lateral osteophytes do not compromise long term functional outcome or implant survival.

## **Conclusion**

This study has demonstrated that in the setting of anteromedial osteoarthritis lateral osteophytes are common, and that their presence does not influence the long term functional outcomes of implant survival following meniscal-bearing UKA. As such the findings of this study are that lateral osteophytes are not a contraindication to medial UKA.

**Acknowledgements:** The authors would like to thank L. Skinner, B.E. Marks, J. Brown and J. Ferris for their assistance with this study. TWH has been supported by the NIHR Biomedical Research Centre, based at Oxford University Hospitals Trust, Oxford. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. Financial support has been received from Zimmer Biomet.

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**Author Contributions:**

TWH developed the initial concept, performed data analysis, interpretation and drafted the manuscript.

RC performed data analysis and critically appraised the manuscript.

CJ performed data collection and critically appraised the manuscript.

SJM performed data collection and critically appraised the manuscript.

CAFD performed data collection and critically appraised the manuscript.

DWM developed the initial concept and was involved in all stages from data collection to drafting of the manuscript.

HGP developed the initial concept and was involved in all stages from data collection to drafting of the manuscript.

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|   | No<br>osteophytes<br>(Grade 0) | Lateral<br>osteophytes<br>(Grade 1 – 3) | <i>p</i> -value | Lateral<br>osteophytes<br>(Grade 3) | <i>p</i> -value |
|---|--------------------------------|---|-----------------|-------------------------------------|-----------------|
| Mean Age<br>(range)                           | 69.0<br>(38 - 87)              | 66.5<br>(40 - 88)                       | 0.01            | 64.2<br>(41 – 83)                   | <0.01           |
| % Male<br>( <i>n</i> )                        | 51<br>(89)                     | 53<br>(151)                             | <i>n.s.</i>     | 48<br>(24)                          | <i>n.s.</i>     |
| Mean BMI<br>(range)                           | 27.5<br>(15 - 52)              | 28.9<br>(18 - 47)                       | 0.01            | 30.5<br>(22 - 46)                   | <0.01           |
| Mean OKS<br>(range)                           | 23.6<br>(9 -47)                | 23.9<br>(7 - 47)                        | <i>n.s.</i>     | 24.1<br>(7 -38)                     | <i>n.s.</i>     |
| Mean AKSS-<br>O<br>(range)                    | 49.1<br>(0 - 95)               | 45.5<br>(6 - 80)                        | <i>n.s.</i>     | 44.5<br>(8 - 70)                    | <i>n.s.</i>     |
| Mean AKSS-<br>F<br>(range)                    | 70.1<br>(35 - 100)             | 68.5<br>(30 - 100)                      | <i>n.s.</i>     | 63.8<br>(35 - 100)                  | <i>n.s.</i>     |
| Median<br>Tegner<br>activity score<br>(range) | 3.0<br>(1 - 6)                 | 3.0<br>(1 - 7)                          | <i>n.s.</i>     | 1<br>(1 - 4)                        | <i>n.s.</i>     |

Table 1: Preoperative demographics

|  | No<br>osteophytes<br>(Grade 0) | Lateral<br>osteophytes<br>(Grade 1 – 3) | <i>p</i> -value | Lateral<br>osteophytes<br>(Grade 3) | <i>p</i> -value |
|--|--------------------------------|---|-----------------|-------------------------------------|-----------------|
| Mean<br>Improvement<br>OKS<br>(Range)                        | 18.4<br>(0 to 29)              | 17.3<br>(1 to 27)                       | <i>n.s.</i>     | 14.3<br>(4 to 18)                   | <i>n.s.</i>     |
| Mean<br>Improvement<br>AKSS-O<br>(Range)                     | 27.4<br>(-25 to 52)            | 36.1<br>(-12 to 90)                     | <i>n.s.</i>     | 24.8<br>(-12 to 40)                 | <i>n.s.</i>     |
| Mean<br>Improvement<br>AKSS-F<br>(Range)                     | 5<br>(-30 to 40)               | 5.8<br>(-10 to 40)                      | <i>n.s.</i>     | 11.7<br>(-30 to 40)                 | <i>n.s.</i>     |
| Median<br>Improvement<br>Tegner<br>activity score<br>(Range) | 0<br>(-2 to 2)                 | 0<br>(-2 to 4)                          | <i>n.s.</i>     | 0<br>(0 to 1)                       | <i>n.s.</i>     |

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Figure 1

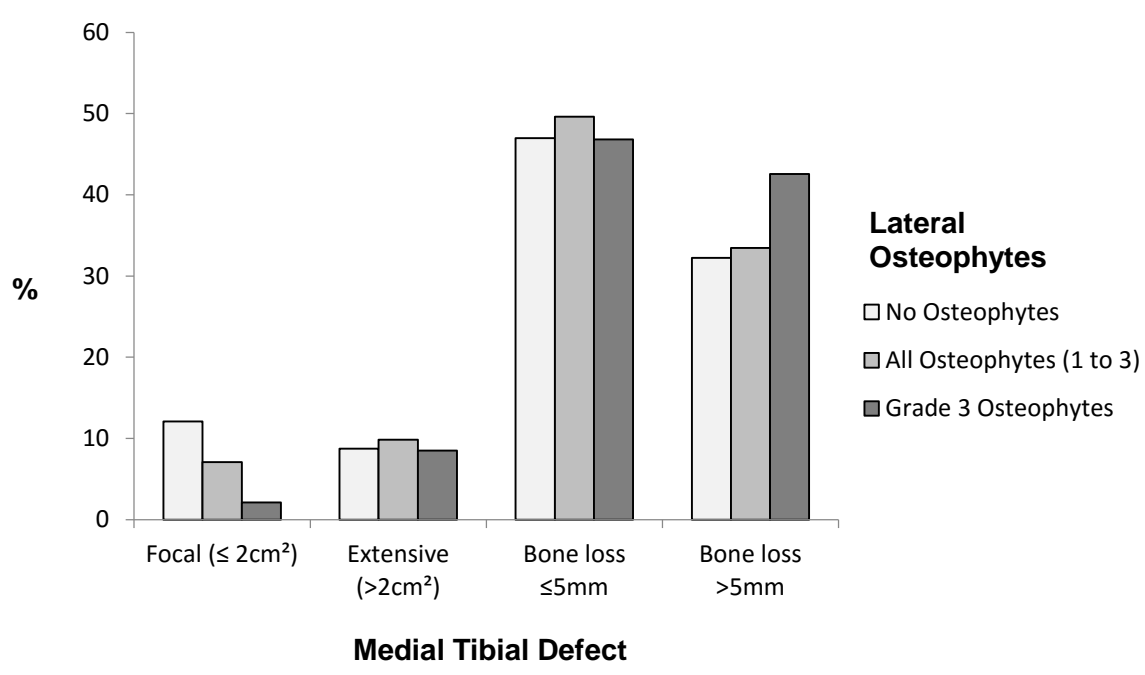


Figure 2

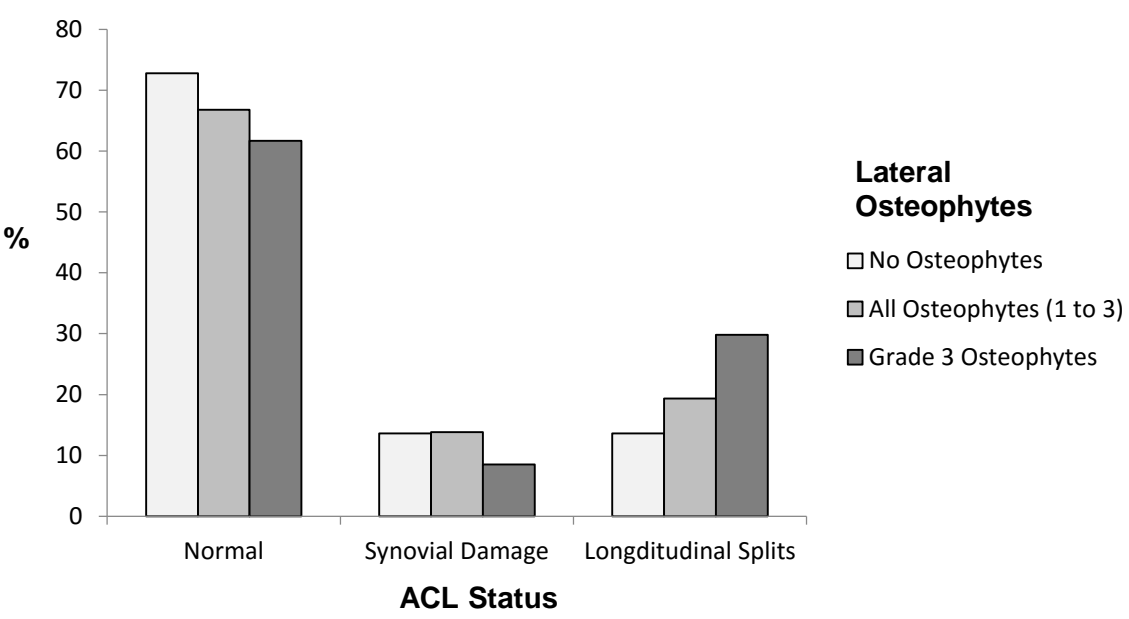


Figure 3

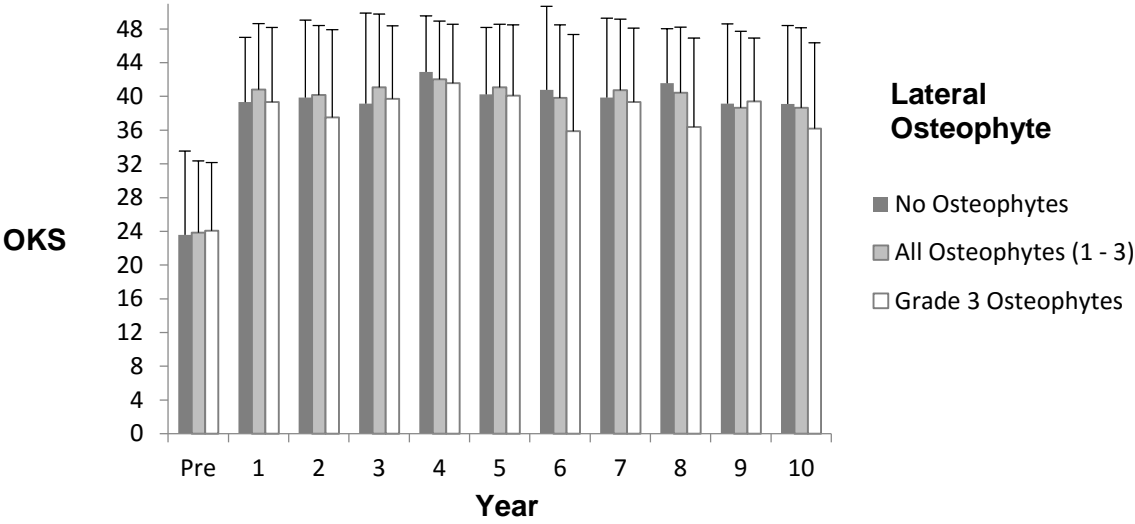


Figure 4

