

Original Research Article

HIGH-RESOLUTION ULTRASOUND FEATURES OF KNEE SYNOVITIS AS PREDICTORS OF CORTICOSTEROID INJECTION FAILURE IN KELLGREN-LAWRENCE GRADE III OSTEOARTHRITIS: A PROSPECTIVE OUTPATIENT COHORT STUDY

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ABSTRACT

Background: Knee osteoarthritis is a major cause of chronic pain and disability, while the degree of synovial inflammation may vary despite similar radiographic severity. High-resolution ultrasound can quantify synovial hypertrophy and Power Doppler vascularity and may help predict response to corticosteroid injection. **Aim & Objectives:** To determine whether baseline ultrasound features of knee synovitis predict corticosteroid injection failure in patients with Kellgren-Lawrence Grade III osteoarthritis.

Materials and Methods: This prospective cohort study included 100 patients aged 45–75 years. Baseline synovial hypertrophy, Power Doppler activity, pain, and WOMAC scores were assessed, followed by clinical follow-up at weeks 2, 6, 12, and 24. Kaplan-Meier and Cox regression analyses were performed.

Results: Treatment failure occurred in 35% of patients. Failure was significantly higher with Grade 2–3 synovial hypertrophy (44.4%), high Power Doppler activity (55.2%), and synovial thickness >5 mm (81.0%). These remained independent predictors of failure.

Conclusion: Baseline ultrasound inflammatory features may effectively predict corticosteroid injection failure.

Keywords: Knee osteoarthritis; Synovitis; Ultrasound; Power Doppler; Corticosteroid injection; Treatment failure.

INTRODUCTION

Knee osteoarthritis (OA) is a common degenerative joint disorder and an important cause of chronic pain, functional limitation, and loss of independence among middle-aged and older adults. Although traditionally considered a disease driven mainly by cartilage loss and mechanical degeneration, current evidence recognizes OA as a whole-joint disorder in which synovial inflammation can contribute substantially to symptoms. In particular, synovial hypertrophy, effusion, and increased synovial vascularity may represent clinically relevant inflammatory components that vary considerably between patients with similar radiographic severity.^[1,2]

Musculoskeletal ultrasound provides a practical method for detecting these inflammatory changes at the point of care. Compared with clinical examination alone, ultrasound can demonstrate synovial hypertrophy and Power Doppler (PD) vascularity, allowing structural and vascular features of synovitis to be assessed directly. Recent studies have demonstrated that greater ultrasound-detected synovial hypertrophy and PD activity are associated with greater pain and symptom severity in knee OA, supporting their potential role as clinically meaningful imaging biomarkers.^[1,2] Importantly, standardized ultrasound assessment has also shown good reliability and reproducibility for evaluating synovial inflammation, strengthening its applicability in prospective clinical studies.^[3]

Intra-articular corticosteroid injection is widely used for short-term symptomatic relief in patients with painful knee OA, particularly when conservative treatment has failed. However, the magnitude and duration of clinical benefit are highly variable. A recent pilot study evaluating ultrasound-defined effusion before corticosteroid injection did not demonstrate a clinically important difference in short-term pain improvement according to the presence or absence of effusion, highlighting the need to examine more specific inflammatory characteristics rather than relying on effusion alone.^[4] Furthermore, studies of patients with advanced OA indicate that synovial tissue pathology and inflammation may have distinct relationships with pain, suggesting that radiographic severity alone does not adequately capture the biological phenotype of symptomatic disease.^[5] These observations are particularly relevant in Kellgren-Lawrence (KL) Grade III OA, where substantial structural degeneration coexists with variable degrees of synovial inflammation. Identifying patients who are unlikely to obtain sustained benefit from corticosteroid injection could improve treatment selection and facilitate earlier consideration of alternative interventions, including total knee arthroplasty. Therefore, assessing baseline synovial hypertrophy thickness and PD vascularity using high-resolution ultrasound may provide a clinically useful method for stratifying patients according to their likelihood of treatment failure. The present prospective cohort study is designed to determine whether these ultrasound features predict time to clinical failure following intra-articular corticosteroid injection over six months and whether baseline inflammatory severity is associated with subsequent changes in WOMAC pain and functional outcomes.^[1,3,4,5]

The present study aims to determine whether baseline high-resolution ultrasound features of knee synovitis, particularly synovial hypertrophy and Power Doppler vascularity, can predict failure of intra-articular corticosteroid injection in patients with KL Grade III knee osteoarthritis. It also seeks to assess their relationship with subsequent changes in pain and functional status, post-injection flare-ups, and clinical progression toward consideration of total knee arthroplasty during six months of follow-up.

MATERIALS AND METHODS

Study design: A prospective outpatient cohort study was conducted to assess whether baseline ultrasound features of knee synovitis could predict failure of intra-articular corticosteroid injection.

Study population: Patients aged 45–75 years with symptomatic, radiographically confirmed KL Grade III primary knee osteoarthritis were enrolled.

Sample size: A total of 100 patients were planned for recruitment.

Study duration: The study was conducted over a 6-month follow-up period for each participant.

Study setting/location: The study was carried out in the outpatient Orthopaedic Department of the study institution.

Inclusion Criteria: Patients aged 45–75 years with KL Grade III knee OA, knee pain for at least 6 months with VAS $\geq 5/10$, and inadequate response to conservative treatment were included.

Exclusion Criteria: Patients with KL Grade I, II, or IV OA, recent intra-articular injections, secondary or inflammatory arthritis, local/systemic infection, or severe comorbidities interfering with treatment or follow-up were excluded.

Statistical Analysis: Data were analyzed using appropriate descriptive and inferential statistical methods. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. The Shapiro–Wilk test was used to assess the normality of continuous variables. Differences between categorical groups were evaluated using the Chi-square test or Fisher’s exact test, as appropriate. Changes in WOMAC pain and functional scores across follow-up visits were assessed using repeated-measures analysis. Time to clinical treatment failure was evaluated using Kaplan–Meier survival analysis, with groups compared using the Log-rank test. Cox proportional hazards regression was performed to identify independent predictors of treatment failure after adjusting for age, BMI, baseline WOMAC score, pain severity, and structural alignment. Hazard ratios with 95% confidence intervals were reported. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

Variable	Category	Frequency (n)	Percentage (%)	p-value
Age group (years)	45–50	16	16	0.021
	51–60	32	32	
	61–70	38	38	
	71–75	14	14	
Sex	Male	42	42	0.114
	Female	58	58	
BMI (kg/m ²)	<25	24	24	0.038
	25–29.9	46	46	
	≥ 30	30	30	

Duration of knee pain	6–12 months	22	22	0.067
	13–24 months	35	35	
	>24 months	43	43	
Baseline VAS pain	5–6	34	34	0.009
	7–8	48	48	
	9–10	18	18	
Baseline WOMAC total	<50	28	28	0.015
	50–70	49	49	
	>70	23	23	
Total	—	100	100	—

Table 2: Baseline Ultrasound Features of Knee Synovitis

Ultrasound Parameter	Category	Frequency (n)	Percentage (%)	p-value
Synovial hypertrophy (OMERACT SH grade)	Grade 0	12	12	<0.001
	Grade 1	34	34	
	Grade 2	38	38	
	Grade 3	16	16	
Inflammatory profile	Low inflammation (Grade 0–1)	46	46	0.003
	High inflammation (Grade 2–3)	54	54	
Power Doppler grade	Grade 0	39	39	<0.001
	Grade 1	32	32	
	Grade 2	21	21	
	Grade 3	8	8	
PD vascularity profile	Low (Grade 0–1)	71	71	0.011
	High (Grade 2–3)	29	29	
Synovial hypertrophy thickness	<3 mm	31	31	0.006
	3–5 mm	48	48	
	>5 mm	21	21	
Total	—	100	100	—

Table 3: Association Between Baseline Ultrasound Inflammation and 6-Month Corticosteroid Injection Failure

Baseline Ultrasound Profile	Treatment Success n (%)	Treatment Failure n (%)	Total	p-value
OMERACT SH Grade 0–1	35 (76.1%)	11 (23.9%)	46	0.002
OMERACT SH Grade 2–3	30 (55.6%)	24 (44.4%)	54	
PD Grade 0–1	52 (73.2%)	19 (26.8%)	71	0.005
PD Grade 2–3	13 (44.8%)	16 (55.2%)	29	
Synovial thickness <3 mm	25 (80.6%)	6 (19.4%)	31	0.001
Synovial thickness 3–5 mm	36 (75.0%)	12 (25.0%)	48	
Synovial thickness >5 mm	4 (19.0%)	17 (81.0%)	21	
Overall	65 (65.0%)	35 (35.0%)	100	—

Table 4: Change in WOMAC Pain and Functional Scores During 6-Month Follow-up

Follow-up	WOMAC Pain Mean ± SD	WOMAC Function Mean ± SD	Mean Change from Baseline	p-value
Baseline	12.8 ± 2.4	43.6 ± 7.8	—	—
Week 2	7.4 ± 2.8	30.2 ± 7.1	–18.8 ± 5.6	<0.001
Week 6	7.9 ± 3.1	31.8 ± 7.6	–16.7 ± 5.9	<0.001
Week 12	9.2 ± 3.5	34.7 ± 8.2	–12.5 ± 6.4	<0.001
Week 24	10.8 ± 3.7	39.1 ± 8.5	–6.5 ± 7.1	0.018

Table 5: Cox Proportional Hazards Analysis of Predictors of Corticosteroid Injection Failure

Predictor	Hazard Ratio (HR)	95% CI	p-value
Age ≥65 years	1.42	0.82–2.46	0.208
BMI ≥30 kg/m²	1.68	1.01–2.80	0.046
Baseline WOMAC total score >70	1.79	1.08–2.97	0.024
Baseline VAS ≥8	1.61	0.97–2.67	0.064
OMERACT SH Grade 2–3	2.31	1.39–3.84	0.001
PD Grade 2–3	2.48	1.46–4.21	<0.001
Synovial thickness >5 mm	2.76	1.57–4.84	<0.001
Malalignment on radiograph	1.51	0.91–2.51	0.109

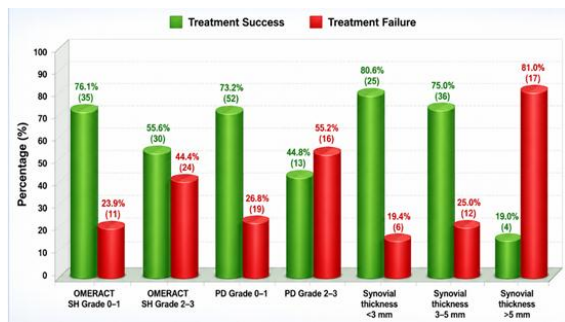


Figure 1: Baseline Ultrasound Profile and Treatment Outcome

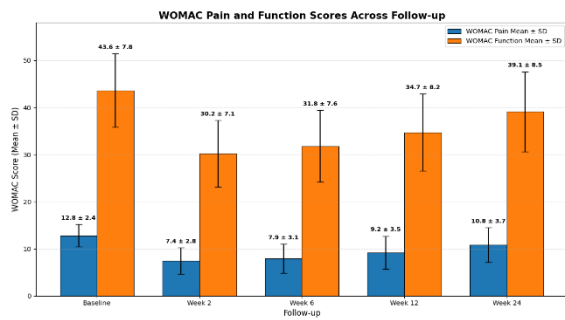


Figure 2: WOMAC Pain and Function Scores Across Follow-up

A total of 100 patients with Kellgren-Lawrence Grade III knee osteoarthritis were included in the study. The largest proportion of participants belonged to the 61–70-year age group (38.0%), followed by 51–60 years (32.0%), while 16.0% were aged 45–50 years and 14.0% were aged 71–75 years; the age distribution was statistically significant ($p=0.021$). Females constituted 58.0% of the study population and males 42.0%, with no significant difference in sex distribution ($p=0.114$). Regarding BMI, 46.0% of patients were overweight (25–29.9 kg/m²), 30.0% were obese (≥ 30 kg/m²), and 24.0% had BMI below 25 kg/m² ($p=0.038$). Knee pain had persisted for more than 24 months in 43.0% of patients, while 35.0% had symptoms for 13–24 months and 22.0% for 6–12 months. Baseline pain severity was moderate to severe, with 48.0% reporting a VAS score of 7–8, 34.0% reporting 5–6, and 18.0% reporting 9–10 ($p=0.009$). Similarly, 49.0% had a baseline WOMAC total score of 50–70, 23.0% had scores above 70, and 28.0% had scores below 50, demonstrating significant variation in baseline functional impairment ($p=0.015$).

Ultrasound examination demonstrated a considerable burden of synovial inflammation among the study participants. According to the OMERACT synovial hypertrophy grading system, 12.0% had Grade 0, 34.0% Grade 1, 38.0% Grade 2, and 16.0% Grade 3 synovial hypertrophy, with a significant distribution across grades ($p<0.001$). When categorized into low and high inflammatory profiles, 46.0% of patients had Grade 0–1 synovial hypertrophy, whereas 54.0% had Grade 2–3 changes ($p=0.003$). Power Doppler assessment showed Grade 0 vascularity in 39.0%, Grade 1 in 32.0%,

Grade 2 in 21.0%, and Grade 3 in 8.0% of patients ($p<0.001$). Overall, 71.0% had low PD activity (Grade 0–1), while 29.0% demonstrated high vascular activity (Grade 2–3), with a significant difference between the groups ($p=0.011$). Synovial hypertrophy thickness was below 3 mm in 31.0%, 3–5 mm in 48.0%, and above 5 mm in 21.0% of patients ($p=0.006$). These findings indicate substantial heterogeneity in the inflammatory phenotype despite all patients having the same radiographic KL Grade III disease.

At six months, 35 patients (35.0%) experienced clinical treatment failure following intra-articular corticosteroid injection, whereas 65 patients (65.0%) maintained treatment benefit. Failure was considerably less frequent among patients with low-grade synovial hypertrophy (Grade 0–1), occurring in 11 of 46 patients (23.9%), compared with 24 of 54 patients (44.4%) with Grade 2–3 synovial hypertrophy ($p=0.002$). A similar pattern was observed with Power Doppler activity. Treatment failure occurred in 19 of 71 patients (26.8%) with low PD activity compared with 16 of 29 patients (55.2%) with high PD activity ($p=0.005$). Synovial thickness demonstrated an even stronger relationship with treatment outcome. Only 6 of 31 patients (19.4%) with thickness below 3 mm experienced treatment failure, compared with 12 of 48 (25.0%) with thickness of 3–5 mm and 17 of 21 (81.0%) with thickness above 5 mm ($p=0.001$). Thus, increasing ultrasound evidence of synovial inflammation was associated with a progressively greater likelihood of corticosteroid injection failure. Following corticosteroid injection, a marked improvement in both pain and functional status was observed during the early follow-up period. The mean WOMAC pain score decreased from 12.8 ± 2.4 at baseline to 7.4 ± 2.8 at week 2, accompanied by an improvement in the mean WOMAC function score from 43.6 ± 7.8 to 30.2 ± 7.1 . The improvement remained significant at week 6, with pain and function scores of 7.9 ± 3.1 and 31.8 ± 7.6 , respectively ($p<0.001$). Thereafter, a gradual deterioration in symptoms was observed. At week 12, the mean pain score increased to 9.2 ± 3.5 and the function score to 34.7 ± 8.2 , although both remained significantly improved compared with baseline ($p<0.001$). By week 24, the corresponding scores were 10.8 ± 3.7 and 39.1 ± 8.5 , representing a smaller but still statistically significant improvement from baseline ($p=0.018$). Overall, the findings suggest that corticosteroid injection provided the greatest symptomatic benefit during the first 2–6 weeks, followed by a gradual reduction in clinical effect over the six-month follow-up period.

Multivariate Cox proportional hazards analysis identified several factors associated with time to clinical treatment failure. BMI ≥ 30 kg/m² was associated with a significantly increased hazard of failure (HR 1.68, 95% CI 1.01–2.80; $p=0.046$), while a baseline WOMAC score >70 was also independently associated with treatment failure (HR

1.79, 95% CI 1.08–2.97; $p=0.024$). In contrast, age ≥ 65 years (HR 1.42, 95% CI 0.82–2.46; $p=0.208$), baseline VAS ≥ 8 (HR 1.61, 95% CI 0.97–2.67; $p=0.064$), and radiographic malalignment (HR 1.51, 95% CI 0.91–2.51; $p=0.109$) were not statistically significant independent predictors. Importantly, the ultrasound parameters showed stronger associations with treatment failure. OMERACT synovial hypertrophy Grade 2–3 was associated with more than a two-fold increased hazard of failure (HR 2.31, 95% CI 1.39–3.84; $p=0.001$), while PD Grade 2–3 was associated with an HR of 2.48 (95% CI 1.46–4.21; $p<0.001$). Synovial thickness >5 mm demonstrated the strongest association, with a hazard ratio of 2.76 (95% CI 1.57–4.84; $p<0.001$). These findings indicate that baseline ultrasound evidence of active synovitis, particularly marked synovial hypertrophy and increased vascularity, may provide clinically useful independent prediction of corticosteroid injection failure in patients with KL Grade III knee osteoarthritis.

DISCUSSION

The present study included predominantly older patients, with 38% aged 61–70 years and 58% females. This demographic pattern is broadly consistent with contemporary knee OA cohorts, in which increasing age and female sex are common characteristics.^[7] The relatively high proportion of overweight and obese participants also supports the recognized contribution of excess body weight to symptom burden and poorer response to conservative treatment.^[8]

More than half of our patients demonstrated moderate-to-severe synovial hypertrophy (OMERACT Grade 2–3), while 29% had high Power Doppler activity. These findings reinforce the concept that radiographically similar KL Grade III knees can have substantially different inflammatory phenotypes. Jiang et al. similarly demonstrated frequent ultrasound-detected synovial abnormalities in middle-aged and older adults with knee OA.^[7] Dima et al. further showed that quantitative ultrasound measurements of synovial hypertrophy correlate well with OMERACT grading, supporting the value of ultrasound-based assessment.^[9] However, de Vries et al. emphasized that ultrasound findings should be interpreted carefully because their agreement with MRI varies according to the severity of synovitis.^[10]

In our cohort, corticosteroid injection failure occurred in 44.4% of patients with Grade 2–3 synovial hypertrophy compared with 23.9% with Grade 0–1 disease ($p=0.002$). Similarly, high PD activity and synovial thickness >5 mm were strongly associated with failure. These findings suggest that greater baseline inflammatory burden may identify patients less likely to achieve sustained benefit. This is clinically relevant because previous evidence has shown that baseline synovitis is not a consistently

reliable predictor of corticosteroid response.^[11,12] The present findings therefore extend previous work by examining graded inflammation and time-to-failure rather than simply the presence or absence of synovitis.

The marked early improvement in WOMAC pain and function, followed by gradual deterioration by week 24, is consistent with contemporary evidence that corticosteroid injections provide their greatest clinically meaningful benefit during the early post-injection period.^[13] Similar improvements after intra-articular therapy have been reported in prospective trials, although longer-term outcomes appear less durable.^[14] Recent meta-analysis also indicates that corticosteroids have comparatively limited sustained benefit beyond the early follow-up period.^[15] Overall, our Cox regression findings, particularly the independent effects of synovial hypertrophy, PD activity, and thickness >5 mm, suggest that high-resolution ultrasound may have practical prognostic value for identifying KL Grade III patients at increased risk of corticosteroid treatment failure.

CONCLUSION

This prospective cohort study demonstrates that high-resolution ultrasound assessment of knee synovitis may provide useful prognostic information in patients with Kellgren-Lawrence Grade III osteoarthritis receiving intra-articular corticosteroid injections. Greater synovial hypertrophy, increased Power Doppler vascularity, and synovial thickness above 5 mm were significantly associated with earlier treatment failure and remained important predictors after adjustment for clinical confounders. Corticosteroid injections produced substantial early improvements in pain and function, although these benefits gradually diminished by six months. Baseline ultrasound assessment may therefore help clinicians identify patients at higher risk of poor response and support more individualized treatment planning, including timely consideration of alternative interventions.

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