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Evaluation Study

NEW TREATMENT OF CHRONIC VERTEBROGENIC LOW BACK PAIN: THE BASIVERTEBRAL NERVE CT-GUIDED RADIOABLATION

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ABSTRACT

Among the causes of chronic low back pain (LBP), vertebrogenic pain is frequently underestimated. A significant source of LBP is vertebral endplate degeneration, characterized by cortical bone damage and subchondral bone inflammatory reaction. The nerve responsible for pain transmission is the basi-vertebral nerve (BVN). Radiofrequency ablation of the BVN (BVA) leads to thermal injury of nerve tissue and interruption of chronic vertebrogenic pain transmission. The aim of this study is to evaluate the effectiveness, in terms of pain and disability reduction, of percutaneous BVA in the treatment of patients affected by vertebrogenic chronic LBP. A second aim is to assess the feasibility and safety of a percutaneous CT- guided technique. We performed percutaneous CT-guided BVN ablation in 56 consecutive patients presenting with vertebrogenic chronic LBP in local anaesthesia using an articulating bipolar radiofrequency electrode. In order to assess the target success of the procedure, a one-month follow-up MRI was performed to evaluate the ablation area. Three months later, a CT study was performed to evaluate bone mineral density to exclude structural bone abnormalities that the treatment might have induced. Pre-and post-procedure pain and disability levels were measured using the visual analogue scale (VAS) and Oswestry disability index (ODI). A 10-point improvement threshold was set as a clinical success for the ODI score, and a 2cm improvement threshold was set as a clinical success for the VAS score. VAS and ODI scores decreased significantly compared to baseline at 3- and 12-month follow-ups. Clinical success was reached in 54/56 patients (96,5%) for pain and 54/56 patients (96,5%) for disability, exceedingly the "minimum clinically important difference". CT-assisted targeting of the ablation zone was determined successfully in all patients. The mean operative time was 32 minutes. No immediate or delayed complications were detected. Percutaneous CT-guided intra-osseous

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BVA seems to be a safe, fast and powerful technique for pain relief in patients with vertebrogenic chronic LBP when the selection of patients is based on a multidisciplinary approach including both conventional nuclear medicine imaging and diagnostic radiology.

KEYWORDS: *pain, spine, disc, ablation, nerve*

INTRODUCTION

Vertebral endplates are a significant source of lower back pain (LBP): the correlation between vertebral endplate damage with a subchondral bone inflammatory reaction, generally identified as "Modic changes", and LBP has been extensively investigated, and the pathological basis of vertebrogenic LBP in patients with Modic changes yet established (1–6).

The nociceptive role of the basi-vertebral nerve (BVN) is supported by histologic, anatomic and immune-histochemical evidence in the pathogenesis of LBP in patients with Modic type I change: Fras et al. (7) and Bailey et al. (8) identified in the BVN as the source of the intraosseous nerves. The BVN enters the posterior vertebral body via the basivertebral foramen and arborizes near the centre of the vertebral body, receiving branches innervating all the cancellous bone and the superior and inferior endplates (*caput medusae*). Findings prove that these nerve endings proliferate in damaged and degenerated endplates and are more numerous than in normal intervertebral space and disc (9). Fras et al. also reported on the presence of Substance-P within the BVN, concluding that these nerves can potentially transmit pain signals from the vertebral endplates (7).

Radiofrequency (RF) ablation of the BVN is a potential technique for treating vertebrogenic LBP, for it interrupts pain transmission from vertebral endplates. This treatment generates definitive thermal damage of tissue proteins within the coagulation zone adjacent to the conducting region of the RF probe. Histologically this area is characterized by the embolization of blood vessels, the disintegration of neural tissues and the Wallerian degeneration of nerves (10). Coagulation is surrounded by a secondary zone of hyperemia, where there is a local release of inflammatory factors, oedema, and changes in blood flow (11). In the post-op MRI scan, the lesion presents the so-called "bull eye appearance" with two concentric zones on T2-weighted images: a central hyper-intensity area surrounded by a hypo-intense rim. After 12 months of ablation, histological studies from animal model demonstrated: hematopoietic marrow in the zone of coagulation replaced by viable fat; new bone growing on preexisting trabeculae, without evidence of avascular necrosis; rudimentary blood vessels and nerves development at the coagulation zone periphery (12).

Regarding the duration of BVN radiofrequency, its outcome is expected to be long-lasting since the BVN does not appear to regenerate spontaneously: the extent of the thermal injury, combined with the intrinsic anatomical characteristics of the BVN, which is non-myelinated, could explain permanent nerve destruction (13, 14).

The present study aims to evaluate the effectiveness, in terms of pain and disability reduction, of radiofrequency ablation of the BVN (BVA) in the treatment of patients suffering from chronic vertebrogenic LBP. In addition, as a secondary endpoint, the purpose was to assess the feasibility and safety of a percutaneous CT- guided technique.

MATERIALS AND METHOD

Patients with chronic LBP were enrolled; all presented failure of at least 6 weeks of conventional conservative therapies. Exclusion criteria were radicular pain, symptomatic spinal canal stenosis, hemorrhagic diathesis, local or systemic infection and poor compliance. Patients signed informed consent as regards diagnosis, treatment, and scientific purposes.

Based on clinical examination, patients with suspected vertebrogenic LBP underwent conventional lumbar MRI study, including axial and sagittal T1-SE, T2-FSE and T2-STIR weighted images. Patients with MRI signs of subchondral bone inflammatory reaction Modic type I or mixed Modic type I and II underwent lumbar bone SPECT/CT. Patient with evidence of focal vertebral body uptake on SPECT/CT imaging underwent CT-guided medial branch block (MBB) to exclude chronic Facet Joint Syndrome (FJS) with an injection of 1 cc of lidocaine in the area of the zygapophyseal nerve at the presumed level, bilaterally. Patients who did not perceive pain relief after lidocaine MBB were finally considered eligible for percutaneous CT-guided BVA for a total of 56 patients (22 males and 34 females; median age 43 years old,

age range 38-52 years): 18/56 patients had 1 segment affected (6 patients L4; 9 patients L5; 3 patients S1), 38/56 patients had 2 segments affected (13 patients L3-L4; 14 patients L4-L5; 11 patients L5-S1).

All the patients presented disc degeneration classified according to Pfirrmann's grading of lumbar disc degeneration (15); 23/56 with Grade IV; 33/56 with Grade V.

Pre-operative pain intensity was rated by the Visual Analogue Scale (VAS) scale, consisting of a 10cm straight line with defined endpoints ("no pain" and "worst pain imaginable") on which the patients were asked to mark their experienced pain at the actual time ("VAS now"). The VAS is a validated clinical instrument with a high degree of reliability. The Oswestry Disability Index (ODI) score was used to rate the pre-operative back-related disability. ODI is a validated scale of ten questions designed to assess pain intensity and activities of daily living. A 10-point improvement threshold was set as a clinical success for the ODI score, and a 2cm improvement threshold was set as a clinical success for the VAS score. These values correspond to the commonly accepted "minimum clinically important difference" in treating chronic LBP (16, 17). Repeat VAS and ODI measurements were performed at the 3- and 12-month follow-ups.

We performed BVA in 56 consecutive patients by a fully percutaneous procedure using a unique bipolar radiofrequency system with an articulating electrode (STAR®, Merit) which contains two thermocouples embedded along the length of the probe for real-time assessment of the ablation zone size. The proximal thermocouple represents the temperature at the outer margin of the ablation zone. The articulating electrode permits transpedicular access and navigation to the desired location within the vertebral body once beyond the pedicle body junction. With the patients in a prone position on the CT table, 5.0 cc of lidocaine was injected using a 20G spinal needle to obtain local anaesthesia into deep muscle tissue and the periarticular area; using a 10G coaxial needle, a unilateral transpedicular approach was employed to access the vertebral body. In order to prevent thermal injuries to the spinal cord and nerve roots, the distal tip of the access needle was deployed 1cm anterior to the posterior wall of the vertebral body. This location corresponds to the outer margin of the ablation area. The coaxial bone biopsy needle is then introduced, obtaining a bone specimen. An articulating osteotome was then inserted to create a preferential path for optimal positioning of the articulating ablation electrode. The centre of the ablation zone, the radiolucent region of the electrode, was then positioned in the centre of the vertebral body, where most vertebral body nerves cluster. After placing the electrode at the targeted location, thermal ablation was performed

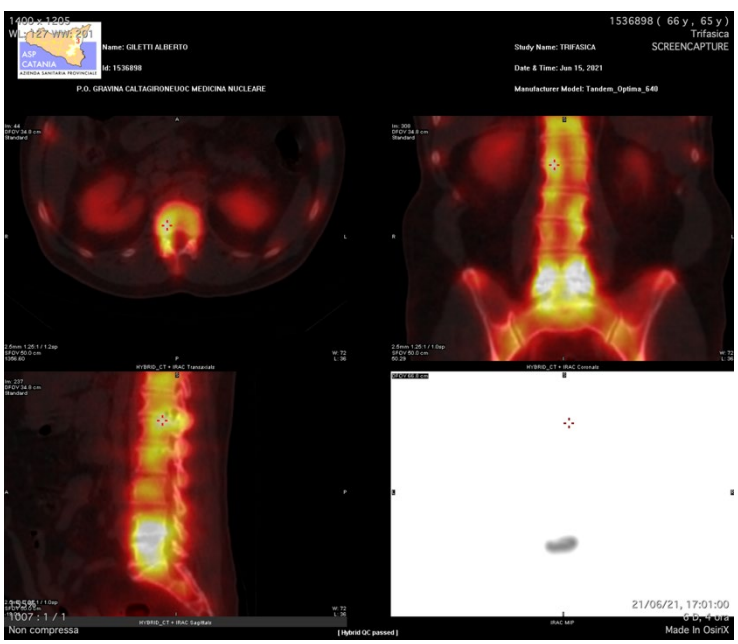


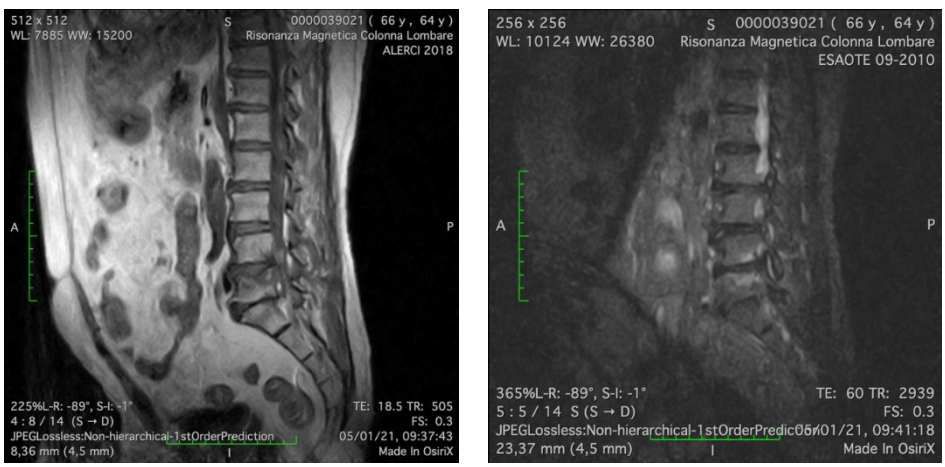
Fig. 1. *66 years male with chronic LBP for 3 years. SPECT-CT on axial, sagittal and coronal recons. Bone scanning clearly depicts severe Tc99 uptake at the L4 and L5 vertebral bodies, confirming the presence of aseptic spondylodiscitis related to chronic mechanical trauma, presumably secondary to disc degeneration.*

using the RF generator until the distal thermocouple reached 55°C-70°C, generating a 15 to 20 mm large ablation zone with a core temperature of approximately 77°C; the RF delivery automatically stopped when the proximal thermocouple reaches 50° C (Fig. 1). The electrode and coaxial needle were then removed, and a post-operative CT performed.
Conventional non-enhanced MRI follow-up studies were performed one month after the procedure, checking for signal abnormality at the level of the endplates and the adjacent intervertebral discs. At the 3-month CT follow-up study, a 0.5 cm^2 "region of interest" (ROI) analysis of the cancellous bone before and after RF ablation was also performed, as well as a comparison between ROI values of the ablated area and the normal non-ablated area in the same vertebral body.

RESULTS

All 56 patients well tolerated the procedure, and no analgo-sedation was necessary. The mean operative time was approximately 32 minutes (range 28-37minutes), with an active ablation time of 5 minutes maximum. No complications occurred at the immediate post-operative CT control scan and the one-month MRI and three-month CT follow-up. Targeting the ablative area was successful in 100% of patients, which consistently included the central portion of the vertebral body along the midline to ensure the BVN ablation. Twelve-month VAS and ODI scores decreased significantly compared to baseline. VAS mean change was -4.3cm (range was -7.5 to -1cm). Clinical success (defined as at least -2.0cm) was achieved in 54/56 patients, in which VAS decreased more than 3.0cm. ODI score meant a change was -32.4 points (range was -6 to -42). Therefore, we decided to evaluate as "clinical success" at least -10 points. This result was achieved in 54/56 patients (96,5%), whose ODI score decreased by more than 20 points. MRI follow-up at 1 month precisely depicts the area of ablation: the centre of the ablated area showed high signal intensity on T2-weighted images, presumably related to a small area of tissue colliquation and necrosis, and a large low signal intensity area, with a concentric reduction in signal intensity, was found both on T1- and T2 weighted scans, related to bone thermal coagulation (Fig. 2). No abnormal signal intensity at the level of adjacent endplates and discs was detected on 1-month MRI follow-up study, excluding presumed vascular damage to the vertebral unit: the endplates remain hypointense on all the sequences, excluding vascular damage or inflammatory-induced reaction at 1 month. No damage was also noted at the level of the disc, both the annulus and the nucleus pulposus.

On the pre-op CT scan, a 0.5cm^2 ROI was placed before treatment on the area to be ablated and the peripheral bone area as an internal control value. This measure was repeated in the same area 3 months after the treatment. Before the treatment, the ROI value of the central core of the vertebral body (the target of the planned RF ablation) was 95.6 Hamsfield Unit (HU – mean value), almost identical to peripheral bone (mean value of 97.3 HU). The 3-month CT



A B

Fig. 2. *66 years male with chronic LBP from 3 years. Sagittal T1SE scan (***A***) and sagittal T2STIR (***B***) images. On MRI a mixed type I and II Modic degeneration can be appreciated at the level of the subcondral somatic bone at L4 and L5, in correspondence to the focal pain referred.*

study demonstrated that the mean bone density value of the ablated area significantly increased to a mean value of 150.9 HU (+57%), while the ROI value of the peripheral cancellous bone area, adjacent to the ablation was not significantly modified (mean value was 96.5HU).

DISCUSSION

The literature shows that Modic changes play an important role in the etiopathogenesis of nonspecific chronic LBP patients (18). Modic type I changes are indicative of oedema and inflammation, the pain being generated by Tumor Necrosis Factors (TNF) release and Protein Gene Products (PGP) (19). In contrast, Modic changes type II are related to bone marrow fatty degeneration, and Modic type III represents sclerosis only as the final evolution of the chronic inflammatory disease. Modic type I changes have a stronger association with pain than Modic II since pain decreases as Modic type I turns into Modic type II (4). Subchondral signal abnormalities represent a dynamic process. Modic type I often converts to Modic type II, but in some cases, lesions can become more extensive or remain unchanged (20-23). Modic type II changes seem to be much more stable, even if there is also some evidence that they may be unstable and change back into type 1 lesions (20-23).

Unfortunately, Modic changes are not an independent and reliable predictor of vertebrogenic chronic LBP and, as for several degenerative changes, are frequently demonstrated on MRI scans in asymptomatic individuals. There is no direct correlation between the size of the Modic type I lesion, clinical presentation, and relevance of LBP or whether recent Modic changes are more symptomatic than longer-lasting ones. Any relationship between symptoms and the duration of such subchondral signal changes remains unknown.

In our study, to confirm the source of chronic LBP in patients with suspected vertebrogenic pain, all participants underwent a SPECT/CT examination (Fig. 3). Bone SPECT/CT is an extremely powerful hybrid imaging system, where SPECT data are merged with conventional CT scans acquired in the same camera. Data from the two modalities are complementary and allow precise localization of the anatomical location of abnormal bone inflammation (24). One of the main advantages of bone SPECT/CT remains the extremely high sensitivity with bone abnormalities becoming apparent earlier than with MRI, CT or any other conventional radiological study. Another SPECT-CT advantage is the capability to image the entire body. Despite the high sensitivity, low SPECT-CT specificity is to be identified as the main drawback: the bone uptake of the tracers, which are usually bisphosphonates labelled with technetium 99m, depends on osteoblast activity and the bone remodelling rate. Therefore, binding is not specific to a specific disease. Consequently, a reliable diagnosis is generally the result of a comparative analysis of CT, MRI and bone scanning (25).

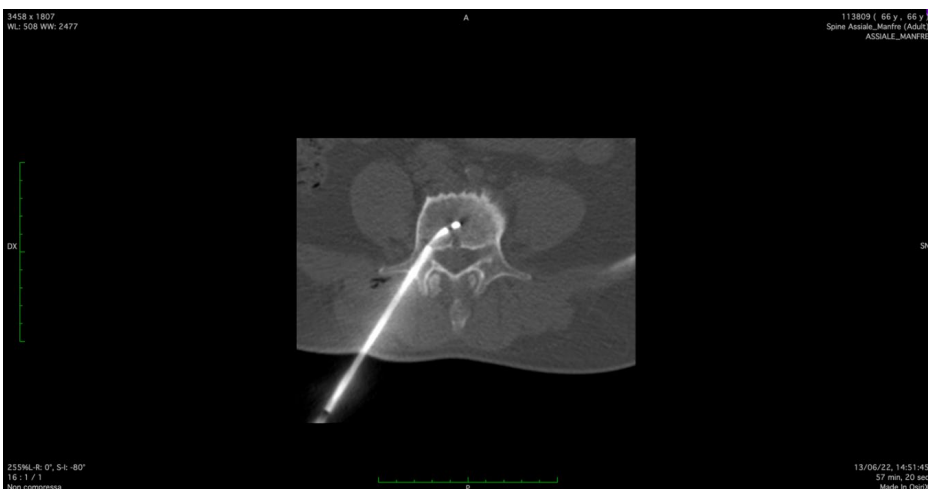


Fig. 3. *66-year-old male with chronic low back pain for 3 years. Basivertebral nerve ablation. CT-guided treatment was performed introducing a steerable radio-probe with a transpeducolar approach inside L4 and L5, reaching the midline at the junction of the anterior 2/3 and posterior 1/3, exactly at the level of the basivertebral nerve rising area.*

In a previous Russo et al. (24) study, the correlation between bone SPECT/CT and Modic changes was investigated. A high positive correlation was found between Modic changes on MRI and increased metabolic activity on bone SPECT/CT imaging. In particular, Modic change type I was the best binary predictor for positivity on bone SPECT/CT. Results showed high metabolic activity in 96.1% of endplates in patients showing Modic type I changes on MRI, 77.8% in cases of Modic type II changes, and only 56% in cases of Modic type III changes. These data suggest that in patients with suspect vertebrogenic pain who might benefit from BVA, the use of bone SPECT/CT compared to conventional MRI for proper selection of patients is a key factor in explaining the high percentage of clinical success obtained.

There are several studies about BVA for the treatment of chronic LBP. However, in all of these studies, the patient selection was made based on MRI imaging only, and results were significantly lower when compared to treatment based on SPECT-CT (24-26).

Moreover, all the BVA treatments in our study were performed using a navigational bipolar RF probe, and CT-guided technique with simultaneous 3D reconstructions obtained intra-operatively so that the best trajectory to the target area in the centre of the vertebra was easily achieved in all cases. Use of a navigational and steerable RF probe permitted safe transpedicular access, trajectory modification once past the pedicle body junction, an action required to reach the target area, and complete ablation of the nerve, reducing the risk of adverse events such as breaching of the pedicle wall and accidental radicular neurovascular thermal injury.

Another issue was the risk of possible damage induced by RF heating transmitted to the peri-ablative area cancellous bone, the endplates and the adjacent disc. For this reason, a 1-month MRI follow-up study and a 3-month CT study were always performed on our population. On the MRI scan, no signal abnormalities were observed at the level of the bone far from the ablated area, the endplates or the adjacent discs, apart from areas through which the probe passed and the target ablation zone. The presumed treatment-related effect on bone integrity was also evaluated by comparing bone mineral density before and 3 months after the procedure: no weakening of the bone was observed. In addition, the results demonstrated sclerosis with an increased bone density of the treated area (+55%) compared to the rest of the vertebral body; this was presumably a result of sclerotic changes induced by the ablation.

All the patients well tolerated conscious sedation using opioids. This technique also reduced any complications related to general anaesthesia.

CONCLUSION

In conclusion, vertebrogenic pain is one of the most frequent and frequently underestimated causes of chronic LBP. The diagnosis cannot rely on CT and/or MRI images alone. Fundamental functional imaging dependent on the metabolic bone activity and SPECT-CT should be considered to increase appropriate patient selection for BVA treatment. Percutaneous CT-guided intra-osseous BVA appears to be a safe, fast and powerful technique for pain relief in patients with vertebrogenic chronic LBP when the selection of patients is based on a multidisciplinary approach, including both conventional diagnostic radiology and bone scanning imaging.

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