Treatment Journey for Nonoperative Symptomatic Knee Osteoarthritis: Data from a New Real-World Registry

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ABSTRACT

Introduction: There is a wide range of nonoperative options to manage symptomatic knee osteoarthritis (OA). This paper aimed to 1) define the treatment sequence for patients undergoing up to four subsequent rounds (i.e., cryoneurolysis) of superficial (Cryo-Superficial) and/or deep genicular nerves (Cryo-Deep/Both),

intra-articular corticosteroid injections (IA-CS), triamcinolone extended-release (IA-TA-ER), hyaluronic acid (IA-HA), or non-steroidal anti-inflammatory drugs (IA-NSAIDs); 2) compare usage of extended-release versus standard corticosteroid injections; and 3) quantify distribution of repeated treatments.

Materials and Methods: We identified 502 patients with symptomatic knee OA and received nonoperative intervention within the Innovations in Genicular Outcomes (IGOR) registry from 2021 to 2024. Treatment journey during follow up was presented aggregating baseline patient demographics, along with sequence of nonoperative treatments per patient, duration, and frequency of repeated use. Repeated use of Round 1 treatment for subsequent treatment rounds was estimated with descriptive statistics.

Results: Fifty-three percent of patients received only the original Round 1 treatment option, either single/repeated dose and did not receive any alternative treatment. Seventy-three percent of patients treated with intra-articular extended-release triamcinolone (IA-TAER) repeated the treatment at least once, whereas 60% of those treated with other treatments did so. No adverse events were reported in patients during repeated treatments.

Conclusion: Patients who received IA-TAER were more likely to repeat the same injection, with 73% repeating at least once and no adverse events were attributed to repeated injections. Approximately half of the patients have switched from the initial treatment offered during follow up, with the use of IA-TAER associated with higher rates of repeated treatment.

SIGNIFICANCE AND INNOVATION

1. **Our study used a newly developed real-world registry IGOR to characterize treatment progression for patients with symptomatic knee OA undergoing up to five rounds of nonoperative treatment.**
2. **Non-surgical interventions included cryoneurolysis, intra-articular injections of NSAIDs, hyaluronic acid injections, corticosteroid, or extended release steroid (triamcinolone) injections.**
3. **We found 73% of patients treated with intra-articular extended-release steroid injections repeated treatment at least once, relative to 60% by other treatments.**
4. **We found approximately half of patients switched from initial treatment offered during follow up, with the use of IA-TAER associated with higher rates of repeated treatment.**

INTRODUCTION

Knee osteoarthritis (OA) is the most prevalent form of OA, affecting 14 million people, or an estimated 19% of all American adults aged 45 years and older.[1,2] Individuals who have symptomatic OA can experience a constellation of symptoms, including pain, stiffness, and an overall decrease in function and ambulation.[3] With the rise of obesity and an aging population, the incidence of symptomatic knee OA is anticipated to increase in the coming years.[2]

Total knee arthroplasty (TKA) remains the gold-standard treatment for managing end-stage knee OA that is unresponsive to non-surgical treatments, with approximately 800,000 cases performed every year in the United States.[4] While there is an abundance of data demonstrating primary TKA is a safe and reliable method to manage end-stage knee OA, there are numerous nonoperative treatment modalities available to postpone or potentially eliminate the need for TKA.[4–6] Nonoperative treatment options can be broadly divided into intra-articular (IA) injections or denervation-based therapies. The IA injections are aimed at decreasing synovial inflammation and pain by downregulating pro-inflammatory mediators and include IA corticosteroids (IA-CS), triamcinolone acetonide extended-release (IA-TAER), hyaluronic acid compounds (IA-HA),[7] non-steroidal anti-inflammatory drugs (IA-NSAIDs), and cellular-based therapies.[5,6,8] Alternatively, denervation-based treatments are aimed at interrupting pain signals from the knee. Cryoneurolysis alleviates pain by applying cold temperatures (between -20 and -100 degrees Celsius) to peripheral nerves, causing Wallerian degeneration and disrupted nerve function.[9–11]

Randomized controlled trials (RCTs) are considered the highest level of evidence for assessing the safety and efficacy of new treatments for knee OA; however, they are often limited by resource constraints, feasibility issues, small sample sizes, and restrictive inclusion and exclusion criteria.[12] In contrast, administrative and claims database studies use retrospective data on knee OA treatments,[13,14] but frequently overlook patient-reported outcome measures (PROMs), disease severity, and patient compliance.[15,16]

Real-world registries offer unique insights beyond those seen in administrative or claims database studies, including factors such as physician or patient preferences and variables such as race, which are often not included in claims databases.[17] These registries also consider the impact of cost and reimbursement on treatment decisions. Unlike randomized controlled trials that adhere to specific treatment protocols, real-world registries collect diverse data reflecting typical clinical practices for treating knee osteoarthritis.[18] They support prospective study designs, standardized data collection, and the inclusion of patient-reported outcomes alongside other clinical and health utilization metrics. In addition, they may offer insights about patient and healthcare provider preferences and approaches for treatment, satisfaction with various treatment alternatives, and the comparative effectiveness of these options. For example, the Innovations in Genicular Outcomes Research (IGOR) registry uses a prospective observational study design to systematically gather data on the clinical efficacy, safety, patient quality of life, and overall healthcare utilization related to various knee OA pain treatments.[18,19]

There is major variability surrounding the nonoperative management of symptomatic knee OA, with the potential for crossover between various treatment options. To characterize this variability, this analysis aimed to (1) define the treatment sequence for patients undergoing up to five rounds of treatment (cryoneurolysis of superficial nerve, deep genicular nerve/both deep and superficial genicular nerves, intra-articular injections of corticosteroids (IA-CS), triamcinolone extended release (IA-TAER), hyaluronic acid (IA-HA), or non-steroidal anti-inflammatory drugs (IA-NSAIDs); 2) compare the repeated usage of extended-release versus standard intra-articular injections of corticosteroids; and (3) quantify the distribution of repeated treatments.

MATERIALS AND METHODS

Registry

The Innovations in Genicular Outcomes Research registry, listed on Clinicaltrials.gov under the identifier NCT05495334, is an ongoing, multicenter, prospective, and longitudinal observational study.[18,19] The IGOR aims to monitor clinical and health-related outcomes over 18 months following different pain treatments for symptomatic knee OA. As a purely observational registry, IGOR allows treating physicians to make all clinical decisions, closely reflecting actual clinical practice. It can catalog a broad range of OA treatments, ranging from oral medications (e.g., NSAIDs, opioids), denervation therapies (radiofrequency ablation, cryoneurolysis), intra-articular injections (corticosteroids, viscosupplementation), and biologic therapies including stem cell products and platelet-rich plasma. As of July 2024, eight academic medical centers and outpatient sites within the United States contribute to IGOR, including: Cedars Sinai Medical Center, Los Angeles, California; Hoag Orthopaedic Institute, Orange, California; Mid State Orthopedics, Alexandria, Louisiana; LSU/Ochsner Medical Center, New Orleans, Louisiana; Sinai Hospital of Baltimore, Baltimore, Maryland; OrthoNebraska, Omaha, Nebraska; RWJ Barnabas Health, Jersey City, New Jersey; and Genesee Orthopedics and Plastic Surgery Associates, P.C., New Hartford, New York, with plans to expand to 15 throughout the United States. Approval was granted by an Institutional Review Board at each location, in accordance with the standards of the U.S. Food and Drug Administration (FDA) Title 21 Code of Federal Regulations Part 56, the International Conference on Harmonization (ICH), and overall Good Clinical Practice (GCP) guidelines.

Individuals eligible for the IGOR registry are those receiving treatment for knee osteoarthritis within 60 days of screening, including options like injections, nerve blocks, or arthroplasty, provided they can provide informed consent. Patients who were excluded were those who were currently enrolled in clinical trials that limited standard care interventions or those enrolled in surgeries not related to the affected knee. After enrollment, patients used HIPAA-compliant, web-based patient-reported outcome (PRO) tools via personal electronic devices to document clinical and health-related data from the beginning and throughout follow-up visits up to 18 months post treatment. Additionally, those undergoing further treatments are monitored in the registry for an additional 18 months from their most recent treatment.

Patient cohorts

We identified patients who have symptomatic knee osteoarthritis who underwent one of the following nonoperative treatments: intra-articular hyaluronic acid injections (IA-HA), intra-articular non-steroidal anti-inflammatory drugs (IA-NSAIDs), intra-articular corticosteroids (IA-CS), intra-articular triamcinolone acetonide extended-release (IA-TAER), cryoneurolysis of the superficial genicular nerve (Cryo-Superficial), or cryoneurolysis of the deep genicular nerve/both nerves (Cryo-Deep/Both). Specific types of IA-HA, IA-NSAIDs, and IA-CS formulations were left to the healthcare provider's discretion. IA-TAER involved the use of ZILRETTA® (32mg) (Pacira BioSciences, Parsippany, New Jersey), an extended-release suspension of triamcinolone acetonide. Cryoneurolysis of superficial or deep genicular nerves was administered by iovera® (Pacira BioSciences, Parsippany, New Jersey).[20] While administration was likewise left to individual providers. Generally, cryoneurolysis is performed via a 20-gauge, 90mm closed-end needle or three 27-gauge, 8mm closed-end needles.[21] This allows exposure of the appropriate nerve to low temperatures, achieved via cryogen (nitrous oxide) flow from the cartridge to the closed-end SmartTip® (Pacira Cryotech, Inc., in Fremont, California).[22,23]

In aggregate, a total of 502 patients who had symptomatic unilateral knee OA were identified between September 21, 2021, and February 1, 2024, with at least 30 days and up to three years of follow up. Of note, the follow-up period was determined on an individual basis by the provider.

Baseline characteristics

Baseline patient demographics were aggregated, including age, sex, race, medical history, body mass index (BMI), surgical history, smoking status, OA

treatment history, prior analgesic medication history, and level of physical activity (Table I). The average time following treatment at study enrollment was 283 days (Table I). There were 81% of patients who received IA injections, including IA-CS (43%, N=215), IA-HA (15%, N=77), IA-NSAIDs (5%, N=46), and IA-TAER (9%, N=72). The remaining 19% of patients were treated with Cryo-Deep/Both treatments (14%, N=70) and Cryo-Superficial (5%, N=23). Overall, patients had an average age of 63 years, with 73% being women. The majority of patients were obese (mean: 35, standard deviation: 11) with at least one chronic comorbidity (61% with cardiac-related disease) and a moderate to severe Kelgren-Lawrence grade (74%). A total of 16% of patients reported use of opioids before study enrollment.

Treatment journey

A patient's treatment journey involved identifying the type of nonoperative treatment for symptomatic knee OA for a patient undergoing up to four subsequent rounds of treatment following Round 1 treatments at study enrollment (i.e., Cryo-Superficial, Cryo-Deep/Both, IA-CS, IA-TAER, IA-HA, NSAIDs). The duration of Round 1 treatment by follow up until Round 2 of treatment (if any) was logged, along with the distribution of repeat use of Round 1 treatment during follow up. The distribution of treatment rounds (up to five) stratified by follow-up period was tabulated.

Data analyses

Descriptive statistics were employed to appropriately characterize baseline patient characteristics among appropriate treatment groups (Round 1). Each patient's treatment path was documented and tabulated, including any subsequent crossovers to other treatment groups (e.g., Cryo-Superficial to IA-TAER). Overall patient follow-up time was tabulated, along with cohort follow-up time since Round 1 (R1) treatment. Patients who underwent repeat Round 1 treatment in Round 2 or other successive treatment rounds were identified and categorized based on the type of Round 1 treatment. The overall distribution of patients who repeated Round 1 treatment options was quantified and tabulated, divided by specific time periods (<6, 6 to 12, 12 to 18, 18 to 24, 24 months or more). The proportion of repeated Round 1 treatment during follow up was estimated and compared between treatment cohorts with Cochran-Mantel-Haenszel tests and adjusted for follow-up time periods. A large language model ChatGPT

Table I
Baseline characteristics in the IGOR cohort

	Cryo-Deep/Both (N=70)	Cryo-Superficial (N=23)	IA-CS (N=215)	IA-HA (N=77)	IA-NSAIDs (N=45)	IA-TAER (N=72)	Total (N=502)	p-value
Follow-up period after treatment (days), mean (SD)	330 (242)	351 (190)	245 (201)	275 (220)	329 (162)	307 (197)	283 (208)	<0.001
Age in years, mean (SD)	66 (9)	59 (12)	61 (10)	64 (11)	58 (9)	69 (9)	63 (10)	<0.001
Women, N (%)	58 (83)	16 (70)	141 (66)	61 (79)	37 (82%	51 (71)	364 (73)	0.023
								0.002
Race, N (%)								
Asian	0	0	6 (3)	2 (3)	0	3 (4)	11 (2)	
Black or African American	12 (18)	10 (43)	83 (39)	13 (17)	23 (51)	13 (18)	154 (31)	
Other/Unknown	2 (3)	0	13 (6)	7 (9)	1 (2)	5 (7)	28 (6)	
White	56 (80)	13 (57)	113 (53)	55 (71)	21 (47)	51 (71)	309 (62)	
Insurance, N (%)								<0.001
Medicare	51 (73)	11 (48)	81 (38)	34 (44)	16 (36)	50 (69)	243 (48)	
Medicaid	0	6 (26)	25 (12)	10 (13)	15 (33)	5 (7)	61 (12)	
Commercial	17 (24)	6 (26)	100 (47)	32 (42)	13 (29)	16 (22)	184 (37)	
Other	2 (3)	0	9 (4)	1 (1)	1 (2)	1 (1)	14 (3)	
BMI, mean (SD)	35 (10)	36 (9)	35 (12)	31 (7)	38 (11)	32 (12)	35 (11)	<0.001
KL grade, N (%)								<0.001
1 (Doubtful)	5 (7)	1 (4)	10 (5)	1 (1)	0	0	17 (3)	
2 (Mild)	11 (16)	1 (4)	50 (23)	20 (26)	6 (13)	12 (17)	100 (20)	
3 (Moderate)	34 (49)	3 (13)	72 (33)	34 (44)	4 (9)	22 (31)	169 (34)	
4 (Severe)	18 (26)	16 (70)	74 (34)	22 (29)	35 (78)	38 (53)	203 (40)	
N comorbidities, N (%)								0.962
0	15 (23)	5 (22)	58 (27)	22 (29)	10 (22)	16 (22)	127 (25)	
1–2	45 (64)	14 (61)	134 (62)	43(54)	30 (67)	49 (68)	315 (63)	
>=3	9 (13)	4 (17)	23 (11)	12 (16)	5 (11)	7 (10)	69 (12)	
Prior opioid use, N (%)								0.047
Yes	18 (28)	7 (30)	28 (13)	11 (14)	5 (11)	10 (14)	79 (16)	
No	52 (72)	16 (70)	187 (87)	66 (86)	40 (89)	62 (86)	423 (84)	

SD=standard deviation, KL=Kelgren-Lawrence

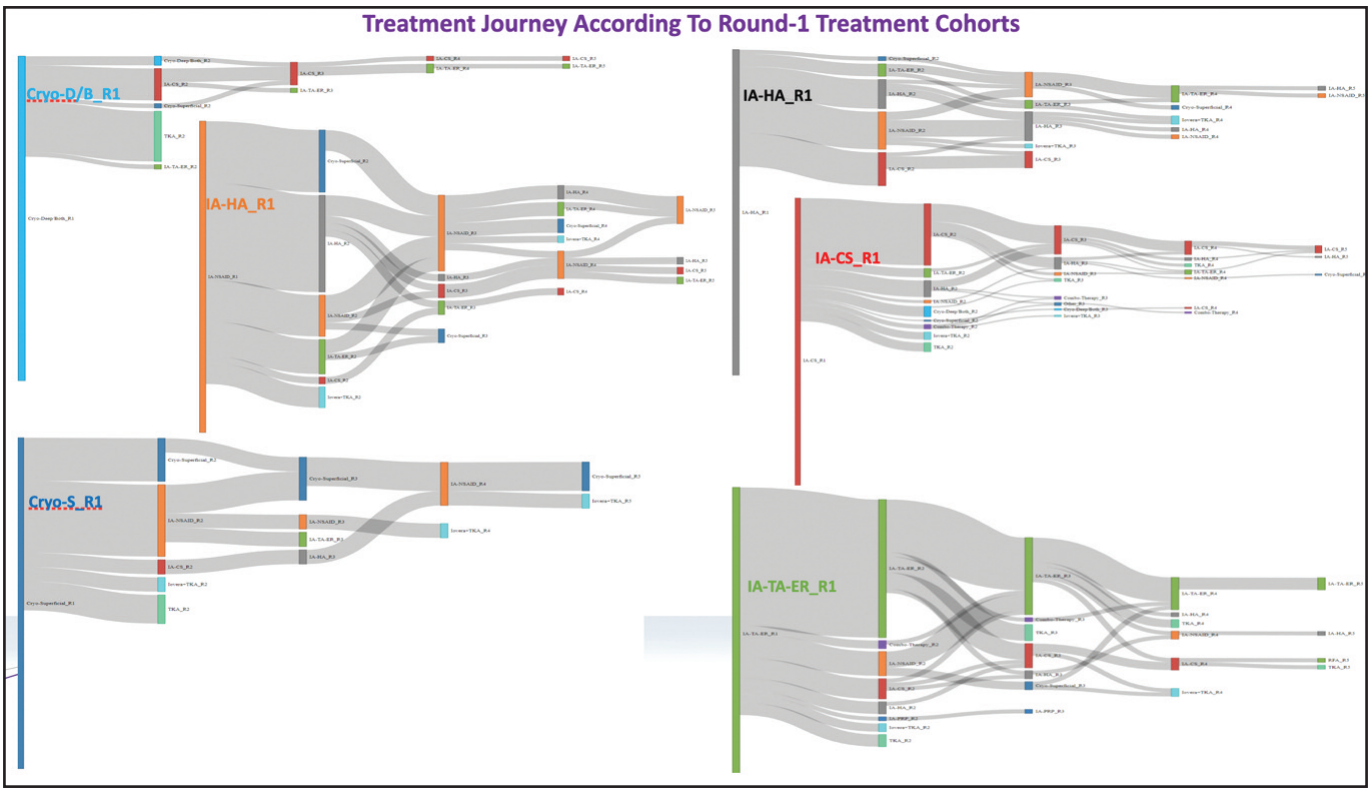

Figure 1. Treatment journey and crossovers according to Round 1 treatment cohorts.

(OpenAI, San Francisco, California) was used to help develop the manuscript and to check for spelling/grammar during the literature review process.

RESULTS

Treatment journey for patients undergoing up to five rounds

The overall treatment journey for patients undergoing up to five rounds of treatments was followed per patient (Fig. 1) and separated by Round 1 treatment cohorts (Cryo-Deep, Cryo-Superficial, IA-HA, IA-NSAID, IA-CS, and IA-TAER). This includes patients who did not undergo further treatment from Round 1 and those who did, including cross-overs to other treatment groups.

IA-TAER was associated with the repeated use of Round 1 treatment during follow up

Among those who underwent subsequent rounds of treatment (N=237), patients who initiated IA-TA-ER treatment (i.e., Round 1) were more likely than other patients to repeat the same injection during follow up, with 73% repeating at least once. In comparison, <60% of patients who received other treatments at Round 1 repeated the same treatment during follow up, with 59% repeats in IA-CS, 50% in IA-HA, 45% in IA-NSAIDs, 41% in Cryo-Superficial, and 13% in Cryo-Deep/Both cohorts. Pairwise comparison with adjustment for follow-up time also showed significantly higher repeated usage with IA-TAER than any other treatments (p-values ≤0.025), except for IA-CS (p-value=0.216).

Distribution of patients in up to five rounds of treatment

Throughout the overall study follow up, 237 patients (47%) have switched to different rounds of treatment. There were 116 (23%), 56 (11%), 38 patients (8%), and 27 (5%) patients who were in Rounds 2, 3, 4, and 5 treatment groups, respectively (Table II). In general, the longer the follow up, the more rounds of treatment were observed.

The overall treatment journey for patients undergoing up to five rounds of treatments was followed per patient (Fig. 1) and separated by Round 1 treatment cohorts (Cryo-Deep/Both, Cryo-Superficial, IA-HA, IA-NSAID, IA-CS, and IA-TAER). This includes patients who did not undergo further treatment from Round 1 and those who did, including cross-overs to other treatment groups.

Although patients who received Cryo-Deep/Both were least likely to repeat the same treatment, they also experienced the longest R1 treatment duration (mean duration >1 year among patients with ≥1 year follow up). Additionally, there were no adverse events reported among patients who repeated Round 1 treatment for subsequent treatment rounds.

Table I
Distribution of patients in five rounds of treatment during follow up

Months	Round 1 (%)	Round 2 (%)	Round 3 (%)	Round 4 (%)	Round 5 (%)
<6	159 60)	43 (37)	10 (18)	4 (11)	0
6 to 12	46 (17)	26 (22)	23 (41)	10 (26)	2 (7)
12 to 18	27 (10)	25 (22)	14 (25)	16 (42)	12 (44)
18 to 24	32 (12)	20 (17)	5 (9)	7 (18)	7 (26)
24 to 30	1 (0.4)	2 (2)	4 (7)	1 (3)	6 (22)
All, N	265	226	56	38	27

DISCUSSION

This analysis aimed to define the treatment sequence for patients presenting with symptomatic knee OA undergoing up to five successive rounds of treatments, quantifying the duration of Round 1 treatment and any rates of subsequent cross-over to other treatment alternatives. Nonoperative interventions included cryoneurolysis of the superficial genicular nerve, cryoneurolysis of the deep genicular nerve, intra-articular nonsteroidal anti-inflammatory drug injections, intra-articular hyaluronic acid injections, intra-articular corticosteroids, or intra-articular extended-release triamcinolone injections. Patients who received IA-TAER were more likely to undergo repeat treatment, with 73% repeating the treatment at least once compared to less than 60% of those who received other treatments. Overall, 53% of patients received only the original Round 1 treatment option and did not receive any alternative treatment through the end of the study period.

A series of guidelines have been established by both the American Academy of Orthopaedic Surgeons (AAOS) and the American Association of Hip and Knee Surgeons (AAHKS) to manage patients who have symptomatic knee OA.[6] Initially, conservative, non-pharmacologic measures are recommended, including weight loss to alleviate joint stress and engaging in low-impact physical activities such as walking, swimming, and cycling to improve strength and flexibility.[24] Both the AAOS and the AAHKS guidelines emphasize the importance of physical therapy aimed at enhancing muscle support around the knee joint. For pain management, the guidelines suggest starting with acetaminophen or NSAIDs, which are effective in reducing pain and inflammation.[6,24] If these medications do not provide sufficient relief, intra-articular corticosteroid injections[7,25] can be considered to reduce inflammation and provide longer-lasting pain relief,[26,27] with evidence "that extended-release IA corticosteroids can be used over immediate release to improve patient outcomes." The AAOS guidelines generally advise against the routine use of hyaluronic acid injections due to inconsistent evidence of their effectiveness.[7,25]

Cryoneurolysis of the superficial and/or deep genicular nerve is a minimally invasive procedure aimed at providing pain relief for patients who have knee OA. It involves the application of extreme cold to targeted nerve fibers, disrupting pain signal transmission. By specifically targeting the genicular nerves, cryoneurolysis can reduce pain in the knee joint with minimal impact on surrounding tissues.[9,28,29] The procedure is performed using a specialized device that precisely controls the temperature and duration of the freezing process. Its benefits have been reported up to three to six months post treatment, including a relatively quick recovery time and the ability to delay or avoid more invasive treatments.[29] A randomized clinical trial (RCT) with a six-month follow up of 141 patients who had symptomatic osteoarthritis receiving cryoneurolysis or not revealed patients had decreased Western Ontario and McMaster Osteoarthritis Index (WOMAC) pain scores even at Day 150.[11] A retrospective study of 80 patients undergoing TKA treated with preoperative cryoneurolysis in opioid-naïve patients revealed use was associated with lower pain severity ($p=0.046$), greater functional improvement, and being 72% less likely to take opioids over six months ($p<0.001$).[30] A single-center study of 267 patients who received cryoneurolysis before primary TKA likewise found that it was associated with 51% lower daily morphine milligram equivalents (MMEs), 22% lower mean pain score ($p<0.0001$), and decreased length of stay ($p<0.0001$).[29] Our study found that the use of cryoneurolysis of the superficial, and/or deep genicular nerves resulted in a longer duration of benefit relative to other treatment groups at all follow-up periods, with a duration lasting up to 12 months.

A marker for the utility and preference of nonoperative treatments is the prevalence of repeated therapies. In our study, 73% of patients who underwent IA-TAER underwent repeat treatment at least once, compared to 60% who received other treatments. Overall, intra-articular injections are a widely used treatment for knee osteoarthritis providing varying duration and intensity of pain relief.[5] Corticosteroid injections are commonly administered due to their potent anti-inflammatory effects, offering major pain reduction that may only last between four and six weeks, necessitating repeat injections.[6,24] Repeat injections, however, may be used cautiously due to concerns about the potential risk of cartilage damage and joint infection with frequent use. Our study had no reported adverse events for repeat injections of IA-TAER during follow up.

Among the various agents used, IA-TAER stands out for its potential for sustained efficacy. In this study, it had slightly prolonged efficacy in the first six months over IA-CS. This may be due to the typical timing by practitioners for these injections and the findings that patients are more likely to request the extended-release formulation, but this needs further study. Triamcinolone acetonide is a corticosteroid that reduces inflammation and pain within the joint.

A phase II open-label study found persistent triamcinolone acetonide from IA-TAER in synovial fluid through 12 weeks, but undetectable levels by week one with standard formulation triamcinolone acetonide. This same study also evaluated plasma levels through 24 hours post injection and detected minimal plasma concentration of triamcinolone acetonide after IA-TAER and significant levels after standard formulation.[31] Also, in a phase II study of well-controlled diabetes mellitus Type II patients, after IA injections of TAER or standard formulation triamcinolone acetonide, change in average daily blood glucose was measured from three days prior through three days post injection. More time was maintained in the target blood glucose range with IA-TAER.[32]

The extended-release formulation is specifically designed to provide prolonged relief by slowly releasing the medication over time, directly targeting the inflamed synovial tissues. A phase III randomized clinical trial of 484 patients revealed those treated with IA-TAER had a significant week 12 improvement in daily pain intensity ($p<0.0001$), extending beyond the primary endpoint to week 16 ($p<0.05$); indicating a 50% improvement from baseline.[33] Another multicenter randomized clinical study of 228 patients found that the use of IA-TAER on patients who have symptomatic knee OA led to improved pain relief through 12 weeks that was superior to immediate-release TA ($p<0.05$ at all time points) as measured through the 11-point numeric rating scale and Western Ontario and McMaster University (WOMAC) subscales.[34] In our study, although 53% of patients did not receive any different treatments from their Round 1 treatment, it is important to appreciate that such treatments are geared towards providing symptomatic relief and may not alter the disease course of knee OA.

The study has several potential limitations, many of which are inherent to a real-world registry-based analysis. The IGOR registry does not follow a standardized treatment protocol, resulting in variable categorization and allocation of patients into treatment groups.[18] This inconsistency can lead to variations in patient care, driven by differing treatment methodologies and indications across various locations and medical specialties.[13,16] There is also a potential for bias to alter potential treatment decisions made by healthcare providers or be influenced by insurance approval or authorization for specific treatments, as well as the capability or desire of certain practitioners to use particular treatment modalities. Another potential bias includes the Hawthorne effect, whereby patients change their behavior because they know they are being observed.[35] Yet another involves follow-up time and individual discussions with providers, which may potentially influence if a patient decides to undergo further nonoperative treatment and, if so, when. Specifically, there is potential bias introduced by measuring treatment duration through time to the next treatment, as this metric may be influenced by clinician-driven scheduling rather than the patient's actual response. Since follow-up visits are likely determined by either clinician's expectation of treatment benefit duration rather than a standardized protocol, concerns for potential harm from more frequent repeat treatments, or non-medical concerns such as insurance coverage intervals, the time to retreatment may reflect scheduling patterns instead of true treatment effectiveness. For instance, a treatment expected to last three months may result in a three-month follow up and retreatment opportunity, whereas a six-month treatment may lead to a longer gap before retreatment. These varying schedules could skew the perceived effectiveness of treatments, as the time to retreatment is influenced by the timing of follow-up visits rather than solely by treatment response. Therefore, the study's assessment of treatment duration may be biased, as it reflects opportunities for retreatment rather than the actual duration of therapeutic benefit.

In addition to these limitations, it is important to understand that the IGOR database includes data from multiple individual sites without oversight from a Contract Research Organization, which opens the possibility for selection bias based on resource allocation and staff availability. Of note, these limitations are present in any observational study; therefore, this may serve as a strength as it represents real-world clinical decision-making by providers unbound by study protocol or criteria. While the use of technology in data collection and aggregation increases user participation, it may potentially skew data towards patients who have higher socioeconomic status and educational levels, who are tech-savvy and able to consistently complete survey forms electronically, and who are unable to capture variations on specific treatments. Nevertheless, the IGOR database is a unique real-world observational study that collates and aggregates data reflecting clinical practice and captures a wide range of potential nonoperative treatment options for knee OA, including clinical efficacy and patient-reported outcomes. The current results are descriptive in nature due to the limited sample size. Nevertheless, such real-world data offers unique insight into the comparative effectiveness and potential patient and healthcare desirability of various treatment alternatives for knee OA. Our results are timely, and more robust analyses will be a more prominent part of future larger studies.

CONCLUSION

This study aimed to characterize the treatment progression for patients who have symptomatic knee osteoarthritis who underwent up to five rounds of nonoperative treatments. Non-surgical interventions considered in the study included cryoneurolysis of the superficial genicular nerves, cryoneurolysis of the deep genicular nerve, cryoneurolysis of both deep and superficial genicular nerves, intra-articular injections of non-steroidal anti-inflammatory drugs (NSAIDs), hyaluronic acid injections, and corticosteroid or extended-release triamcinolone injections. We found that 73% of patients treated with intra-articular extended-release triamcinolone (IA-TAER) repeated the treatment at least once, whereas 60% of those treated with other treatments did so. There were no safety concerns attributed to repeated treatments. By the end of the study period, 53% of patients had not switched from their initial treatment.

AUTHORS' DISCLOSURES

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