

Total Knee Conversion Rates and Functional Outcome After Calcium Phosphate Injection for Bone Marrow Lesions of the Knee

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Abstract

Untreated osteoarthritis (OA)-related bone marrow lesions (OA-BML) can hasten the progression of knee OA. Previous studies have shown that fluoroscopically guided intraosseous calcium-phosphate (CaP) injections of OA-BML during knee arthroscopy can lead to pain reduction, improved functionality, and prolonged time until conversion to total knee arthroplasty (TKA). The purpose of this retrospective study is to compare the clinical outcomes of patients who underwent knee arthroscopy and CaP injection for OA-BML versus knee arthroscopy for non-OA-BML pathologies. Two-year follow-up data and patient-reported outcomes including knee injury and operative outcome scores, joint replacement scores (KOOS, JR) were available for 53 patients in the CaP group and 30 patients in the knee arthroscopy group. Results indicate that patients in the CaP group had less frequent conversion to TKA compared with patients in the knee arthroscopy group. Statistical analysis demonstrated a statistical difference between preoperative and postoperative KOOS, JR within the CaP group but not for the knee arthroscopy group. Two-year postoperative KOOS, JR for CaP patients was statistically greater than the 2-year postoperative KOOS, JR of knee arthroscopy patients. Results indicate greater improvement in functional outcomes with knee arthroscopy and CaP injection of OA-BML compared with knee arthroscopy alone for non-OA-BML diagnoses. The results of this retrospective study help to distinguish the benefits of knee arthroscopy accompanied by CaP intraosseous injection from that of knee arthroscopy alone.

Keywords

- ▶ osteoarthritis
- ▶ knee arthroscopy
- ▶ subchondroplasty
- ▶ calcium phosphate
- ▶ bone marrow lesion

Osteoarthritis (OA)-related bone marrow lesions (OA-BML) are areas of subchondral bone that have been identified as precursors to symptomatic OA and risk factors for an increased rate of OA progression.^{1–3} Etiologies include degenerative changes, acute traumatic injuries, or inflammatory arthropathies.⁴ OA-BML are associated with pain and decreased functionality in addition to an increased likelihood of pursuing total knee arthroplasty (TKA).^{5,6} TKA is a reliable procedure for the treatment of arthritis,

but patient-reported outcomes have been suboptimal with as few as 22% of patients claiming excellent results.⁷ In addition, according to one meta-analysis, 82% of TKAs demonstrate 25-year survival before revision is indicated, making TKA a less attractive option for younger patients.⁸ Due to low satisfaction and the risk of revision TKA, minimally invasive arthroscopic surgical treatment of OA-BML offers a promising alternative for patients who wish to delay arthroplasty.

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Table 1 Inclusion and exclusion parameters

Inclusion study group	Exclusion from study
Tibial OA-BML	Smoking at time of surgery
Failure of conservative treatment (cortisone, bracing, physical therapy, etc.)	Chronic narcotic use
K-L score 0–3	Femoral OA-BML
	Hemoglobin A1C over 7.5 at time of surgery
	K-L score of 4
	Arthroscopic anterior cruciate ligament reconstruction

Abbreviations: K-L, Kellgren–Lawrence; OA-BML, osteoarthritis (OA)-related bone marrow lesions.

OA-BML present on magnetic resonance imaging (MRI) as areas of increased signal intensity on fat-suppressed T2-weighted images.^{4,9,10} On water-sensitive sequences such as T-weighted imaging, OA-BML take on diffuse shapes with poorly defined borders.¹¹

The subchondroplasty (SCP) procedure is a surgical technique utilizing an orthobiologic ceramic.¹² SCP entails a fluoroscopy-guided injection of an engineered osteoconductive nanocrystalline calcium-phosphate (CaP [$\text{Ca}_{10-x} [\text{M}]_x [\text{PO}_4]_{6-x} [\text{HPO}_4, \text{CO}_3]_x [\text{OH}]_{2-x}$]) via a cannula at the site of an OA-BML.¹³ The goal of CaP injection is to improve bone strength while providing scaffolding for subchondral bone remodeling.^{14,15}

A previous meta-analysis has demonstrated that CaP injection provides a decrease in pain and an increase in

functionality.¹⁶ While CaP injection as a treatment for OA-BML has been studied in the past, the outcomes data are limited. In addition, no publications have compared the outcomes of knee arthroscopy without CaP injection to knee arthroscopy with CaP injection. The primary purpose of this study is to compare the conversion rate to TKA of patients who underwent arthroscopic CaP injection for OA-BML to those who underwent knee arthroscopy for non-OA-BML diagnoses. The secondary purpose of this study is to compare the difference in postoperative pain and functionality of both groups.

Materials and Methods

The inclusion and exclusion parameters of the study are defined in **Table 1**.

A retrospective analysis was performed of patient-reported outcome data, medical records, and radiographs to evaluate patients selected based on a 2-year follow-up, with a date of surgery between January 2015 and June 2020. Patients were evaluated in an orthopaedic clinic. The study was approved through a local Institutional Review Board.

MRI was used to determine the presence, size, and location of an OA-BML in the tibia of patients in the CaP cohort (Figs. 1B and 2B). Patients with pathology requiring an arthroscopic procedure which does not include CaP injection (e.g., meniscal debridement, osteophyte removal) were placed in the knee arthroscopy cohort (**Table 2**). Patients in both cohorts received an OA grade determined by the Kellgren–Lawrence grade in a radiographic review done by a fellowship trained orthopedic surgeon (**Figs. 1A, 2B, and 3**).

Table 2 Procedures performed for patients in the CaP and knee arthroscopy group

Arthroscopy type	SCP (n = 53)	No SCP (n = 30)
Partial medial meniscectomy	40	27
Partial lateral meniscectomy	20	12
Microfracture medial femoral condyle	20	12
Microfracture lateral femoral condyle	3	2
Microfracture tibial condyle	0	2
Microfracture medial tibial plateau	1	0
Microfracture of trochlea	7	3
Patellofemoral abrasion chondroplasty	13	13
Lateral tibial articular surface chondroplasty	2	0
Plica resection	1	1
Lateral tibia abrasion chondroplasty	1	0
Synevectomy	2	1
Implantation of amniotic stem cells	1	1
Femoral abrasion chondroplasty	1	9
PRP injection	3	0
Pseudogout debridement	0	1
DeNovo juvenile cartilage transplant	0	2

Abbreviations: CaP, calcium-phosphate; PRP, platelet-rich plasma; SCP, subchondroplasty.

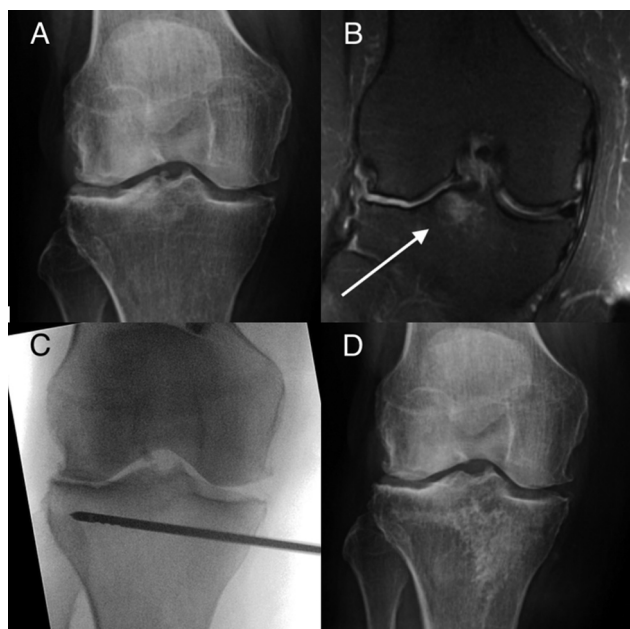


Fig. 1 (A) AP radiograph of CaP survivor preoperatively, KL score of 3. (B) Preoperative coronal PD fat saturation MRI with arrow indicating OA-BML at the lateral tibial plateau. (C) AP intraoperative fluoroscopic imaging of cannula placement through medial to the lateral tibial plateau. (D) Two months postoperative AP radiograph with area of increased density within the medial plateau.

All surgical procedures were performed by a fellowship-trained orthopaedic surgeon. Patients were selected for knee arthroscopy based on moderate-to-severe pain lasting more than 2 months with failure of conservative treatments.

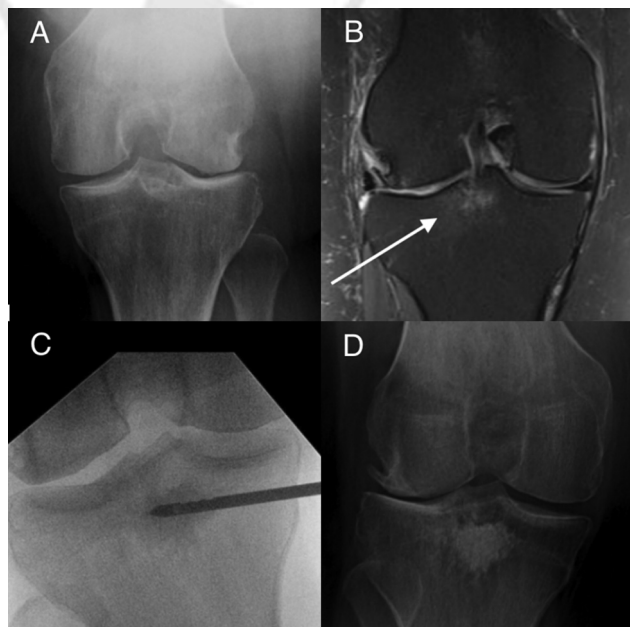


Fig. 2 (A) AP radiograph of CaP conversion preoperatively, KL score of 3. (B) Preoperative coronal PD fat saturation MRI with arrow indicating OA-BML at the proximal tibial plateau. (C) AP intraoperative fluoroscopic imaging of cannula placement through medial to the proximal tibial plateau. (D) Three months postoperative AP radiograph with area of increased density within the medial plateau.

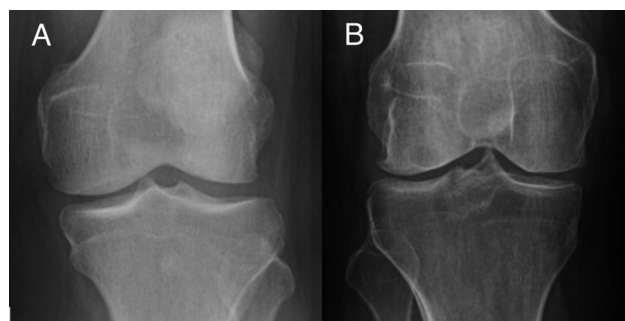


Fig. 3 (A) AP radiograph of a knee arthroscopy conversion, KL score of 1. (B) AP radiograph of a knee arthroscopy survivor, KL score of 2.

Nonoperative treatments include corticosteroid intra-articular injection, physical therapy, and oral nonsteroidal anti-inflammatory drugs. After a physical evaluation and MRI, candidates for CaP injections were educated using an informational handout, visual, schematic, web-based education about the procedure, and discussion of the risks/benefits of the operation. Informed consent was obtained for all patients who underwent surgery.

Of the 133 patients who had CaP between 2015 and 2020, 53 patients were selected for retrospective study based on inclusion/exclusion parameters and a 2-year follow-up. Out of 60 patients who had knee arthroscopy between 2015 and 2020, 30 patients met the criteria for retrospective analysis of knee arthroscopy without a CaP injection based on the same parameters.

CaP injection procedures followed techniques outlined in previous publications.^{17,18} CaP injection was fluoroscopically guided intraoperatively through AP and lateral fluoroscopic views of the knee. Patients who underwent tibial CaP injections were preoperatively evaluated for pathologies which might require arthroscopic surgeries including femoral condyle microfracture, osteophyte removal, or meniscal repair, and procedures were performed as indicated (–Table 2).

A standardized knee arthroscopic clinical protocol was utilized for all surgical procedures. Patients adhered to crutch use for 3 days postoperatively, after which patients were advised to begin weight-bearing and range of motion as tolerated with crutches as an assistive device as needed. Patients returned to the clinic 12 days postoperatively for suture removal and then began physical therapy twice weekly for 6 weeks. At 6 weeks postoperatively, patients were permitted to resume activities as tolerated.

Two years postoperatively, patients were encouraged to complete outcome surveys. Patients who maintain their natural knee were considered survivors; patients who transition to knee arthroplasty were considered conversions. In addition, postoperative outcomes in CaP patients were measured using knee injury and operative outcome scores, joint replacement scores (KOOS, JR). Baseline KOOS, JR scores were measured preoperatively and compared with 2-year postoperative KOOS, JR scores. For those patients who converted to TKA prior to 2-years, the KOOS, JR from the appointment immediately prior to the TKA was used.

Table 3 Comparison of CaP and knee arthroscopy group outcomes and demographics

	CaP group	Knee arthroscopy group	p-Value
Total number of patients (n)	53	30	–
Sex % female	68%	73%	0.8
Avg. age (range)	57.6 (19–80)	62.9 (35–80)	0.064
Avg. BMI (range)	29.6 (16.9–47.4)	30.2 (22.8–40.0)	0.38
K-L Score	1.6	1.33	0.23
% Survivorship (out of 52)	88.70%	80.00%	0.33
Time until conversion in months (range)	13.5 (6–20)	12 (6–20)	0.63

Abbreviations: Avg., average; BMI, body mass index; CaP, calcium-phosphate; K-L, Kellgren–Lawrence; PRP, platelet-rich plasma; SCP, subchondroplasty.

All subjects included are analyzed for survivorship. Patients were only considered for paired analysis if they submitted a baseline KOOS, JR, as well as a 2-year or greater (2+ year) KOOS, JR. Two-tailed paired *t*-test was used within groups, and two-tailed unpaired *t*-test was used between groups. Fisher's exact test was used for categorical differences (sex, survivorship). The null hypothesis was that there was no significant difference between populations in paired groups.

The minimum clinical importance difference (MCID) was evaluated for baseline and 2+ year KOOS, JR. The MCID for KOOS, JR is a 15.1-point difference.¹⁹

Results

Calcium-Phosphate Cohort (Total Follow-Up Population)

► **Table 3** shows the outcomes and demographics for patients in both groups.

In total, 88.7% of patients in the CaP group were survivors and did not transition to a TKA within 2 years. The average time until conversion was 13.5 months for converting patients.

In total, 80% of patients in the knee arthroscopy group were survivors within the 2-year follow-up. The average time until conversion was 12 months for converting patients.

There was no statistical difference in demographics or outcomes between both groups.

Survivor Functional Outcome Analysis

Patient-reported outcomes and demographics for the survivor groups are shown in ► **Table 4**.

In the CaP group, there was a 20.7 point increase ($p < 0.001$) in KOOS, JR from baseline to the 2+ year time point. The KOOS, JR scores for 87.5% of patients (21/24) improved after 2+ years. Two patients had no change in score, and one patient had a reduction in their score.

In the knee arthroscopy group, the average 2+ year KOOS, JR score showed an increase of 10.1 points ($p > 0.05$) compared with baseline values. The KOOS, JR scores for 66.7% of patients (6/9) improved after 2+ years, 1 patient had no change in score, and 2 patients had a reduction in their score.

The 2+ year KOOS, JR ($p < 0.05$) and KL scores ($p < 0.05$) were statistically significant between groups (► **Figs. 4–9**).

Functional Outcome Analysis for Total Knee Arthroplasty Conversion

Patient-reported outcomes and demographics for the conversion groups are shown in ► **Table 5**.

For patients in the CaP group, the average KOOS, JR decreased 2.4 points ($p > 0.05$) from baseline upon the

Table 4 Results showing demographics and outcomes for nonconverting patients in both the CaP group and the knee arthroscopy group

	CaP (survivors)	Knee arthroscopy (survivors)	p-Value
Number of patients (n)	24	9	–
Sex % female	83.30%	88.90%	1
Avg. age (range)	58.0 (35–80)	62.1 (47–80)	0.16
Avg. BMI (range)	30.5 (16.9–47.4)	30.4 (25.4–40.0)	0.96
K-L score	1.7	0.89	0.018
Baseline KOOS, JR (range)	53.3 (39.6–76.3)	48.9 (24.9–66.0)	0.31
2+ year KOOS, JR (range)	74.6 (52.5–100)	59 (24.9–84.6)	0.029
Preoperative to postoperative KOOS, JR change (within group)	20.7	10.1	0.084

Abbreviations: Avg., average; BMI, body mass index; CaP, calcium-phosphate; K-L, Kellgren–Lawrence; KOOSJR, knee injury and operative outcome scores, joint replacement scores.

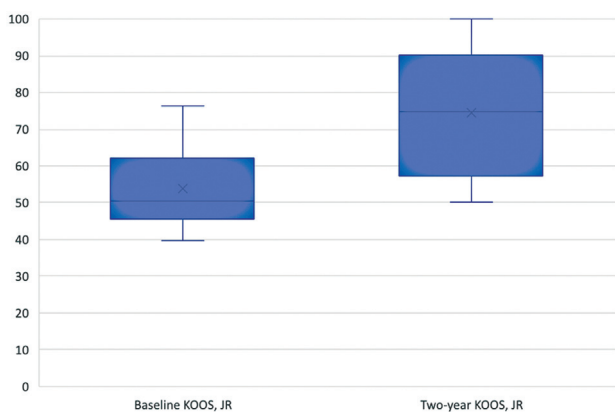


Fig. 4 CaP survivor group box and whisker plot of preoperative and 2-year postoperative KOOS, JR.

decision to convert to a TKA. The time until conversion was an average of 15 months. Of the four patients, 50% (2 out of 4) showed increased KOOS, JR at the time of conversion compared with their baseline values.

In the knee arthroscopy group, the average KOOS, JR decreased 3 points ($p > 0.05$) upon the decision to convert to a TKA. The time until conversion was an average of 10.3 months. Of the three patients, 66.7% (two out of three) showed increased KOOS, JR at the time of conversion compared with their baseline values.

The average age ($p < 0.05$) was statistically significant between groups.

Discussion

OA-BML are a risk factor for an increased rate of OA progression, a cause of pain, and a source of decreased functionality.⁵

Untreated OA-BML are correlated with an increased likelihood of TKA as illustrated by a 3-year follow-up of patients diagnosed with an OA-BML.⁶ Joint preserving treatments are a promising alternative for patients who wish to prolong the time until TKA. Considering the outcomes of this study, treatment of OA-BML via CaP injection offers a beneficial treatment option in return of function, prolonged time with the natural knee, and pain reduction.

The CaP group had 88.7% survivorship for the 2+ year follow-up timeline. In comparison, knee arthroscopy patients showed 80% survivorship for the same timeline. There was no statistical significance between groups for survivorship.

Preoperative KOOS, JR scores were similar at the preoperative baseline for both groups. KL scores were statistically lower in the knee arthroscopy group (meaning less preoperative evidence of OA on plain weight-bearing X-rays). There was a postoperative increase in KOOS, JR scores in both the CaP group and the knee arthroscopy group. The CaP group met the criteria for the KOOS, JR MCID with an average increase of 20.7 points. The knee arthroscopy group did not meet the criteria for the KOOS, JR MCID with an average increase of only 10.1 points. The CaP group's improvement in average 2-year KOOS, JR as compared with the knee arthroscopy group's had statistical significance despite similar baseline average scores, age, and BMI. It is of interest that patients in the CaP survivor group had greater 2-year postoperative KOOS, JR scores despite having significantly higher KL scores preoperatively.

Multifactorial logistical regression showed no correlation between age and/or BMI for either group (Table 5 shows a significant p -value for the age difference between two conversion groups, i.e., older people with pure knee

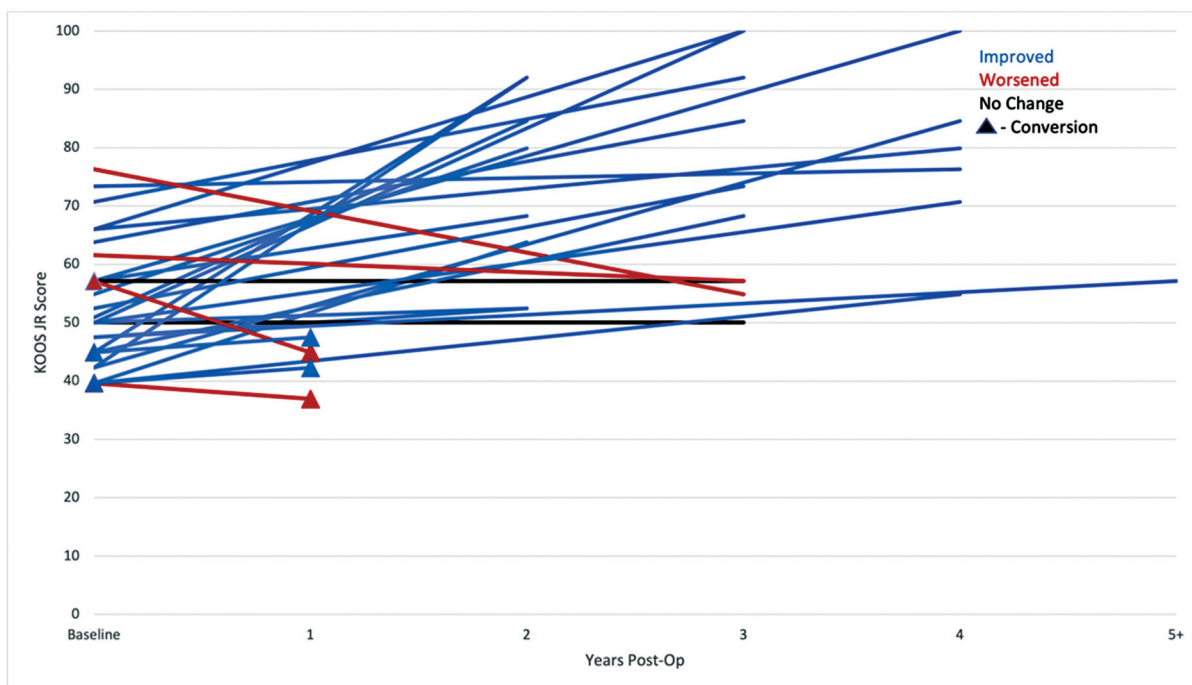


Fig. 5 Change in KOOS, JR for CaP patients, plotted in years from preoperative baseline score to time point of final KOOS, JR obtained.

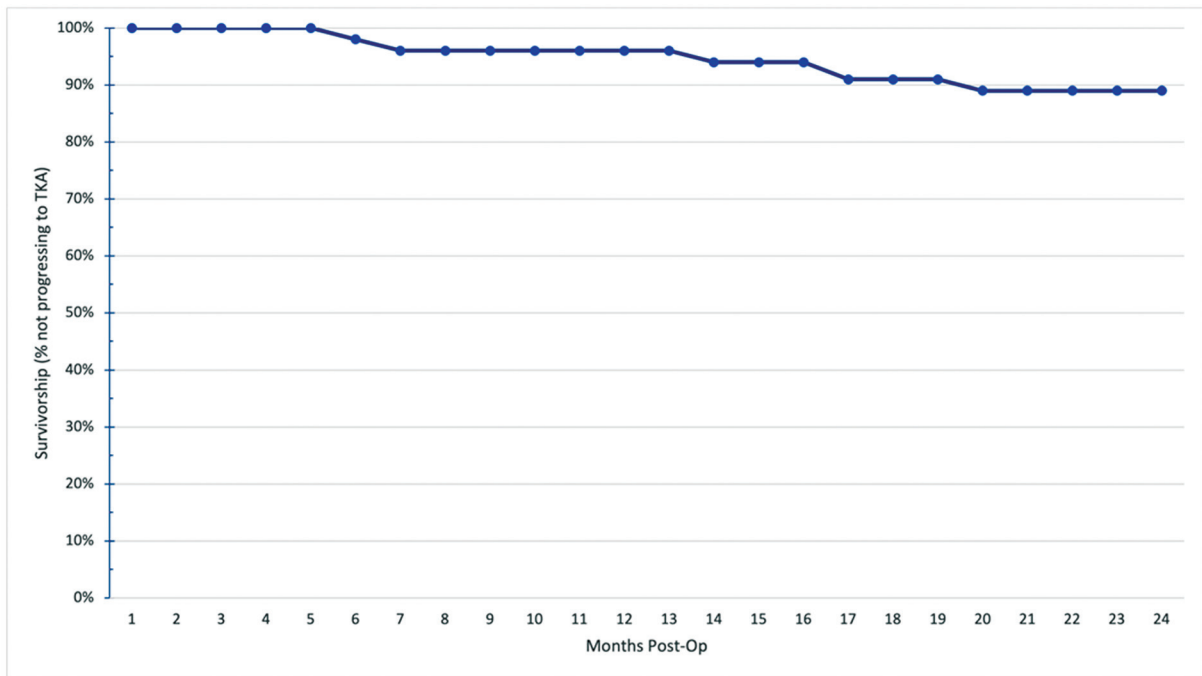


Fig. 6 Survivorship of CaP treated patients over 2 years.

scope had a higher conversion rate despite lower KL score preoperatively).

There are some limitations to this study. Most patients with OA-BML require procedures in addition to CaP injection which presents a confounding variable to our research. The arthroscopy cohort was included to reduce this variable's impact, but the difference in underlying diagnoses makes them an imperfect control group. In addition, knee arthroscopy protocol (including arthroscopy with CaP injection) typically does not require follow-up beyond 6 weeks unless

pain/decreased function persists. This limitation may have contributed to a small sample size and lower postoperative outcomes at 2 years postoperatively. Finally, future studies may include a group of patients with isolated OA-BML treated without surgery, though given the success of the aforementioned surgical intervention, the ethics of such a study may be questionable. When attempted previously, patients refused to be randomized into two cohorts.

Results of this study mirrored the results of past publications. In a retrospective study of 66 patients with a

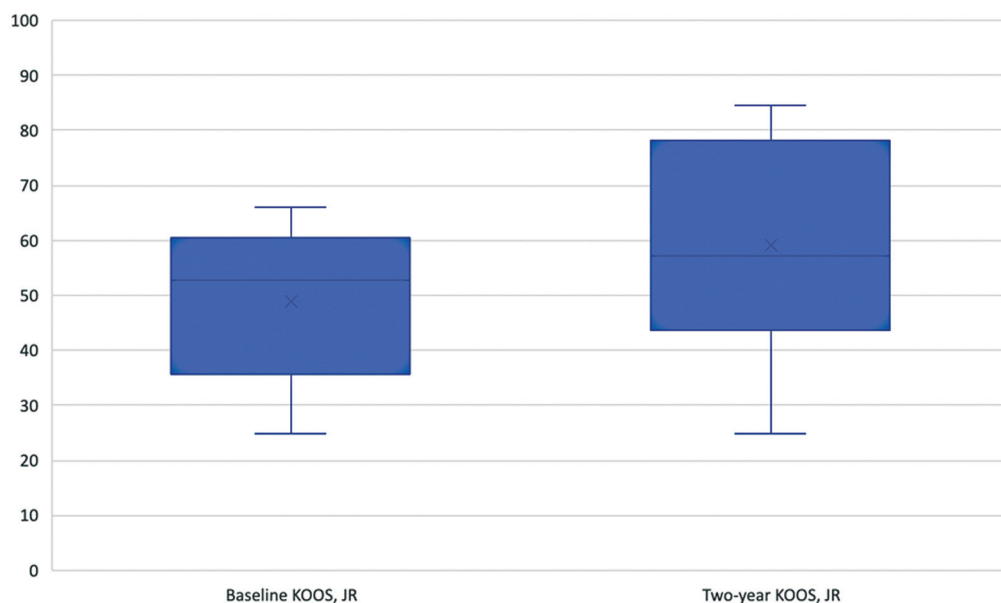


Fig. 7 Knee arthroscopy box and whisker plot of preoperative and 2-year postoperative KOOS, JR.

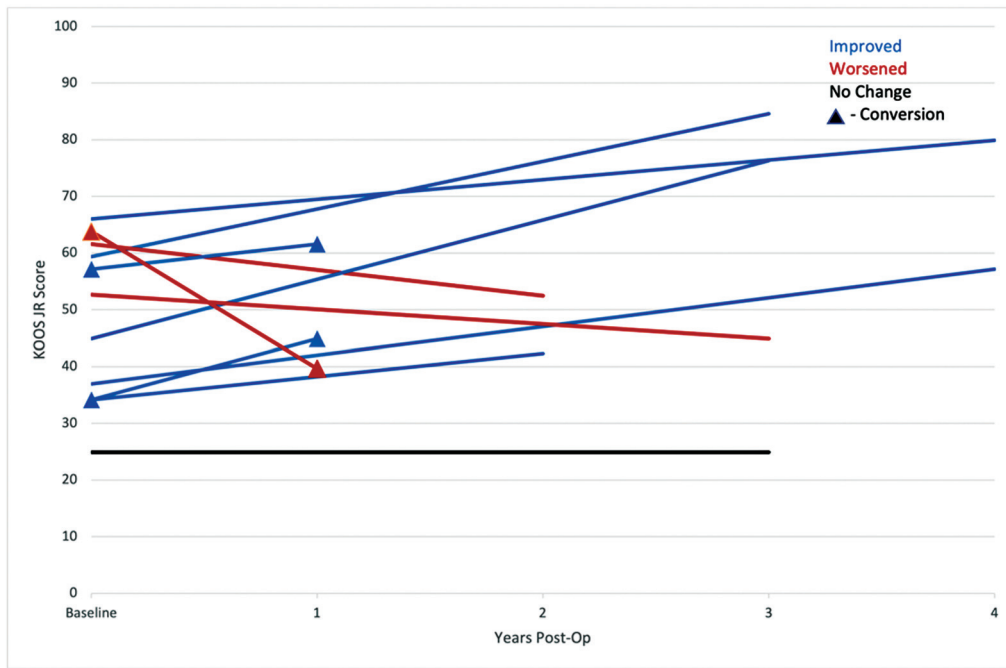


Fig. 8 Change in KOOS, JR for knee arthroscopy patients, plotted in years from preoperative baseline score to time point of final KOOS, JR obtained.

primary diagnosis of OA-BML and a 2-year follow-up, CaP injection for the treatment of OA-BML yielded 70% survivorship, statistically significant improvement in VAS and IKDC and met MCID criteria for IKDC and VAS.²⁰ In another retrospective follow-up of 50 patients with a 14-month follow-up, treatment of OA-BML with CaP injection resulted in 88% of patients reporting a decrease in pain, 72% of patients reporting a greater distance walked, and 92% survivorship.²¹ Lastly, in a retrospective study of 12 patients with an average 36-month follow-up, results indicate that MCID

was met for preoperative to postoperative change in VAS score and 83% survivorship after CaP injection.²²

Previous studies have made efforts to determine 2-year survivorship in patients who underwent CaP injection. This study is the first of its kind to compare the outcomes of knee arthroscopy and CaP injection to knee arthroscopy for non-OA-BML pathologies. This retrospective, single-surgeon study was conducted to determine whether relief in pain and increase in functionality was due to the treatment of issues addressed in knee arthroscopy (meniscectomy and

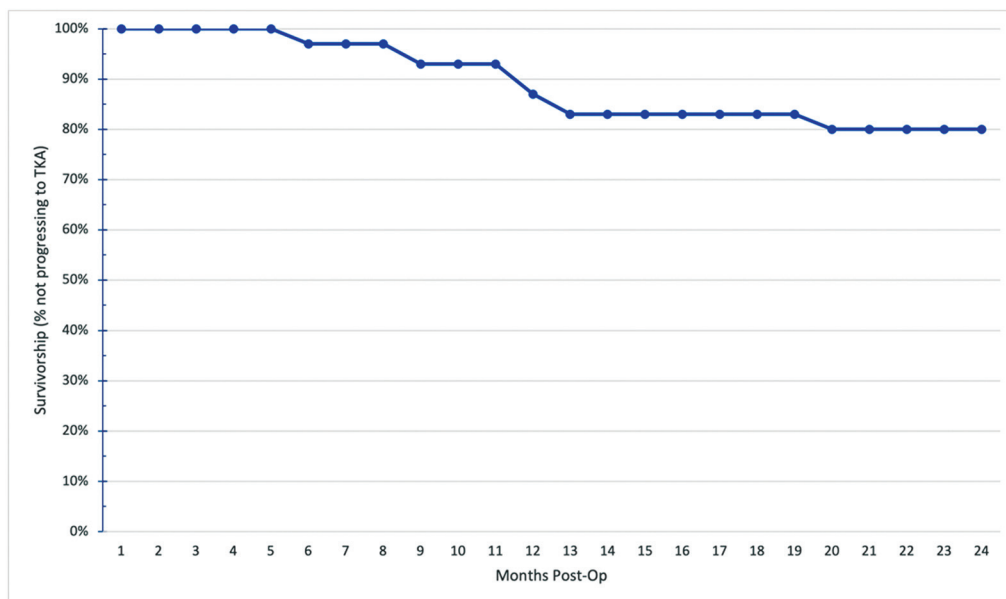


Fig. 9 Survivorship of knee arthroscopy treated patients over 2 years.

Table 5 Results showing demographics and outcomes for converting patients in both CaP cohort and knee arthroscopy cohort

	CaP (conversions)	Knee arthroscopy (conversions)	p-Value
Number of patients (n)	4	3	–
Sex % (#F to M)	75%	67%	1
Avg. age (range)	51.8 (41–60)	70.0 (65–79)	0.03
Avg. BMI (range)	32.5 (20.9–42.4)	31.3 (26.2–36.8)	0.85
K-L score	2.5	1.3	0.27
Baseline KOOS, JR (range)	45.3 (39.6–57.1)	51.7 (34.2–76.3)	0.51
KOOS, JR at conversion (range)	42.9 (37.0–47.5)	48.7 (39.6–61.6)	0.39
Time until conversion (months)	15 (6–20)	10.3 (6–13)	0.3

Abbreviations: Avg., average; BMI, body mass index; CaP, calcium-phosphate; K-L, Kellgren–Lawrence; KOOSJR, knee injury and operative outcome scores, joint replacement scores.

microfracture) or treatment of the OA-BML itself. It is possible that as imaging techniques advance, OA-BMLs will be more easily visualized and identified in patients who present with knee pain but have normal radiographic imaging. The results of this study indicate the treatment of OA-BML with CaP results in a higher survivorship and statistically greater functional outcome compared with knee arthroscopy alone for non-OA-BML diagnoses.

Conclusion

Untreated OA-BML correlate with an increased rate of OA progression. Due to the suboptimal satisfaction rates and high cost or contraindications to TKA, patients with OA-BML may wish to seek joint-preserving treatments. This study analyzed patient outcomes by comparing survivorship and KOOS, JR for patients who received CaP injection for OA-BML during knee arthroscopy versus patients who only received knee arthroscopy for non-OA-BML pathologies. Overall, patients in the CaP cohort had higher 2+ year KOOS, JR scores and a higher percent survivorship. Results suggest that knee arthroscopy and CaP injection of OA-BML may be more beneficial than knee arthroscopy alone for non-OA-BML diagnoses. This retrospective study agrees with previous CaP bone substitute studies but expands on them by helping to distinguish the benefits of CaP from that of knee arthroscopy. While further research is needed, CaP injection has been shown through this study and others to be a viable method of treatment for OA-BML.

Conflict of Interest

None declared.

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