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Sacral Insufficiency Fractures: a Review of Risk Factors, Clinical Presentation, and Management

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Abstract

Purpose of the Review Sacral insufficiency fractures (SIF) are a common and often underdiagnosed source of low back pain. In patients with SIF, there is both a compromised sacroiliac joint and weakened sacrum, resulting in decreased resistance to torsional stress, leading to fracture. While conservative medical management is a safe option, minimally invasive intervention may provide improved short and long-term relief of low back pain in patients presenting with SIF. This comprehensive review is undertaken to provide an update to the current understanding of SIF with description of risk factors, clinical presentation, and management.

Recent Findings Sacroplasty is a minimally invasive procedure in which polymethylmethacrylate (PMMA) cement is inserted into bone to improve its structural integrity and alleviate symptoms. Balloon sacroplasty (BSP) has also been successful in alleviating pain with minimal cement leakage in SIF patients. Various other interventional techniques, including navigation-assisted screw fixation have been used to address SIF and have shown improvement in pain with minimal side effects.

Summary This review included various modalities of treatments available to manage SIF. This review shows that in comparison with nonsurgical management, sacroplasty has been shown to have greater pain reduction and improved mobility.

Keywords Sacroplasty · Sacral insufficiency fracture · Pathological fracture · Balloon sacroplasty · Osteoporosis

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Introduction

Sacral insufficiency fractures (SIF) are a common and often underdiagnosed source of low back pain.

Low back pain is one of the common conditions with significant healthcare expenditure burden and disability [1, 2]. In fact, Dieleman et al. have shown significant increases in healthcare utilization with $87.6 billion spent on back and neck pain in 2013. During the same period, opioid-related deaths have increased substantially in the USA, with policies currently being directed toward controlling opioids and improving access to non-opioid modalities [3–6]. In addition, numerous modalities of non-opioid techniques have been increasing with extensive utilization with increasing healthcare costs [7•, 8, 9, 10•, 11–19], even though some procedures have shown a significant decline in utilization [20–22].

Among the multiple causes of intractable low back pain, vertebral osteoporotic fractures and SIF has been described [19, 23–26, 27•, 28•, 29–33]. Benign SIF were described in

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1982 by Lourie, as a common disabling cause of low back pain and immobilization, especially in elderly patients with osteoporosis. Patients with SIF present with vague back pain, but some patients present with radiating pain or even neurological deficits [28•, 29–33]. Patients with SIF are offered multiple modalities of treatments. While conservative medical management is a safe option, minimally invasive intervention with sacroplasty may provide improved short- and long-term relief of low back pain in patients presenting with SIF [26–33]. The aim of this review is to provide a comprehensive update to the current understanding of SIF diagnosis and treatment.

Epidemiology

Earlier studies have reported the incidence of SIF to be 1.0–1.8%; however, rates as high as 5% have been reported [32]. A recent study looked at 250 patients that presented to the emergency department and underwent imaging with computed tomography (CT) for suspected pelvic injury. Of the forty-six patients who were diagnosed with pelvic fractures, eleven of the patients (4.4%) were found to have SIF. The variance in SIF incidence can be attributed to the delay of diagnosis due to nonspecific symptoms and SIF appearing more subtly than other types of fractures on initial X-ray assessment [33].

Pathophysiology

The sacrum, comprised of 5 fused vertebral segments, articulates superiorly with the fifth lumbar vertebrae (L5) and inferiorly articulates with the coccyx. On each side of the sacrum, the two lateral projections of the sacrum, the alae, articulate with the ilium to form the sacroiliac joint. Lateral to the sacral bodies and central canal are the anterior and posterior neural foramina. The sacrum is essential in the stabilization of the pelvis and lumbar support [34, 35].

During normal gait, a torsional stress is created around the sacrum as each lower extremity alternates between flexion and extension. As part of the biomechanics of the spine and legs, the sacroiliac joint relieves the torsional stress that is created during normal gait. In cases where the sacroiliac (SI) joint has pathology, such as rheumatoid arthritis, then the mechanical load is then transferred to the sacrum. If the sacrum is weak, such as in patients with osteoporosis, then the sacrum cannot withstand the offloaded stress and the sacrum is prone to fracture. Therefore, in patients with SIF, there is both a compromised sacroiliac joint and weakened sacrum, resulting in less resistance to the torsional stress and decreased stabilization of the pelvis with physiological stress [34]. Anatomy and innervation of sacrum has been well described [35].

Risk Factors

Risk factors associated with the development of SIF include osteoporosis, steroid-induced osteopenia, postmenopause, pelvic radiation, and rheumatoid arthritis [36–43]. There are fewer cases reported in the literature for other metabolic bone disorders such as osteomalacia, Paget's disease, hyperparathyroidism, and osteodystrophy, and five reported cases of lumbosacral fusion [43]. Osteoporosis is one of the most common associated conditions with SIF; therefore, SIF are mostly found in patients older than 55 years and predominates in those with a mean age of 70–75 years old. Other commonly associated conditions with SIF include rheumatoid arthritis, Paget's disease, hyperparathyroidism, malignancy, and steroid-induced osteopenia. Interestingly, one study examined stress injuries in 312 younger patients under the age of 18 who had been running regularly and found that 1.6% had sacral injuries found on magnetic resonance imaging (MRI) [42].

Pelvic radiation therapy for the treatment of pathologies including cervical cancer, sacral chordoma, or sacral metastasis has been highly associated with SIF [36]. In 61 cervical cancer patients who received whole pelvic radiation therapy, 11 patients (61%) were diagnosed with SIF on CT [36]. In another study, 21 of the 40 (52.5%) cervical cancer patients who received radiotherapy were found to have SIF on technetium Tc 99 m-labeled methylene diphosphonate PET [37]. In a retrospective study of patients with sacral chordomas treated with radiotherapy, 52% had SIF. This group of patients underwent a pelvic MRI every 3 months for follow-up in the first year, followed by every 6 months thereafter. SIF was detected on MRI with a range of 1–62 months and a median of 11 months post-follow-up. In another study, 2 years after receiving stereotactic radiotherapy, 79% occurrence of sacral fractures was detected on MRI [38].

In contrast, in a study of 252 patients who had stereotactic body radiation therapy (SBRT), many had vertebral fractures; however, there was only one reported SIF. A 76-year-old female with a history of myxoid chondrosarcoma of the left femur and oligo-metastasis at the right sacral bone had received SBRT and subsequently developed SIF in the left sacral alae on CT [39].

Postpartum sacral stress fractures have also been reported. One case of a 36-year-old woman, who presented with low back and buttock pain 2 days following her cesarean delivery, described a diagnosis of SIF on MRI and CT scan [40]. It was concluded that while the cesarean delivery was not a traumatic cause for SIF, pregnancy alone could be a risk factor for developing SIF [40]. During pregnancy, many associated factors occur that can be causal for SIF, including weight gain and increased lumbar lordosis. In addition, the pelvic ligaments are loosened and result in decreased stabilization of the pelvis. It has been noted that during labor, mechanical stress may

put females at risk for SIF. Lactation can also cause osteopenia and osteoporosis, which have been noted as risk factors as well [41].

Clinical Presentation and Diagnosis

As a result of nonspecific symptoms on presentation and variable findings on X-ray, SIF may be missed or misdiagnosed. Physical exam findings can be entirely normal; however, some patients may have diminished ankle reflexes or restricted back extension. In such patients, X-ray findings can similarly be entirely unremarkable; however, fracture is most often seen in the sacral ala. Often, there is a delay of 40–55 days in obtaining sacral radiographs. Moreover, only 20–38% of SIF are visible on X-ray, while only 12.5% have visible fracture lines [34]. MRI may show disc degeneration, lumbar stenosis, or hyper-intensity with foraminal stenosis in the sacral region. Late in the disease course, MRI may reveal associated edema in the sacral region.

In one study of 50 patients with SIF presenting with nonspecific symptoms, 74% of patients were definitively diagnosed with SIF using MRI, whereas only 12% were diagnosed by CT and only 12% by X-ray. To better highlight sacral fractures, MRI imaging used in this study was T1-weighted for low intensity regions and T2-weighted for high intensity. In addition, 1% of patients were diagnosed with the bone scintigraphy scan using the Tc 99m-labeled methylene diphosphonate. Therefore, in older patients with lower extremity or lower back pain and have associated risk factors for fractures such as osteoporosis or corticosteroid use, MRI would be the recommended imaging modality for SIF diagnosis [42].

X-rays have low sensitivity for SIF and should be used as an initial imaging modality, to rule out other potential causes of low back pain. Anterior-posterior (AP) and lateral lumbar spine and AP pelvis X-rays are recommended. Overlying bowel gas, soft tissue, calcifications from nearby vessels, and spinal anatomy may obscure radiographic findings of SIF [44]. If the X-rays are negative and there is a suspicion for SIF, MRI should be used. CT can also be used but it is less sensitive than MRI. However, if X-rays do show evidence of SIF, then it is not necessary to proceed with an MRI. Bone scintigraphy scanning is not specific, as SIF can appear similarly to degenerative disc disease, arthritis, and synovitis. Still bone scintigraphy can be used as a supplemental imaging modality to MRI or CT. Bone scans do take more time, and therefore cross-sectional imaging is recommended above bone scans for SIF in the cases of negative X-ray [45]. E.

Diagnosis of SIF may prove difficult due to the presence of nonspecific symptoms or the pain being in the back and legs; the workup tends to involve the lumbar region rather than the sacrum. Interestingly, one study of 42 patients showed that L-spine MRI showed diagnosed SIF in patients who had SIF of 64.3%, whereas pelvis MRI was 9.5% and CT pelvis was 14.3% [46]. Patients who have SIF may also have vertebral or iliac fractures which may further complicate the presentation with reports of hip and thigh pain [47, 48, 49•, 50]. Bone scans are a useful modality for diagnosis of SIF and additionally fractures in the lower vertebra. As such, a diagnostic bone scan can be especially useful in earlier stages of SIF when there is atypical or unspecific pain.

The Denis classification describes different types of traumatic sacral fractures as well as the various SIF. There are three "zones" in the Denis classification. The first zone describes a sacral fracture that is most lateral and involves the sacral ala. Zone 1 is the most common location of fracture for patients with SIF. In patients with osteoporosis, there may be more trabecular bone loss in the sacral ala than in the vertebral bodies, resulting in a compromised sacral ala that is prone to SIF. Zone 2 is a sacral fracture involving the neural foramina, and zone 3 is medial involving the sacral bodies and transverse central canal. These fractures tend to fracture vertically; however, there can be a horizontal component as well that can be seen on MRI as the "Honda" or "H" sign. Typically, this occurs in the later stage when the central area of the sacrum weakens and fractures horizontally due to decreased ability to withstand the weight of the upper body [42]. In a retrospective observational study of lumbar spine MRI versus non-lumbar imaging modalities in the diagnosis of SIF, Kim et al. [44] showed that SIF are more commonly diagnosed by lumbar spine MRI than non-lumbar imaging modalities such as bone scan, pelvic bone CT, and pelvic MRI, because of symptoms that mimic lumbar spine pathology and variable comorbid causes of pain. The authors concluded that lumbar spine MRI reveals SIF, and it is essential to be familiar with sacral insufficiency features on lumbar spine MRI, which would help to increase the sensitivity in detecting unrecognized SIF.

Management

Until recently, the mainstay of treatment for SIF centered around physical therapy, modified bed rest, injection therapy, and other traditional analgesic efforts. Sacroplasty and balloon sacroplasty (BSP) are minimally invasive percutaneous procedures which address the underlying cause of back pain in a more targeted effort. In these procedures, polymethylmethacrylate (PMMA) cement is injected into the compromised bone, improving its structural integrity [46].

Mortality following benign SIF is substantial [27•]. Park et al. [27•] described multiple risk fractures with 43% of the patients with a history of malignancy, and 22% of the patients have undergone pelvic radiation therapy before fracture diagnosis. Among these, 6.5% underwent sacroplasty, and the others underwent conservative management after fracture

diagnosis. They showed that significant factors associated with increased mortality were male gender, malignancy history, lumbosacral fusion with distal fusion at S1, stroke history, low total femur bone mineral density score, and low body mass index (BMI).

Medical Management

Conservative management of SIF primarily focuses on early rehabilitation and pain control. In the past, bed rest was the mainstay of initial treatment. It was recommended that patients remain relatively immobile for approximately 3 to 6 months following a fracture. However, recent literature suggests that early mobilization may improve outcomes and lead to fewer complications. Prolonged bed rest has been associated with a number of adverse effects including increased risk of deep vein thrombosis, decreased muscle strength, and cardiac dysfunction [47]. Immobility may increase osteoclastic bone resorption and further diminish bone mineralization. In contrast, early mobilization stimulates osteoblastic bone formation leading to increased bone strength. Traditional weight-bearing exercises, the use of assistive devices, and aqua therapy have all been successful in aiding in rehabilitation after fractures. A majority of patients with SIF report improvement in symptoms after 1–2 weeks of conservative management, with many showing significant reduction in pain and increase in mobility after 6 months [48].

Pain control is an important consideration in treating SIF. Opioids, acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed analgesics for fractures. Although NSAIDs are commonly used, recent literature has suggested that NSAIDs should be used judiciously for fractures as they may impair endochondral ossification during fracture healing [49•]. In addition, NSAIDs may reduce bone mineral density and delay fracture healing early in treatment [50]. Further research is still needed to determine the safety of NSAIDs in fracture healing.

Furthermore, management of underlying osteoporosis is critical to treatment of SIF. Sufficient levels of vitamin D and calcium are essential for bone mineralization. As such, patients should take the recommended daily dosages of 1200 mg calcium and 800 IU vitamin D daily [24, 51]. Oral bisphosphonates, which inhibit bone resorption, such as alendronate, have also been approved for the treatment of osteoporosis. However, long-term use of bisphosphonates has been shown to reduce bone remodeling and may cause bone microdamage [52•]. For now, it is recommended that providers reassess bisphosphonate therapy after the first 5 years of treatment [53].

Teriparatide, a recombinant form of parathyroid hormone (PTH), has recently emerged as a new treatment for SIF. A number of studies have demonstrated that teriparatide has positive effects on bone healing such as increasing bone mineral density, increasing osseous tissue volume, and reducing fracture healing time [54–57]. In a retrospective, case-controlled study, 41 patients with MRI-confirmed SIF were divided into two groups, teriparatide versus control. Those who received 20 μg of teriparatide for 3 months had an improvement of VAS score from 6.9 to 3.8, while the control had an improvement of 6.5 to 5.1. Analgesic use at 3 months was 28.6% in the teriparatide group and 55% in the control group. The mean time to mobilization (1.2 vs. 2.0) was shorter in the teriparatide group. The mean time to fracture healing was 7.4 weeks compared to 13.6 weeks in the control group [43]. A case report of a patient with bilateral sacral stress fractures who failed traditional management reported improvement after 6 months of treatment with teriparatide [58]. The efficacy of long-term management of teriparatide is not yet known. However, after 2 years of use, there appears to be a reduction in bone mineral density and increase in porosity [59].

Interventional Management

Sacroplasty is a minimally invasive procedure in which PMMA cement is injected into bone to improve its structural integrity and alleviate symptoms. Sacroplasty was first introduced as a treatment for pelvic lesions resulting from metastasis. The practice was later realized to be a viable option for other osteological pathologies such as SIF [26, 28•, 60–67]. However, literature on SIF is sparse compared to vertebral augmentation procedures. However, the literature is emerging.

In patients with SIF, sacroplasty has been demonstrated not only to improve pain scores but also to increase patients' participation in activities of daily living (ADL). One study investigated 16 patients who presented with complaints of low back, groin, or buttock pain and underwent sacroplasty upon radiologic confirmation of SIF. Prior to undergoing sacroplasty, the mean reported pain score was 7.5 on the visual analog scale (VAS) compared to 4.1 on postoperative day one, 3.3 on 1-month follow-up, and 3.2 on 3-month follow up. In this study, ADLs were measured using the Oswestry Disability Index (ODI), with a mean initial score of 59% and a mean 3-month postoperative score of 14.8% [60]. Similarly, in a prospective study of 15 patients diagnosed with SIF, which were unresponsive to a conservative treatment protocol, sacroplasty was found to offer immediate pain relief and furthermore maintained pain relief at 1-year follow-up. In these patients, a reduction in average VAS scores immediately following the procedure was noted to decrease to 1.7 from 7.9. After 12 months, the average VAS score reported was 2.4 [61].

Kortman et al. [26] in a multicenter study assessed the effectiveness and safety of sacroplasty in patients with osteoporotic SIF or pathological sacral lesions. They studied 243 patients with 204 with painful SIF and 39 with symptomatic

sacral lesions. The average pre-treatment VAS score of 9.2 ± 1.1 was significantly improved after sacroplasty to 1.9 ± 1.7 in patients with SIF. The average pre-treatment VAS score of 9.0 ± 0.9 in patients with sacral lesions was significantly improved after sacroplasty to 2.6 ± 2.4. There were no major complications or procedure-related deaths. The authors concluded that CT-guided percutaneous sacroplasty is a safe and effective procedure in the treatment of painful SIF or lesions. Further, they also concluded that it was associated with prompt and durable pain relief and should be considered as an effective treatment option in this patient population.

In 2017, a 10-year study was concluded which had followed a group of 244 SIF patients, 34 of whom received nonsurgical management (NSM), and 210 of whom were treated with sacroplasty [28•]. This was the first long-term study and is valuable for investigating the consequent pain improvement, patient satisfaction, and opioid, non-opioid, and OTC analgesic use. Although both groups had a comparable average initial VAS score, after 2 weeks, the sacroplasty group experienced an average pain score reduction of 66%, while the NSM group only experienced a 27.2% reduction. After 2 years, the radiofrequency sacroplasty group caught up slightly, showing an average of 85% reduction in VAS; however, the sacroplasty group still demonstrated better outcomes with an average VAS reduction of 92%. In the sacroplasty group, 77% were using opioids for pain control before the procedure. However, in the first postoperative follow-up, only 33 were still using opioids, and at the 10-year follow-up, all 117 who were available for follow-up reported that they were no longer using any analgesic medication. Non-opioid analgesic use was originally 33%, and OTC analgesic drug use was 31%. After the procedure, it was 0.005% for the former and 0.07% for the latter. The most common complication reported was PMMA leakage, which caused little to no clinical detriment. The authors concluded that sacroplasty should be considered a long-lasting, safe, and effective means to treat SIF [28•]. Cumulatively the results of these studies suggest that sacroplasty should be considered an effective, low-risk option for patients with intractable pain and disability from SIF.

BSP, akin to balloon kyphoplasty, utilizes a balloon catheter that is insufflated first, in order to compact fractured vertebral pieces and to create a precise and sufficient space for PMMA injection. In order to assess the value of this technique in sacroplasty, 45 patients with SIF were evaluated in a study, where 18 underwent the procedure with balloon assistance, and 27 underwent the procedure without balloon assistance. Both groups achieved remarkable improvement of symptoms; and while the BSP took significantly longer to perform, there was substantially less cement leakage noted [46]. Radiofrequency sacroplasty (RFS) offers another variation in which a flexible osteotome, rather than a balloon, is used to create a sufficient space for plaster insertion. The PMMA cement is then activated by radiofrequency before being inserted into the enlarged cavity. When RFS and BSP, with CT guidance, were compared in a group of 40 SIF patients, both procedures were equally successful in alleviating pain with minimal leakage, leading the authors to subsequently conclude that surgeons may simply choose whichever method they are most comfortable with [63].

Surgical

Transiliac-transsacral screw stabilization is a surgical technique that may offer rapid and complete pain relief for patient's refractory to conservative management. Follow-up studies indicate patients remain mobile and pain-free for at least 12 months after the surgery. Furthermore, patient satisfaction after transiliac-transsacral screw implantation was high, and many reported that they would undergo the procedure again [64]. In one study of 41 elderly patients, 16 patients were treated with transiliac-transsacral screw fixation, and 25 were treated nonoperatively. Those treated with screw fixation had a greater improvement in VAS of 3.9 versus 0.6 in the control group. Compared to 20% of patients that have conservative treatment, 75% of those that undergo transiliac-transsacral screw fixations were discharged home [65]. Transsacral bar insertion is a reliable method for stabilizing sacral fractures and achieving high interfragmentary compression in comparison to transiliac screw fixation [66]. Iliosacral screw fixations are also commonly used to treat SIF; however, some studies have indicated that these may be mechanically insufficient and predispose to screw loosening [67]. In patients with neurological side effects due to unstable SIF, lumbosacral fixation is also an option to alleviate symptoms and improve mobility [68].

The nature of SIF presents some challenges to surgical fixation. Given that SIF tends to affect osteoporotic bone, achieving adequate stability with screw fixation may prove difficult. Cement augmentation of implanted screws may enhance structural stability though further long-term studies are needed. Collinge et al. [69] described a novel technique in which a screw is inserted percutaneously, and then the screw itself is used as conduit for the introduction of aqueous calcium phosphate cement. The cement augmentation provides an amenable medium for the screw fixation, allowing the screw to enhance the structural stability.

Sacroplasty for the Management in Pathologic Fractures

In addition to management of SIF, sacroplasty is a promising treatment for pathologic fractures. In a case of an 81-year-old male with multiple myeloma and severe pathologic sacral lesions with severe pain, sacroplasty resulted

in immediate pain relief and reduction of pain for 2 years after the procedure [70]. In another report, a 71-year-old patient with castrate-resistant metastatic prostate cancer underwent sacroplasty for severe pain. After the procedure, the patient had significant pain reduction and improvement in his overall mobility [71].

Patients with prior radiation treatment are often not candidates for surgery such as screw fixation and pelvic ring stabilization; therefore, sacroplasty is a valuable treatment option to these patients [72]. Patients with periosteal destruction due to lytic or blastic lesions may be better treated with sacroplasty than other methods such as radiofrequency ablation or corticosteroid injections [73]. Patients with metastatic disease often have debilitating pain, and BSP can be an important palliative care treatment. One study investigated BSP in 10 patients with metastatic destruction of the sacrum. Patients reported significant pain relief based on the VAS for 6 months postoperatively and reported high rates of satisfaction with their procedures [74].

In addition to pain relief, sacroplasty for pathologic fractures results in improved functional mobility using the functional mobility scale (FMS) and decreased dependence on oral pain medications. In a retrospective review of 53 patients, there were statistically significant reductions in FMS, VAS, and analgesic scale scores (AS) for all patients who underwent sacroplasty [75]. The complications associated with sacroplasty include hemorrhage, infection, and cement leakage. There may be an increased incidence of these complications when treating pathological fractures compared to SIF. However, this may be due to the nature of the tumors and lesions associated with metastasis [76]. Larger cohort studies are needed to further examine this. One complication of sacroplasty is the inability to fully visualize the needle tip and potential damage to internal organs or nerves. Sacroplasty under fluoroscopic guidance may be safer than traditional sacroplasty and also results in significant pain relief [77]. Further studies are needed to determine the long-term durability of sacroplasty in pathologic fractures as many studies have only obtained follow-up for 6 to 9 months. In elderly patients with significant immobility due to painful fractures, sacroplasty can provide a significant improvement in quality of life often making a difference of whether patients remain independent in functioning or need caretakers. It may be performed in office settings similar to kyphoplasty [78].

Conclusion

SIF commonly occur in the elderly population and are associated with a high mortality rate. These fractures are thought to occur due to sacroiliac joint pathology and a compromised sacrum secondary to conditions such as rheumatoid arthritis, Paget's disease, steroid-induced osteopenia, radiation therapy, and osteoporosis. Due to nonspecific in presenting clinical symptoms, SIF can be misdiagnosed and improperly managed. Anteroposterior or lateral lumbar spine X-rays along with MRI are recommended for accurate diagnosis of SIF. In the past, bed rest, physical therapy, and analgesics were the mainstay of treatment for SIF. Recent literature however has shown that sacroplasty is a promising technique to treat SIF. Sacroplasty is a minimally invasive procedure in which PMMA cement is inserted into bone to improve its structural integrity and alleviate symptoms. BSP has been successful in alleviating pain with minimal cement leakage in SIF patients. Various other interventional techniques, including navigation-assisted screw fixation, have been used to address SIF and have shown improvement in pain with minimal side effects. In comparison with nonsurgical management, sacroplasty has been shown to have greater pain reduction and improved mobility. Furthermore, sacroplasty may be utilized in patients who were previously refractory to conservative or medical management. Further large-scale studies are needed to study the long-term effects and safety of sacroplasty in the treatment of SIF.

Compliance with Ethical Standards

Conflict of Interest Ivan Urits, Vwaire Orhurhu, Jessica Callan, Nishita V. Maganty, Sara Pousti, Thomas Simopoulos, Cyrus Yazdi, Rachel J. Kaye, Lauren K. Eng, Alan D. Kaye, Laxmaiah Manchikanti, and Omar Viswanath declared that they have no conflict of interest.

Alan Kaye is a Section Editor for *Current Headache and Pain Reports*. He has not been involved in the editorial handling of this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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