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REVIEW

Best Practice Guidelines on the Diagnosis and Treatment of Vertebrogenic Pain with Basivertebral Nerve Ablation from the American Society of Pain and Neuroscience

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Abstract: Chronic low back pain is a worldwide leading cause of pain and disability. Degenerative disc disease has been the presumptive etiology in the majority of cases of chronic low back pain (CLBP). More recent study and treatments have discovered that the vertebral endplates play a large role in CLBP in a term defined as vertebrogenic back pain. As the vertebral endplates are highly innervated via the basivertebral nerve (BVN), this has resulted in a reliable target in treating patients suffering from vertebrogenic low back pain (VLBP). The application of BVN ablation for patients suffering from VLBP is still in its early stages of adoption and integration into spine care pathways. BVN ablation is grounded in a solid foundation of both pre-clinical and clinical evidence. With the emergence of this therapeutic option, the American Society of Pain and Neuroscience (ASPN) identified the need for formal evidence-based guidelines for the proper identification and selection of patients for BVN ablation in patients with VLBP. ASPN formed a multidisciplinary work group tasked to examine the available literature and form best practice guidelines on this subject. Based on the United States Preventative Task Force (USPSTF) criteria for grading evidence, gives BVN ablation Level A grade evidence with high certainty that the net benefit is substantial in appropriately selected individuals.

Keywords: back pain, vertebrogenic pain, lumbar degenerative disc, radiofrequency ablation, basivertebral nerve, guidelines

Introduction: background and Pathophysiology of Vertebrogenic Pain

Degenerative disc disease (DDD) has been the presumptive source for a significant portion of chronic back pain cases. However, the advent of histological, immunological and radiological evidence has elucidated a precise etiology of a pain generator: the vertebral endplates, leading to vertebrogenic pain.[1] The endplates are involved in the salient role of dispersing adjacent intradiscal pressures to prevent disc bulging and provides nutrients to the disc via diffusion from the segmental spinal arteries within the endplates.[2] The basivertebral nerve (BVN), originating from the

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sinuvertebral nerves (SVN), enters the vertebral body through the central vascular foramen with branches into the superior and inferior endplates (Figure 1).[3,4] These nociceptive nerve fibers are the presumptive primary pain generators, and histological images denote the proliferation of nerve fibers at the endplates in the presence of disc degeneration.[4]

The highly innervated vertebral endplates can become susceptible to progressive degradation from physiological aging, calcifications, traumatic injuries, intraosseous edema, and localized inflammation (Figure 2). Insults to the vertebral endplates result in the secretion of proinflammatory and neurogenic factors, causing proliferation of basivertebral nerves at the endplate, thus increasing sensitivity to pain from compressive forces.[2] A protein arrays study has found increased levels of 20 inflammatory factors, with many having nociceptive effects within the damaged intravertebral discs. This induces neuronal plasticity and neo-innervation.[4,5] These factors can then further proliferate endplate damage by increasing the diffusion between the vertebral body and disc leading to further degradation, hence worsening vertebrogenic pain.

Dr. Modic, a radiologist, was the first physician to publish a classification of the degenerative changes of the endplate based on magnetic resonance imaging (MRI), with three types highlighting the evolutionary stages.[6] Type 1 denotes acute degeneration commonly associated with pain as fibrovascular changes occur within the subchondral bone marrow resulting in edema and inflammation. On MRI, the endplates are hypointense on T1 and hyperintense on T2-weight images. Type 2 classifies subacute and chronic changes as fatty bone marrow infiltration occurs within the vertebral body with the MRI demonstrating hyperintense signals on both T1 and T2 weighted images. The progression of chronic changes may lead to bony sclerosis at the endplates, observed within the Type 3 Modic classification. These changes are visible on MRI as hypointense on T1/T2.[6] A recently proposed scoring system ("Mo-di-disc") including Modic changes, fatty infiltration in the paraspinal muscles and disc degeneration was found to be the most significant predictor for patients with more intense low back pain.[7] Yet, although Modic type 1 and 2 changes are highly specific for low back pain,[2] MRI findings should always be correlated with clinical findings. Furthermore, the advent of MRI modalities with ultrashort time to echo (UTE) may help increase the sensitivity of perceived Modic changes as it increases visualization of the endplates, thus accurately identifying the vertebrogenic pathology (Figure 3).[2] Recently, it has been proposed that changes in disc degeneration through decades of human life along with Modic changes have specific gear-up periods in human life associated with disc degeneration, particularly increasing at the end of the 2nd decade and at the beginning of the 3rd decade, while Modic changes are more common at the end of the 4th and at the beginning of the 5th decade. Furthermore, the onset of severe intervertebral disc degeneration has been documented to be ahead of endplate changes

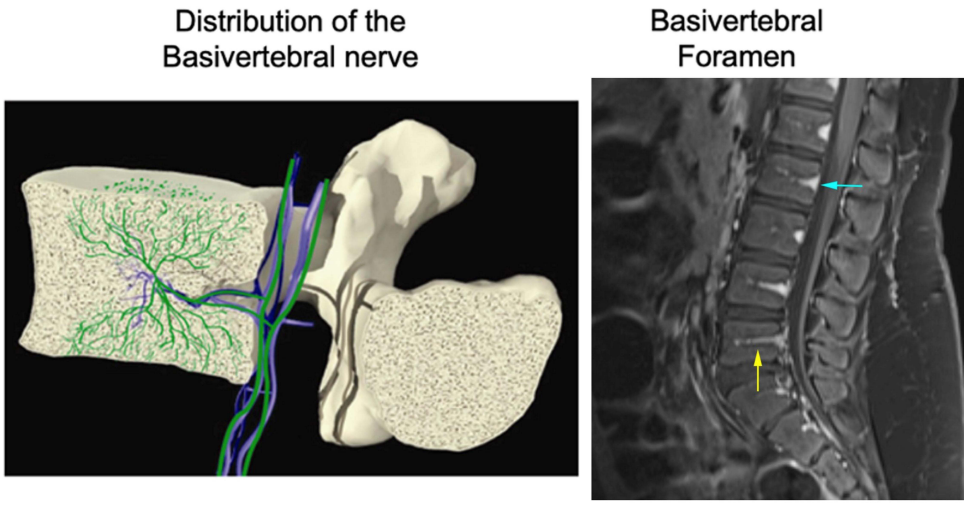

Figure 1 The BVN (white arrows) branches from the SVN as it enters the vertebral body through the central vascular foramen, accompanied by the basivertebral vessels, bifurcating to the endplates. Reprinted with permission from Fischgrund JS, Rhyne A, Franke J, et al. Intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 2-year results from 415 a prospective randomized double-blind sham-controlled multicenter study. Int J Spine Surg. 2019;13(2):110–119, Copyright © International Society for the Advancement of Spine Surgery 2019. Creative Commons licensing agreement CC BY-NC-ND.[3] Reprinted with permission from Traylor K, Murph D. Spinal Vascular Anatomy. The Neurosurgical Atlas. https://www.neurosurgicalatlas.com/volumes/neuroradiology/spinal-corddisorders/spinal-vascular-anatomy.[54]

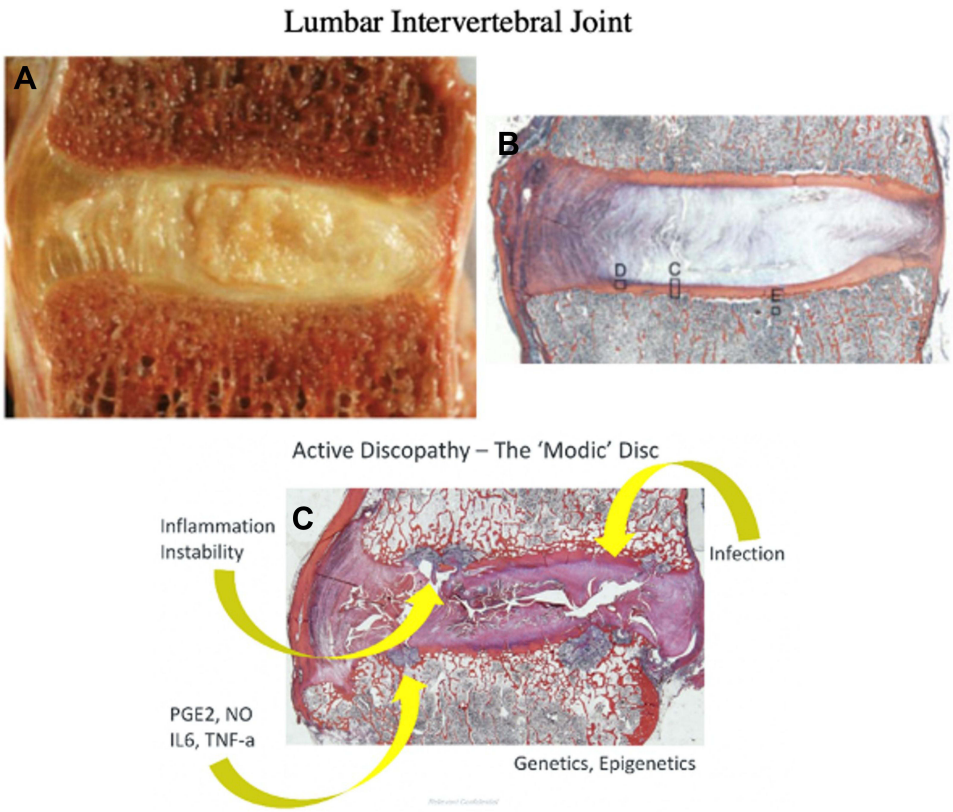

Figure 2 (**A**) Gross morphology of the lumbar intervertebral joint, (**B**) with the corresponding histological stain. (**C**) Histological depiction of endplate damage. Reproduced with permission from otz JC, Fields AJ, Liebenberg EC. The role of the vertebral end plate in low back pain. Global Spine J. 2013;3(3):153–164, Copyright 2013, SAGE Publication;[2] and Dudli S, Fields AJ, Samartzis D, Karppinen J, Lotz JC. Pathobiology of Modic changes. Eur Spine J. 2016;25(11):3723–3734, copyright 2016, Spring Nature.[55]

by nearly one decade, thus patients with vertebrogenic pain and endplate degeneration may require treatment for early on or at any time along this degenerative cascade course.[8]

Ongoing scientific evidence supports that pathological neurotization of the BVN may lead to significant disability by causing axial low back pain that is worse with sitting and forward flexion.[1] Therapeutic modalities aimed at ablation of the BVN have been shown to be very effective for the treatment of chronic low back pain (LBP).[1,9]

Evidence for BVN Ablation

Basivertebral nerve ablation (BVNA) is a specific intervention targeting chronic axial low back pain from a vertebrogenic etiology, phenotypically identified by vertebral endplate damage, often described as Modic changes on MRI.[6,10] Although vertebral endplate changes are a radiological finding characterized by endplate disruption, fissuring, degeneration and active inflammation, the nociceptive input from these damaged endplates is carried by the BVN, supporting the hypothesis that this is a particularly unique subset etiology of chronic axial low back pain. Numerous studies have reported a strong association of vertebrogenic pain to severe, debilitating, chronic, greater frequency and worse functional impairment, with pain refractory to conservative management.[2,11–16] Limited interventions exist to treat vertebrogenic pain, and for the past few years BVNA has gained significant attention due to numerous clinical trials and clinical reviews published examining clinical efficacy, safety and future considerations.[1,3,4,17–30]

Currently, there is one Food and Drug Administration (FDA) cleared procedural platform to ablate the BVN of the L3 through S1 vertebrae, indicated for patients with axial LBP greater than 6 months of duration who are refractory to conservative nonsurgical management and have evidence of type 1 and/or type 2 Modic changes of vertebral endplates on diagnostic images.[31,32] As of January 2022, two current procedural terminology (CPT) codes

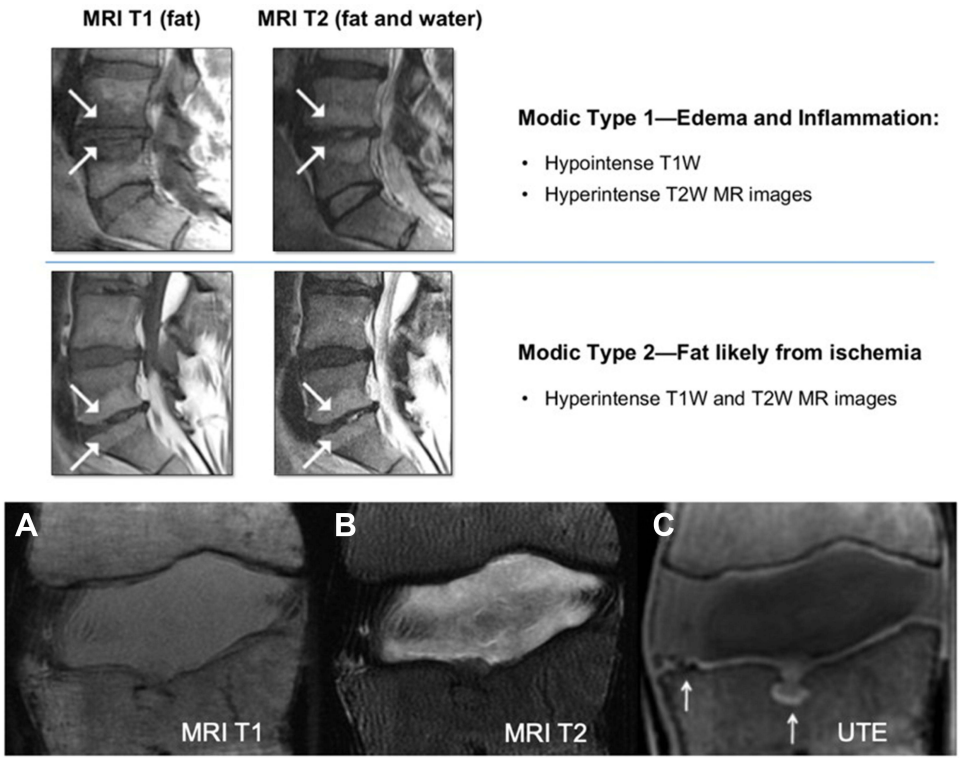

Figure 3 (Top) White arrows pointing to Modic changes appreciated on MRI T1/T2. (Bottom). (**A**) Midsagittal T1-weighted MRI; (**B**) T2-weighted MRI; and (**C**) ultra-short echo time (UTE) MRI, further elucidating endplate damage of L1-L2 motion segment. Reproduced with permission from Otz JC, Fields AJ, Liebenberg EC. The role of the vertebral end plate in low back pain. Global Spine J. 2013;3(3):153–164, Copyright 2013, SAGE Publication;[2] and Dudli S, Fields AJ, Samartzis D, Karppinen J, Lotz JC. Pathobiology of Modic changes. Eur Spine J. 2016;25(11):3723–3734, copyright 2016, Spring Nature.[55]

have been established to report the BVNA procedure, 64,628 (first two vertebral bodies) and 64,629 (each additional vertebral body). The diagnosis code that applies for this procedure is M54.51 (vertebrogenic low back pain/low back pain vertebral endplate pain).[31,33]

BVNA clinical evidence is supported by Level I randomized clinical trials and Level II studies with long-term data beyond five years endorsing a greater than 60% decrease in Oswestry Disability Index (ODI) functional scores from baseline, in addition to a greater than 65% decrease in pain, reported using the visual analog scale (VAS) sustainable at five years.[3,18,21,23] The most recent evidence described on a prospective, randomized, multicenter clinical study by Koreckij et al 2021 demonstrated significant improvement in pain, function and quality of life sustained through 24 months, with greater than 50% reduction in pain reported by 72% of subjects, with 31% of these being pain-free at 2-year follow-up and the study reported no serious adverse events.[1] Similarly, the prospective, open label, randomized controlled trial by Smuck et al 2021 exhibited significant improvement in pain and function in the BVNA treatment arm over standard of care arm, with treatment results sustained through 12 months. Furthermore, 64% of subjects in the BVNA treatment arm demonstrated greater than 50% improvement in pain scores and 29% were pain free, compared to the control group.[27]

Early data has demonstrated an excellent safety profile and improvements in pain, function, quality of life, patient satisfaction, and opioid utilization. Regarding opioid utilization, the prospective, multicenter, open label single arm by Truumees et al 2019 noted a discontinuation of opioid therapy in 50% of subjects at 3-month follow-up post BVNA,[20] while the prospective, randomized, double-blind, sham-controlled multicenter study by Fischgrund et al 2019 reported that 60.7% of patients taking opioid at baseline reduced their opioid medication use and 46.4% completely eliminated the use of opioids at the 12-month follow-up.[3] Similarly, the prospective, multicenter, randomized clinical study by Koreckij et al 2021 demonstrated opioid utilization reduction up to the 24 month follow-up, with 62% of subjects reducing their baseline dose.[1] The study by Markman et al 2020 reported that there is an association between functional improvement following BVNA and lower dose opioid utilization.[22] However, the prospective, multicenter, randomized study by Khalil

et al 2019 and the clinical study by Markman et al 2020 reported that no change in opioid utilization at 3-months post procedure, like the results by Smuck et al 2021.[21,22,27]

Most clinical studies on BVNA describing functional outcomes utilize the ODI as a measurement tool. Based on the current literature there is an agreement among all studies reporting statistically significant and meaningful clinical improvement in functionality with a sharp improvement in ODI scores at 3 months, sustained at 6, 12, 24 and 60 months follow-up, when compared.[3,18,23] The systematic review performed by Conger et al 2021 supported these findings concluding that there is moderate-quality evidence that BVNA is an effective intervention for the reduction of disability and improvement in function at the short and long-term follow-up.[28] Pain reduction measured by the visual analog scale (VAS) has also been reported by all clinical studies, including single arm or double arm, sham-controlled randomized trials. Important to note, all studies considered a meaningful clinically important difference (MCID) of at least 2 points for the VAS. Concurrently to the sharpest improvement in function at 3 months follow-up, the strongest improvement in pain scores compared to baseline were also at 3 months post-procedure and are sustained at 6, 12, 24 and 60 month follow-up.[3,18,23] There is moderate-quality evidence to support BVNA for pain reduction in the treatment of vertebrogenic pain based on systematic analysis of cumulative data.[28] The aggregate statistics also endorsed improvement in quality of life, measured by the short-form 36 post BVNA, yet one study did not find a meaningful clinically significant difference at the 12-month follow-up.[18] However, at the 24-month follow-up, there was statistically significant improvement in quality of life.[3] There is limited evidence suggesting that BVNA improves quality of life.[1,3,17,18,20,21,24] Patient satisfaction has been reported by two clinical studies, and both suggested a strong association with good to excellent satisfaction post-BVNA, and none of the subjects across both studies reported poor outcomes. Truumees et al 2019 reported that 78% of subjects considered their treatment a success, while Kim et al 2018 reported a 93% success rate.[19,24]

BVNA has demonstrated superiority to standard of care for vertebrogenic pain at short and long-term follow-up. Of note, the standard of care treatment arm included medications, physical therapy, manipulation, acupuncture and spinal injections.[21,27] Systematic analysis reviewing multiple studies on BVNA agreed that there is moderate-quality evidence that BVNA is superior to standard of care management for improvement in pain and function at 3 months follow-up in strictly selected patients with vertebrogenic pain.[28] These findings are supported by the prospective, multicenter, randomized clinical trial by Smuck et al 2021 reporting that BVNA exhibited statistically significant and clinically meaningful improvements in function, pain and quality of life, when compared to standard of care at 3 and 6 months with durability of the treatment response at 12 months.[27] It is important to note that there were no device-related patient deaths or serious adverse events based on the available published literature. BVNA has an excellent safety profile, when compared to other interventions.[31] Adverse events are relatively rare and only minor and self-limited events were reported, such as transient motor or sensory deficits, incisional pain, transient radiculitis, and one case of vertebral compression fracture in an osteoporotic patient (on the sham group) and a case of retroperitoneal hemorrhage due to misdirected pedicle access have been reported among studies.[18,20,21] Post-procedure diagnostic imaging at longer follow-ups did not reveal any advanced disc degeneration, avascular necrosis or spinal cord injuries post BVNA and the rate of adverse events was very rare.[26,28,29]

Cumulative data has established that there is moderate-to-high quality evidence supporting BVNA to improve pain, function, quality of life, opioid utilization reduction, and has demonstrated high patient satisfaction and statistical significance and clinically meaningful superiority of BVNA in contrast to standard of care for the management of vertebrogenic pain in strictly selected patients.[1,3,4,17–25,27,28,30] Based on the United States Preventive Services Task Force (USPSTF) criteria for quality of evidence,[34] with modifications for interventional pain studies, the ASPN work-group gives a BVNA ablation a Level A grade for high certainty that the net benefit is substantial in appropriately selected individuals (Table 1).

Diagnostic Approach to Vertebrogenic Pain

Diagnosis of vertebrogenic pain requires correlating clinical symptoms with radiographic findings indicative of intraosseous changes and damage at the vertebral endplate as shown in Figure 4. In the clinical setting, these patients present with axial low back pain. The pain is generally described as deep, aching and burning in quality. Many

Table 1 Quality of Evidence Ranking Using United States Preventative Services Task Force Criteria Modified for Interventional Spine Procedures

Grade	Definition	Suggestions for Practice
A	The ASPN BVN group recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The ASPN BVN group recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The ASPN BVN Group recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The ASPN BVN Group recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
IStatement	The ASPN BVN group concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Abbreviations: ASPN, American Society of Pain and Neuroscience; USPSTF, United States Preventive Services Task Force.

patients with vertebrogenic pain may have weeks of being asymptomatic or have low levels of low back pain interspersed with four to five days of severe flares. Patients will often describe worsening of pain with sitting, bending forward, and changing from sitting to standing position. Physical exam in these patients will demonstrate reproduction of familiar pain with flexion-based movements with stress placed on the anterior column and may have tenderness on percussion at the vertebral level of concern. In addition to these clinical features, radiographic evidence of endplate degeneration confirms the diagnosis of vertebrogenic pain.[31,35,36] MRI, particularly T1 and T2 weighted sequence, can identify intraosseous changes near damaged endplates. Three types of endplate changes, called Modic changes, can be appreciated on T1 and T2 weighted MRI.[6,31] In a type 1 Modic change, the endplate will appear

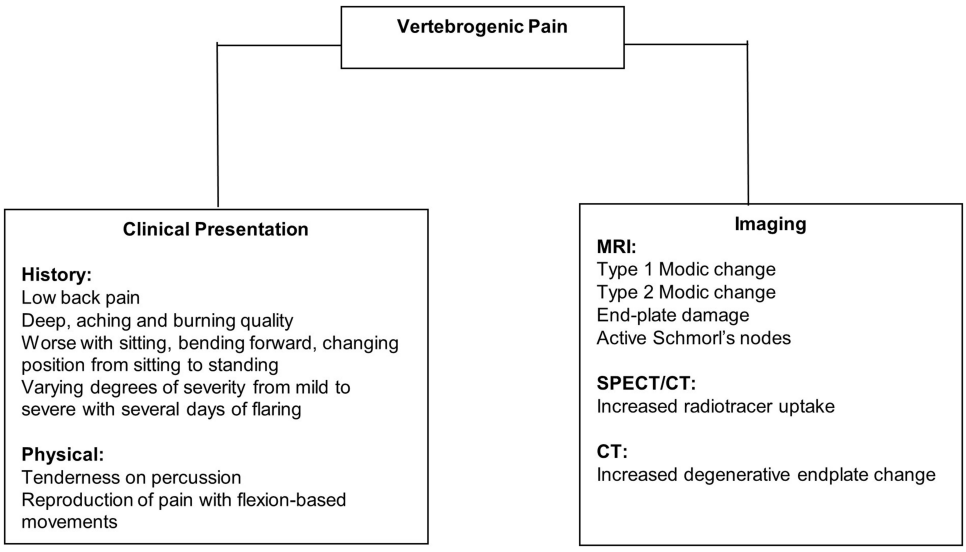

Figure 4 Diagnostic approach to vertebrogenic pain requires concordance of clinical presentation and radiographic finding on MRI.

hypointense in T1 weighted sequence and hyperintense in T2 weighted sequence. Type 1 Modic change indicates edema and inflammation. Type 2 Modic change is charactered by a hyperintense signal on both T1 and T2 weight MRI and indicates fatty infiltration of the bone marrow. Finally, a type 3 Modic change will show a hypointense signal on T1 and T2 weighted MRI and is indicative of bone sclerosis. The combination of typical clinical features along with Type 1 and 2 Modic changes are highly diagnostic of vertebrogenic pain.

There is emerging evidence supporting the utility of radiologic modalities other than MRI for identification of vertebrogenic pain. Single photon emission computed tomography (SPECT) is a hybrid radiographic technique where a bone scan with radiotracer uptake is overlaid on three-dimensional CT imaging. This modality relies on the fact that inflamed and metabolically active endplates would have increased uptake of radiotracer. In fact, recent studies have shown strong agreement between Modic changes and increased radiotracer uptake on SPECT imaging.[37,38] In particular, the type 1 Modic change was highly correlated with significant radiotracer uptake on SPECT.[37,38] Computed tomography alone can serve a useful radiographic tool to identify vertebrogenic pain. In a recent population-based study, there was a strong association found between Modic changes and endplate defects.[39] Given the sensitivity of CT imaging to identify degenerative endplate defects, this type of radiographic modality can be an alternative when MRI is contra-indicated or not feasible.

Treatment Modalities for Vertebrogenic Pain

The term "vertebrogenic back pain" has been utilized interchangeably in the past to describe back pain originating from the vertebral column due to a variety of pathological areas in the spine such as "the degenerative disc disease", disc displacement or extrusion (with or without radiculopathy), metastatic disease, or inflammatory disease.[40,41] This gets even more confusing when vertebrogenic pain has also been defined and recognized as a unique entity associated with vertebral endplate changes due to irritation from inflammatory factors from adjacent diseased disc cells, that the term was distinctly utilized for this condition.[2]

As with most chronic low back pain, initial conservative therapy includes treatment with nonsteroidal anti-inflammatory drugs, muscle relaxants, and physical therapy but the relief has been shown to be limited.[42,43] Vertebrogenic pain refractory to conservative treatment can be treated with BVNA, a safe procedure which leads to improved pain and functional outcomes.[18,21,29]

It has been implicated that the inflammation of the BVN can be partially attributed to the intervertebral disc itself.[2] Several therapies have been utilized in the past to treat discogenic back pain including intra-discal electrothermal therapy (IDET) and intradiscal allograft supplementation (Figure 5). Review of the available literature on IDET shows that the therapy improved subjective outcomes but has inconsistent evidence when evaluating high powered randomized

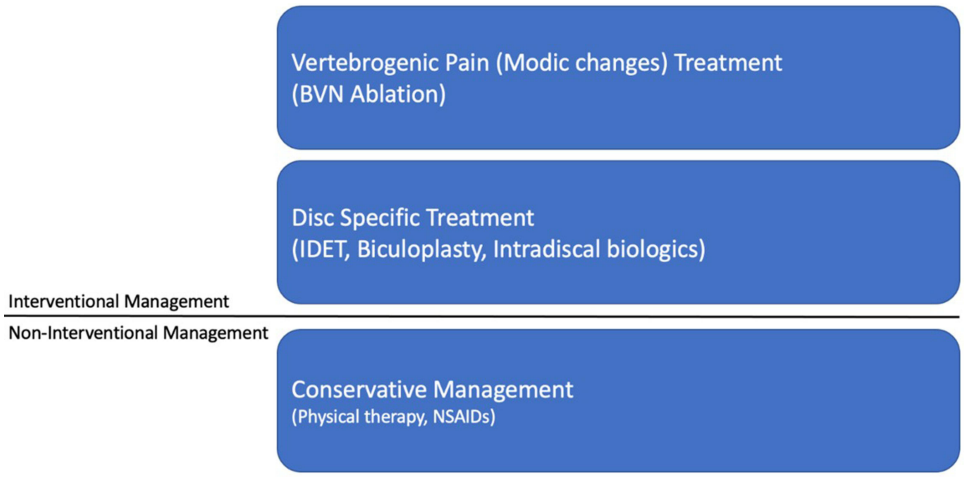

Figure 5 Potential management options for vertebrogenic pain.
Abbreviation: BVN, basivertebral nerve; IDET, intra-discal electrothermal therapy; NSAIDs, non-steroidal anti-inflammatory drugs.

controlled trials for objective improvement. Further, significant complications such as device malfunction, disc herniation, cauda equina syndrome, and osteonecrosis have been reported after IDET.[44,45] Though promising, the results from intervertebral disc allograft supplementation are limited and require further studies to fully evaluate efficacy and safety.[46]

It is important to note that only BVNA has been shown to be beneficial in patients with vertebrogenic back pain as defined by Modic changes. As such, inferences of whether intradiscal therapies can be utilized for treatment of vertebrogenic back pain and not discogenic back pain is only speculative at this time as patients evaluated in the respective studies were not evaluated for concurrent Modic changes.

Procedural Technique

Once the appropriate diagnosis of vertebrogenic low back pain has been made based on history, physical exam, and spinal imaging, patients can be considered for BVNA. Degenerative endplate changes may be visualized as Modic Type 1 or Type 2 endplate changes on MRI or significant endplate sclerosis on CT scan, bone scan or SPECT scan.

The traditional approach to basivertebral nerve ablation incorporates transpedicular access to the vertebral body, whereas probe positioning for BVNA at the S1 vertebral body is unique to the anatomy of the lumbosacral junction and iliac crests.

Patients for BVNA should be comfortably placed in the prone position with all pressure points padded well. The addition of support structures to lessen the lumbar lordosis should be implemented by the proceduralist as needed based on the patient's specific anatomy. Antibiotics to cover appropriate skin flora are recommended, and any previous history of surgical site infections should be thoroughly explored and accounted for in antibiotic selection. BVNA can be performed either under conscious sedation or general anesthesia.

Patients with a high thrombotic or bleeding risk, highlighted in Table 2, should be carefully evaluated prior to their procedure. There is strong evidence supporting a multidisciplinary approach involving cardiology, hematology and internal medicine to optimize medical management. The Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile International Normalized Ratio [INR], Elderly, Drugs/Alcohol Concomitantly (HAS-BLED) and BleedMAP (one point for each risk factor: history of prior bleeding [Bleed], mechanical mitral heart valve [M], active cancer [A], and low platelets [P]) scoring systems can help identify potential risk factors in patients that increase their risk of bleeding (although neither system was designed specifically for BVN ablation).[47] Patients with an increased risk of bleeding should have preprocedural labs evaluating their hemoglobin and platelet count. Anticoagulation and antiplatelet medication specific recommendations are also important to be aware of before performing BVN ablation and are highlighted in Table 3.[48]

Following usual sterile prep and drape, a fluoroscopic C-arm should be utilized to identify the target lumbar segment. To ensure targeting the proper lumbar segment, proceduralists should consider counting lumbar segments from the sacrum as well as the first rib and correlating this to pre-procedural imaging. The C-arm should be moved into position to visualize the target vertebral body in the anterior-posterior (AP) and lateral plane.

Table 2 Factors Associated with Increased Bleeding and Thrombotic Risk

High Risk of Thrombosis	Increased Bleeding Risk
• Any mitral valve prosthesis, any caged-ball/ tilting disk aortic valve, any rheumatic valvular heart disease • Stroke or transient ischemic attack within 6 months of the procedure • CHA_2DS_2-VASc score >7 • Venous thromboembolism (VTE) within 3 months, recurrent idiopathic VTE • Patients with a VTE of any duration and history of severe thrombophilia • Cancer associated thrombosis	• Bleeding episode within 3 months or during similar procedure in the past • Known history of platelet abnormality/ dysfunction • Supra-therapeutic INR • History of mechanical mitral valve • Bleeding episode with prior bridging therapy • Platelet count <50 x 10^9/L for high risk procedures • Active cancer

Note: Table adapted from published guidelines.[47]

Table 3 Periprocedural Considerations and Management of Anticoagulants and Antiplatelet Medications

Medications/Class	Considerations Prior to BVN Ablation	When to Stop Beforehand	When to Resume Afterwards
Acetylsalicylic acid (ASA)	- When used for primary prophylaxis (patient has no history of prior cardiovascular event/ disease) discontinue low dose ASA. - When low dose ASA is used for secondary prophylaxis (in patients with history of cardiovascular disease), confer with the prescribing physician about the risk of bleeding vs risk of stopping it.	- **Primary Prophylaxis**: 6 days - **Secondary Prophylaxis**: Shared decision with prescribing physician	24 hours
Nonsteroidal anti-inflammatory drugs (NSAIDs) (Non-ASA)	- Can be stopped without negatively affecting cardiac and cerebral function. - Consider discontinuing before the procedure and allow 5 half-lives of the specific medication to pass to mitigate impact on platelet function. - Patients with hypoalbuminemia, hepatic dysfunction, or renal dysfunction are an exception to this "5 half-life" rule due to altered volumes of distribution, medication metabolism, and increased elimination half-life. - Cyclooxygenase 2 (COX-2) selective inhibitors do not need to be stopped.	5 half lives	24 hours
Phosphodiesterase Inhibitors (cilostazol and dipyridamole)	- Discuss discontinuation with patient and prescribing physician regardless of whether it is taken with or without ASA.	2 days	Cilostazol can be resumed within 24 hours (discuss resuming dipyridamole with prescribing physician, especially in patients also taking ASA)
Platelet receptor (P2Y12) inhibitors	- In patients with (1) hepatic/ renal disease, (2) prior history of abnormal bleeding, (3) taking concurrent antiplatelet medications, or with (4) advanced age we recommend discussing cessation of the medication with the prescribing physician. - Consider bridge therapy using low molecular weight heparin (LMWH) in patients with a high risk of thromboembolic events after discussing with prescribing physician. The bridge LMWH can be stopped 24 hours before the planned procedure.		
Clopidogrel		7 days	12–24 hours**
Prasugrel		7–10 days	24 hours
Ticagrelor		5 days	24 hours
Cangrelor		3 hours	24 hours
Coumadin	- Stop Coumadin for 5 days prior to procedure and INR should normalize to ≤1.2 before procedure. - In patients with high thromboembolic risk, consider bridging with LMWH after discussing with prescribing physician.	5 days (and normal INR)	6 hours
Heparin		- IV: 6 hours - Sub-Q: 24 hours	- IV: 2 hours (24 hours if there was increased procedural bleeding) - Sub-Q: 6–8 hours

(*Continued*)

Table 3 (Continued).

Medications/Class	Considerations Prior to BVN Ablation	When to Stop Beforehand	When to Resume Afterwards
LMWH		- Prophylactic: 12 hours - Therapeutic: 24 hours	- Prophylactic: 12–24 hours - Therapeutic: 12–24 hours
Fondaparinux		4 days	24 hours
New oral anticoagulants (NOACs)	- For any of the NOAC medications, allow 5 half lives to pass from the time of discontinuation before performing the procedure. - In patient's with a high risk of venous thromboembolisms, bridge therapy should be provided with LMWH after conferring with patient's prescribing physician (LMWH should be stopped 24 hours before the planned procedure). - When resuming these medications in patients with high VTE risk, discuss the plan with the prescribing physician (consider administering half the usual dose 12 hours after the procedure rather than waiting a full 24-hour interval).		
Dabigatran		4 days (5–6 days for impaired renal function)	24 hours
Rivaroxaban		3 days	24 hours
Apixaban		3 days	24 hours
Edoxaban		3 days	24 hours

Notes: Table adapted from published guidelines that reviewed recommendations for higher risk interventional spine procedures such as vertebroplasties and kyphoplasties.[48] **The normal daily dose of 75 mg of Clopidogrel can be resumed 12 hours after the procedure. A full 24 hours should pass if a loading dose of Clopidogrel is used.

The C-arm should then be rotated to square off the superior endplate at the target level and rotated approximately 35 degrees to the right or left to obtain an oblique view with the facet centered at the midpoint of the vertebral body (Figure 6). The superolateral border of the target pedicle should be identified as the skin entry point. The overlying skin and subcutaneous tissue is then infiltrated with the local anesthetic chosen by the proceduralist (lidocaine 1% is recommended). A spinal needle can be used to anesthetize the track towards the pedicle's periosteum and confirm the introducer cannula trajectory. A skin incision is then made with a 10 blade. The 8-gauge introducer cannula with either the diamond or bevel tip is then introduced through the skin, subcutaneous tissue and paraspinal muscle until bony contact is made.

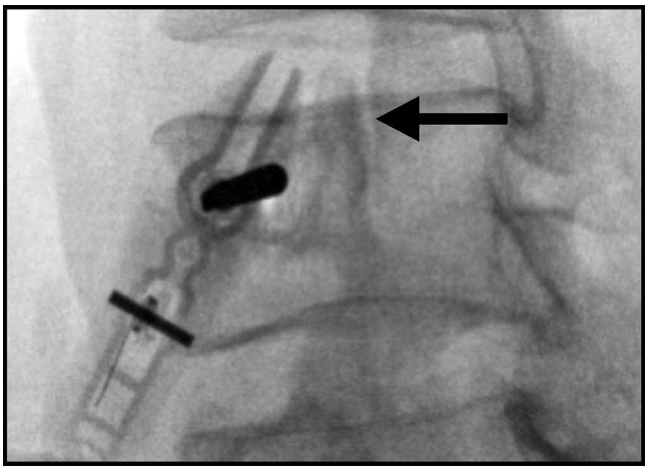

Figure 6 Oblique view of lumbar vertebrae with squared off endplates and facet centered at the midpoint of the vertebrae (arrow).

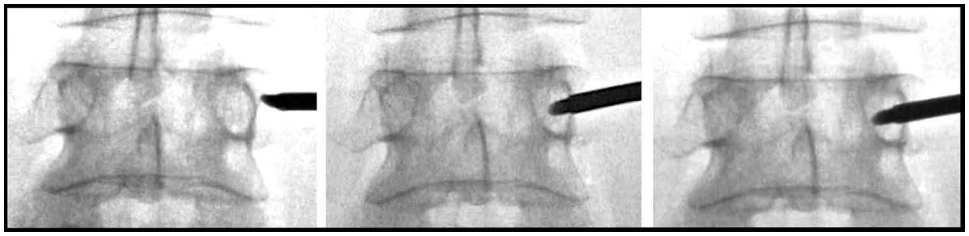

Figure 7 AP view showing progression of the trocar from the lateral to medial pedicle border while simultaneously traversing towards the posterior aspect of the lumbar vertebral body. As the trocar is advanced it is important that the stylet tip not pass the medial border of the lumbar pedicle in the AP view until it breaches the posterior vertebral body wall in the lateral view.

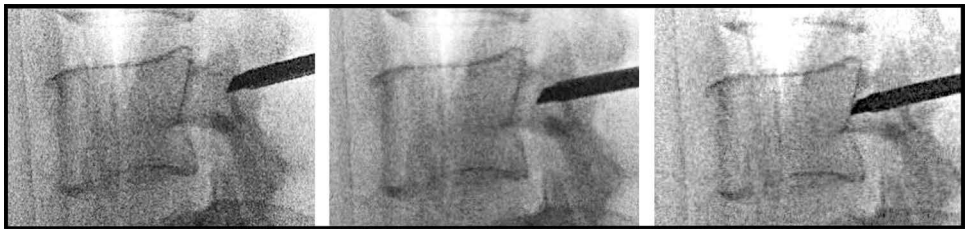

Figure 8 Lateral view showing progression of the trocar towards the posterior aspect of the lumbar vertebral body while simultaneously advancing the trocar from the lateral to medial pedicle border.

At this point, the position of the introducer cannula should be checked in the AP and lateral plane. Using a mallet, the trocar is then advanced through the pedicle to the posterior aspect of the vertebral body. A combination of AP and lateral views are used to ensure the pedicle is appropriately traversed without breaching its medial border (Figures 7 and 8). Once the trocar is in the posterior aspect of the target vertebral body, the trocar is removed from the cannula and the curved cannula assembly (CCA) with the nitinol J-stylet is inserted. The wingnut is rotated counterclockwise permitting excursion of the J-stylet.

The curved cannula assembly is then advanced using a mallet in 1–2 mm increments. The J-stylet is observed to traverse the vertebral body in the AP and lateral views. The ideal placement is reached when the tip of the stylet is noted to be between 30–50% anterior to the posterior wall of the vertebral body in the lateral view, halfway between the superior and inferior endplates, and across the midline of the target vertebral body's spinous process in the AP view (Figure 9). The stylet is then removed. The bipolar radiofrequency (RF) probe is then connected to the generator and then inserted into the introducer cannula (Figure 10). The wingnut is rotated clockwise to retract the polyether ether ketone

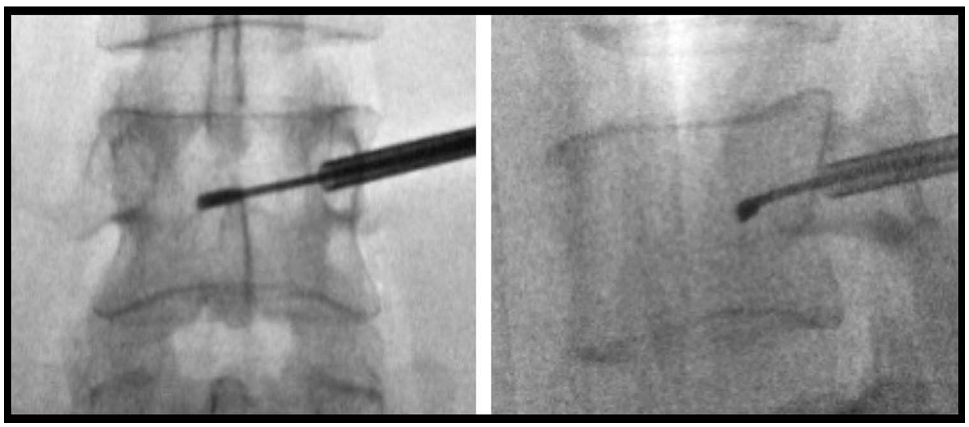

Figure 9 AP view (left) and lateral view (right) images showing final placement of J-stylet tip in lumbar vertebrae.

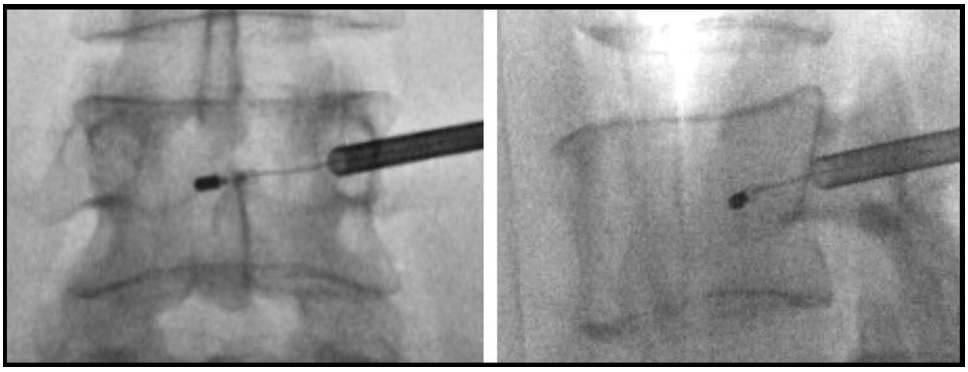

Figure 10 AP view (left) and lateral view (right) images showing final placement of bipolar radiofrequency (RF) probe in the lumbar vertebrae.

(PEEK) sleeve to expose the proximal electrode on the radiofrequency probe. Current evidence is based on the BVN nerve being ablated at 85 degrees Celsius for 15 minutes using an RF generator standard algorithm.[17,18,49]

While the ablation is occurring at the first target level, the C-arm can be moved to visualize the second target vertebral level (L3-L5) using the same technique described above.

S1-Level BVNA

To perform BVNA at the S1 level, the C-arm should be moved to visualize the left or right target pedicle at the superolateral aspect of S1. The C-arm should be rotated to a Ferguson view to square off the superior endplate of S1 as well. The skin entry point should be identified and infiltrated with local anesthetic chosen by the proceduralist (lidocaine 1% is recommended) (Figure 11). A spinal needle can be used to anesthetize the track towards the pedicle's periosteum and confirm the introducer cannula trajectory. A skin incision is made with a 10 blade. Then the 8-gauge introducer

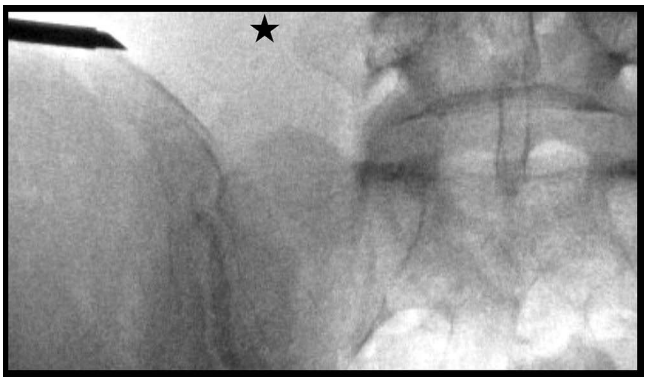

Figure 11 Trocar tip marks skin entry site when targeting the S1 pedicle. Once a Ferguson view is obtained, extend an imaginary line from the L5 transverse process (star) to the ipsilateral iliac crest and this marks the entry site of the introducer cannula assembly.

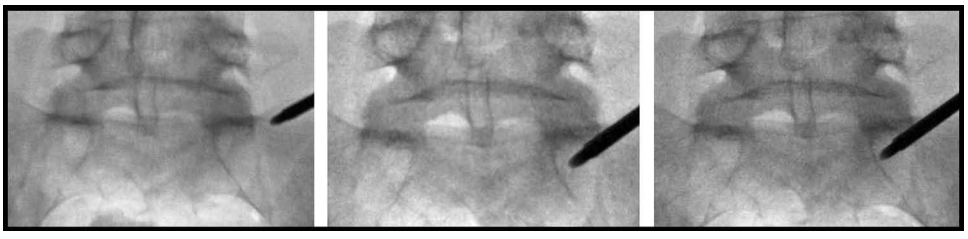

Figure 12 AP view showing progression of the trocar from the lateral to medial S1 pedicle border while simultaneously moving towards the posterior aspect of the S1 vertebral body. As the trocar is advanced it is important that the stylet tip not pass the medial border of the S1 pedicle in the AP view until it breaches the posterior vertebral body wall in the lateral view.

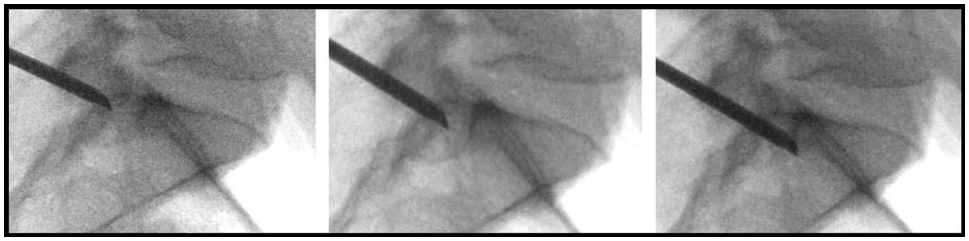

Figure 13 Lateral view fluoroscopic image showing progression of the trocar towards the posterior aspect of the S1 vertebral body while simultaneously advancing the trocar from the lateral to medial S1 pedicle border.

cannula with either the diamond or bevel tip is introduced through the skin, subcutaneous tissue and paraspinal muscle until bony contact is made. The proper position should be checked in the AP and lateral plane.

Using a mallet, the trocar is then advanced through the pedicle towards the posterior aspect of the vertebral body. A combination of AP and lateral views are used to ensure the pedicle is appropriately traversed without breaching its medial border (Figures 12 and 13). Once the trocar is in the posterior aspect of the S1 vertebral body, the trocar is removed from the cannula and the curved cannula assembly with the nitinol J- stylet is inserted. The wingnut is rotated counterclockwise permitting excursion of the J-stylet. The curved cannula assembly is then advanced using a mallet in 1–2 mm increments. The J-stylet is observed to traverse the vertebral body in the AP and lateral views. The J-stylet is then removed and replaced with the straight stylet to reach the BVN target.

The proper target is reached when the tip of the stylet is approximately 50% anterior to the posterior wall of the S1 vertebrae in the lateral view, 40% inferior to the superior endplate and across the midline of the S1 spinous process in the AP view. The stylet is then removed. The bipolar RF probe is removed from the previous vertebral body, cleaned and then inserted into the introducer cannula (Figure 14). The wingnut is rotated clockwise to retract the PEEK sleeve to expose the proximal electrode on the radiofrequency probe. Current evidence is based on the BVN nerve being ablated at 85 degrees Celsius for 15 minutes using an RF generator standard algorithm.[17,18,49]

With all ablations completed, the instruments should be removed from the vertebral bodies. The surgical wounds can be closed with liquid adhesive (cyanoacrylate tissue adhesive) and/or steri-strips followed by a sterile pressure dressing.

Special Procedure Considerations, Challenges, Pearls and Alternative Techniques

Considerations

Successful basivertebral nerve ablation depends on special considerations and proper surgical planning. MRI has heightened the importance of surgical planning. After confirming Modic changes, the surgeon plans the angle of entry into the pedicles, taking into consideration the curved cannula has a working turn between 75° and 85°. Our practice is to draw a line on the

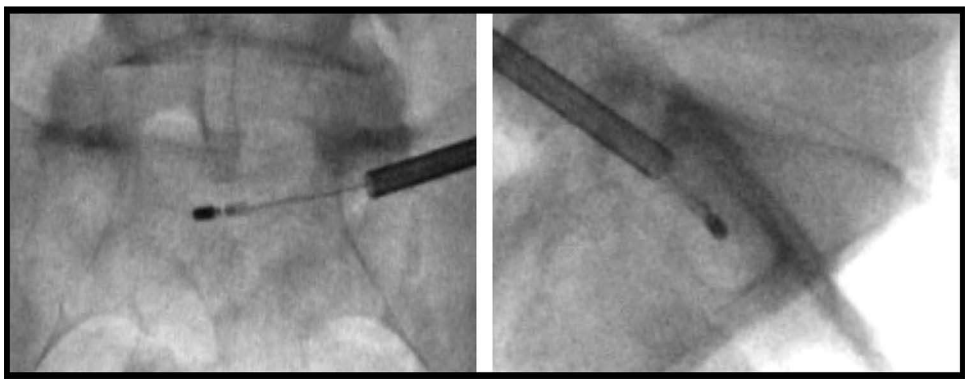

Figure 14 AP view (left) and lateral view (right) images showing final placement of bipolar radiofrequency (RF) probe in S1 vertebrae.

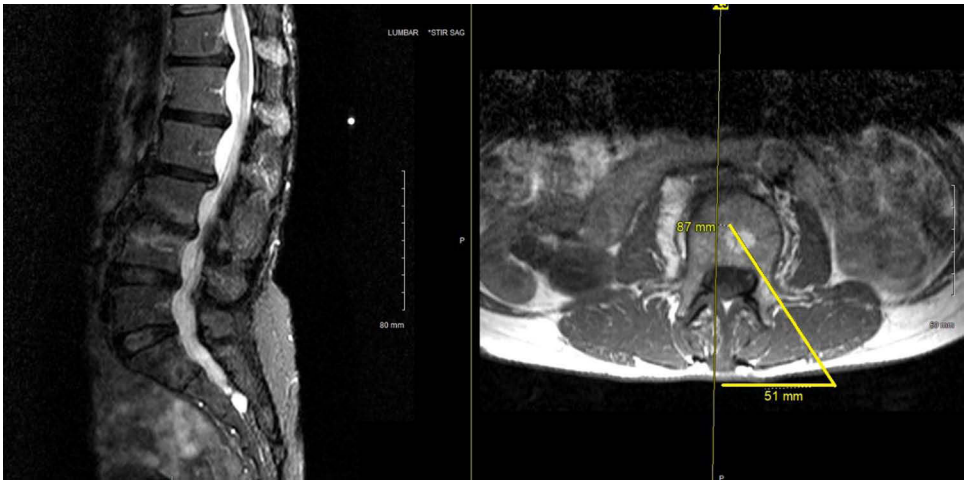

Figure 15 On the left, note the Modic changes at L3/4 on short tau inversion recovery (STIR) MRI. On the right, the first line starts in the vertebral body, passing the anteromedial pedicle, going through the posterolateral pedicle and terminating at the skin. The measurement from the spinous process to the terminus of the first line gives the best starting position for entry into the pedicle.

axial MRI images that originates at the anteromedial aspect of the pedicle through the posterolateral aspect of the pedicle and extends to the skin. From the terminus of this line, we measure the distance to the spinous process. This distance gives the surgeon a simpler starting location for skin, which saves time in the operating room by eliminating guesswork in finding the appropriate angle of entry into the pedicle and vertebral body (Figure 15).

Challenges

The challenges associated with basivertebral nerve ablation are similar to the challenges of kyphoplasty or sacroplasty, with the unique challenge of this procedure being the precision of probe placement. With BVN ablation, the trajectory down the pedicle is from superior lateral to inferior medial. This ensures the curved cannula will make a smooth approach to the target ablation zone.[32]

Specific challenges associated with this procedure include narrow pedicles, hard bone, multiple levels, a high riding pelvis, and difficulty with sacral levels. When narrow pedicles are encountered, preoperative surgical planning is of heightened importance to ensure the proper angle of entry so as to not violate the medial border of the pedicle. With special attention already placed on the narrow pedicle, it is imperative to take more AP and lateral imaging during the procedure, taking especial care to advance in the AP view, while the safety view is the lateral view. When encountering hard bone, multiple images again help to ensure you are not violating the cortex of the pedicle. We have found entering into the posterior aspect of the vertebral body is where there is particularly dense cancellous bone, and it may require additional force to tap through. Alternatively, a hand drill may be used to drive through into the vertebral body.

When multiple levels are being treated, efficiency is vital. In our experience, it is easiest to start on the left side, so that the C-arm does not potentially strike a right sided RF probe. In this manner, we prefer to finish with a right sided pedicle to decrease the risk of inadvertently disrupting the RF probe with the C-arm frequently changing from AP to lateral. Finally, accessing the subsequent vertebral body should be started and achieved while the other level is completing its burn time.

When encountering anatomical difficulties such as sacral levels or a high riding pelvis, diligent and proper preoperative planning pays many dividends. In the case of sacral levels, pedicles are frequently large and shallow while the sacred body is also quite shallow appeared this requires on occasion a rather abrupt turn if the angle of entry is too shallow. Sometimes this is necessary when there is a high riding pelvis, and the iliac crest is in the way. Our recommendation would be to take as oblique of an approach as possible, paying particular attention not to violate the cortex of the iliac crest.

Pearls

In our experience of this procedure, we have discovered a number of pearls. We have found it easiest to start on the left side when anatomy, number of levels, and logistics allow. There are advantages to starting with the superior most segment or the inferior most segment. When starting superiorly, it tends to allow for easier navigation of the C-arm, while starting inferiorly, allows the RF probe to stay out of your way while working on the next superior segment. In either case, a best practice is to start entering into the next vertebral body while the RF probe is ablating the nerve of the previous segment.

Some strategies to reduce post-operative pain include performing an interlaminar epidural at the middle level of the treatment to potentially mitigate neuritis. Anecdotally, this has allowed for less postoperative pain with improved patient satisfaction amongst some of the authors of this guideline. One alternative option for post-operative pain control is providing the patient with a medial branch block at the pedicle to be entered and the level above.

Alternative Techniques

To our knowledge, there are no FDA-approved alternative techniques to this procedure. Some surgeons prefer an extrapedicular approach versus transpedicular, but these approaches are within the described guidelines of the procedure. Future techniques are likely to improve the tools and decrease burn time. Future tools should account for reliability of the curved cannula, and smaller tools decrease the chance of violating the pedicle. The ASPN BVN work group will make updates to the procedural techniques and operational platforms at appropriate intervals.

Algorithmic Approach to Vertebrogenic Pain with BVN Ablation

The diagnosis of vertebrogenic low back pain is based on history, physical examination, and imaging. Because low back pain is multifactorial, it is important to have an algorithmic approach to identify the right patient for the right therapy (Figure 16). Most therapy failures are a result of poor patient selection and not the therapy itself.[50] In general, the etiology of low back pain can be anatomically characterized as primarily generating from the anterior, middle, or posterior column. Because the fulcrum of the spine is the posterior third of the vertebral column, pain generators that are worse with extension are posterior to this line, whereas pain generators worse with flexion are anterior to this line.[51]

Initial patient evaluation involves identifying anterior column pain, which commonly manifests as pain with sitting, driving, lifting, tying shoelaces, and/or putting on socks.[29] Patients often cannot tolerate remaining in one position for too

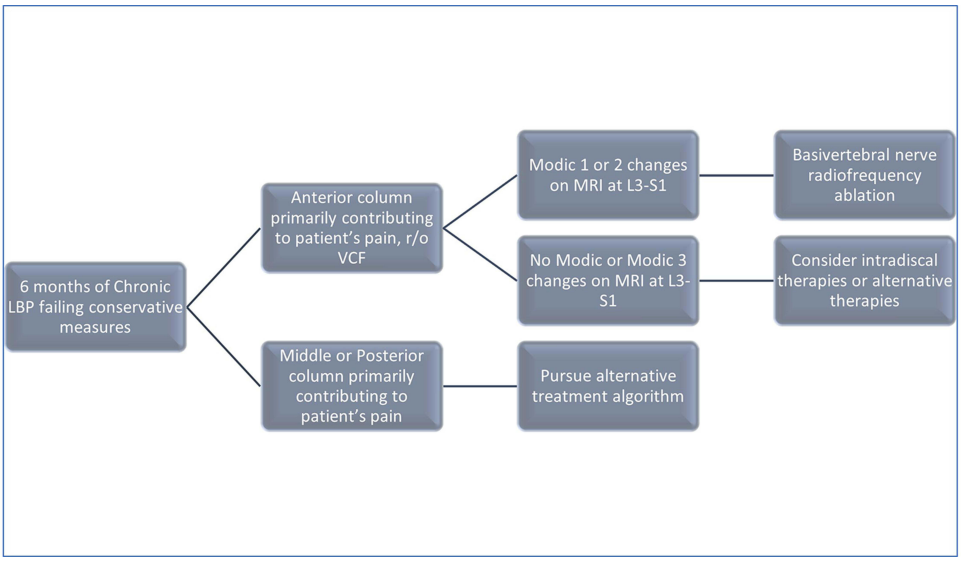

Figure 16 Schematic diagram outlining the algorithmic approach to BVN ablation.
Abbreviations: LBP, low back pain, r/o VCF, rule out vertebral compression fracture.

long and find themselves frequently shifting positions or standing rather than sitting. Such positional triggers can be picked up on the intake form or during the history portion of the exam.

Physical examination generally is used to exclude other pain generators. The physical examination of the patient with vertebrogenic pain may include patients with midline pain, pain with sustained hip flexion, and increased pain with flexion with loading.[52]

Imaging is the third step in identifying a patient with vertebrogenic pain. Identifying Modic 1 or 2 changes on MRI from L3-S1 in these patients supports the diagnosis of vertebrogenic pain. Patients need not have pan-endplate Modic changes to qualify. For patients who cannot obtain MRI, other imaging modalities may support degenerative endplate changes even when Modic cannot be specifically identified.

Anterior column pain generators include discogenic, vertebrogenic, and vertebral compression fracture pain. While these are three distinct pathologies, the nociceptive pathways among these pain generators are likely similar and involve the basivertebral nerve, sinuvertebral nerve, and sympathetic fibers, to varying degrees.[31,53] It is important to note, however, that there exists a debate concerning the similarities and differences between discogenic and vertebrogenic pain. The majority of the evidence at this time suggests that the two pathologies exists on a continuum that may start with discogenic pain and evolve into vertebrogenic pain.[29]

Because patients with chronic low back pain often have multiple spinal pathologies, it is not uncommon for patients to present with multiple pain generators.[29] In this scenario, diagnostic blocks may be performed to rule in or rule out those pathologies. Once the diagnoses have been identified, the pain generators should be ranked based on patient input. Each diagnosis should have a treatment algorithm which is evidence-based and made with consideration to the patient's own assessment of the risks and benefits of each proposed treatment as it relates to their quality of life.

Vertebrogenic pain does not require diagnostic blockade to confirm its diagnosis unlike facetogenic pain.[29] While a functional anesthetic discogram (FAD) may be useful to identify the appropriate level to treat in a situation where a patient has multiple levels of Modic changes on MRI, performing an FAD must be weighed against the risks inherent to the procedure, including the rare, though challenging management of diskitis. Of note, the published literature on the use of BVNA did not use discography as diagnostic test prior to treatment.

Many candidates for basivertebral nerve radiofrequency ablation have failed many other therapies and have suffered through years of low back pain before finding their solution. These are typically the patients who continue around the therapeutic carousel, possibly on unending opioids, never finding a solution to their problem. Fortunately, the advent of BNVA has provided an effective tool to treat vertebrogenic pain, with strong evidence to support durable pain relief.

Conclusion

BVNA represents a promising treatment for patients suffering from chronic LBP of a vertebrogenic nature. As LBP is known to arise from numerous etiologies, careful diagnosis and patient selection for those with vertebrogenic pain as the primary source of symptomatology is vital for optimal outcomes. Current evidence supports long term improvement in pain and function in properly selected patients for BVNA. The ASPN best practice guidelines for BVNA provides guidance to clinicians for appropriate, effective, and safe implementation of BVNA into clinical practice. The ASPN BVN guidelines are intended to be a living document with updated guidelines published at appropriate intervals in the future.

Abbreviations

AP, anterior-posterior; ASA, acetylsalicylic acid; BleedMAP, one point for each risk factor: history of prior bleeding [Bleed], mechanical mitral heart valve [M], active cancer [A], and low platelets [P]); BVN, basivertebral nerve; BVNA, basivertebral nerve ablation; CCA, curved cannula assembly; COX-2, cyclooxygenase 2; CPT, current procedural terminology; CT, computed tomography; DDD, degenerative disc disease; FAD, functional anesthetic discogram; FDA, Food and Drug Administration; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/alcohol concomitantly; IDET, intra-discal electrothermal therapy; INR, international normalized ratio; IV, intravenous; LBP, low back pain; LMWH, low molecular weight heparin; MCID, meaningful clinically important difference; MRI, magnetic resonance imaging; NOACs, new oral anticoagulants; NSAIDs, non-steroidal anti-inflammatory drugs; ODI,

Oswestry Disability Index; PEEK, polyether ether ketone (thermoplastic polymer); P2Y12, platelet receptor; RF, radiofrequency; SPECT, single-photon emission computed tomography; STIR, short tau inversion recovery (MRI); SVN, sinuvertebral nerves; USPSTF, United States Preventive Services Task Force; UTE, ultrashort time to echo (MRI); VAS, visual analog scale; VCF, vertebral compression fracture; VTE, venous thromboembolism.

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Disclosure

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