

# Journal Club: Effect of Repeated Corticosteroid Injections for Knee Osteoarthritis

Alex Hu |



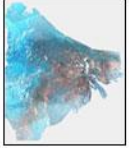
## Introduction

Epidemiology

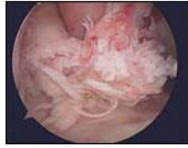
Pathophysiology

- Knee osteoarthritis is a leading cause of disability and medical costs, estimated to affect more than 9 million individuals in the United States
- Traditionally, it is taught that knee corticosteroid injections can be given every 3 months

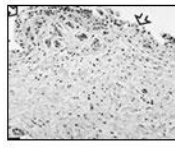
Meniscal damage



Ligament tears

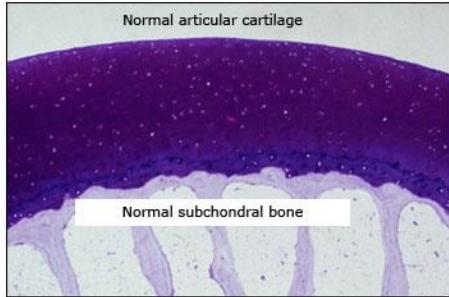


Synovitis



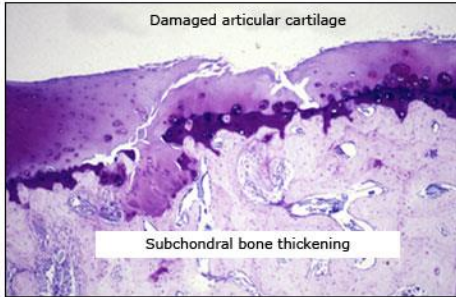
Cytokines, chemokines, growth factors, MMPs

Normal articular cartilage



Normal subchondral bone

Damaged articular cartilage



Subchondral bone thickening

- Studies have found inflammation is common in knee osteoarthritis and is associated with progression of cartilage damage
- Suppression of inflammation using corticosteroid injections may limit the progression of osteoarthritis

JAMA | Original Investigation

# Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis

## A Randomized Clinical Trial

Timothy E. McAlindon, DM, MPH; Michael P. LaValley, PhD; William F. Harvey, MD; Lori Lyn Price, MAS; Jeffrey B. Driban, PhD; Ming Zhang, PhD; Robert J. Ward, MD

- What are the effects of intraarticular injection of 40mg of triamcinolone every 3 months on progression of cartilage loss and knee pain in patients with knee osteoarthritis?



## Study Design

Methods

Intervention

Eligibility

Outcomes

- 2-year, double-blinded, randomized control trial that was conducted at Tufts Medical Center
- Participants were either injected with 40mg (1ml) of triamcinolone or 0.9% (1ml) of NaCl. Neither was mixed with local anesthetic
- Administered every 12 weeks for 2 years

# Eligibility

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45 years or older

Knee osteoarthritis defined  
by American College of  
Rheumatology criteria

Discontinue analgesics for 2  
days prior to assessment



Other disorders affecting the  
knee joint (rheumatologic,  
septic joint, etc.)

Prior use of oral or chronic  
corticosteroids

Recent corticosteroids or  
hyaluronic acid injections

# Outcomes

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Change in knee cartilage  
volume in the index  
compartment

Change in pain using the  
WOMAC subscale



All other outcomes were  
considered exploratory

Functional testing, Cartilage  
Damage, VAS pain score,  
Decrease in Tylenol Use,  
Change in A1c

## Baseline Characteristics

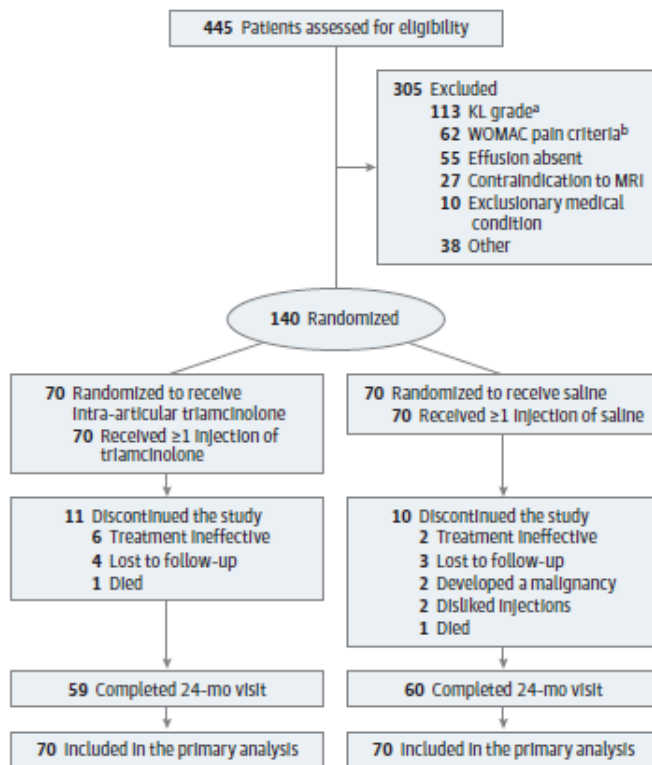
Table 1. Participant Characteristics at Baseline

	Mean (SD)	
	Triamcinolone (n = 70)	Saline (n = 70)
Age, y	59.1 (8.3)	57.2 (7.6)
Women, No. (%)	37 (52.9)	38 (54.3)
White, No. (%)	47 (67.1)	42 (60.0)
BMI	30.8 (5.1)	31.7 (6.6)
Varus or valgus malalignment, No. (%)	53 (75.7)	55 (78.6)
Synovial pouch depth, mm	4.2 (1.9)	4.5 (2.0)
KL score, No. (%)		
2	29 (41.4)	29 (41.4)
3	41 (58.6)	41 (58.6)
Clinical		
VAS pain score <sup>a</sup>	38.4 (22.2)	42.6 (22.1)
WOMAC score <sup>b</sup>		
Pain	8.2 (3.0)	8.4 (3.0)
Function	28.3 (10.8)	30.1 (9.5)
Stiffness	3.7 (1.6)	4.0 (1.4)
20-m Walk, s	19.8 (6.7)	18.2 (3.8)
Chair stand, s	18.3 (8.6)	17.2 (6.5)
SF-36 score <sup>c</sup>		
Physical	36.7 (9.1)	35.4 (9.7)
Mental	52.6 (10.2)	52.2 (10.0)
Hemoglobin A <sub>1c</sub> , mean (SD), %	6.0 (0.8)	6.0 (0.6)
C-reactive protein, mean (SD), mg/L (log)	0.6 (1.2)	0.4 (1.1)



## Patient Flow

Figure 1. Flow of Patients With Knee Osteoarthritis Through the Study



Dropout is defined as not attending the 24-month visit.

<sup>a</sup> Patients who scored neither a Kellgren-Lawrence (KL) grade of 2 nor 3 were excluded.

<sup>b</sup> Patient scored 2 or higher on the weight-bearing question or 8 or less on the weight-bearing pain score according to the Western Ontario and McMaster Universities (WOMAC) index.



## Results

- 85% of patients in the triamcinolone group and 86% in the saline group completed the final visit
- 88% of all possible intraarticular injections were administered

# Structural Outcomes

Table 2. Treatment Effect on Structural Outcomes of Knees With Osteoarthritis<sup>a</sup>

Measurement	Mean (95% CI)		Mean (95% CI)		Between-Group Difference in Change	P Value
	Triamcinolone (n = 70)		Saline (n = 70)			
	Baseline	2-Year Change	Baseline	2-Year Change		
<b>Cartilage thickness, mm</b>						
Index compartment	2.43 (2.27 to 2.58)	-0.21 (-0.29 to -0.14)	2.34 (2.19 to 2.50)	-0.10 (-0.16 to -0.04)	-0.11 (-0.20 to -0.03)	.01
Total mean cartilage thickness	5.58 (5.35 to 5.81)	-0.29 (-0.43 to -0.15)	5.61 (5.38 to 5.84)	-0.13 (-0.23 to -0.03)	-0.16 (-0.31 to -0.01)	.04
<b>Cartilage damage index, mm<sup>3,b</sup></b>						
Index compartment <sup>c</sup>	973.56 (855.78 to 1091.34)	-133.66 (-177.39 to -89.93)	884.60 (767.49 to 1001.70)	-72.41 (-114.16 to -30.66)	-61.25 (-121.78 to -0.72)	.048
Total	2654.79 (2482.92 to 2826.67)	-177.63 (-257.20 to -98.06)	2678.45 (2508.23 to 2848.67)	-82.01 (-145.42 to -18.60)	-95.62 (-194.93 to 3.68)	.06
<b>Area of denudation, mm<sup>2,d</sup></b>						
Index compartment	3.09 (2.37 to 3.81)	0.41 (0.06 to 0.77)	3.35 (2.61 to 4.06)	0.41 (0.17 to 0.66)	0.00 (-0.44 to 0.43)	.99
Total	4.40 (3.67 to 5.13)	0.36 (-0.69 to 1.42)	4.49 (3.77 to 5.20)	0.32 (-0.11 to 0.76)	0.04 (-1.11 to 1.20)	.93
<b>Semiquantitative measures, mm<sup>3</sup></b>						
Bone marrow lesion volume (log) <sup>d,e</sup>	7.79 (6.47 to 9.11)	0.89 (-0.29 to 2.08)	6.80 (5.47 to 8.13)	1.11 (-0.33 to 2.57)	-0.22 (-2.04 to 1.59)	.80
Effusion volume (log) <sup>d,e</sup>	10.70 (10.48 to 10.92)	-0.09 (-0.44 to 0.25)	10.80 (10.57 to 11.02)	-0.32 (-0.56 to -0.09)	0.23 (-0.11 to 0.57)	.17

<sup>a</sup> Estimates and test for treatment by time interaction from repeated-measures, random intercept model, adjusted for KL and sex. Time used is months from baseline examination as a linear trend.

<sup>b</sup> Mean thickness: lower baseline values indicate worse structural damage; high change values, worse damage.

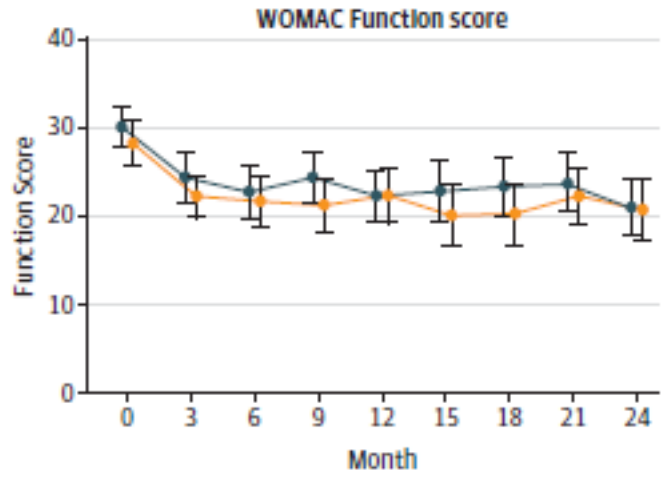
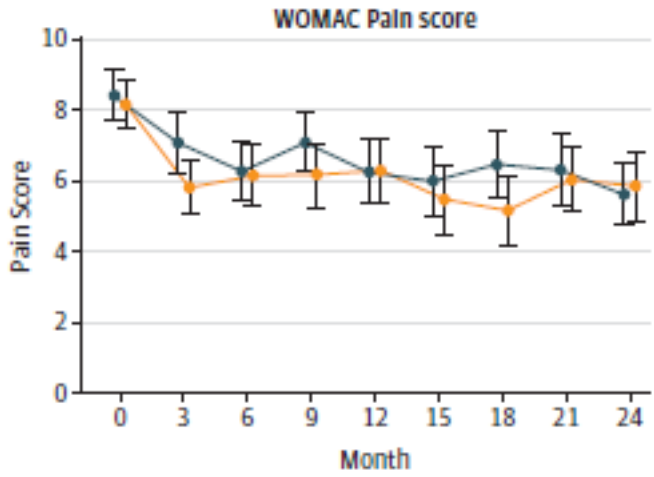
<sup>c</sup> Index compartment indicates compartment with greatest joint space narrowing.

<sup>d</sup> Denudation, BML, effusion: Higher baseline values indicate worse structural damage; high change values indicate worse damage.

<sup>e</sup> Higher natural log values for bone marrow lesions and effusion denote greater volumes affected by these findings. The natural log transformation was used for these measures due to pronounced skewness.

# Clinical Outcomes

Figure 2. Pain and Function Scores of Patients With Knee Osteoarthritis Treated With Triamcinolone vs Saline



No. of participants	
Saline	70 68 63 64 61 62 58 58 59
Triamcinolone	70 68 66 61 60 59 55 56 59

70 68 63 64 61 62 59 58 59
70 68 66 61 60 59 55 56 59

# Secondary Outcomes

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Outcome	Significance
20 minute walk	No
Chair Stand	No
VAS Pain Score	No
WOMAC Function	No
WOMAC Stiffness	No
A1c	Yes

## Key Finding

- In patients with knee osteoarthritis, intraarticular triamcinolone when compared to saline, increased cartilage volume loss and had no effect on knee pain over 2 years.



## Discussion

- Although cartilage loss was not associated with worsening of clinical outcomes, rates of cartilage loss have been associated with higher rates of arthroplasty
- Results raise questions about role of inflammation in progression of osteoarthritis
- Prior studies have suggested a possible benefit of intraarticular saline, but did not control for placebo effect
- Change in A1c was likely due to chance

# Advantages and Limitations

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Generalizable to the overall population

Randomized control study using intention to treat analysis

Objective measures of cartilage loss with MRI



Does not evaluate the short term impact of injections at 4 weeks

Unclear clinical significance of cartilage loss

Limited to those with mild and moderate arthritis





- Corticosteroid injections may still be appropriate for those who require relief of pain in the short term or those with severe osteoarthritis
- For those receiving consistent injections consider maximizing other therapies to decrease frequency of injections
- Consider other types of injections when available, such as hyaluronic acid or PRP

**Thanks!**

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