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Predictors of Outcome in Conservative and Minimally Invasive Surgical Management of Pain Originating From the Sacroiliac Joint

A Pooled Analysis

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Study Design. A pooled patient-level analysis of two multicenter randomized controlled trials and one multicenter single-arm prospective trial.

Objective. The aim of this study was to identify predictors of outcome of conservative and minimally invasive surgical management of pain originating from the sacroiliac joint (SIJ).

Summary of Background Data. Three recently published prospective trials have shown that minimally invasive SIJ fusion (SIJF) using triangular titanium implants produces better outcomes than conservative management for patients with pain originating from the SIJ. Due to limitations in individual trial sample size, analyses of predictors of treatment outcome were not conducted.

Methods. We pooled individual patient data from the three trials and used random effects models with multivariate regression analysis to identify predictors for treatment outcome separately for conservative and minimally invasive surgical treatment. Outcome was measured using visual analogue scale (VAS), Oswestry Disability Index (ODI), and EuroQOL-5D (EQ-5D).

Results. We included 423 patients assigned to either nonsurgical management (NSM, n = 97) or SIJF (n = 326) between 2013 and 2015. The reduction in SIJ pain was 37.9 points larger [95% confidence interval (95% CI) 32.5–43.4, $P < 0.0001$] in the SIJF group than in the NSM group. Similarly, the improvement in ODI was 18.3 points larger (95% CI 14.3–22.4), $P < 0.0001$). In NSM, we found no predictors of outcome. In SIJF, a reduced improvement in outcome was predicted by smoking ($P = 0.030$), opioid use ($P = 0.017$), lower patient age ($P = 0.008$), and lower duration of SIJ pain ($P = 0.028$).

Conclusion. Our results support the view that SIJF leads to better treatment outcome than conservative management of SIJ pain and that a higher margin of improvement can be predicted in nonsmokers, nonopioid users, and patients of increased age and with longer pain duration.

Key words: disability, fusion of the sacroiliac joint, low back pain, opioid use, sacroiliac joint pain.

Level of Evidence: 1

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The sacroiliac joint (SIJ) contributes to 15% to 30%[1–5] of all chronic low back pain (LBP) with an even higher contribution (35–43%[6–8]) after lumbar fusion. Patients with SIJ pain have decreased quality of life[9] with levels similar to other common surgically treated spine conditions.[10] Nonsurgical treatments for SIJ pain, including physical therapy, chiropractic, intraarticular SIJ steroid injections, and radiofrequency neurotomy of sacral nerve root branches, have some literature support,[11–15] but high-quality evidence supporting long-term improvements and describing potential predictors of favorable outcomes is lacking.

Surgical treatments for SIJ dysfunction include open and minimally invasive SIJ fusion (SIJF). Most published evidence on minimally invasive SIJF reports use of triangular titanium implants (TTIs), including retrospective case series,[16–27] a combined multicenter case series,[28] comparative case series against open SIJF,[29–31] systematic reviews,[32–34] and three prospective multicenter clinical trials.[35–37] Even though previously published results from the three prospective trials have shown concordant improvements in pain, disability and quality of life after SIJF compared with nonsurgical management (NSM), the number of patients included in each of those trials was too low to identify potential predictors of clinical outcomes both for conservative management and SIJF. We therefore conducted a patient-level pooled analysis using the data from all three prospective multicenter TTI clinical trials to determine whether patient characteristics predicted clinical outcomes after either surgical or nonsurgical treatment.

MATERIALS AND METHODS

Data Sources

The three pooled trials are prospective clinical trials of SIJF with TTI. Trial characteristics are presented in Table 1. Literature searches using Medline, Embase, and ClinicalTrials.gov [primary search terms: sacroiliac joint AND (arthrodesis OR fusion)] revealed no other ongoing prospective TTI trials.

INSITE, a prospective 2-year multicenter randomized controlled trial (RCT) conducted at 19 centers in the US,[28] included 148 patients with diagnosed SIJ dysfunction unresponsive to at least 6 months of conservative care. Patients were included between January 2013 and May 2014. Diagnosis was based on history, physical examination tests,[38] and a $\geq$50% decrease in SIJ pain after image-guided joint block with local anesthetic.[39–42] Subjects were randomized in a 2:1 fashion to either SIJF as previously described[35] or NSM. NSM included anti-inflammatory and opioid pain medications, physical therapy, intra-articular SIJ steroid injections, and radiofrequency neurotomy, delivered serially as needed to manage pain and disability. Assessments included SIJ pain using a visual analog scale, Oswestry Disability Index (ODI),[43] EuroQoL-5D (EQ-5D),[44] and Short Form-36 (SF-36).[45] In the NSM group, crossover to surgical care was allowed only after the 6-month visit was complete.

iMIA, a prospective multicenter randomized controlled clinical trial (n = 103), was conducted at nine European centers.[36] Patients were included between June 2013 and May 2015. Key differences between iMIA and INSITE include 1) iMIA used 1:1 randomization, 2) nonsurgical treatment in iMIA included only physical therapy per European guidelines,[46] 3) iMIA included Zung Depression Scale[47] but not SF-36, and 4) iMIA included a functional test[48] and self-reported walking distance.

SIFI is a prospective, multicenter, single-arm clinical trial (n = 172) conducted at 26 centers in the US.[37] Patients were included between August 2012 and December 2013. All subjects underwent SIJF. SIFI subjects underwent computed tomography (CT) scan at 1 year; otherwise, study parameters were identical to INSITE.

Surgical Revisions and Wound Infections

Adverse events, defined broadly using an international clinical trial standard, were collected continuously during the trials. Events of interest included wound-related problems and early and late surgical revisions of the target SIJ.

Statistical Analysis

We applied random effects models, performed using the nlme[49] and lme4[50] R[51] packages, that used appropriate covariance structures to take into account individual patient characteristics (fixed effects) as well as repeated measures and site-level factors (random effects). Both univariate and multivariate regression techniques were used, including interaction terms. Outcomes assessed in a single trial only were not evaluated. As both RCTs allowed crossover from NSM to SIJF after month 6, the treatment effect in the NSM cohorts was estimated using only 1, 3, and 6-month data. Models regarding patient age and pain duration used values grouped by quartiles. Opioid use was defined as continuous daily opioid use, including oral medication and/or transdermal application.

RESULTS

Four hundred twenty-three patients in three trials were analyzed, including 326 who underwent SIJF and 97 who underwent NSM. Two-year follow-up data were available from the two completed US studies; 1-year data are currently available from the European RCT.

Baseline Characteristics

In the three pooled trials, mean (SD) age was 50.4 (11.2) years, most (70.4%) subjects were women, and pain duration averaged 5.4 years (SD 6.7, Table 2). Mean baseline SIJ pain (80 points, SD 12.5) and ODI scores (56 points, SD 12.7) were high. Quality of life was diminished (mean EQ-5D Time Trade-off Index (TTO) of 0.43, SD 0.20 and mean SF-36 Physical Component Summary of 31, SD 5.9). Body mass index, baseline pain scores, the proportion using opioids, and the proportion with prior SIJ steroid injections were higher in the two US studies; smoking was less common in US patients. In the two RCTs, baseline characteristics (age, body mass index, pain duration, baseline pain, and ODI and QOL scores) were distributed equally across groups. Current smoking and a history of prior RF ablation were more common in the SIJF group ($P = 0.0100$ and 0.0197, respectively). Operative characteristics were similar across studies: Operating time averaged 48 minutes and three implants were used in most cases, with no significant variation in the mean number of implants used across studies ($P = 0.970$). Mean hospital length of stay was longer in the European RCT (3.6 days) *versus* US studies (0.8 days, $P < 0.0001$).

TABLE 1. Trial Characteristics of Studies Included In Pooled Analysis

Characteristic	Study		
	INSITE	iMIA	SIFI
NCT number	NCT01681004	NCT01741025	NCT01640353
Number of study centers	19	9	26
Number enrolled/treated	148	103	172
Geography	US	EU	US
Enrollment period	2013–2014	2013–2015	2012–2013
Design	RCT	RCT	SAT
Randomization ratio (surgery:nonsurgery)	2:1	1:1	NR
Control group	NSM	CM	—
Data availability, mo	24	12	24
Percent of subjects with available data at long-term follow-up*	85%	92%	87%
Inclusion criteria			
Age 21–70 yrs	✓	✓	✓
SIJ pain for >6 mo	✓	✓	✓
Diagnosis of SIJ dysfunction based on Fortin Finger Test, 3/5 positive exam and block	✓	✓	✓
ODI at least 30%	✓	✓	✓
SIJ pain at least 50 points	✓	✓	✓
Exclusion criteria			
Severe back/hip pain due to something else	✓	✓	✓
Other known sacroiliac pathology	✓	✓	✓
History of recent (<1 yr) major pelvic trauma	✓	✓	✓
Previously diagnosed osteoporosis	✓	✓	✓
Osteomalacia or other metabolic bone disease	✓	✓	✓
Chronic rheumatologic condition	✓	✓	✓
Condition or anatomy making iFuse treatment infeasible	✓	✓	✓
Chondropathy	✓	✓	✓
Known allergy to titanium or titanium alloys	✓	✓	✓
Use of medication known to have detrimental effects on bone	✓	✓	✓
Neuropathy that would interfere with physical therapy	✓	✓	✓
Current local or systemic infection	✓	✓	✓
Currently receiving long-term worker's compensation, disability, involved in injury litigation	✓	✓	✓
Pregnant or planning pregnancy in next 2 years	✓	✓	✓
Prisoner	✓	✓	✓
Known or suspected alcohol or drug abuse	✓	✓	✓
Uncontrolled psychiatric disease	✓	✓	✓
Participating in another study	✓	✓	✓
Fibromyalgia	✓		
Spine surgery in the past 12 months		✓	

CM indicates conservative management; mo, months; NR, not relevant; NSM, nonsurgical management; RCT, randomized controlled trial; SAT, single-arm trial.

**SIJF group only.*

TABLE 2. Baseline Characteristics of Patients Included in Pooled Analysis

Characteristic	Study			Total	*P* Across Studies*	*P* Across Treatment†
	INSITE (n = 148)	iMIA (n = 103)	SIFI (n = 172)			
Age, yrs, mean [range]	51.3 [26–72]	48.1 [23–70]	50.9 [23–72]	50.4 [23–72]	0.2073	0.7480
Women, n (% female)	103 (69.6%)	75 (72.8%)	120 (69.8%)	298 (70.4%)	0.8322	0.2425
Race, n (%)						
White	141 (95.3%)	ND	166 (96.5%)	307 (95.9%)	0.3370	0.8681
Black	5 (3.4%)	ND	2 (1.2%)	7 (2.2%)		
Ethnicity						
Hispanic or Latino, n (%)	8 (5.4%)	ND	7 (4.1%)	15 (4.7%)	0.7654	0.1817
Body mass index, mean [range]	30.4 [17–50]	27.1 [16–44]	29.4 [17–51]	29.2 [16–51]	0.0085	0.7567
Smoking status, n (%)						
Current smoker	29 (19.6%)	39 (37.9%)	44 (25.6%)	112 (26.5%)	0.0287	0.0100
Former smoker	43 (29.1%)	22 (21.4%)	49 (28.5%)	114 (27.0%)		
Never smoker	76 (51.4%)	42 (40.8%)	79 (45.9%)	197 (46.6%)		
Prior lumbar fusion (n, %)	58 (39.2%)	37 (35.9%)	76 (44.2%)	171 (40.4%)	0.3732	0.8458
Years of pain, mean [range]	6.4 [0.48–41]	4.7 [0.45–44]	5.1 [0.43–41]	5.4 [0.43–44]	0.2515	0.1052
Prior treatments						
Physical therapy	107 (72.3%)	59 (57.3%)	111 (64.5%)	277 (65.5%)	0.0456	0.9074
Steroid SI joint injection	127 (85.8%)	75 (72.8%)	162 (94.2%)	364 (86.1%)	<0.0001	0.2677
RF ablation	25 (16.9%)	17 (16.5%)	27 (15.7%)	69 (16.3%)	0.9575	0.0197
Taking opioids (n, %)	99 (66.9%)	53 (51.5%)	131 (76.2%)	283 (66.9%)	<0.0001	0.1654
Questionnaire scores, mean (SD)						
VAS	82.3 (11.3)	75.3 (12.8)	79.8 (12.8)	79.6 (12.5)	0.0056	0.0631
ODI	56.8 (13.2)	56.6 (14.0)	55.2 (11.5)	56.1 (12.7)	0.4531	0.3670
EQ-5D	0.45 (0.18)	0.36 (0.25)	0.43 (0.18)	0.4 (0.2)	0.1837	0.5518
PCS	30.4 (6.2)	ND	31.7 (5.6)	31.1 (5.9)	0.0476	0.5709
MCS	43.1 (11.6)	ND	38.5 (11.3)	40.6 (11.7)	0.0029	0.8356

EQ-5D indicates EuroQOL-5D Time Trade-off Index; MCS, SF-36 Mental Component Summary; ND, not done; ODI, Oswestry Disability Index; PCS, SF-36 Physical Component Summary; SI, sacroiliac; VAS, visual analogue scale.

**Mixed model across studies.*

†Mixed model across treatment groups (SIJF vs. NSM, RCTs only).

Treatment Effect

Taking into account all assessments before month 6, the adjusted reduction in SIJ pain was 37.9 points larger [95% confidence interval (95% CI) 32.5–43.4, $P < 0.0001$] in the SIJF groups *versus* the NSM groups. Similarly, the improvement in ODI was 18.3 points larger (95% CI 14.3–22.4), $P < 0.0001$) and the improvement in EQ-5D TTO index was 0.24 points larger (95% CI 0.17–0.30, $P < 0.0001$). Extensive modeling was used to evaluate for effect modifiers (*i.e.*, interaction terms), but none were found.

Predictors of Treatment Outcome

Table 3 and Figure 1 show associations of clinical characteristics with treatment outcomes for NSM and SIJF. In the NSM cohort (n = 97), none of the examined variables showed a significant association with pain, disability (ODI), or quality of life (EQ-5D) at 6 months of follow-up. For the SIJF group (n = 326), predictors of treatment outcome were assessed over the 24-month follow-up period. For SIJ pain, we found that older age [effect size (ES) 9.1 points; $P = 0.0080$] and longer pain duration (ES 7.7 points; $P = 0.0282$) were associated with larger improvements after SIJF, while current smokers (ES 5.9 points; $P = 0.0299$) and patients using opioids at baseline (ES 6.4 points; $P = 0.0166$) had smaller responses. For disability (ODI), improvements after SIJ were smaller among current smokers (ES 4.4 points; $P = 0.0292$) and those using opioids at baseline (ES 6.1 points; $P = 0.0029$). For EQ-5D, only longest pain duration was predictive of statistically significantly greater improvements after SIJF (ES 0.105 points; $P = 0.0035$).

TABLE 3. Associations Between Baseline Patient Characteristics and Treatment Outcome

	SIJ Fusion			Nonsurgical Management		
	VAS SIJ	ODI	EQ-TTO	VAS SIJ	ODI	EQ-TTO
Age quartile						
1 (<24 yrs)	Ref	Ref	Ref	Ref	Ref	Ref
2 (42–50)	−2.3 (0.5135)	1.92 (0.4643)	−0.0294 (0.4219)	5.5 (0.2976)	5.3 (0.1374)	−0.001 (0.9905)
3 (50–59)	−4.7 (0.1750)	0.17 (0.9482)	−0.0231 (0.5210)	5.8 (0.3026)	−0.6 (0.8725)	−0.041 (0.6536)
4 (>59)	**−9.1 (0.0080)**	−1.39 (0.5921)	0.0013 (0.9707)	2.4 (0.6745)	1.4 (0.6940)	0.026 (0.7664)
Pain duration quartile						
1 (<1.5 yrs)	Ref	Ref	Ref	Ref	Ref	Ref
2 (1.5–3)	−4.9 (0.1677)	0.88 (0.7417)	0.057 (0.1147)	0.74 (0.8831)	1.2 (0.7237)	−0.103 (0.2037)
3 (3–6)	**−7.7 (0.0282)**	−0.19 (0.9431)	0.067 (0.0644)	3.42 (0.5048)	−1.5 (0.6693)	−0.082 (0.3234)
4 (>6)	−5.2 (0.1384)	−0.26 (0.9235)	**0.105 (0.0035)**	1.50 (0.7872)	−3.9 (0.2969)	−0.101 (0.2619)
Current smoker	**5.9 (0.0299)**	**4.4 (0.0292)**	0.0027 (0.9232)	−4.9 (0.3028)	−1.2 (0.7189)	0.112 (0.1423)
Male gender	−1.3 (0.6324)	−2.4 (0.2453)	−0.029 (0.3111)	3.1 (0.4344)	−0.52 (0.8493)	−0.030 (0.6418)
Bilateral SIJF	2.1 (0.5172)	1.5 (0.5484)	0.027 (0.4155)	—	—	—
History of lumbar fusion	3.0 (0.2236)	1.6 (0.3868)	−0.027 (0.2841)	1.9 (0.6403)	0.17 (0.9501)	0.044 (0.4959)
Opioids at baseline	**6.4 (0.0166)**	**6.1 (0.0029)**	−0.025 (0.3656)	5.1 (0.1922)	2.2 (0.3970)	−0.042 (0.5001)

Each entry shows the regression coefficient for the subgroup level for changes in SIJ pain, ODI, or EQ-5D TTO index for the SIJF group and NSM group separately. Negative values indicate a decrease. Associated P values are given in parentheses. Significant values (P < 0.05) are bolded.

EQ-TTO indicates EQ-5D Time Trade-off Index; ODI, Oswestry Disability Index; Ref, reference level; VAS SIJ, visual analog scale sacroiliac joint pain.

Surgical Revisions and Wound Infections

Of the 326 patients undergoing SIJF, 1.2% (n = 4) underwent early surgical revision (<1 month). In each of those patients, one of the implants had been inadvertently placed into a sacral neuroforamen, causing postoperative neuropathic symptoms and requiring surgical repositioning of the implant. Late revision surgery (>1 month), performed in 2.8% (n = 9), was typically done to address pain, sometimes associated with poor implant position, with placement of additional implants in most cases. Signs of wound infection occurred in eight subjects overall, including deep wound infection requiring surgical washout (n = 1), drainage from wound treated with antibiotics (n = 3), redness treated with antibiotics (n = 3), and slow healing treated with antibiotics (n = 1). No subject had bony infection or implant removal for infection.

DISCUSSION

Combining data from three separate prospective studies allowed us to assess in more detail which patient groups may have a better chance of benefitting from conservative or minimally invasive surgical treatment of chronic SIJ pain. Our principal findings are that, within the patient cohort undergoing SIJF, two factors (current smoking and opioid use at baseline) predicted lower and two factors (higher patient age and longer duration of SIJ pain) predicted higher degrees of improvement in SIJ pain and pain-related disability. Older age also predicted higher improvements in quality of life (EQ-5D TTO). Even though one may argue that each of these differences may be of relatively modest clinical significance, it is important to note that they all reached statistical significance. Moreover, subgroups with smaller improvements after SIJF, such as smokers or opioid users, still displayed larger and clinically important improvements compared with patients in the NSM cohort. Another important difference between SIJF and NSM was that within NSM, we found no predictors of treatment outcome at all.

In the SIJF cohort, smokers showed reduced pain response (by 5.9 VAS points) and higher disability levels (by 4.4 ODI points) than nonsmokers. These results are consistent with previously published data describing a significant negative association between smoking and spine surgery outcomes.[52]

Patients using opioids at baseline also benefitted less from SIJF (by 6.4 VAS points and by 6.1 ODI points) when compared with opioid-naive patients. These findings add to the somewhat controversial discussion regarding opioids as part of LBP treatment overall, as current evidence suggests an absence of long-term superiority of opioids over placebo in the treatment of LBP, which has led some authors to call for avoiding any opioid use in LBP treatment.[53,54] Opioid use may even increase the risk of recurrence of already existing depression as well as the risk of developing new onset depression.[55]

In the SIJF cohort, patients younger than 45 years displayed a reduced pain response (by 9.1 VAS points) compared with patients in the oldest age quartile. Whether young age reflects a true biologic effect or is a marker for more severe disability is not known, but our results suggest that SIJF should be discussed with greater caution in younger patients. However, our findings are in line with previously published reports on patients undergoing lumbar fusion surgery, which found that older patients were not at a higher risk of poor treatment outcomes.[56]

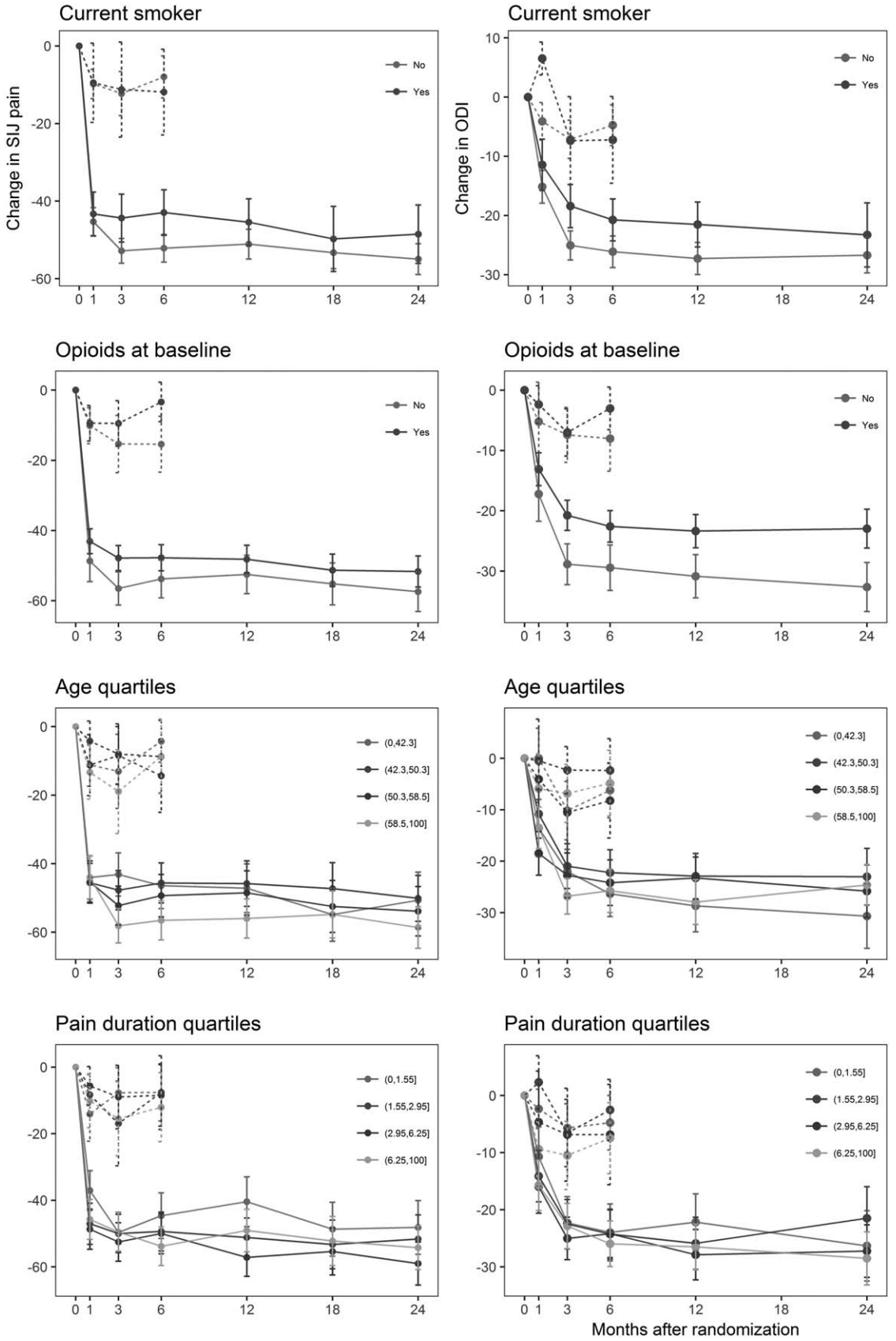

Figure 1. Changes in pain (by VAS, left) and disability (by ODI, right) over time for NSM (dotted lines) and SIJF (solid lines) in relation to baseline smoking, opioid use, patient age, and pain duration.

Within the SIJF cohort, we observed that patients in the third quartile of pain duration (3–6 years) had a larger improvement in pain. Also, patients in the fourth pain duration quartile (>6 years) had larger improvements in quality of life (EQ-5D). The significance of this finding is uncertain and is therefore the most difficult to integrate into decision-making during patient selection. However, as increased pain duration has been described to be a risk factor for poor treatment outcome in LBF,[57] our contrasting results provide reassurance that in patients with long-standing pain originating from the SIJ, SIJF is a reasonable option.

Procedure-related safety was reasonable in our analysis, with a low rate of wound problems and a low surgical revision rate consistent with a previous report in the commercial setting.[58]

Combined with retrospective case series,[16–31] our findings provide high-level evidence for the safety and effectiveness of SIJF with TTI and support its use as a relevant treatment choice in patients with SIJ dysfunction unresponsive to NSM.

Minimally invasive SIJF is gaining increasing attention in spine surgery. Two different surgical approaches to SIJF have been reported. In the dorsal approach, which was not used in the trials evaluated in our analysis, a midline dorsal incision is made with dissection to the dorsal ligamentous recess followed by device placement. Stabilization is achieved through ligamentotaxis. Published outcomes from this approach are scant.[59] In the lateral-to-medial approach, which was used in the trials analyzed by us, the implants transfix the SIJ. Published TTI studies include the three trials we summarized as well as retrospective case series,[16–28] including some with 3-,[26] 4-,[22] and 5-year[24] follow-up, and comparative case series *versus* open SIJF.[29–31] Three additional case series report good outcomes with hollow modular anchor screws[60–62] and a recent small case series suggests good outcomes with an additional transfixing device.[63] Minimally invasive SIJF using TTI was shown to not only improve the LBP component of SIJ pain but also the referred leg pain component.[64] Because of differences in approaches, device design, acute impact on the joint, and long-term fusion strategies, it is unclear whether results from our analysis apply to other laterally transfixing devices or to devices placed *via* a dorsal approach.

The main strength of our analysis is that all three pooled studies were of high quality, used standardized enrollment and diagnostic criteria, and were rigorously monitored. The two RCTs were designed to directly estimate the clinical value of surgery compared with a nonsurgical treatment control group. However, certain limitations should be mentioned. First, because the study protocols of iMIA and INSITE allowed crossover from nonsurgical to surgical treatment after 6 months and the majority of patients made use of this option, long-term information for NSM (beyond 6 months) was not evaluated in our analysis. Nevertheless, while crossover prevented calculation of treatment ES after month 6, it allowed us to completely avoid early crossover, which has complicated interpretation of other surgery *versus* nonsurgery trials.[65,66] Another limitation of our analysis is that all trials included were not blinded and therefore patient-specific expectations cannot be ruled out as potential confounders to overall outcome results. Nevertheless, the large observed ES suggest a true underlying effect. Finally, the fact that all three trials included in our analysis were industry-sponsored may be viewed by some as a limitation. However, industry-sponsorship is the norm in spine surgery device trials.[67]

CONCLUSION

Our pooled analysis suggests that the success of conservative management of SIJ pain is limited and difficult to predict. In contrast, improvements in pain, disability, and quality of life with minimally invasive SIJF were large; moreover, the extent of improvement was modestly associated with smoking, opioid use, patient age, and duration of pain. Procedure-related safety of SIJF was reasonable.

➢ Key Points

- ❑ Recent evidence suggests that minimally invasive surgical treatment of pain originating from the sacroiliac joint (SIJ) may be a relevant alternative to frequently unsuccessful conservative management.
- ❑ We pooled data from the only existing prospective trials using triangular titanium implants to treat SIJ pain to identify predictors of treatment outcome.
- ❑ Minimally invasive surgical management produced significantly better outcome than conservative management.
- ❑ We found no predictors of outcome for conservative management of SIJ pain.
- ❑ For minimally invasive surgical management, we found that smoking and opioid use predicted poorer outcome, while higher patient age and longer duration of pain were associated with better outcome.

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Study Groups

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