

Prospective, Multicenter, Randomized, Crossover Clinical Trial Comparing the Safety and Effectiveness of Cooled Radiofrequency Ablation With Corticosteroid Injection in the Management of Knee Pain From Osteoarthritis

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Background and Objectives: Osteoarthritis (OA) of the knee affects the aging population and has an associated influence on the health care system. Rigorous studies evaluating radiofrequency ablation for OA-related knee pain are lacking. This study compared long-term clinical safety and effectiveness of cooled radiofrequency ablation (CRFA) with intra-articular steroid (IAS) injection in managing OA-related knee pain.

Methods: This is a prospective, multicenter, randomized trial with 151 subjects with chronic (≥ 6 months) knee pain that was unresponsive to conservative modalities. Knee pain (Numeric Rating Scale [NRS]), Oxford Knee Score, overall treatment effect (Global Perceived Effect), analgesic drug use, and adverse events were compared between CRFA and IAS cohorts at 1, 3, and 6 months after intervention.

Results: There were no differences in demographics between study groups. At 6 months, the CRFA group had more favorable outcomes in NRS: pain reduction 50% or greater: 74.1% versus 16.2%, $P < 0.0001$ (25.9% and 83.8% of these study cohorts, respectively, were nonresponders). Mean NRS score reduction was 4.9 ± 2.4 versus 1.3 ± 2.2 , $P < 0.0001$; mean Oxford Knee Score was 35.7 ± 8.8 vs 22.4 ± 8.5 , $P < 0.0001$; mean improved Global Perceived Effect was 91.4% vs 23.9%, $P < 0.0001$; and mean change in nonopioid medication use was CRFA $>$ IAS ($P = 0.02$). There were no procedure-related serious adverse events.

Conclusions: This study demonstrates that CRFA is an effective long-term therapeutic option for managing pain and improving physical function and quality of life for patients with painful knee OA when compared with IAS injection.

Clinical Trial Registration: ClinicalTrials.gov (NCT02343003).

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Osteoarthritis (OA) of the knee is a noninflammatory degenerative disease of the knee joint consisting of 3 large categories: conditions that block normal synchronous movement, conditions that produce abnormal pathways of motion, and conditions that cause stress concentration resulting in changes to articular cartilage.¹ Total knee arthroplasty is an established terminal treatment for late-stage OA of the knee. Yet, not all patients are appropriate because of age, comorbidity, or other factors. Intra-articular corticosteroid injection provides short-term pain relief,² may require repeated treatment, and may cause cartilage damage over an extended exposure time.³ Anatomical studies have identified the superior lateral, superior medial, and inferior medial genicular nerves as possible targets for cooled radiofrequency ablation (CRFA) as a proposed therapeutic strategy to provide analgesia.⁴ Favorable outcomes have been reported using CRFA for sacroiliac joint pain⁵ and discogenic lumbar pain.^{6,7} Similarly, initial reports on knee denervation to provide extended analgesic effects in patients with OA were largely positive, but included a small cohort of patients or short follow-up.^{8–11}

The current randomized controlled study was designed to test the hypothesis that CRFA was noninferior or superior to intra-articular steroid (IAS) injection at 6 months to treat OA-related knee pain. The primary efficacy end point was the proportion of subjects whose knee pain was reduced by 50% or greater from baseline at 6 months after treatment. Secondary end points included change in knee function, subjects' perception of treatment effect, and analgesic drug use 6 months following study interventions.

METHODS

Study approval was obtained by the Western Institutional Review Board (Puyallup, Washington) and Rush University Medical Center Institutional Review Board (Chicago, Illinois). All patients properly consented prior to initiating screening activities. The study was registered in ClinicalTrials.gov (NCT02343003) on January 15, 2015.

Study Subjects

Consecutive subjects presenting to study investigators with signs and symptoms of knee OA were considered for the trial. More specifically, radiographic confirmation of a patient having had OA within 12 months before study screening was required,

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with no other etiology demonstrated as the source of knee pain. Patients reported that they had suffered from OA pain for approximately 10 years (Table 1), and most entered the study with prior diagnoses of OA of the knee as evidenced by prior treatments received, medications taken, and independent radiographic assessment. The diagnosis was reconfirmed by study investigators before entry into the trial using this previous information, as well as patient presentation and physical examination. Subjects with bilateral knee OA were not excluded; only 1 knee was screened and enrolled as the “index knee” for treatment. Inclusion criteria included (1) knee pain for 6 months or more that was unresponsive to conservative treatments (physical therapy, oral analgesics, intra-articular injections with steroids, and/or viscosupplementation); (2) Numeric Rating Scale (NRS) pain score of 6 or greater for the index knee; (3) radiological confirmation of OA grades 2 to 4 noted within 12 months of enrollment; (4) Oxford Knee Score (OKS) of 35 or less; (5) positive diagnostic genicular nerve block (defined as a decrease of $\geq 50\%$ in NRS score); and (6) if the patient was taking an opioid or other morphine-equivalent medication, the dose must have been clinically stable ($<10\%$ change in dosage for ≥ 2 months prior to the screening visit). Exclusion criteria included (1) body mass index of greater than 40 kg/m^2 ; and (2) history of systemic inflammatory conditions such as rheumatoid arthritis or uncontrolled diabetes, cancer, previous total knee arthroplasty, previous knee RF block or ablation, or coagulopathy.

Study Design

Described here is a prospective, randomized, open-label, multicenter (eleven sites) clinical study with a parallel-group

design to compare CRFA utilizing the Coolief System (Halyard Health Inc, Alpharetta, Georgia) with IAS injection. Enrolled subjects underwent CRFA or corticosteroid injection in a 1:1 randomization scheme, and study follow-up visits occurred at 1, 3, and 6 months after study interventions. At the 6-month follow-up visit, patients randomized to the IAS cohort were allowed to “cross over” and receive CRFA treatment.

Subjects were permitted to use analgesics as needed during the study, but the total daily dose had to be the equivalent of or less than 60 mg of morphine at intake. Dosing for membrane stabilizers and antidepressants for pain remained constant throughout the study, unless approved otherwise by the investigator. Additional treatments to the index knee were prohibited during the study.

Diagnostic Blocks

Subjects underwent fluoroscopically guided blockade of the superomedial and inferomedial branches of the saphenous nerve and the superolateral branch of the femoral nerve⁶ using 1 mL of local anesthetic (preferably Marcaine [bupivacaine] 0.5% or similar) at each site (with an ideal volume of 0.60–0.75 mL/site). A “positive” responder experienced a decrease in score on the NRS scale of 50% or greater⁸ at least 15 minutes after the injection. All positive responders were eligible for the study and randomized independently of the block results. Needle placement for diagnostic blockade was identical to Figure 1.⁴

Cooled Radiofrequency Ablation

Subjects randomized to the CRFA study arm underwent genicular ablation with the Coolief System. Cooled radiofrequency

TABLE 1. Study Subject Demographics

| | CRFA (n = 76) | IAS (n = 75) | P |
|---|---------------|---------------|-------|
| Mean (SD) age at consent, y | 63 (12) | 66 (13) | 0.12* |
| Sex distribution, n | | | |
| Female | 50 | 49 | 0.95† |
| Male | 26 | 26 | |
| Race distribution, n | | | |
| American Indian or Alaska Native | 0 | 0 | 0.72† |
| Asian | 0 | 1 | |
| Black or African American | 17 | 10 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| White | 59 | 60 | |
| Other | 0 | 4 | |
| Mean (SD) body mass index, kg/m^2 | 30.6 (5.5) | 30.4 (6.3) | 0.82* |
| Mean (SD) duration of knee pain, mo | 127.9 (138.9) | 102.9 (108.7) | 0.3‡ |
| Medication use for knee pain, n | 61 | 54 | 0.23† |
| Index knee radiographic evaluation results, n | | | |
| Grade 1/no OA | 0 | 0 | 0.62† |
| Grade 2/mild OA | 26 | 27 | |
| Grade 3/moderate OA | 32 | 35 | |
| Grade 4/severe OA | 18 | 13 | |
| Mean (SD) knee pain level (NRS score) prior to diagnostic block | 7.2 (1.2)§ | 6.9 (1.4) | 0.37 |
| Mean (SD) percent decrease in pain (NRS score) postdiagnostic block | 83.2 (17)§ | 80.8 (17.9) | 0.42 |

*Student *t* test for independent means.

† χ^2 Test.

‡Wilcoxon test for location.

§n = 75.

||Wilcoxon rank sum test.

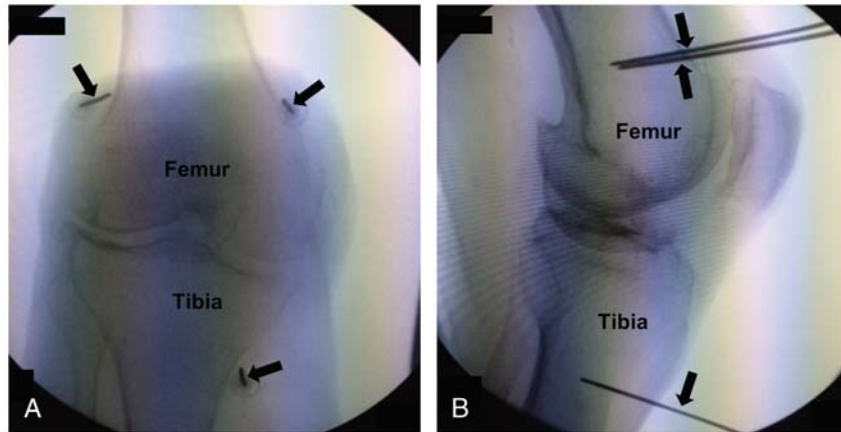


FIGURE 1. A, True anteroposterior image of distal femur with CRF probes (3; at arrows) in place and (B) true lateral image of proximal tibia with probes (3; at arrows) in place.

ablation of the index knee was performed using fluoroscopic visualization of anatomical landmarks for proper cooled radiofrequency (CRF) probe placement (Fig. 1). Subjects were placed supine on a radiolucent table, with the treatment knee slightly flexed on a bolster. After anesthetizing the skin and soft tissue, a 75- or 100-mm, 17-gauge CRF introducer was placed at the appropriate locations. If blood or fluid was observed after removing the stylet, the CRF probe was repositioned and reaspirated. True lateral fluoroscopic visualization, making sure to account for valgus or varus deformities, confirmed accurate probe positioning at 50% depth of the femur and tibia (Fig. 1B). A 4-mm, 18-gauge, internally cooled active tip electrode was placed into the introducer needle, and positioning was reaffirmed in the anteroposterior (Fig. 1A) and lateral (Fig. 1B) fluoroscopic views. Motor stimulation at 2.0 V established no muscular contractions, and sensory stimulation at less than 0.5 V in all 3 locations reproduced concordant knee pain. Motor stimulation was required in all cases solely as an additional safety check to ensure that there were no motor nerves present in the area being lesioned. The optional sensory stimulation provided supplemental confirmation that the target nerve locations identified during blocks were accurate and ensured proximity of the probe to each of these nerves prior to lesioning. Most of the initially treated subjects required local anesthesia, whereas 19 (28%) of the 67 required conscious sedation.

Each neural element was anesthetized with 1% lidocaine prior to CRFA at 60°C for 150 seconds. The heat generated from the RF energy produces thermal energy with average maximum tissue temperatures greater than 80°C.¹² The needles were then removed, and study subjects were allowed to properly recover prior to discharge. All subjects were discharged to home with instructions for self-care.

Intra-Articular Steroid Injection

Study subjects randomized to IAS underwent 1 corticosteroid injection in the index knee. Subjects were placed supine, with the index knee prepared in a sterile fashion. A topical anesthesia was accomplished using ethyl chloride spray or local anesthetic. An appropriately sized needle per the investigator's routine practice was placed into the suprapatellar pouch, and a steroid dose equivalent to 40 mg Depo-Medrol (methylprednisolone acetate) was injected into the joint space. Across the study, Depo-Medrol, Kenalog (triamcinolone topical), and betamethasone were used in 70%, 18%, and 12% of treatments, respectively. Subjects were discharged to home with instructions for self-care.

Study Outcomes

The primary efficacy end point was the proportion of subjects whose knee pain was reduced by 50% or greater from baseline at 6 months after treatment. The 11-point NRS captured the amount of index knee pain at all study time points.^{13,14} Secondary end points included (1) change in knee function detected by OKS,¹⁵ (2) subjects' perception of treatment effect as reflected by the Global Perceived Effect (GPE) score,¹⁶ and (3) opioid and nonopioid (nonsteroidal anti-inflammatory drugs) analgesic use, as measured by subject self-reported average daily dosage used. Assessments of these study end points were made at baseline and at 1, 3, and 6 months following treatments. Outcome data were captured according to subjects' impressions made during the week preceding data collection at each study visit (baseline to 6 months).

All subjects were evaluated for adverse events (AEs) and serious AEs (SAEs) at each visit. Adverse events were any unfavorable and/or unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with the study procedure, regardless of relationship to the device. Serious AEs included events deemed life threatening or resulting in death, requiring inpatient hospitalization or prolonging existing hospitalization, resulting in persistent significant disability or incapacity, or warranting intervention to avoid the aforementioned SAEs.

Data Analysis

A noninferiority evaluation was used to estimate the study sample size. The sample size was based on the estimated success rates of 59%⁸ (success = $\geq 50\%$ NRS score reduction) and 47%¹⁷ (success = $\geq 30\%$ NRS score reduction) in the CRFA and standard groups, respectively, and a noninferiority margin of 15%. Assuming an attrition rate of 20% and a 2-sided significance level of 5%, 144 subjects enrolled into the study would yield 114 subjects at the primary end point.

Continuous data were reported using descriptive statistics, and categorical data were summarized as counts and percentages with 95% confidence intervals (CIs). The statistical tests used for comparisons are described in the referenced tables and figures. Results of study end points that appear in text only are accompanied by descriptions of the statistical tests used for those comparisons. All statistical tests were 2-sided and performed at the 5% level of significance (α) except for the following prespecified end points: (1) change from baseline in OKS at 6 months: adjusted

$\alpha = 0.0083$, and (2) change from baseline in opioid analgesics usage at 6 months: adjusted $\alpha = 0.025$.

Subjects in each study group may not have provided all observations at each follow-up time point. The number of subjects from which data were collected to make each assessment determination is indicated in the presentation of study results.

RESULTS

Two-hundred thirty-three subjects were screened, and 151 were randomized to study cohorts (CRFA, $n = 76$; IAS, $N = 75$) (CONSORT diagram; Fig. 2). Of those subjects, 138 proceeded to treatment (CRFA, $n = 67$; IAS, $n = 71$), and 13 others did not because of withdrawal ($n = 9$), being lost to follow-up ($n = 2$), and protocol deviations ($n = 2$). At 1 and 3 months after treatment, 136 and 133 subjects remained in the study, whereas at 6 months, 126 subjects (CRFA, $n = 58$; IAS, $n = 68$) were evaluated for study outcomes. Overall, a less than 20% dropout rate for the primary end point analysis occurred, with 87% (58/67) of the CRFA group and 96% (68/71) of the IAS group returning at 6 months to contribute data. Results presented in this article are according to those in the full analysis set. A last observation carried forward (LOCF) analysis was also conducted to accommodate missing data points, and selected data are shown to reinforce the LOCF achievement of the primary end point.

Study Population

No differences at baseline existed between groups regarding age, sex, race, mean body mass index, mean duration of knee pain, and analgesic medication utilization. No baseline differences existed

between groups in knee OA severity, mean index knee pain levels (NRS scores) before diagnostic block, and the extent of index knee pain reduction postdiagnostic block (Table 1). The mean reduction in pain by blocks was 83.2% in the CRFA group and 80.8% in the IAS group ($P = 0.42$). Logistic regression analysis did not identify a correlation between response to blocks and response to CRFA treatment. Regarding prior knee procedures, 48.7% and 54.7% of the CRFA and IAS groups, respectively, reported having a previous IAS injection in the index knee ($P = 0.46$), and 22.4% and 29.3% of these study groups reported prior viscosupplementation ($P = 0.33$).

Numeric Rating Scale

Mean baseline pain scores in the CRFA ($n = 76$; 7.3 ± 1.2) and IAS ($n = 75$; 7.2 ± 1) cohorts were not different ($P = 0.55$, Wilcoxon rank sum test) (Fig. 3). Within both study groups at 1, 3, and 6 months, mean pain score was reduced ($P < 0.0001$ at each data point, paired Student t test) relative to baseline.

At each follow-up interval, the mean knee pain score was less in the CRFA group than in the IAS group (Fig. 3) (1 month: CRFA [$n = 67$], 3 ± 2.3 ; IAS [$n = 69$], 3.9 ± 2.2 , $P = 0.025$; 3 months: CRFA [$n = 65$], 2.8 ± 2.2 ; IAS [$n = 68$], 5.2 ± 2 , $P < 0.0001$; 6 months: CRFA [$n = 58$], 2.5 ± 2.3 ; IAS [$n = 68$], 5.9 ± 2.2 , $P < 0.0001$) (Wilcoxon rank sum test). Mean reductions in the average NRS scores from baseline in the CRFA group were greater than those in the IAS group at all follow-ups (1 month: CRFA [$n = 67$], -4.2 ± 2.5 , IAS [$n = 69$], -3.3 ± 2.3 , $P = 0.02$; 3 months: CRFA [$n = 65$], -4.4 ± 2.3 , IAS [$n = 68$], -1.9 ± 2.1 , $P < 0.0001$; 6 months: CRFA [$n = 58$], -4.9 ± 2.4 , IAS [$n = 68$], -1.3 ± 2.2 , $P < 0.0001$) (paired Student t test).

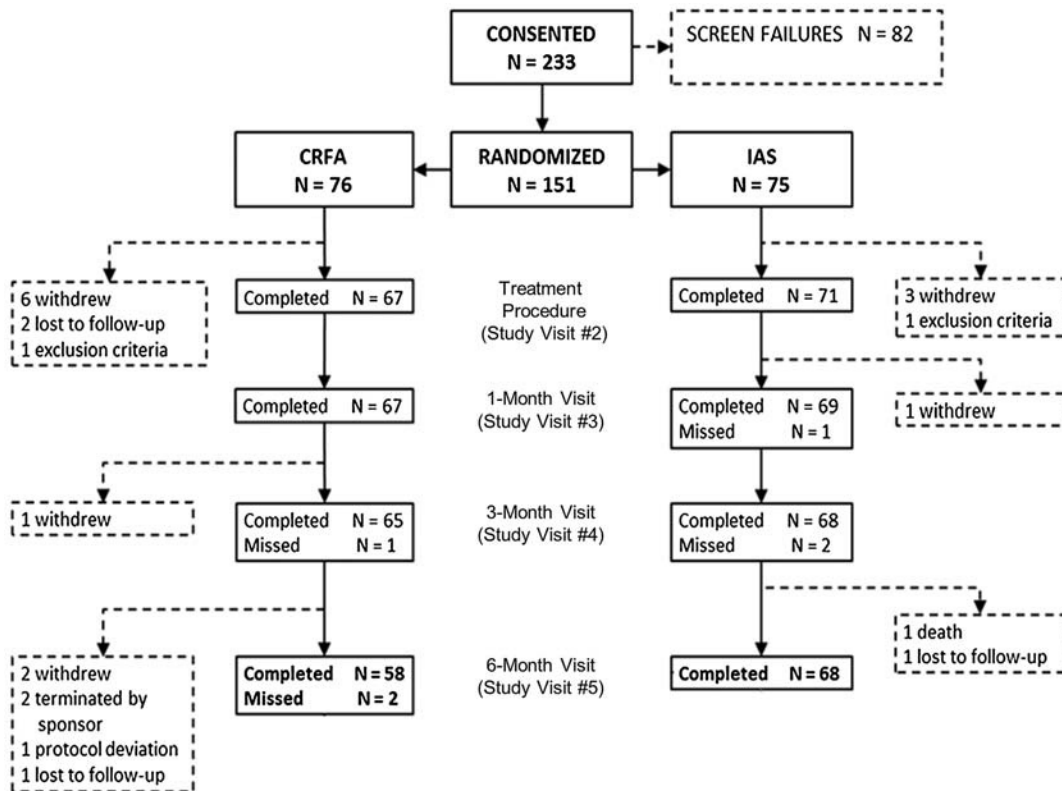


FIGURE 2. Disposition of study volunteers and study timeline, including follow-up time points for data collection. *Reasons for screen failures: 6 patients failed the diagnostic block entry criterion, 15 presented with grade 1 OA, 3 had evidence of a structural abnormality other than OA that affected their gait, function, and/or pain, 8 withdrew consent during the screening period because of a non-AE reason, 7 failed the OKS requirement, 25 were excluded for multiple reasons, and the remaining 18 patients violated other unique inclusion/exclusion criteria.

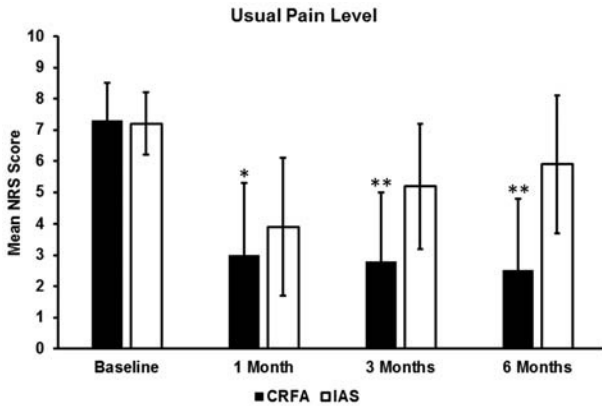


FIGURE 3. Numeric Rating Scale—mean usual knee pain. Mean CRFA and IAS study group NRS scores are indicated by bars, and SDs are expressed as whiskers. * $P < 0.05$ and ** $P < 0.0001$ (Wilcoxon rank sum test) versus IAS means at same time points.

Seventy-four percent (43/58) (95% CI, 62.9–85.4) of the CRFA group and 16% (11/68) (95% CI, 7.4–24.9) of the IAS group met successful outcome criteria ($\geq 50\%$ reduction in NRS score) at 6 months ($P < 0.0001$, χ^2 test), whereas 25.9% (15/58) and 83.8% (57/68) of these study cohorts, respectively, were non-responders. None of the subjects in the CRFA group reported worse pain at 6 months, whereas 15% (10/68) of the IAS cohort experienced exacerbation of usual knee pain during the follow-up period ($P < 0.0024$, χ^2 test). Twenty-two percent (13/58) (95% CI, 11.4–33.5) of the CRFA group and 4% (3/68) (95% CI, 0–9.4) of the IAS group reported “no pain” (100% reduction) 6 months after treatment ($P < 0.0026$, χ^2 test). In the CRFA group, 6.9% (4/58) of the population had no change in usual pain following the 6-month time point compared with 23.5% (16/68) of the IAS group (Fig. 4).

Oxford Knee Score

The mean OKS in each study cohort was equivalent at baseline (Table 2). Mean OKSs improved at all end points within both study groups ($P < 0.0001$ at each data point, paired Student t test) relative to baseline scores. The mean OKSs were greater in the CRFA group than in the IAS group at 1, 3, and 6 months (Table 2). Increasingly higher OKSs in the CRFA group were noted over the course of the 6-month time frame, whereas scores in the IAS group exhibited an opposite trend from 1 to 6 months. Index knee function improved in the CRFA group, whereas it declined in the IAS group from 1 to 6 months after treatment.

Interestingly, while the number of subjects in each study group considered to have “severe (knee) arthritis” symptoms were not different at baseline, beginning at 1 month, more subjects in the CRFA group than in the IAS group had “satisfactory joint function,” and at 3 and 6 months, more subjects in the CRFA had “mild to moderate arthritis” or “satisfactory joint function” than in the IAS group. These latter OKS classifications were not applicable to any study subjects at baseline (Table 3).

Global Perceived Effect

At 1 month, there was no difference ($P = 0.1$, χ^2 test) in the proportions of subjects who reported perceived improvement as a consequence of treatment for chronic knee pain between the CRFA (79% [53/67]; 95% CI, 69.1–89.1) and IAS (67% [46/69]; 95% CI, 55.3–78.1) groups. In contrast, at the 3-month time point, a higher proportion of the CRFA group reported improvement (80% [52/65]; 95% CI, 70.0–90.0) compared with the IAS group (31% [21/68]; 95% CI, 19.6–42.1) ($P < 0.0001$). At 6 months, 91% (53/58) (95% CI, 83.9–98.8) of the CRFA cohort versus 24% (16/67) (95% CI, 13.4–34.4) of the IAS group ($P < 0.0001$) reported improved global perceived effect.

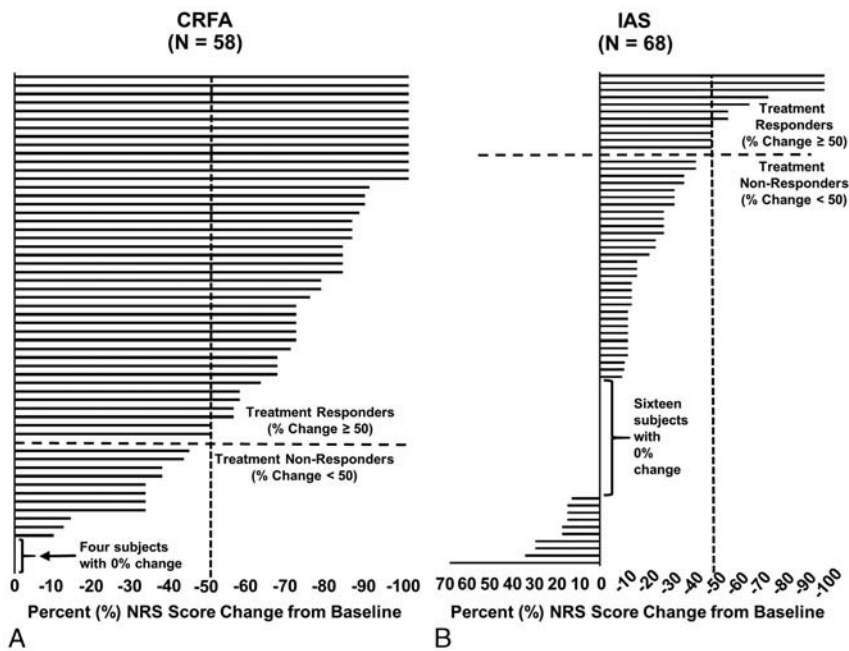


FIGURE 4. Numeric Rating Scale—changes in usual knee pain at 6 months. Changes in CRFA (A) and IAS (B) study group NRS scores from baseline at 6 months are indicated by the horizontal black bars. The treatment “responder” qualification required an NRS score decrease from baseline of 50% or greater.

TABLE 2. Oxford Knee Score

| | Baseline | | 1 mo | | 3 mo | | 6 mo | |
|---|---------------------------|----------|----------------------------|------------|-----------------------------|------------|-----------------------------|------------|
| | CRFA | IAS | CRFA | IAS | CRFA | IAS | CRFA | IAS |
| No. subjects | 76 | 75 | 67 | 69 | 65 | 68 | 58 | 67 |
| Mean (SD) | 16.7 (4) | 16.9 (5) | 33.3 (9.2) | 29.4 (8.5) | 34.6 (8.3) | 24.6 (7.6) | 35.7 (8.8) | 22.4 (8.5) |
| Difference between means: CRFA-IAS (95% CI) | -0.2 (-1.8 to 1.3) | | 4 (0.98 to 7) | | 10 (7.28 to 12.7) | | 13.3 (10.28 to 16.4) | |
| Statistically significant difference | No (<i>P</i> = 0.83*) | | Yes (<i>P</i> = 0.004) | | Yes (<i>P</i> < 0.0001) | | Yes (<i>P</i> < 0.0001) | |

*Wilcoxon rank sum test.

Pain Medication Use

At baseline, 19 subjects in the CRFA group (25% [19/76]; 95% CI, 15.0–35.0) and 26 subjects in the IAS group (35% [26/75]; 95% CI, 23.6–45.7) required opioid analgesic medication. The average total daily dose (morphine equivalence) was not different between study groups (CRFA, 28 ± 28.9 mg; IAS, 27.2 ± 22.1 mg; *P* = 0.75, Wilcoxon rank sum test). Mean opioid drug use at each time point was not different (*P* ≥ 0.17 at each data point, Student paired *t* test) than baseline within each group, and mean changes in doses used were not different between cohorts at each follow-up.

Thirty-three patients in the CRFA group (43% [33/76]; 95% CI, 32.0–54.8) and 34 patients in the IAS group (45% [34/75]; 95% CI, 33.8–56.9) required nonopioid medication at baseline. The daily average dose of nonopioid medications at each time point was not different (*P* ≥ 0.06 at each data point, Student paired *t* test) from baseline within each study group. However, there was a difference in mean nonopioid drug dose use between study groups at baseline (CRFA [*n* = 33], 899.5 ± 625.1 mg; IAS [*n* = 34], 500.3 ± 443.5 mg; *P* = 0.002, Wilcoxon rank sum test). Although changes in such drug use were not different between groups at 1 month (CRFA [*n* = 33], 0 ± 0 mg; IAS [*n* = 33], 94.8 ± 354.5 mg; *P* = 0.08) or 3 months (CRFA [*n* = 31], -16.1 ± 89.8 mg; IAS [*n* = 32], 64.7 ± 201.4 mg; *P* = 0.03), the average changes were different between cohorts at 6 months (CRFA [*n* = 29], -34.5 ± 128.9 mg; IAS [*n* = 32], 135.5 ± 391 mg; *P* = 0.02) (Wilcoxon rank sum test).

Adverse Events

Subjects were screened for all AEs regardless of relatedness to disease state or procedure. There were 61 and 65 AEs reported

among 34 and 30 subjects in the CRFA and IAS cohorts, respectively, with the majority of them in each group having an “unrelated” or “unlikely” relationship to study intervention (CRFA, 77% [47 events/61 total events]; IAS, 97% [63/65]). Three subjects in the CRFA group experienced 4 SAEs, whereas 7 subjects in the IAS group experienced 8 SAEs. Three (75%) of the 4 SAEs in the CRFA cohort involved the respiratory system: (1) exacerbation of asthma, (2) severe acute asthma, and (3) acute respiratory failure), and 1 (25%) involved urogenital function (pyelonephritis). The majority (50% [4/8]) of the 8 SAEs in the IAS group involved gastrointestinal function: (1) nausea and vomiting, (2) worsening of hiatal hernia, (3) gastric volvulus, and (4) abdominal pain secondary to small bowel obstruction, whereas 2 (25%) pertained to the cardiovascular system (heart attacks, 2 subjects), and 2 (25%) were categorized as “other”: (1) opioid overdose and (2) death. None of the SAEs were related to the study treatments.

DISCUSSION

Cooled radiofrequency ablation reduced index knee pain by at least 50% at 6 months in 74.1% of treated subjects compared with 16.2% in the IAS-treated subjects. Consistent with this, the LOCF data revealed that the number of subjects who experienced at least a 50% drop in pain at 6 months was higher in the CRFA group (67.2%; 95% CI, 55.9–78.4) than in the IAS group (15.7%; 95% CI, 7.2–24.2). The CRFA group consistently experienced greater pain relief throughout the study, with a mean NRS reduction of 4.9 compared with 1.3 in the IAS group at 6 months. A greater proportion of CRFA study subjects (60%) reported low-level residual knee pain (NRS score ≤2 at 6 months) compared with the IAS study group (7%).

TABLE 3. Oxford Score Classification Distributions

| | Baseline | | 1 mo | | 3 mo | | 6 mo | |
|---|---------------------------|-----|--------------------------|-----|-----------------------------|-----|-----------------------------|-----|
| | CRFA | IAS | CRFA | IAS | CRFA | IAS | CRFA | IAS |
| Total no. subjects in group | 76 | 75 | 67 | 69 | 65 | 68 | 58 | 67 |
| Score 0–19 (severe), <i>n</i> | 51 | 47 | 6 | 8 | 2 | 17 | 3 | 25 |
| Score 20–29 (moderate to severe), <i>n</i> | 25 | 27 | 16 | 27 | 17 | 36 | 12 | 30 |
| Score 30–39 (mild to moderate), <i>n</i> | 0 | 1 | 26 | 26 | 26 | 13 | 20 | 10 |
| Score 40–48 (satisfactory function), <i>n</i> | 0 | 0 | 19 | 8 | 20 | 2 | 23 | 2 |
| Statistically significant difference | No (<i>P</i> = 0.54*) | | No (<i>P</i> = 0.56) | | Yes (<i>P</i> < 0.0001) | | Yes (<i>P</i> < 0.0001) | |

Parentetical descriptors under score distributions describe status of (knee) arthritis (scores 0–39) or indicate satisfactory knee function (“satisfactory function”).

*χ² Test.

At 6 months, a greater proportion of the CRFA group (40%) reported satisfactory knee function on the OKS compared with the IAS group (3%). Patient self-perceived overall health status (GPE) improved in 91% of the CRFA compared with 24% in the IAS group. A greater proportion of the CRFA cohort (36%) compared with the IAS cohort (3%) experienced both low-level (NRS score ≤ 2) index knee pain and concurrent satisfactory knee joint function (OKS ≥ 40) at 6 months. Despite statistically significant reduction in knee pain and disability, concomitant opioid analgesic use was not different between the 2 groups and remained similar to baseline use. Possible reasons for this include the fact that (1) the study protocol did not include a plan to wean opioids; (2) 43% and 60% of patients in the CRFA and IAS groups who were taking opioids as of the study's baseline assessment were using such medication for medical indications beyond OA-related knee pain; and (3) patients who were using opioids at baseline indicated that they had been taking that medication for a significant period of time (mean, 2.3 [SD, 3.3] and 2.4 [3.4] years, CRFA and IAS, respectively) before the study's inception. Thus, the study's ability to identify a decrease in opioid usage was limited given these findings. Further research in a patient population using opioids strictly for OA-related knee pain would eliminate the confounding nature of opioid use in this current study and may reveal opioid use changes that are commensurate with the respective effects of CRFA and IAS on pain in this study. In contrast, a reduction in nonopioid analgesic medication did occur coupled with improvements in pain and function.

The results of IAS injection seen in this research are consistent with those that previously cited the limited effectiveness of corticosteroid injections to elicit analgesia for those with knee OA.¹⁸ These results suggest that, compared with a single IAS, CRFA provides a clinically meaningful reduction in knee pain associated with improved knee function.

Cooled radiofrequency ablation is a safe, target-specific treatment that can be performed on an outpatient basis with minimal sedation required and in a short period (typically <45 minutes). As ablated peripheral nerves regenerate,¹⁹ knee pain and disability may reemerge. Longer-term (12-month) data are being gathered to assess the durability of the treatment effect beyond 6 months. As has been reported with medial branch neurotomy,²⁰ repeat neuroablative procedures reinstate pain relief. Therefore, if the index knee pain eventually did return, repeating the CRFA procedure would be reasonable and sensible, especially if in the interim the patient enjoys reduction in pain, disability, and the need for less specific oral analgesics.

The limitations of this study include the following: the comparison group (IAS subjects) underwent a singular injection rather than multiple IAS injections, and the 6-month time point at which the primary outcome was assessed is not consistent with the expected duration of effectiveness of a steroid injection.¹⁸ The IAS injections are not truly a "control" intervention, given that corticosteroids are analgesics.¹⁸ This was an open-label trial, and so not all study site observers were blinded to procedures. To help mitigate this bias, questionnaires (ie, NRS, OKS, GPE) were self-administered by study subjects. Medication diaries were not used to record medication usage in this study, which introduced potential for error and/or inability to identify acute changes in medication dosage during the study. The effect of each treatment on opioid use for OA-related knee pain could not be specifically measured, because patients in both study groups used opioids for medical indications other than OA-related knee pain. Although there were no specific mobility instructions for the affected joint or a medication utilization protocol, the study outcomes were not influenced by these standardization absences.

Nonetheless, the findings of this study indicate that CRFA (Coolief) for genicular nerve ablation is superior to a single corticosteroid injection in osteoarthritic subjects for managing knee pain. Cooled radiofrequency ablation is a safe and effective nonopioid option for managing pain and improving physical function and quality of life (ie, based on OKS and GPE results) for patients with OA-related knee pain compared with IAS injection.

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