SacroIliac Joint Fusion vs Sham Operation for treatment of sacroiliac joint pain

A prospective double blinded randomized controlled multicenter trial

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Table of contents

INTRODUCTION *3*

PATIENTS AND METHODS *4*

Study design 4

Patients 4

Table 1: Inclusion and exclusion criteria 5

Interventions 6

Cases/Surgery 6

Controls/Sham surgery 6

Figure 1: Flow-chart of trial timeline. 7

Sample size 8

Outcomes 9

Primary outcome 9

Secondary outcomes 9

Table 2: Timeline of outcome measures 10

Study procedures 10

Randomization 10

Blinding 11

Withdrawal 11

Postoperative care 11

Data analysis plan 12

Research questions, objectives and hypotheses 12

Data collection 13

Data set and variables 13

Data analysis 15

Shell tables 16

DISCUSSION *19*

Ethics, registration, funding and potential conflicts of interest *20*

Aknowledgements *21*

References: *21*

INTRODUCTION

Sacroiliac joint (SIJ) pain is increasingly recognized as a possible pain generator in low back pain (LBP) (Sembrano et al. 2009). In as many as 15-30% of patients with LBP, the sacroiliac joint may be the cause of pain, and to an even greater extent in patients suffering from "failed back surgery" (Sembrano et al. 2009, DePalma et al. 2011).

The sacroiliac joint transfers force from the spine through the pelvis to the lower extremities (Vleeming et al. 2012). Dysfunction of the joint's articular congruity, ligamentous structures and motor control might be a cause of pain (Aldabe et al. 2012). The joint is richly innervated and contains mechano- and nociceptive receptors (Sakamoto et al. 2001, Szadek et al. 2008). Even though pain can arise from the sacroiliac joint, the diagnosis of sacroiliac joint pain is challenging. Patient history and radiological imaging have low sensitivity and specificity for the diagnosis of sacroiliac joint pain (Elgafy et al. 2001, Vleeming et al. 2008). Single clinical tests show little diagnostic strength for sacroiliac joint pain, but composites of clinical tests have fair sensitivity and specificity (Laslett et al. 2005, Vleeming et al. 2008). To strengthen the diagnosis, clinical tests are combined with intraarticular sacroiliac joint injection with local anesthetics (Kennedy et al. 2015).

Sacroiliac joint pain can be severe, disabling and reduce quality of life similarly to other spine conditions (Cher et al. 2014). Non-operative treatment consists of physiotherapy, pain medication, intra-articular sacroiliac joint steroid injections, prolotherapy and radiofrequency neurotomy of sacral nerve branches. There is limited evidence of effect of these treatment modalities (Luukkainen et al. 2002, Cohen et al. 2008, Kim et al. 2010, Patel et al. 2012) . In many patients non-operative treatment fails (Polly et al. 2016a). Historically open surgery has often been unsuccessful, due to intense postoperative pain and severe complications (Smith-Petersen et al. 1926). Recent multiple minimally-invasive sacroiliac joint fusion studies have reported pain relief and improved function to a greater extent than non-operative treatment and open surgery, and with low frequency of complications (Ledonio et al. 2014, Polly et al. 2016a, Sturesson et al. 2016, Whang et al. 2019). The increase in both available implants for minimally invasive sacroiliac joint fusion and their use is demonstrated by a growing number of publications. However, many are industry-sponsored and of poor quality (Sachs et al. 2012, Sachs et al. 2013, Miller et al. 2014, Rappoport et al. 2017, Fuchs et al. 2018).

Although the literature suggests superiority of minimally invasive sacroiliac joint fusion to non-operative treatment, some of the effect may be explained by placebo; to what extent is

not known. Therefore, we designed a non-industry sponsored prospective multi-center, double-blind, randomized sham-surgery controlled trial (RCT) in accordance with the SPIRIT recommendations to test the null-hypothesis that there is no difference in pain reduction between sham surgery and minimally invasive sacroiliac joint fusion.

PATIENTS AND METHODS

Study design

The trial is designed as a prospective multi-center, double-blinded, randomized sham-surgery controlled trial with 2 parallel groups. Participants, investigators, and data analysists are blinded for group allocation until the primary endpoint. The primary end-point is group difference in sacroiliac joint pain intensity on the operated side at 6 months postoperatively, measured by Numeric Rating Scale (NRS).

60 participants will be included after oral and written study information is given, and with written consent from the participant. There are 2 recruitment sites; Oslo University Hospital (OUS) in Norway and Karolinska University Hospital in Sweden. The recruitment phase started in April 2018, and the 1st participant was recruited in August 2018 in Norway and December 2019 in Sweden. Due to the corona virus pandemic there were large delays in inclusion in both countries. Inclusion was completed October 2021. All patients are followed for 6 months before unblinding, and for a total of 2 years postoperatively. The studies primary endpoint, the 6 month follow-up was finished by May 2022.

Patients

Referrals from general practitioners and from departments of orthopedic surgery or physical medicine and rehabilitation are screened for eligibility by an orthopedic consultant in the 2 departments and all patients whose referral includes information about pain originating from the sacroiliac joint are taken in for evaluation. This baseline evaluation is performed at the hospital's outpatient clinics with standardized clinical examination in accordance with inclusion and exclusion criteria (Table 1). Those who fulfill the inclusion criteria are invited to participate in the RCT.

Table 1: Inclusion and exclusion criteria

INCLUSION CRITERIA

1. Suspected SIJ pain for >6 months, or >18 months for pregnancy induced pelvic girdle pain.
2. Between 21-70 years old
3. Diagnosis of the SIJ as the suspected primary pain generator based on both of the following:
   A. Pain pointed with a single finger (Fortin Finger Test) at or close to the posterior superior iliac spine (PSIS) with possible radiation into buttocks, posterior thigh or groin
   B. At least 3 of 6 clinical tests for SIJ pain (Laslett et al. 2005; Vleeming et al. 2008)
   1. Compression
   2. Posterior Pelvic Pain Provocation test – P4
   3. Palpation of the long dorsal sacroiliac ligament
   4. Patrick FABER's test
   5. Active Straight Leg Raise (ASLR) test
   6. Gaenslen´s test
4. Reduced SIJ pain (NRS) of at least 50% of the pre injection NRS score after fluoroscopically or computed tomography guided controlled injection of local anesthetic into the SIJ.
5. Oswestry Disability Index (ODI) score of at least 30%.
6. SIJ pain of at least 5 on the Numeric Rating Scale (NRS), where 0 is no pain at all and 10 is worst imaginable pain.
7. Bilateral SIJ pain, if one dominant side. If eligible the dominant painful SIJ will be treated in the study.
8. Mentally and physically able to comply with study protocol.
9. Signed study-specific informed consent.

EXCLUSION CRITERIA

1. Pain due to other causes, such as lumbar disc degeneration, lumbar disc herniation, lumbar spondylolisthesis, lumbar spinal stenosis, lumbar facet degeneration, and lumbar vertebral body fracture.
2. Sacroiliac pathology caused by auto-immune disease (e.g. ankylosing spondylitis), neoplasia or crystal arthropathy.
3. History of recent (<1 year) fracture of the pelvis with documented malunion, non-union of sacrum or ilium or any type of internal fixation of the pelvic ring.
4. Spine surgery during the past 12 months.
5. Previously diagnosed or suspected osteoporosis (defined as T-score <-2.5 or history of osteoporotic fracture).
6. Documented osteomalacia or other metabolic bone disease.
7. Any condition or anatomy that makes treatment with the iFuse Implant System infeasible.
8. Patients with prior SIJ surgery.

The orthopedic department at Oslo University Hospital is currently the only center in Norway that performs minimally invasive sacroiliac joint. Approximately 40-60 patients are evaluated per year in the outpatient clinic. Sweden has evaluated twice the number of patients annually, and minimally invasive sacroiliac joint fusion is performed at 2 centers. One of the centers in Sweden participate in the study.

Interventions

Patients are randomized to either receive minimally invasive sacroiliac joint fusion or a sham procedure (Figure 1). All patients will receive the same pre- and postoperative assessment (i.e. blood samples, general anesthesia, draping, wound care and pain medication). They will not be randomized before they are under general anesthesia. Patients are kept under general anesthesia for 40 to 50 minutes regardless of intervention group as this operation on average lasts for 45 minutes. The operations will be done by 1 or 2 surgeons and the theater will be closed to all other personnel. After the procedure is completed the participants will be treated with standard post-operative care as given after minimally invasive sacroiliac joint fusion regardless of randomization group. The post-operative follow-up during the hospital stay will be done by health staff blinded for treatment allocation.

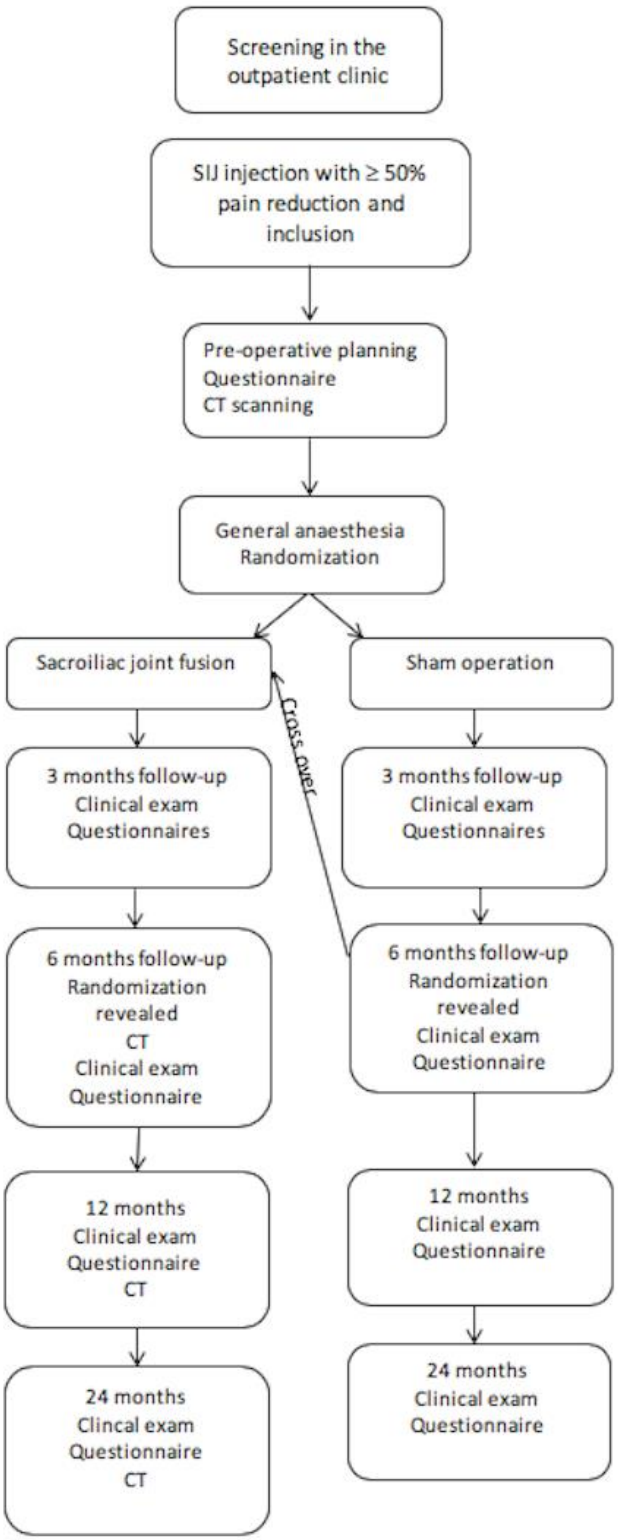
Cases/Surgery

Patients randomized to sacroiliac joint fusion receive treatment with triangular titanium implants according to the surgical technique manual (iFuse®, SI BONE, Inc.) (SI BONE 2020). The procedure starts with a 3-5cm long skin incision over the posterolateral aspect of the pelvis. Blunt dissection is performed through the subcutaneous tissue, fascia and muscle. Guide pins are inserted over the SIJ at the desired entry-point, verified by fluoroscopy. The surgeon drills and broaches over the pins, and 3 triangular titanium implants are inserted. The wound is then closed. An injection of the sacroiliac joint with local anaesthetic is performed under guidance of fluoroscopy at the time of the procedure. A subcutaneous injection of local anaesthetic is given around the skin incision.

Controls/Sham surgery

The control group consists of participants randomized to sham operation. The sham operation consists of the surgeon making the same skin incision as the surgical group receives. Blunt dissection is performed through the subcutaneous tissue, fascia and muscle. Guide pins are

Figure 1: Flow-chart of trial timeline.



inserted to the ileum, but do not enter the bone. The wound is then closed. Participants will be under general anesthesia while the procedure is simulated. All instruments needed are smeared with blood from the skin incision in order to keep the 2 procedures as similar as possible. An injection of the sacroiliac joint with local anaesthetic is performed under guidance of fluoroscopy during the procedure. A subcutaneous injection of local anaesthetic is given around the skin incision.

The surgeon will use a standard phrasing for the surgical report for both cases and controls. For controls pre-operative planned implants are reported and for intervention cases the actual implants used are reported.

Initially 2 methods of sham intervention (Norway vs Sweden) were described in the protocol section on ClinicalTrials.gov. The reason for this was due to different criteria for obtaining ethical approval in the 2 countries. However, after observing the 2 different sham intervention methods the study group concluded that the differences where insignificant and therefore could be described similarly.

Sample size

The average mean pre-operative NRS in previous studies has been reported to be 7.0-8.5 (Kibsgard et al. 2013, Sachs et al. 2013, Duhon et al. 2016, Polly et al. 2016b). There are 2 RCT´s that have compared minimally invasive sacroiliac joint fusion to non-operative treatment (Polly et al. 2016a; Sturesson et al. 2016). These report a mean decrease in global NRS of respectively 4.3 and 5.3 (Polly et al. 2016a; Sturesson et al. 2016). The same 2 studies showed a mean 0.5-1.3 points decrease in NRS in the group treated with non-operative treatment. We assume our trial´s case group to have at least mean 3 points decrease in NRS and the control group to experience a mean 1 point decrease in NRS. 2 previous studies have suggested that 2 points reduction in NRS represents a clinical important difference (Farrar et al. 2001, Hagg et al. 2003). For the sample size calculation, we assumed a change that would result in a mean 2 point difference between the groups for the main outcome in NRS on the operated side 6 months postoperatively. The standard deviation (SD) was set to 2.5 points since the SD has been reported in previous studies to vary between 1.0-2.9 at 6 months follow-up after sacroiliac joint fusion (Kibsgard et al. 2013, Sachs et al. 2013, Polly et al. 2016b, Duhon et al. 2016). The probability of a type 1 error (alpha) was set to 0.05. Based on these assumptions we calculate 25 participants in each group with 80% power using an online

sample size calculator (http://www.clincalc.com). Due to a possible dropout of 20% we will include 30 participants in each group, giving 60 participants in the study.

Outcomes

Primary outcome

The primary outcome is group difference in pain intensity on the operated side at 6 months postoperatively, measured by NRS, where 0 is no pain at all and 10 is worst imaginable pain. NRS is used as a primary outcome in other studies on minimally invasive sacroiliac joint fusion and will make it possible to compare our results with existing literature (Polly et al. 2016a; Sturesson et al. 2016).

Secondary outcomes

Secondary outcomes are patient-related-outcome-measures (PROMs), functional tests and pain-scores measured with NRS for global pelvic pain, contralateral sacroiliac joint pain and leg pain (Table 2). The PROMs collected are Oswestry Disability Index (Copay et al. 2016), Pelvic Girdle Questionnaire (Stuge et al. 2011) and the Euroqol 5 dimension (EQ-5D-5L) and EQ visual analogue scale (EQ-5D Foundation 2017). The functional tests consist of the active straight leg raise test, the 6 minute walking test and Timed Up and Go test. Furthermore, data on work status, ambulatory status, adverse events including re-intervention in target sacroiliac joint, implant loosening and fractures are recorded. Patient assessment of treatment and patient satisfaction with treatment is also collected. All assessments at 3- and 6-months follow-up are performed by blinded investigators who are qualified health personnel. After 6 months patients and investigators are un-blinded. Follow-up is continued for 2 years after the operation.

Table 2: Timeline of outcome measures

Endpoint/outcome	Baseline	Preoperative	Postoperative	3 months	6 months	12 months	24 months
NRS operated SIJ/side	x	x	x	x	x	x	x
Global NRS	x	x	x	x	x	x	x
NRS non-operated SIJ/side	x	x	x	x	x	x	x
Leg pain NRS	x	x	x	x	x	x	x
ODI	x	x		x	x	x	x
PGQ	x	x		x	x	x	x
EQ-5D-5L, including EQ-VAS scale	x	x		x	x	x	x
Clinical tests: • Patrick´s test (FABER) • Posterior Pelvic Pain Provocation test (P4) • Gaenslens test • Mennells test • Distraction • Compression • Palpation of the long dorsal ligament and sacrotuberal ligament	x	x		x	x	x	x
Functional tests • ASLR • ASLR range test • 6MWT • TUG	x	x		x	x	x	x
Ambulatory and work status	x	x		x	x	x	x
Adverse Events (including device breakage, migration, loosening etc)			x	x	x	x	x
Re-intervention of target SIJ				x	x	x	x
Patient satisfaction with treatment				x	x	x	x
Patients assessment of treatment				x	x	x	x

Abbreviations and explanations: **SIJ** = Sacroiliac joint. **NRS** = Numeric Rating Scale (measured on scale 0-10 where 0 is no pain and 10 is worst imaginable pain). **ODI** = Oswestry Disability Index (scale 0-100, where 0 is normal function,100 is bedridden). **PGQ** = Pelvic girdle questionnaire (score converted to percentage 0-100%, where 0 is worst pelvic health, 100 is best pelvic health). **EQ-5D-5L**: describes quality of life through scores in 5 dimensions all scored between 1 = no problems to 5= extreme problems. **EQ-VAS** (scale from 0-100: where 0 is worst health and 100 is best health). **ASLR** = Active Straight Leg Raise test (scale 0-5 where 0 = no difficulty raising leg, 5 = severe difficulty. Measured per leg.). **ASLR range test** = Active Straight Leg Raise Range test (measures how high a straight leg can be raised from examination table to the nearest 5 degree). **6MWT** = 6 minute walking test (measures the distance in meters walked in 6 minutes in one round). **TUG** = Timed Up and Go (Measures the time it takes a patient to sit in chair, raise, walk 3 meters back and forth and sit back in chair. Mean time of two rounds is recorded).

Study procedures

Randomization

Participants who give consent to participate in the trial and who fulfill the inclusion criteria will be randomized by the operating surgeon at each site (1 per site) after the participant has been anesthetized. Participants will be randomly assigned to either minimally invasive

sacroiliac joint fusion or sham surgery. Randomization is performed as block randomization with blocks of 4 or 6 with a 1:1 allocation to minimally invasive sacroiliac joint fusion or sham surgery. The randomization sequence is pepared by an independent statistician and the randomization sequence was unknown to the researchers. Allocation is completed with a computer generated randomization stratified by site through a specific website (Viedoc ©Viedoc Technologies (Viedoc 2021) provided by OUS). This website can only be accessed with personified username and password, and only the operating surgeon has access to randomize participants.

Blinding

All other parties than the operating surgeon and assisting staff in the operating theatre are blinded as to which intervention the participant has received. This includes trial participants, care providers, investigators and data analysts. No other than the operating surgeons have access to randomization prior to follow-up. Un-blinding occurs after completed 6-months follow-up. Participants that have undergone sham intervention and wish to cross over to surgical intervention are allowed to when the 6-month follow-up is completed. Both participants who were randomized to minimally invasive sacroiliac joint fusion initially and participants who cross-over to minimally invasive sacroiliac joint fusion are then followed for at least 2 years postoperatively (Figure 1). Participants who have undergone surgical intervention with implants can undergo surgery of the opposite sacroiliac joint if they wish after the initial 6-month follow-up.

Un-blinding of participants may take place if there is a suspicion of a severe adverse event in which knowledge of implant positioning is essential for patient management. Example of such events can be severe pain, new neurological deficits, or other injuries of such severity that it demands radiological examination to ensure adequate emergency medical care.

Withdrawal

The participant may withdraw from the study for any reason at any time. The investigators may also withdraw participants from the study in order to protect their safety and/or if they are unwilling or unable to comply with the required study procedures.

Postoperative care

All participants are informed of partial weight bearing on crutches for the first 4-8 weeks postoperatively. After 12 weeks there are no restrictions.

CT scan of the sacroiliac joint is performed pre-operatively and at 6, 12, 24 months follow-up to evaluate proper implant placement and lack of radiological signs of loosening.

Data analysis plan

Research questions, objectives and hypotheses

Research questions:

1. What is the efficacy of minimally invasive sacroiliac joint fusion?
2. Are there any tests, signs, symptoms or patient reported outcomes which can predict the outcome of minimally invasive sacroiliac joint fusion?

Objectives:

The main objective of this trial is to test the null-hypothesis that there is no difference in pain intensity between the sham surgery and minimally invasive sacroiliac joint fusion groups at follow-up.

Secondary objectives are to test the secondary hypotheses listed below and investigate the following research questions:

1. Is there a difference in pain intensity between minimally invasive sacroiliac joint fusion and sham at follow-up?
2. Is there a group difference in reduction in pain intensity from baseline to 3 months to 6 months between the sacroiliac joint fusion group and the sham group?
3. Is there a difference in functional outcomes measured with PROMs, clinical tests and functional tests between the sacroiliac joint fusion group and the sham group?
4. Is there a difference in the proportion of individuals that reach a clinically significant improvement of 2 points or more on the NRS scale in the sacroiliac joint fusion group and the sham group?
5. Is there a difference in the usage of analgesics at 3 and 6 months in the sacroiliac joint fusion group and the sham group?
6. Is there a difference in the rate of complications at 3 and 6 months in the sacroiliac joint fusion group and the sham group?
7. Is there a difference in the proportion of individuals that are on full or partial sick leave at 3 and 6 months in the sacroiliac joint fusion group and the sham group?

Hypotheses:

1. There is no difference between the groups in pain intensity on the operated SIJ in the sacroiliac joint fusion group compared to the sham group
2. Pain improves similarly in the sacroiliac joint fusion group as in the sham group between baseline and 3 months.
3. Pain improves similarly in the sacroiliac joint fusion group as in the sham group between 3 months and 6 months.

4. Pain improves similarly in the sacroiliac joint fusion group as in the sham group between baseline and 6 months.
5. There is a similar improvement in physical function, measured with functional tests and subjective questionnaires, in the sacroiliac joint fusion group as in the sham group.
6. The same proportion of individuals in the sacroiliac joint fusion group achieve a clinically significant improvement of 2 points or more on the NRS scale as in the sham group.
7. Individuals in the sacroiliac joint fusion group use the same amount of analgesics at 3 and 6 months as individuals in the sham group.
8. The proportion of individuals with complications at 3 and 6 months is similar in the sacroiliac joint fusion group as in the sham group.
9. The proportion of individuals that are on full or partial sick leave at 3 and 6 months is similar in the sacroiliac joint fusion group as in the sham group

Data collection

Baseline data on age, sex, diagnosis of sacroiliac joint pain, level of sacroiliac joint pain and response to injection if applicable, is registered on all eligible individuals evaluated at the outpatient clinic in order to evaluate reasons for failure to include individuals and for exclusion.

All data from both trial centres is collected into the Viedoc website (©Viedoc Technologies (Viedoc 2021)) provided by OUS. The data is confidential and not available as the trial is not completed and recruitment is still ongoing. Data collection is done either by direct electronic registration into the Viedoc Database or by forms, subsequently transcribed into Viedoc by the investigators. If there are missing data these will be collected by contacting the participant or by medical records review. Any adjustment of data entry has to be documented and is registered and reported by the database.

Data set and variables

The data set is exported from the Viedoc database as an excel-file. Only data from baseline, preinjection, postinjection, preoperative, postoperative, 3 months and 6 months time-points are used in this data analysis.

Variables

Independent or Predictor variables		Dependent or outcome variables	
Continuous	Categorical	Continuous	Categorical
Age (years)	Sex (F/M)	Numeric Rating Scale (NRS) (0-10 scale): - Operated SIJ - Contralateral SIJ - Leg pain - Global pelvic pain	EQ-5D-5L
Weight (kg)	Etiology of SIJ pain: - Idiopathic - Related to pregnancy - Trauma Other	EQ-5D-5L index	
Height (cm)	Civil status		
Clinical tests (pos/neg): - Patrick´s test (FABER) - Posterior Pelvic Pain Provocation test (P4) - Gaenslens test - Mennells test - Distraction test - Compression test - Palpation of Long Dorsal Ligament and Sacrotuberal Ligament.	Employment status		Clinical tests (pos/neg): - Patrick´s test (FABER) - Posterior Pelvic Pain Provocation test (P4) - Gaenslens test - Mennells test - Distraction test - Compression test - Palpation of Long Dorsal Ligament and Sacrotuberal Ligament.

Oswestry Disability Index (%)	Comorbidities (number of previous illnesses)	Oswestry Disability Index (%)	
Pelvic girdle questionnaire (%)	SIJ pain specific questions (Y/N)	Pelvic girdle questionnaire (%)	Adverse Events (Y/N)
EQ-5D VAS scale (0-100)		EQ-5D VAS scale (0-100)	Re-intervention of operated SIJ (Y/N)
Children (number of children)			Patient satisfaction with treatment (0-5)
Timed Up and Go (sec) 6 minute walking test (meters)		Timed Up and Go (sec) 6 minute walking test (meters)	Patient assessment of treatment (0-5)
Functional tests: - ASLR (0-5) - ASLR range test (0-90degrees)	Pain medication use (No of medication per category)	Functional tests: - ASLR (0-5) ASLR range test (0-90degrees)	Pain medication use (No of medication per category)

Data analysis

Data from the intervention groups will be compared based on the intention to treat (ITT) principle). Statistical comparisons in order to test differences between 2 independent groups will be made by the Student´s t-test or, in the case of a non-normal distribution, the Mann-Whitney U-test. To assess contingency tables, the chi square test will be used or, in the case of small expected frequencies, Fischer´s exact test. Descriptive statistics will be used to characterize the data. A p-value of <0.05 will be considered as significant. A sensitivity analysis will be performed comparing the intention to treat data against the per-protocol data exclusively from patients who complied with the study protocol. The proportion of patients in both intervention groups who obtain a clinically significant improvement of 2 points and more on the NRS scale will be compared.

In addition, a linear mixed model for repeated measures with a subject-specific random intercept will be used to assess results at the different follow-up time points using the outcome measurements during follow-up as dependent variable and the outcome variable at baseline, time, intervention and the interaction term between time and intervention as fixed effects.

For the primary outcome measure NRS for the operated sacroiliac joint measured at the day of the 6-month follow-up is used.

For the secondary outcomes the baseline value will be taken from the preinjection time point. Where such data is not available at this time point, baseline data will be collected from the preoperative measure point. These baseline values will be compared with values at 3 and 6 month follow-up.

All statistical analysis will be performed by a blinded statistician. The code for group belonging will not be broken until the analyses and interpretations of the results have been performed. Data will be analyzed using IBM SPSS statistical software, version 28.0.1.1 (14). An independent blinded statistician will do additional analyses using STATA statistical software.

Shell tables

10. Demographics

Variable	**Intervention group (N=n, CI 95%)**	**Control group(N=n, CI 95%)**
Age **20-29:N=** **30-39: N=** **40-49:N=** **50-59: N=** **60-70: N=**	Age groups: 20-29:N= 30-39: N= 40-49:N= 50-59: N= 60-70: N=	Age groups: 20-29:N= 30-39: N= 40-49:N= 50-59: N= 60-70: N=
Sex - **Female**	Female N= / male N=	Female N= / male N=

- Male		
Civil status - Married - Partner - Single		

Employment status:
 	
- Employed
- Sick leave:
  ○ Partial (<25%, 25-50%, 50-75%)
  ○ Full (100%)		

No of Children		
BMI and Weight/Height		
Ambulatory without assistance		
Prior Lumbar fusion		
Underlying diagnosis n(%) - Pregnancy - Trauma - Idiopathic		
Previous comorbidities (number of)		
Taking opioids, n (%)		

Preinjection:
 	
- ODI, score, mean (+/- SD)
- PGQ, score, mean (+/-SD
- NRS, score, mean (+/- SD)
  ○ operated SIJ
  ○ contralateral SIJ
  ○ global pelvic pain
  ○ leg pain
- Eq-5D index		

11. Group difference in NRS sacroiliac joint fusion group versus sham group. Improvement NRS sacroiliac joint fusion group versus sham group. Also demonstrated graphically.

Months	Group difference between surgical group and control group of pain intensity in operated SIJ measured with NRS
Baseline (0)	n/N and mean score, CI 95%
3months	n/N and mean score, CI 95%
6 months	n/N and mean score, Ci 95%

12. NRS values in sacroiliac joint fusion group compared to sham group. Also demonstrated graphically.

Months	NRS operated SIJ	
	Surgery	Sham
Baseline (0)	n/N and mean score, CI 95%	n/N and mean score, CI 95%
3months	n/N and mean score, CI 95%	n/N and mean score, CI95%
6 months	n/N and mean score, Ci 95%	n/N and mean score, CI 95%

13. Improvement in NRS shell table proportions

Months	NRS operated SIJ improvement of 2 points or more		NRS global pelvic pain improvement of 2 points or more	
	Surgery	Sham	Surgery	Sham
Baseline (0)	n/N and %	n/N and %	n/N and %	n/N and %
3months	n/N and %	n/N and %	n/N and %	n/N and %
6 months	n/N and %	n/N and %	n/N and %	n/N and %

14. Improvement in ODI and PGQ

Months	ODI		PGQ	
	Surgery	Sham	Surgery	Sham
Baseline (0)	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%
3months	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%
6 months	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%

15. Improvement in TUG and 6MWT

Months	TUG		6MWT	
	Surgery	Sham	Surgery	Sham
Baseline (0)	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%
3months	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%
6 months	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%	mean score, CI 95%

7. Shell tables for other outcomes will look and contain similar content as the examples above.

DISCUSSION

Minimally invasive sacroiliac joint fusion is increasingly used worldwide with reported reduced pain, improved physical function and quality of life compared to non-operative treatment in two industry-sponsored RCTs (Polly et al. 2016a; Sturesson et al. 2016). Both showed a clinically and statistically significant difference between the surgically and non-operatively treated groups with greater pain reduction in the surgically treated group (Polly et al. 2016a; Sturesson et al. 2016). It is a weakness that the studies were industry-sponsored. Further, a placebo effect might have contributed to the reported superiority of minimally invasive sacroiliac joint fusion.

To what extent a placebo effect influences the result after minimally invasive sacroiliac joint fusion is not known. A placebo effect after surgery has been shown to be an important factor in efficacy (Turner et al. 1994). Both patient and health care provider can influence a placebo effect on treatment results. This has particularly been shown in treatment of chronic pain, where the psychological component is believed to be important. Patients with long-lasting diseases seem to be poorer placebo responders, but on the other hand placebo tend to work better in patients expecting to have changes in sensation of pain (Vandana et al. 2001). Several sham controlled studies in orthopedic surgery have shown comparable pain relief in both groups, such as Moseley et al (2002) and Schrøder et al. (2017). Hence, the effect of minimally invasive sacroiliac joint fusion might be explained by placebo, but this is yet to be examined.

The ethical dilemma of sham surgery is relevant. To ask patients to undergo general anaesthesia for sham surgery might seem unethical. However, a German study of 1,37 million anaesthetic procedures with elective patients, graded as ASA classification physical status I and II, showed 7,3 cases of death or serious complication per million cases, corresponding to a very low risk (Schiff et al. 2014). All types of surgery are associated with risks of complications, and so also for minimally invasive sacroiliac joint fusion (Shamrock et al. 2019). In the control group the risks for surgical complications should be very low. A possible result showing sham surgery to be equal to minimally invasive sacroiliac joint fusion might spare thousands of people from undergoing unnecessary elective surgery with the risk and costs such surgery entail. We therefore find it ethically acceptable to complete a sham-controlled double-blinded randomized prospective study.

Ethics, registration, funding and potential conflicts of interest

Ethical approval for the study has been granted in Norway by the Ethics Committee Health Region Southeast, Oslo, Norway (2017/1892/REK sør-øst A), and in Sweden from The Regional Ethics Committee in Stockholm, Sweden (nr: 2018/1463-31).

The protocol of this study is registered with clinicaltrials.gov (NCT03507049)

The final result from this study will be published in peer-reviewed international journals and also disseminated through international congress lectures.

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