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Literature Review

RECENT ADVANCES IN INTERVENTIONAL PAIN MANAGEMENT

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ABSTRACT

Introduction: Due to limited access to therapy, 60 million individuals worldwide suffer from chronic pain, with a frequency of 20–25% in some nations. Low- and middle-income countries (LMICs) are disproportionately affected by this condition. The yearly cost of diabetes, cancer, and heart disease—including medical expenses, lost productivity, and disability programs—is less than that of pain complaints. Pain management techniques, the most recent discoveries in pain research, and the most recent advancements in pain therapy technology can work together to reduce the prevalence of chronic pain and lessen the financial burden that comes with pain syndrome. **Objective**: To determine the extent to which the latest technological developments in interventional pain management to personalized treatment techniques according to patient complaints and conditions. The scope of technological development here is not only pain intervention techniques but also advances in understanding the pathophysiology of pain, nerve and tissue regeneration, as well as the modalities of technology used for pain interventions. **Review:** By conducting literature searches including journals, systematic reviews, library surveys, and case reports from the last 10 years on the latest interventional pain management techniques and serial cases. **Summary:** Many new minimally invasive pain intervention techniques have been developed and used in the treatment of chronic pain within the past 10 years. The necessity for standardization of processes, safety, efficacy, cost, and accessibility to new technology and techniques are among the issues and debates surrounding technical advancements and strategies for managing chronic pain. Intervention pain management techniques have grown in importance as a less intrusive method of treating chronic pain. For optimal outcomes, used in conjunction with other pain management modalities such as medication, physical therapy, cognitive behavioral change therapy, and others.

Keywords: Access and Essential Health Care Services; Chronic Pain; Coblation; Cryoneurolysis; Interventional Pain Management

ABSTRAK

Pendahuluan: Secara global, ada 60 juta orang yang menderita nyeri kronis, dengan prevalensi berkisar antara 20 dan 25 persen di beberapa negara. Karena keterbatasan akses ke perawatan medis, penyakit ini berdampak secara tidak proporsional pada negara-negara berpenghasilan rendah dan menengah (LMIC). Biaya tahunan untuk penyakit jantung, kanker, dan diabetes, termasuk biaya medis, program disabilitas, dan penurunan produktivitas, lebih rendah daripada biaya untuk keluhan nyeri. Kemajuan dalam penelitian fisiologi nyeri dan teknologi terapi nyeri terbaru dapat membantu mengurangi jumlah kasus nyeri kronis dan biaya yang disebabkan oleh sindrom nyeri. Kombinasi dari berbagai metode penanganan nyeri dapat membantu mengurangi jumlah uang yang dihabiskan karena sindrom nyeri. **Tujuan:** Untuk menentukan sejauh mana perkembangan teknologi terbaru dalam manajemen nyeri intervensional untuk mencapai teknik pengobatan yang dipersonalisasi sesuai dengan keluhan dan kondisi pasien. Menggunakan teknologi tidak hanya untuk mengatur nyeri, tetapi juga untuk mengerti nyeri patofisiologi, regenerasi saraf dan jaringan, serta modalitas teknologi yang digunakan untuk mengatur nyeri. **Review**: Dilakukan dengan cara melakukan pencarian literatur termasuk jurnal, tinjauan sistematis, tinjaun Pustaka dan laporan kasus dari 10 tahun terakhir tentang teknik dan manajemen nyeri intervensional yang terbaru, baik yang sudah teruji maupun yang masih dalam tahap serial kasus. **Kesimpulan**: Dalam sepuluh tahun

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terakhir, sejumlah teknik intervensi nyeri yang minimal invasif telah ditemukan dan digunakan dalam pengobatan nyeri kronis. Teknik manajemen nyeri intervensi telah menjadi bagian penting dari pengobatan nyeri kronis dengan cara yang minimal invasif. Untuk mencapai hasil terbaik, teknik ini harus digunakan bersama dengan modalitas nyeri tambahan seperti obat-obatan, fisioterapi, terapi perubahan, dan terapi lain. Namun, ada tantangan dan kontroversi terkait standarisasi prosedur, keamanan, efektivitas, dan biaya.

Kata kunci: Akses dan Layanan Perawatan Kesehatan Penting; Nyeri Kronis; Koblasi; Krioneurolisis; Manajemen Nyeri Intervensional

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INTRODUCTION

Pain is a reflexivity that encompasses sensory, affective, and cognitive components, making it challenging to define, characterize, and understand (1). Pain is often seen as a failure of healthcare efforts to address the underlying cause, which frequently worsens and evolves into chronic pain. The 2010 Global Burden of Disease (GBD) study revealed that 1-4% of the global population suffers from chronic back pain, which is associated with both somatic and psychological disorders. On a global scale, disability is the primary cause of this condition, which is largely unknown (2). Arthritis and cancer cases continue to rise year after year, putting a strain on the healthcare system in terms of addressing the causes. Resulting in rising medical costs and decreased productivity (3,4).

According to the 2008 Medical Expenditure Panel Survey (MEPS), heart disease ($309 billion), cancer ($243 billion), and diabetes ($188 billion) are less expensive than pain-related healthcare in the US. These expenses, which include lost productivity, disability programs, and medical bills, vary from $299 to $335 billion (5,6). The opioid crisis in the US and Canada, the side effects of opioid usage, and the failure of non-pharmacological therapies to reduce pain and lower maintenance expenses are some of the additional difficulties associated with managing persistent pain (7,8).

Combining new pain management methods with the latest advances in pain physiology research and pain therapy technology will create new opportunities for reducing the incidence of chronic pain and lowering the financial burden due to pain syndrome (9). By better understanding the concept of multifaceted pain, existing technologies, and methods can be applied in parallel. Healthcare providers can provide individualized care that is tailored to each patient's condition through internal and external technologies, pharmacotherapy, and evolving surgical and percutaneous techniques with a variety of patient management options, including medications, non-pharmacological approaches, and interventional techniques (10). Treating patients with compassion and precision can lessen the toll that chronic pain has on individuals, their families, and the healthcare system as a whole.

REVIEW

History of Pain Management

Pain management has been practiced since ancient times. The Code of Hammurabi, which consists of 282 ancient Mesopotamian laws, includes provisions for pain treatment. The Edwin Smith Papyrus, a medical manuscript from around 1500 BC, describes techniques for pain management, reflecting the Egyptians' evolving understanding of pain control. Galen, a Greek physician, developed a method of pain

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management based on the concept of balance. Both the Greeks and Romans had a thorough understanding of how to manage pain (11).

Subsequently, there was an increase in the use of the opium plant as a medication, willow bark, and leaves as natural sources of salicylic acid, pain pathways, ether and chloroform for anesthesia, cocaine, morphine, and heroin, as well as minimally invasive methods for pain intervention such as radiofrequency and vertebral augmentation (vertebroplasty and kyphoplasty) in later stages (12). The least invasive nerve interventions can utilize ultrasonography and fluoroscopy. This study focuses on techniques that use fluoroscopy. Literature searches include journal articles, original research, systematic reviews, and case studies on the application of new technologies for health interventions and the need for such advancements in the coming years.

Advancement in Pain Intervention Techniques

1. Regenerative Medicine

The growth of healthcare has led to a shift in the paradigm, moving away from viewing illness solely as a threat and preventing its spread (13). Inflammatory conditions, matrix-degrading enzymes and their upstream effectors, vascular and nerve ingrowth, and cellular aging are all examples of catabolic processes that could be stopped by regenerative therapy. Moreover, boosting cell division and the availability of anabolic growth hormones and antioxidants might improve anabolic processes. In regenerative medicine, viscosupplementation, prolotherapy, platelet-rich plasma, and mesenchymal stem cells are the main techniques for managing pain.

A. Viscosupplementation

The viscosity and flexibility of osteoarthritic synovial fluid can be restored by injecting hyaluronic acid (HA) into the intra-articular region. HA is essential for lubrication, stress absorption, and the viscoelastic characteristics of synovial fluid (14).

B. Proloterapy

The injection of a remedy known as proloterapy encourages sclerosis at the injection site and restores an inadequate structure. Unlike other regenerative medicine procedures, pluritherapy uses an injectate that is devoid of any biological component. Hypertonic dextrose is the most often utilized prolotherapy solution because it triggers the body's inflammatory cascade (15).

C. Platelet-rich plasma

Because platelet-rich plasma (PRP) has regenerative, analgesic, and anti-inflammatory properties, it produces bioactive proteins that promote the body's ability to repair (16).

D. Mesenchymal Stem Cells (MSC)

Adipose tissue and bone marrow MSCs can develop into adipogenic, chondrogenic, and osteogenic lineages. By repairing disc tissue and regulating nociceptive pain, MSCs can lessen lower back discomfort. However, a constraint on long-term results is MSC survival (12,15).

2. Neuromodulation Techniques

Techniques that use chemicals or electrical stimulation to change the activity of neurons. Neuromodulation modifies the activity of neurons and neural circuits to influence a range

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of physiological and psychological processes. Neuromodulation modifies the excitability or responsiveness of neurons to other stimuli, as opposed to direct stimulation, which elicits a response. Chemical, electrical, and bioelectrical neuromodulation are some of the classes into which neuromodulation methods are divided into several classes (16).

Table 1. Mechanisms of Neuromodulation (16).

No	Mechanism	Groups	Mode of Action
1	Chemical Neuromodulation	Neurotransmitter	Chemicals such as dopamine, serotonin, and norepinephrine modulate neuronal activity. Imbalances can affect mood, cognition, and behavior.
		Neuromodulator	Substances such as acetylcholine and neuropeptides modulate neurotransmitter release or receptor sensitivity.
2	Neuromodulasi of electrics	Deep Brain Stimulation	Involves implanting electrodes in specific areas of the brain to treat disorders such as Parkinson's disease and depression.
		Transcranial Magnetic Stimulation	Non-invasive methods that use magnetic fields to stimulate nerve cells in the brain, are often used in the treatment of depression.
		Transcranial Direct Current Stimulation	Uses low electrical currents applied to the scalp to modulate brain activity.
3	Bioelectronics	Vagus Nerve Stimulation	Implantation of a device to stimulate the vagus nerve, used for epilepsy and depression.
		Sacral Nerve Stimulation	To treat bladder control issues and chronic pain by stimulating the sacral nerve.
4	Gene therapy	Genetic modulation	Modifying gene expression to affect neuron function or repair damaged neural circuits.

Table 2. Various Invasive Neuromodulation Technologies for Pain Intervention and Their Major Indications (12) (16) (17)

No	Invasive Neuromodulation Technology	Major Indications
1	Stimulation of the Spinal Cord (SCS)	Complex regional pain syndrome (CRPS), the syndrome of failed back surgery, neuropathic pain, such as diabetic neuropathy, Peripheral vascular disease, and vascular discomfort
2	Stimulation of the Dorsal Root Ganglion (DRG)	Neural discomfort for the hands, chest, abdomen, foot, knee, or groin associated with focal CRPS
3	The stimulation of peripheral nerves (PNS)	Discrete neuropathies, headache acute pain, neuropathic pain, and chronic pain
4	DBS, or deep brain stimulation	Phantom limb pain (CRPS), discrete neuropathies neurodegenerative conditions such as Parkinson's disease
5	Neurostimulation for Restorative	Persistent low back ache caused by machinery
6	Pump-Based Intrathecal Drug Delivery	Pain associated with cancer Incongruity

Pain-transmitting sensory neurons are destroyed using radiofrequency (RF). Over 70 years, this method has improved to reduce tissue damage and regulate lesion size. Nociceptive pain, including facet joint arthralgia, sacroiliac joint pain, and discogenic low back pain, responds better to radiofrequency (RF) treatment. Novel approaches, such as pulsed RF and bipolar RF, expand pain treatment options. To stimulate peripheral nerves and lessen pain, a procedure known as peripheral neurostimulation (PNS) entails implanting electrodes close to peripheral nerves (16).

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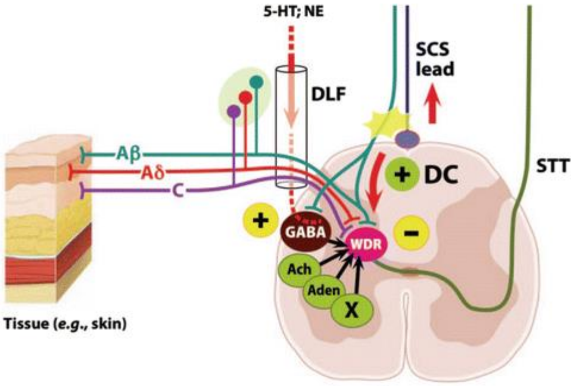

Figure 1. Segmental Spinal and Supraspinal Regulation using Neurotransmitters including GABA, Acetylcholine, and Adenosine is Required for SCS-Mediated Pain Alleviation (18).

3. Neuroablative Procedures

Techniques in medicine include removing or destroying a section of the nerve tissue to cure a range of neurological illnesses. The main goal of these procedures is to manage nerve anomalies that are difficult to treat with other means or to reduce pain. Well-established neuroablative techniques include chemical neurolysis, pulsed radiofrequency, radiofrequency ablation (RFA), and electrothermal therapy.

Table 3. Long-established Neuroablative Procedures (16).

No	Procedure of Neuroablation	Technique	Indication
1	Radiofrequency Ablation (RFA)	This technique uses radiofrequency waves to heat and destroy nerve tissue that causes pain. Electrodes are placed near the target nerve, and radiofrequency energy is used to heat and destroy portion of the nerve.	The treatment targets hronic pain, including lower back, neck, and joint pain.
2	Chemical Neurolysis	Injection of chemicals, such as phenol or alcohol, into nerve tissue to destroy the nerve. These chemicals cause nerve cell death and reduce pain.	Used to manage chronic pain, especially when other methods are ineffective.
3	Pulsed Radiofrequency	This technique involves using pulsed radiofrequency waves to stimulate nerves without causing permanent damage. It can reduce pain differently compared to RFA.	Neuropathic pain and chronic pain that is difficult to treat
4	Electrothermal Therapy	This procedure uses electrical energy to generate heat that destroys nerve tissue. Electrodes are inserted into the target area, and heat is produced to destroy the painful tissue.	Joint pain and lower back pain.

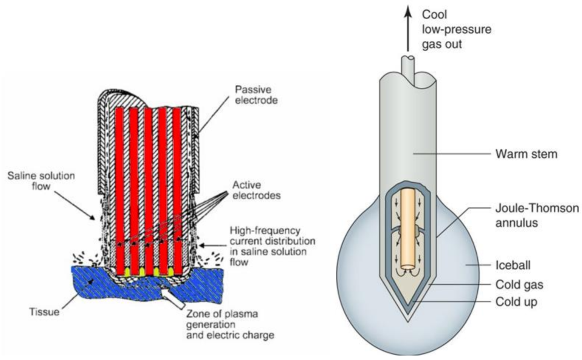

Figure 2. The Mechanism of Coblation and Cryoneurolysis (22).

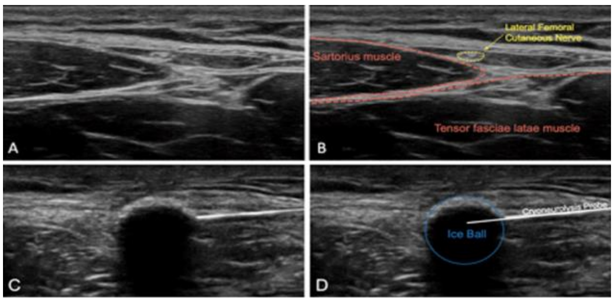

Figure 3. Cryoneurolisis to the Lateral Femoral Cutaneous Nerve (23).

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Table 4. Recent Neuroablative Procedure (16).

No	Procedure of Neuroablation	Technique	Indication
1	Coblation	Non-heat-driven process of tissue dissolution. Plasma generates hydrogen (H) and hydroxyl (OH) ions. The OH radicals cause protein degradation. This technique works by using low-pressure plasma energy to cut or destroy tissue. The energy is produced from ionized gas (usually argon) flowing through electrodes and directed to the target tissue. This process generates relatively low temperatures, reducing the risk of damage to surrounding tissues.	Phantom limb and stump discomfort. Peripheral nerve treatments may be more successful than neuroma, orthopedic surgery for trigeminal neuralgia, disc herniation, cervical discogenic pain, and tendinitis (19–22).
2	Cryoneurolysis	The procedure involves cooling the nerve to cause damage to the vasa nervorum (the blood vessels supplying the nerve). This results in endoneurial edema (swelling within the nerve sheath), increased pressure, and subsequent axonal destruction (damage to the nerve fibers). The target temperature is between -20 and -100^{0}C.	It is effective in treating acute pain such as chest wall pain after surgery or trauma, chronic pain in knee osteoarthritis, chronic head pain et causa occipital neuralgia, and specific nerves such as lateral femoral cutaneous, and neuropathic pain (23,24).
3	Basivertebral nerve (BVN) ablation	Methods that injure the spinal nerve. Disc degeneration is one possible cause of chronic low back pain and has been consistently linked to it. The vertebral endplates next to each disk play a crucial role in the pathologic disease presentations and increase the vulnerability to inflammation and damage. They maintain the balance between providing structural support for the spine and serving as the main blood and nutrient supply pathway for the disc.	Vertebrogenic pain. The following patient requirements apply to basivertebral nerve ablation: type 1 or type 2 modic alterations at one or more levels from L3-S1, as well as chronic low back pain for whom conservative treatment has been tried for more than six months (16).

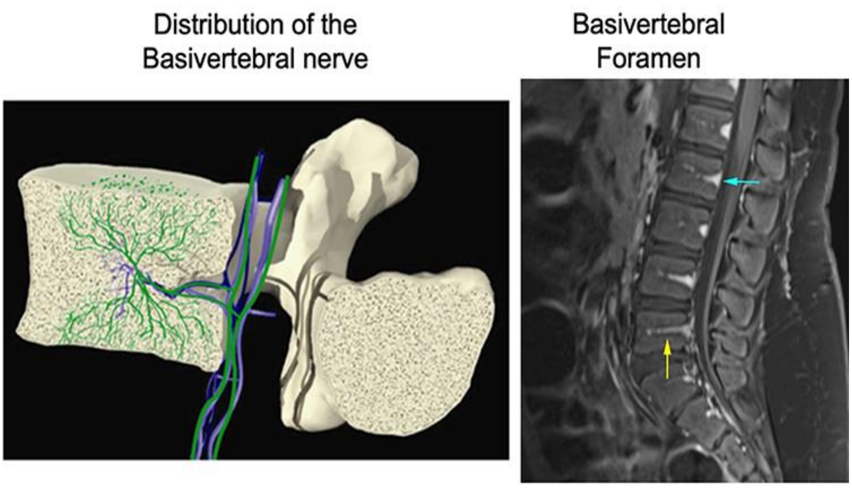

Figure 4. Distribution of Basivertebral Nerve dan Foramen (16).

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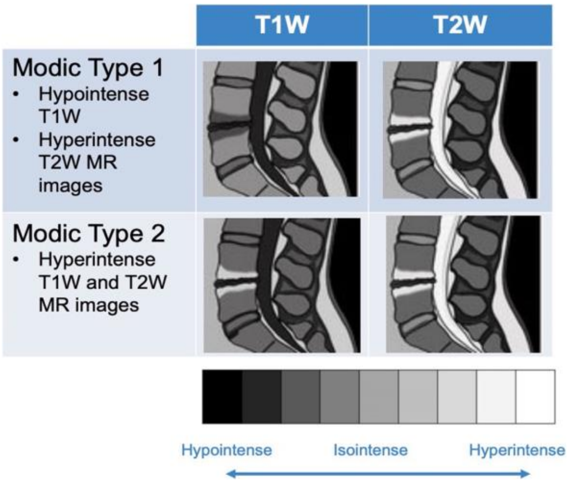

Figure 5. Modic Changes. (Photo credit: Relievant Medsystems. All rights reserved. 2021) (16).

The first human subjects BVN ablation pilot experiment was carried out in 2017 by Becker et al. The study included 17 patients with MC1 or MC2 abnormalities and chronic low back pain (CLBP) who had either received conservative treatment or had been treated for six months. For this cohort, the baseline values of the Oswestry Disability Index (ODI) were 52 and the Visual Analog Scale (VAS) was 61. During the 3-month follow-up after surgery, both the VAS and the ODI showed statistically significant improvement; the ODI dropped by 29 points to an average of 23. Sustained improvement was also seen in the 12-month follow-up (12).

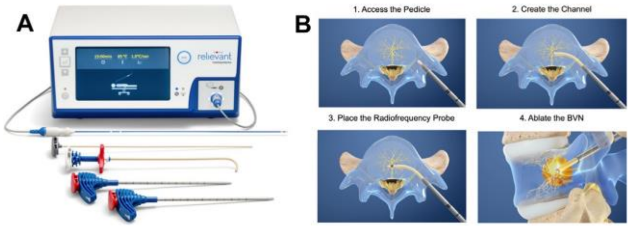

Figure 6. Intraceptive Technique. (A): Intracept apparatus. The Intracept Steps (B). (Photos by Relievant Medsystems. All rights reserved. a2021) (16).

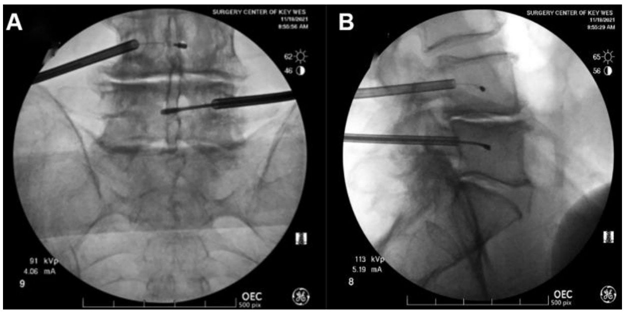

Figure 7. The X-ray View in AP and Lateral for Basivertebral Nerveablation (16).

Table 5. MILD technique (16, 25–28)

Major options	Advantages	Disadvantages	Technique and procedures	Indication
Direct decompression	Minimum of invasive. Quick recovery, and Minimum of risk	Limited access	Percutaneous Discectomy Percutaneous Laser Discectomy Microscopic Decompression	Patients who are not likely to have favorable surgical results or who would choose a less invasive operation include those with central spinal stenosis, hypertrophy of the ligamentum flavum measuring more than 2.5 cm, and diseases with or without instability.
Indirect decompression	Less invasive reversible	Variable outcome Device complication	Interspinous spacer	Patients who are adults with moderate spinal stenosis who have attained skeletal maturity and are exhibiting symptoms.

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The procedure is performed unilaterally with the patient in a prone position; either general or conscious sedation is administered. Using standard anatomic landmarks, the location of the entry pedicle at each level to be treated is determined and marked. Under fluoroscopic guidance, an introducer cannula is advanced through the pedicle until the trocar just breaches the posterior vertebral wall. The introducer trocar is exchanged with a smaller plastic cannula/curved nitinol stylet assembly, which facilitates the creation of a curved path from the posterior wall to the pre-determined target located at the terminus of the BVN, located near the center of the vertebral body. Finally, the curved nitinol stylet is removed and an RF probe is introduced and positioned at the terminus of the BVN. The bipolar RF probe is activated and the temperature at the tip is maintained at a constant 85 °C for 15 min (Figure. 7)

4. Minimally Invasive Lumbar

A less intrusive method than standard surgical approaches, lumbar decompression (MILD) is a minimally invasive surgical technique intended to minimize scarring in the lower back. The most common ailments this surgery is used to treat include disc herniation, spinal stenosis, and posterior back discomfort. Neurogenic claudication, a severe condition, can result from degenerative constriction of the spinal canal, nerve roots, or foramen in individuals with symptomatic lumbar spinal stenosis (LSS) (29).

Ligamentum flavum or facet hypertrophy, osteophyte development, and intervertebral disc bulging are the three potential pathophysiologies for LSS. Functional disability, claudication, and compressive discomfort can result from any of these disorders. As of right now, there are primarily two methods available: direct decompression, which is frequently accomplished via a percutaneous method, and indirect decompression, which is accomplished with percutaneous interspinous spacers (16).

Percutaneous interspinous spacers can only be implanted at two consecutive levels in adult patients with up to symptomatic moderate spinal stenosis who satisfy the following requirements for placement: they must have been on conservative treatment for a minimum of six months.

Individuals with spinal stenosis extending from the L1-L2 level to the L4-L5, ligamentum flavum hypertrophy more than 2.5 cm, and central or lateral stenosis in particular. Using the percutaneus, do lumbar decompression. The main goal of percutaneous lumbar decompression is to debulk the ligamentum flavum and lamina using an epidurogram and image-guided dissection (16)

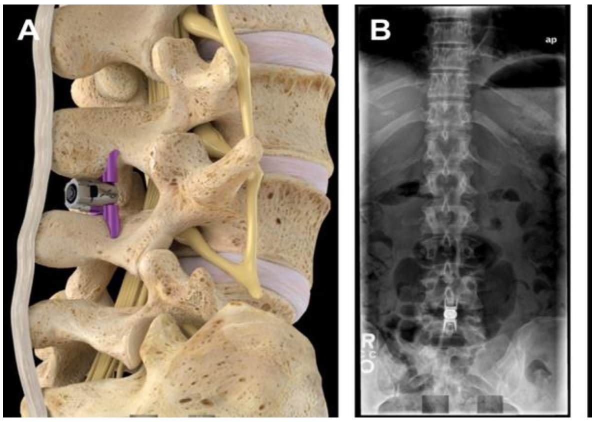

Figure 8. A. Percutaneous Interspinous Spacers Seen Laterally. B. Anteroposterior (AP) Radiography Image of the Interspinous Spacer's Final Location. (Figure supplied by Boston Scientific with permission) (16)

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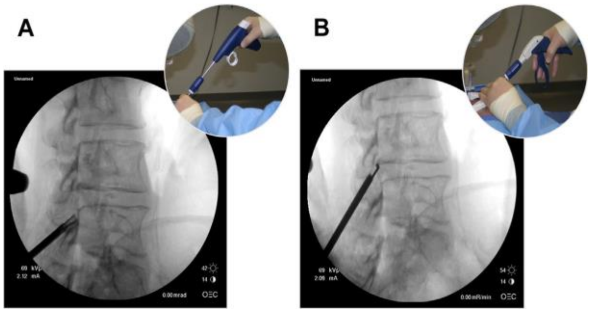

Figure 9. (A): Bone Rongeur: The Bone Rongeur is Introduced, and Lamina Pieces are Removed from the Superior and Inferior Lamina. **(B): Tissue Sculpter**: After Adequate Removal of the Lamina, the Tissue Sculpter is Introduced to Reduce the Ligamentum Flavum(16).

Pain management is a crucial component of healthcare to lessen suffering and improve the quality of life for patients with both acute and chronic pain. The best methods for managing pain effectively are as follows:

1. Through evaluation of history, physical examination, and psychosocial assessment.
2. Pain management through multiple modalities
   A. Pharmacologic treatments: When necessary, combine non-opioid analgesics (such as acetaminophen and NSAIDs), adjuvant drugs (such as antidepressants and anticonvulsants), and opioids.
   B. Non-medical interventions: For comprehensive pain management, combine chiropractic adjustments, acupuncture, physical therapy, and other non-pharmaceutical methods.
   C. Pain interventions: adjust the availability of human resources and technologies.
3. The patient-centred method consists of individualized care plans, patient education, and stewardship of opioids to avoid addiction and overdose. Adapt pain management techniques to the unique requirements and medical circumstances of the patient. Educate patients on the nature of their pain, available treatments, and the significance of following the recommended course of action.
4. Managing chronic pain with behavioural therapies and functional objectives.
5. Research and Education:
   A. Ongoing Training: Educate and train healthcare professionals on the most recent methods and best practices for managing pain.
   B. Clinical Research: Encourage and participate in research to create fresh approaches to pain management.

The challenges and controversy surrounding the use of technology and chronic nail art are as follows: there is a need for standardization in intervention techniques, patient identification, and the type of agent used to enhance treatment outcomes and consistency. Both efficiency and safety are critical, as all new techniques require extensive research to ensure their effectiveness and safety. Lastly, cost and accessibility are concerns because integrating new technology involves adjusting costs, accessibility, and training requirements for clinical practice (30).

When it comes to the future of pain management interventions, new technologies are continuously being developed, including more advanced stimulation systems and more precise pain assessment tools. It is expected that these innovations will enhance patient outcomes. However, further research is required to evaluate and optimize these new techniques and to establish more evidence-based practices.

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SUMMARY

Techniques for interventional pain treatment have grown in importance as a minimally invasive approach to managing chronic pain. While radiofrequency ablation, spinal cord stimulation, and nerve blocks are still common practices today, other methods including targeted drugs and regenerative medicine are now being used.

Technologies and approaches that make use of our growing understanding of the intricate details of human biology are developing at the same time. A pain management specialist of the future will be able to accurately evaluate each patient's condition with the use of internal and external technology, medications, and sophisticated surgical and percutaneous methods. Physicians may assist lower the risk of chronic illness for patients, their families, and the whole healthcare system by thoroughly and precisely examining their patients.

All things considered, the development of new technology and minimally invasive treatment approaches has given patients who struggle to control their pain new hope. These patients now have safer, more accurate solutions available to them.

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Conflict of Interest

The authors declare that there are no conflicts of interest related to this study.

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Authors' Contributions

1. Ratri Dwi Indriani: Contributed to the study design, data analysis, and manuscript writing.
2. Abdurrahman: Supervised the research and provided funding support.
3. Dedi Susila: Conducted the research and manuscript.
4. Muzaiwirin: Data collection.
5. Muhammad Ainur Rosyid Ridho: Assisted with data interpretation and provided critical revisions to the manuscript.

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