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Narrative Review

A Comprehensive Review of Treatment Approaches to Ilioinguinal Neuralgia

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Background: Ilioinguinal neuralgia is a frequent cause of pain in the lower abdomen, genitals, and upper thighs and is commonly caused iatrogenically. Patients with ilioinguinal neuralgia often have a history of surgical interventions such as hernia repairs, appendectomies, or hysterectomies.

Objectives: The objective of this narrative literary review is to catalog and provide an organized level of evidence for the available interventions for treating ilioinguinal neuralgia.

Methods: Research databases, including PubMed, CINAHL and Google Scholar, were searched for characterization, diagnosis, and treatment of ilioinguinal neuralgia. The included results comprised case studies, randomized trials, and meta-analyses. Interventions were organized from least to most invasive and sorted into 3levels (A-C). Level A consisted of data derived from multiple randomized clinical trials or meta-analyses. Level B consisted of data derived from single randomized trials or nonrandomized studies. Level C was composed of consensus opinions of experts, case studies, or standards of care.

Results: The review finds the greatest level of evidence in support of the conservative management of pain through various classes of medications and topical treatments. Although injection-based interventions and neuromodulation approaches have been developed in the past few years, these techniques lack level A evidence from studies such as multiple randomized clinical trials or meta-analyses. The most invasive treatment discussed is surgical neurectomy, which also lacks level A evidence but has garnered support from retrospective reviews and prospective studies.

Limitations: Attempts were made to gather studies from large databases. However, we acknowledge that our efforts do not cover all known publications on the management of ilioinguinal neuralgia.

Conclusions: Based on the present literary review, the method of ilioinguinal neuralgia management with the strongest level of evidence in its favor is taking conservative measures, including topical and oral medications. The paper and accompanying original Table 2 provide a good summary of what current literature supports which treatment options.

Key words: Ilioinguinal neuralgia, thigh pain, spinal cord stimulation, peripheral nerve, dorsal root ganglion

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The entrapment of peripheral nerves secondary to trauma or surgical procedures can result in significant pain and debility. A frequent cause of pain in the lower abdomen and upper thigh is injury to the ilioinguinal nerve. Since the ilioinguinal nerve is a mixed sensorimotor nerve from T12 and L1 nerve roots, it carries sensory information segmentally and supplies motor innervation to the transverse abdominis and internal obliques (1). Ilioinguinal neuralgia, which is diagnosed clinically, is often characterized by tenderness to palpation along the inguinal canal, neuropathic pain in the inguinal region, and impaired sensation along the nerve's cutaneous distribution (2). Affected areas often include the lower abdomen, labia majora, mons pubis, penile root, anterior scrotum, and upper thigh. If there is high concern for ilioinguinal neuralgia, the condition can be clinically diagnosed through physical exams and electrophysiologic studies and confirmed by ultrasound-guided nerve blocks.

It is difficult to accurately assess the prevalence of this condition because of its multifactorial etiology and the inconsistent time span between nerve injury to symptom presentation. For ilioinguinal neuralgia, he most common etiology overall is iatrogenic. Among patients who receive elective hernia repair, a noted prevalence of postoperative chronic pain arises after the procedure, and this pain ranges from 18-37% in the ilioinguinal nerve distribution (3). Other surgical procedures that may cause damage to the ilioinguinal nerve include appendectomies, hysterectomies (Pfannenstiel incision), and orchiectomies. As for other causes of traumatic ilioinguinal nerve injury, stretching of the nerve during pregnancy is common, as is abdominal trauma during high-impact sports or femoral catheterization (such as during the placement of a central line) (4). Additionally, idiopathic nerve entrapment is noted, which is thought to be secondary to musculoaponeurotic connective tissue abnormalities often found in locations such as the inguinal canal, rectus borders, iliac crest, and paravertebral muscles (5) (Table 1).

Clinical Presentation

Patients with ilioinguinal neuralgia typically present with complaints of pain in the setting of recent surgical intervention of the abdomen or pelvis. The burning, continuous pain happens in the lateral aspect of the iliac fossa, around the lower quadrants of the abdomen, and in the upper thigh, with radiation from these regions to the scrotal/labial or inguinal region. Patients can also report dysesthesia, paresthesia, hyperesthesia, or hypoesthesia with the presence of tenderness to palpation (6). Common differential diagnoses with similar presentations include genitofemoral neuralgia, lumbosacral radiculopathy, and plexopathy, and these possibilities should be considered (7). Importantly, an injury to a nerve can also lead to more than just pain. There may also be notable loss of function in muscle groups such as the transverse abdominis and internal oblique as well as in the small area on the upper anteromedial thigh. Hair loss and trophic changes may also occur (8).

Diagnostics

Several modalities can be used to narrow down the diagnosis of ilioinguinal neuralgia. These modalities are centered around direct visualization with ultrasound and magnetic resonance imaging (MRI) or through electromyography and/or diagnostic blocks.

Electromyography is noted to have limited benefit in diagnosing ilioinguinal nerve injury; however, the technique is important in excluding lumbar radiculopathy and plexopathy. There is a high possibility of mistaking branches of the iliohypogastric nerve or co-stimulating adjacent iliohypogastric nerves when the positioning of the electromyogram needle is based on anatomical landmarks alone (9).

Ultrasound has proven to be a valuable tool for tracing the nerve. When using ultrasound to diagnose a possible case of ilioinguinal neuralgia, it is recommended that tracing be started at the iliac crest and followed to the superficial inguinal ring. The purpose of tracing is to visualize any possible entrapments from redundant tissues, trauma, or masses (10).

MRI of the lumbosacral spine should be conducted to provide a confirmatory modality for excluding lumbar radiculopathies. The potential drawbacks of MRI include access restrictions, time investments, and cost.

A confirmatory anesthetic block can also be performed under ultrasound guidance to diagnose ilioinguinal neuralgia. This technique is both diagnostic and potentially therapeutic (if steroids are used). The region of pain is flooded with local anesthetic, and improvement in pain is monitored. In a study conducted by Gofeld and Christakis (10), the researchers noted a high anatomical variability in the nerve distribution when attempting to target the nerve using the anterior superior iliac spine (ASIS) as a landmark. The study noted that the nerve consistently passed between the internal oblique and transverse muscles above the ASIS; however, accessing the nerve at that point was precarious given its deep location and the potential danger of the physician

perforating the abdominal cavity and intestines. Notably, the course of the nerve as described by anatomical textbooks truly correlates in only about 41.8% of patients (10). In fact, patients may demonstrate variability in innervation, with the iliohypogastric nerve replacing the ilioinguinal nerve at rates as high as 12.5% (10).

Table 1. *Likely etiology of nerve injury based on location*

Location	Cause
Retroperitoneal	Surgical incisions (e.g. nephrectomy)
	Retroperitoneal tumors
Lower Abdomen	Entrapment in abdominal muscle layers
	Surgical incisions
Inguinal canal	Herniorrhaphy
	Endometriosis
	Lipoma, leiomyoma
Unknown	After childbirth
	Spontaneous

Adapted from Stewart J. Focal peripheral neuropathies. Raven Press New York 1993, p. 411-418.

Treatment

Conservative

The treatment of ilioinguinal neuralgia is a spectrum, spanning from conservative management to surgical interventions (Table 2). Conservative management focuses on pain control with topical applications of compounded ointments and oral medications. The latter category includes nonsteroidal anti-inflammatories, opioids, and, most recently, antidepressants, such as duloxetine. Duloxetine has emerged as a dual-action medication, treating the neuropathy while addressing the patient's mood and reactive depression from chronic discomfort (12). Another type of treatment consists of specific lifestyle modifications centered around physical therapy and the avoidance of exacerbating positions, such as leaning forward or hyperextension of the hip joint. Rehabilitation-specific interventions include the utilization of transcutaneous electrical nerve stimulation (TENS), acupuncture, and myofascial release techniques to alleviate potential tissue interruption of the nerve.

Pharmacological Approaches to General Neuropathic Pain

The development of new pharmacological medications over the past several years has afforded a plethora of options to manage general neuropathic pain. Typically, the first-line agent for neuropathic pain is gabapentin, which was initially used as an anticonvulsant agent (13). Today, gabapentin is used for a wide range of indications, primarily for neuropathy stemming from type 2 diabetes but also for postherpetic neuralgia and other pain syndromes with neuronal etiology (14). In the 2017 Cochrane Pain, Palliative and Supportive Care Group review of gabapentin for neuropathic pain, 37 studies encompassing 5,914 participants showed substantial benefits in pain relief (defined as at least 50% pain relief from the baseline) at daily doses ranging from 1,800 mg to 3,600 mg. Among postherpetic neuralgia patients, 32% showed substantial benefits over those who had received a placebo, and 35% of participants diagnosed with diabetic neuropathy also experienced substantial benefits (15). Although Level A studies supporting gabapentin use for other causes of neuropathic pain are scant, the theoretical benefit of its use persists: disruption of nerves that generate chronic pain. The mechanism of action of gabapentin is at the voltage-gated calcium channels that inhibit the release of excitatory neurotransmitters presynaptically (16). The adverse effects of gabapentin are relatively mild, consisting of somnolence, dizziness, and, in some cases, ataxia (14).

Pregabalin has a similar mechanism of action as gabapentin and is also a first-line medication for the management of neuropathy. Notably, the absorption of pregabalin is reported to be much faster than that of gabapentin, at a rate 3 times greater (17). The same group that studied gabapentin efficacy also studied pregabalin in postherpetic neuralgia, painful diabetic neuropathy, unclassified post-traumatic neuropathic pain, and central neuropathic pain. In 45 studies encompassing 11,906 patients, pregabalin at daily doses of 150 mg, 300 mg, and 600 mg were studied. Across all indications, increased doses resulted in increased pain relief. However to obtain at least 30% relief, patients in the unclassified post-traumatic neuropathy group required the maximal studied dose of 600 mg per day (18). Gabapentin and pregabalin are noted to have similar side effects.

Antidepressant medications have proved to be efficacious at managing neuropathic pain. Although their exact mechanism of action is not clear, antidepressants have been shown to improve chronic pain in as quickly as a few days' time, whereas weeks are required before mood benefits become evident (19). Commonly utilized antidepressants for neuropathic pain include tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SNRIs). To some extent, TCAs and SNRIs both inhibit the reuptake of noradrenaline transport-

Table 2. *Evidence based interventions for ilioinguinal neuralgia.*

		Level A Data derived from multiple randomized clinical trials or meta-analysis	Level B Data derived from a single randomized trial or nonrandomized studies	Level C Only consensus opinion of experts, case studies or standard of care
Least invasive	Conservative Treatment	- Lunn et al (24) (meta-analysis) - Duehmke et al (28) (meta-analysis) - Cooper et al (29) (meta-analysis) - Gaskell (30) (meta-analysis)	- Wiffen et al (15) (systematic review) - Darry et al (18) (systematic review) - Binder et al (27) (double-blind, placebo controlled, parallel-group, multicenter study)	- Kachiko et al (12) (case report) - Sommer et al (32) (narrative review)
Injectionable Interventions	Radio Frequency Ablation		-Kastler et al (40) (retrospective comparison cohort study)	
	Cryoablation			- Chiles et al (42) (case report) targeting femoral component of genitofemoral nerve
	Selective Spinal Nerve Block		-Kale et al (43) (retrospective study)	
	Anesthetic Block of IIN		- Lim et al (36) (randomized single blind study) -Khedkar et al (39) (randomized prospective observational study)	- Kulacoglu et al (35) (cadeveric study)
	Botox Injection			- Tereshko et al (41) (case report)
Neuromodulation	Spinal Cord Stimulation		- Lepski et al (46) (prospective study) - Yakovlev et al (44) (prospective study) - Levine et al (47) (prospective study)	- Elias et al (41) (case report)
	Peripheral Nerve Stimulation		- Lepski et al (46) (prospective study)	- Stinson et al (48) (case report) - Rauchwerger, Paicius (50) (case series) - Reddy (53) (retrospective case series) - Staats et al (54) (case report)
	Dorsal Root Ganglion Stimulation		- Deer et al (56) (randomized comparative trial) - Kretzschmar et al (58) (prospective study) - Mol et al (59) (multicenter, randomized controlled study)	- Bullis et al (61) (case series)
Most Invasive	Surgical Neurectomy		- Kim et al (62) (retrospective review) - Rosen et al (63) (prospective study)	

ers (20). This increase in noradrenaline in turn drives the inhibition of calcium channels in the dorsal horn of the spinal cord by way of inhibitory G protein-coupled alpha-2 adrenergic receptors. Loss of calcium prevents the release of excitatory neurotransmitters in the primary afferent (pain-relaying) fibers. Concurrently, the G protein-coupled receptors also open potassium channels, which hyperpolarize the postsynaptic spinal cord dorsal horn and prevent the propagation of action potential (21). TCAs for neuropathic pain should be used with caution, since these medications tend to affect multiple targets and cause side effects such as dry mouth, urinary retention, constipation, and other anti-cholinergic symptoms (22). The recommended daily dose of TCAs is under 100 mg (23). Meanwhile, the use of SNRIs for neuropathic pain has been studied extensively. In a meta-analysis by Lunn et al (24), 18 trials encompassing 6,407 patients showed efficacy in pain reduction with duloxetine doses ranging from 60 mg to 120 mg daily for patients with diabetic neuropathy. According to the Lunn et al study, no efficacy was appreciated at lower doses. The same study noted lower-to-moderate-quality evidence supporting duloxetine for the treatment of other chronic pain

syndromes, such as fibromyalgia (24). Side effects of SNRIs include diarrhea, constipation, loss of appetite, and sexual dysfunction (25).

Generally used as a medication of last resort when the above approaches show minimal benefit for the patient, opiates are a strong analgesic for neuropathic pain. Opioids are primary agonists at the mu-opioid receptor, propagating decreased pain sensation (26). Based on their affinity to the receptor, opioids can be classified as low-potency or high-potency. Due to the addictive properties of opioids, it is imperative to administer them to patients at the medications' lowest efficacious dose (27). Initially, tramadol can be used, which is a partial mu agonist that also has effects on serotonin reuptake. In a meta-analysis of 6 randomized, double-blind studies involving 438 patients, tramadol at daily doses of 100 mg to 400 mg offered at least a 50% reduction in pain (28). Stronger opioids include morphine and oxycodone. A meta-analysis of 5 randomized, double-blind, cross-over studies encompassing 236 patients who took morphine at doses of 90 mg to 180 mg per day concluded that there was insufficient evidence to support or refute the use of oral morphine as a treatment for neuropathy (29). Similarly, a meta-analysis of 5 studies encompassing 687 patients diagnosed with either painful diabetic neuropathy or postherpetic neuralgia found very low-quality evidence that oxycodone at any dose was a valuable treatment option (30). Side effects of opioids include respiratory depression, sedation, dizziness, nausea, vomiting, constipation, and physical dependence (31).

Topical Therapies for Neuropathic Pain

Currently, 2 topical therapies can be used for neuropathic pain: lidocaine 5% patches and capsaicin 8% patches. Notably, when compared to pregabalin for the treatment of peripheral neuropathic pain etiologies, capsaicin 8% patches demonstrated noninferior efficacy, and lidocaine 5% patches also demonstrated efficacy (although theirs did not qualify as non-inferior) (32). Analgesic effects can be observed within a few days of starting patch treatment. In a double-blind, placebo-controlled, parallel-group, multicenter study, 265 patients with postherpetic neuralgia were treated with 5% lidocaine patches for 12 hours per day. Of the patients, 51.7% reported at least moderate pain relief over that which they experienced with the placebo, expressing notable improvement in pain, allodynia, quality of life, and sleep (33). Emerging trends within the literature also support conjunction therapies with oral and topical modalities, particularly for the sake of decreasing opioid dosages. Unfortunately, the relief obtained from topical therapies is fairly short-lived and often disappears after patch removal (34). Due to the patches' minimal effect on cutaneous A-beta fibers, cutaneous anesthesia is usually not observed. The primary side effect to be wary of when considering either of these topical therapies for neuropathic pain is skin irritation at the site of application (34).

Invasive Pain Management Strategies

Nerve Blocks

Historically, ilioinguinal nerve blocks were commonly performed with a blind technique, which involved injecting local anesthetic close to the ASIS and into the planes between the external and internal oblique muscles or the internal and transverse muscles (35). However, the blind technique has a failure rate of up to 30% and is associated with adverse effects, such as colonic puncture and femoral nerve palsy (36-38).

A study comparing the conventional blind technique to ultrasound-guided nerve blocks found that the ultrasound-guided technique resulted in an earlier onset of sensory and motor blocks and decreased dose requirements. In the conventional group, patients were injected with anesthetic 2 cm medially and 2 cm caudally to the ASIS. The ultrasound-guided technique involved direct visualization of the ilioinguinal nerve between the transverse abdominis and the internal oblique (39).

Radiofrequency Ablation

Radiofrequency ablation may be utilized for patients who have demonstrated pain reduction after nerve blocks. A retrospective comparison cohort study of 42 patients found that the patients who underwent radiofrequency ablation of the ilioinguinal nerve experienced a significantly longer duration of pain relief (12.5 months) than did those who underwent local anesthetic infiltration to the ilioinguinal nerve (1.6 months) (40).

Botox Injections

Botulinum toxin type A has been used in cases of refractory genitofemoral neuralgia. A case report described a 78-year-old woman who received 3 treatments of botulinum toxin injections, resulting in a significant temporary relief of symptoms (41). While this case involved genitofemoral neuralgia, the approach may be applicable to ilioinguinal neuralgia, pending further trials to determine the efficacy of the treatment.

Cryoablation

Cryoablation has been used to target the femoral component of the genitofemoral nerve in patients with chronic groin pain. A case report noted that a patient experienced complete pain relief at a 2-month follow-up after a cryoablation procedure (42). This technique may also be effective for pain related to the ilioinguinal nerve.

Selective Spinal Nerve Block

Selective spinal nerve blocks have been employed for patients whose groin pain did not respond to peripheral nerve blocks. A retrospective study involving 17 patients with ilioinguinal, iliohypogastric, and genitofemoral neuralgia found that 4 patients who did not reach substantial relief with peripheral nerve blocks subsequently underwent T12 and L1 selective spinal nerve blocks and thereafter experienced improvements in or the resolution of the pain (43).

Neuromodulation

Spinal Cord Stimulation

Spinal cord stimulation (SCS) is a well-established treatment for chronic neuropathic pain. A study following 15 patients with chronic postoperative groin pain who received spinal cord stimulators reported that all 15 patients experienced pain reduction of over 75% at 12 months, according to the visual analog scale (VAS) (44). Another case report detailed 2 patients with intractable post-herniorrhaphy pain who found relief with SCS (45).

A prospective study compared SCS with peripheral nerve stimulation in 4 patients with persistent neuropathic post-hernia pain. The study demonstrated significant pain reduction during a 14-day trial phase, particularly when both spinal and inguinal electrodes were activated (46).

Another prospective study compared SCS and dorsal nerve root stimulation in patients with various pain distributions, including groin pain. At 12 months, both groups showed comparable and statistically significant decreases in pain, improvements in quality of life, and reduced opioid dosages. However, groin pain is harder to target with SCS, highlighting the potential of peripheral nerve and dorsal nerve root stimulation for ilioinguinal neuralgia (47).

Peripheral Nerve Stimulation

Given that the pathology of ilioinguinal nerve pain is primarily peripheral, neuromodulation with peripheral nerve stimulation (PNS) implants is emerging as a novel treatment modality with promising outcomes. Most research in this space has come from case series. In 2001, Stinson et al reported 3 cases of peripheral nerve stimulator implantation for chronic pain after inguinal herniorrhaphy. At the baseline, the patients' pain scores ranged from 8 to 10 on the VAS. Six weeks after the implantation, patients reported a pain score of 0 (48). Subsequent case series have also shown pain reduction, varying from 6 to 12 months after implantation of the stimulators (49,50). In 2013, a combined spinal cord stimulator (SCS) and peripheral nerve field stimulation (PNFS) study was conducted by Lepski et al (51), who observed 4 cases and 36 controls. The baseline pain score of 7.2 decreased to 4.7 with PNFS, 3.4 with SCS, and 2.4 with combined stimulation, averaged 3 days after implantation.

Among all studies conducted, it was important to have a stringent selection process for the implantation of nerve stimulators. Pre-implantation requirements included previously failed treatments, psychiatric evaluations, and a 3-5-day trial with temporary stimulator placement (52).

A unique, short, in-office trial method for PNS candidates is described by Reddy et al (53). They used an Arrow® StimuCath® kit (Teleflex Technologies) and ultrasound guidance to approach target nerves with lead wires and stimulate them for 30 minutes while monitoring patients' pain scoring as reported on the VAS. A trial was considered successful if the patient achieved greater than 50% reduction in pain. Reddy et al (53) found no difference between traditional trialing methods and the use of the Arrow® StimuCath® kit for 17 patients who were followed for a mean duration of 3 years after permanent PNS implantation.

With advancements in technology, the size of the stimulator has decreased drastically, resulting in the micro-implantable pulse generator (micro-IPG). Preliminary case reports have shown pain ratings decreasing from 6/10 to 1/10 at 3 and 6 months post-implantation. These devices are well tolerated—their smaller size reduces pain associated with stimulator location, and each has an 18-year service life (54).

Dorsal Root Ganglion Stimulation

A newly emerging technology in neuromodulation is dorsal root ganglion (DRG) stimulation, which has been effective in providing analgesia for various neuropathic pain syndromes. Although DRG stimulators are not pure spinal cord stimulators, the former are associated with complications, such as migration of leads and positional variance (55). In a randomized comparative trial known

as ACCURATE, analgesic effects by way of DRG stimulation were compared directly to traditional SCS in patients diagnosed with complex regional pain syndrome of the lower extremities. Interestingly, DRG stimulation was associated with greater efficacy, improvements in quality of life, better psychological dispositions, and less postural variation in stimulation (56). Complications to consider with DRG implants include pain at the pulse generator pocket site, lead fracture, lead migration, and infections (57).

Because ilioinguinal neuralgia often has a traumatic etiology, the use of DRG stimulation for treatment of pain caused by trauma to peripheral nerve injuries was studied by Kretzschmar et al (58) in 2021. They found significant pain relief ($P < 0.001$) at 3 (58%), 12 (66%), 18 (69%), 24 (71%), and 36 months (73%) in 21 patients, respectively. To study post-surgical inguinal pain specifically, the SMASHING (Spinal Modulation After failed Surgery for chronic pain following Hernia treatment in INGuinal area) trial was initiated by Mol et al (59) in 2018. Their target population was patients who did not respond favorably to previous pain treatment regimens (including neurectomy) for post-surgical inguinal pain due to an open hernia repair or Pfannenstiel incision (59). Unfortunately, the trial failed to enroll the researchers' target of 78 patients and conducted data analysis on only the 18 who were enrolled. Notably, Mol et al (59) observed an average pain reduction of 50% with DRG stimulation. However, 9 of 15 patients who met the endpoint criteria suffered adverse events, such as lead dislocation or pocket pain (60). More specifically, a case series with 7 patients—five of whom had a pre-existing diagnosis of ilioinguinal neuralgia and 2 of whom had well-defined chronic neuropathic pain in the penis and groin—showed that 6 of the patients experienced 80% or greater pain relief with DRG stimulation at T12, L1, and/or L2 (61).

Surgical

Surgical interventions are reserved for intractable cases in which all previous management techniques, such as conservative measures and anesthetic blocks of the nerve, have failed. Surgically, a neurectomy is performed, in which the nerve is dissected in the region proximal to previous trauma (62). This surgery can be performed laparoscopically or openly, and good patient satisfaction and pain improvement can occur with either approach (63).

Limitations

Further study is needed to determine which treatments will best address differing patient needs, etiology of injury, character of pain, and level of disability. Attempts were made to gather studies from large databases. However, we acknowledge that those efforts did not cover all known publications about the management of ilioinguinal neuralgia.

Conclusions

Based on the literary review, the treatment method for ilioinguinal neuralgia with the strongest level of evidence in its favor is taking conservative measures, including topical and oral medications. Injection-based interventions and neuromodulation approaches have been developed in the past few years but lack level A evidence from studies such as multiple randomized clinical trials or meta-analyses. The most invasive treatment discussed is surgical neurectomy, which also lacks level A evidence but has garnered support from retrospective reviews and prospective studies. A summarized approach to diagnosing and treating ilioinguinal is shown in Fig. 1.

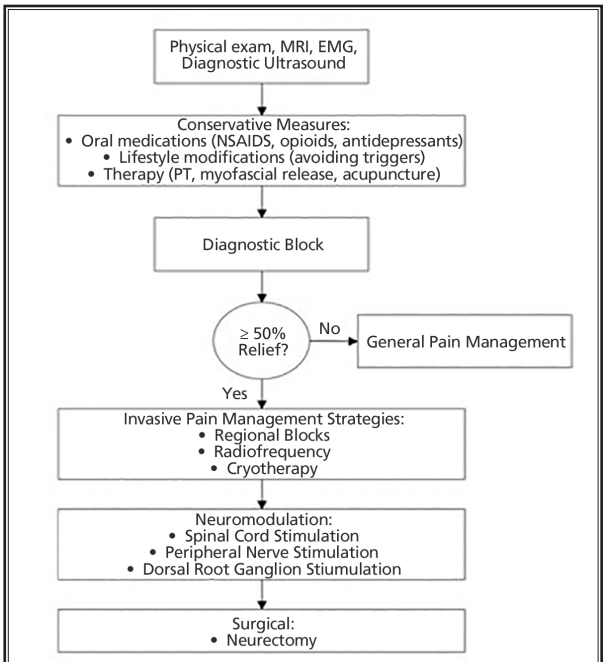

Fig. 1. *A methodical approach to diagnosis and treatment.* Adapted and modified from Liem L and Mekhail N. Management of post-herniorrhaphy chronic neuropathic groin pain: a role for dorsal root ganglion stimulation. *Pain Practice* 2016:7:915-923

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