Observational Study

The Effect of Sedation on Diagnostic Lumbar Medial Branch Blocks for Facetogenic Low Back Pain: An Observational Study

Nimesh Patel, MD[1], Katherine Nowak, PhD[1,2],Ashwin Vaidyanathan, MD[1], Hannah Milad, MD Candidate[2], Katie Adlaka, MD Candidate[2], Cameron Rubino, MD Candidate[2], Erika Taco Vasquez, MD[1], Lakshmi Nerusu, MD[3], Behnoosh Rahavard, MD[4], Mohamed Fayed, MD[1], Patrick Forrest, MD[1,2], Sarah Money, MD[1,2], Samvid Dwivedi, MD[1,2], Lara Zador, MD[1,2], Roger Haddad, DO[1,2], Daanish Khaja, MD[1,2], Nabil Sibai, MD[1,2], and Rohit Aiyer, MD[5]

From: [1]Department of Anesthesiology, Pain Management and Perioperative Medicine- Henry Ford Health System, Detroit, MI; [2]Wayne State University School of Medicine, Detroit, MI; [3]Deparment of Anesthesiology, Ohio State University, Columbus, OH; [4]Synovation Medical Group, Rancho Mirage, CA; [5]Integrative Sports and Spine, Irvine, CA

Address Correspondence:
Nimesh Patel, MD
Henry Ford Health System
2799 E Grand Blvd,
Detroit, MI 48202
E-mail:
patelnimesh112@gmail.com

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Background: Lumbar medial branch blocks (MBB) are some of the most commonly performed pain procedures in the United States. Diagnostic MBBs are performed to confirm if the generator of low back pain is the facet joint. However, with diagnostic injections, false positive blocks may occur.

Objectives: Our prospective observational study aims to investigate the effects of midazolam sedation on patients' perceived intensity of pain relief following lumbar MBB.

Study Design: This is a single-center multi-site prospective observational study registered on clinicaltrials.gov (NCT04453449).

Setting: The study was approved by the Henry Ford Health System Institutional Review Board (IRB) in June 2020 (IRB# 14010) and registered on clinicaltrials.gov in July 2020 (NCT04453449). This manuscript adheres to the applicable EQUATOR STROBE guidelines for an observational cohort study.

Methods: Patients that underwent MBB without sedation were compared to sedated patients. Patients were asked to complete the Numeric Rating Scale (NRS) at baseline, one day after their diagnostic blocks, as well as 4 weeks and 8 weeks after their lumbar radiofrequency ablation (RFA). The primary outcome is the difference between baseline NRS pain scores and the lowest reported score in the 8 hours following MBB. For patients who proceed to RFA, the frequency of false positive blocks was evaluated. A patient was considered to have a false positive block when they failed to achieve 50% pain relief from RFA after 2 successful sequential MBBs.

Results: There was no significant difference in the NRS pain score change between the sedated and non-sedated groups for diagnostic block one ($P = 0.167$) and diagnostic block 2 ($P = 0.6145$). There was no significant difference of false positive rates between non-sedation and sedation patients at 4-weeks post-RFA ($P = 0.7178$) and at 8-weeks post-RFA ($P = 1.000$).

Limitations: Some of the limitations of this study include its nonrandomized design, patient self-reported pain scores, as well as the small variability in the injection technique of proceduralists and in the anatomical location of the injection site.

Conclusions: This study showed that midazolam did not change patients' perceived intensity of pain following MBB, as well as false positive rates after RFA. Larger studies are required to draw definitive conclusions.

Key words: Medial branch blocks, diagnostic, radiofrequency ablation, back pain, chronic pain, facet joint, medial branch ablation

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In the past few decades, there has been an exponential increase in the use of injections to treat chronic pain. Medicare data from 1997 to 2006 indicates a nearly 200% increase in interventional pain procedures with total costs of facet joint interventions increasing by 79% from 2009 to 2018 (1,2). Moreover, since COVID-19 pandemic Medicare data has shown an overall decrease in the rate of facet joint injections by 17.5-18.5% from 2019-2020 (3,4).

The lumbar zygapophysial joint, commonly known as the lumbar facet joint, is a well-known generator of chronic back pain. The cited prevalence of facet arthropathy is widely variable, ranging from 15% to 60%, depending on the technique of diagnosis as well as the background of the observer (7). Facet joint injections and lumbar medial branch blocks (MBB) are the second most-commonly performed interventional pain procedures in the United States (8). Diagnostic injections are utilized to identify the specific sources of pain prior to definitive therapeutic intervention (5). Diagnostic lumbar MBBs are performed to confirm if the generator of low back pain is the facet joint. If a patient has sufficient pain relief after the MBB, which makes the block positive, the patient is recommended to receive therapeutic medial branch radiofrequency ablation (RFA). However, some patients do not respond to the subsequent RFA, even if they experienced pain relief from the MBB. This is considered a false positive block (type 1 error), and may occur due to a variety of factors, including a placebo response, expectation bias, heavily used sedation with opioids, and/or circulatory absorption of local anesthesia (9). The high frequency of false positive blocks, among other reasons, including financial reasons, has led many interventional pain physicians to recommend two diagnostic injections to diagnose low back pain arising from facet arthropathy (10).

The literature presents various findings regarding the association of sedation with the rate of false positive blocks (9,11). For instance, in a series of randomized studies performed by Manchikanti et al, the impact of sedation on diagnostic validity was assessed in patients with cervical and lumbar facet joint pain (12-14). Three of these studies suggested that sodium chloride (placebo), midazolam, or fentanyl may be a confounding factor as patients who were given these for sedation had improved pain scores and were able to perform previously painful movements (12-14). A fourth randomized study evaluated the broader role of placebo and nocebo effects when opioids and sedation are administered for interventional pain procedures (15). This study reported a placebo response in 13-30% of patients receiving sodium chloride, midazolam, or fentanyl and a nocebo response in 3-8% of patients (15). In these studies, sedation and pain relief were assessed before and after the drug was administered but not after the block or procedure was performed. In addition, these studies suggest that if strict threshold criteria are used, midazolam or fentanyl would have minimal effects on cervical and lumbar mediated facet pain. However, in a randomized, controlled, crossover study by Cohen et al (9) which evaluated the use of sedation while placing diagnostic blocks, patients who were sedated reported a significantly larger reduction in pain diary scores and lower procedure-related pain compared with patients who received no sedation. Furthermore, a higher proportion of blocks administered to patients with sedation led to > 50% and > 80% post-procedure pain relief suggesting that sedation increases positive diagnostic block rate (9). Thus, if sedation can influence the rate of false positive blocks, then this simple addition to clinical approaches could potentially lead to a change in clinical management and utilization patterns of interventions.

Midazolam is the most commonly used benzodiazepine for procedural sedation around the world. Being water-soluble and rapid-acting, midazolam has been known to provide reliable sedation, amnesia, and anxiolysis (16). Unlike opioids, midazolam has no analgesic properties, which is advantageous for its use during diagnostic blocks such as MBBs. In a prospective, randomized, double-blind, placebo-controlled study by Manchikanti et al. evaluating sedation as confounding factor for lumbar facet joint pain, administration of midazolam resulted in 5% of patients being able to perform previously painful movement suggesting that it may influence false-positive rate (14). Recent practice guidelines by the American Society of Interventional Pain Physicians (ASIPP) state that the use of sedation for MBBs can help reduce procedure-related anxiety, increase patient satisfaction, reduce body movement during the procedure, and improve follow-up compliance (17-19). However, sedation can potentially increase the false positive rate since benzodiazepines can increase relaxation of skeletal muscle and improve activity levels, leading the patient to believe that the diagnostic block was effective (20). In fact, current guidelines from Cohen et al.'s consensus practice guidelines published in Regional Anesthesia & Pain Medicine and ASIPP do not recommend the routine use of sedation, and sug-

gest titrating to the lowest dose possible without the addition of opioids if administered to patients (17,21). Furthermore, it is advised that when sedation is used, patients should be counseled on the increased risk of a false-positive block (21).

The current literature on the threshold for pain relief cut-off of the lumbar facet diagnostic block reveals a lack of consensus and clarity. For instance, in Cohen et al.'s multicenter prospective correlational study they found no significant difference in lumbar RFA outcomes when thresholds between 50-100% were used (22). The study suggested that adopting more rigorous selection criteria might lead to the exclusion of a potentially beneficial procedure (22). On the other hand, a retrospective analysis conducted by Manchikanti et al. reported that patients who experienced > 80% pain relief from lumbar facet joint nerve block procedures showed better outcomes in the 2-year follow-up compared to patients who experienced 50-80% pain relief (51% vs 89.5%) (23). The current study will follow consensus practice guidelines as outlined by Cohen et al (21), which states that in order to maximize access to care a threshold of > 50% pain reduction should be used when evaluating if a block was effective.

This prospective observational study investigated the effects of midazolam sedation on perceived pain relief following lumbar MBB in patients diagnosed with lumbar spondylosis without myelopathy. The objectives were to determine if patients who receive midazolam sedation during their MBB report more pronounced pain relief, and if there is a higher frequency of reported positive blocks in sedated patients. Our hypothesis is that the use of midazolam sedation will increase the perception of pain relief from diagnostic MBBs and cause a higher number of positive MBBs in sedated patients, contributing to a higher number of false positive results after the RFA procedure.

Methods

This single-center, multi-site, prospective, observational study evaluated the effects of midazolam sedation on the perceived pain intensity of patients diagnosed with facetogenic low back pain following lumbar MBBs. The study was approved by the Henry Ford Health System Institutional Review Board (IRB) in June 2020 (IRB# 14010) and registered on clinicaltrials.gov in July 2020 (NCT04453449). This manuscript adheres to the applicable EQUATOR STROBE guidelines for an observational cohort study.

The research team identified patients scheduled for upcoming MBBs at 5 different pain clinics in the Henry Ford Health System (HFHS), making this a multi-site study, and determined if they met the eligibility criteria through a manual chart review based on the HFHS EPIC electronic medical record database. Patients had to be at least 18 years old, with a history of axial low back pain for at least 3 months, indicated for lumbar MBB, reporting pain scores ≥ 4 on a 0-10 numeric rating scale (NRS), and diagnosed with facetogenic low back pain arising from the L3-L4, L4-L5 or L5-S1 facet joints bilaterally. Patients were diagnosed with facetogenic low back pain by board-certified pain physicians based on clinical presentation of axial low back pain suspected to arise from the lumbar facet joints and on imaging findings of lumbar spondylosis. Patients were excluded if they had lower back pain with radicular symptoms, uncontrolled major depression or other psychiatric disorders, a history of adverse reaction to either midazolam, fentanyl, or lidocaine, focal neurological deficits or cognitive impairment. Patients were also excluded if they were pregnant or lactating, unable to understand the informed consent and protocol, unwilling to participate in the study, nonEnglish speaking, hearing impaired, or suffering from other conditions with overlapping complaints, such as fibromyalgia or lumbar spinal stenosis.

Eligible patients were contacted by a study team member prior to their procedural clinic appointment and the study was introduced to them. Patients were explained that participation in the study would not lead to any change in conduct of the MBB and that each patient could choose to use sedation at the discretion of the proceduralist. On the day of the procedure, standard HFHS protocol was followed to determine if a patient should receive midazolam sedation or not. If the patient expressed that they were anxious about the upcoming procedure, the clinician offered the option of intravenous midazolam to help them relax. Before sedation, the risks and benefits of using midazolam were discussed with the patient, including the possibility that the use of midazolam may result in a false positive block. After the patient had made their decision, a study team member approached the patient to explain the study and obtain informed consent.

Patients requesting sedation were intravenously administered 0.25-2.5 mg of midazolam shortly after timeout and were given midazolam titrated in increments of 0.25-0.5 mg during the procedure for patient comfort. The clinician assessed comfort by conversing with the patient during the procedure and monitoring

patient's vital signs and behavior to accordingly titrate midazolam to bring the patient to a state of moderate relaxation. Patients who did not choose sedation received no sedatives prior to or during their procedure.

Bilateral L3, L4, or L5 lumbar MBBs were performed under fluoroscopic guidance by board certified pain physicians or by interventional pain fellows under 1:1 supervision. Oblique fluoroscopy (ranging from 20°-40°) was used to clearly identify the junction of the superior articular process (SAP) and transverse process (TP) which was targeted to block the L3 and L4 medial branches (the L4 SAP-TP junction for L3 MBB, and the L5 SAP-TP junction for L4 MBB). The L5 dorsal ramus was blocked at the junction of the S1 SAP and its corresponding sacral ala using antero-posterior fluoroscopy. The 22-gauge, Quincke spinal needles were used for all MBBs. Each site was injected with 0.5 mL of 0.5% bupivacaine during the diagnostic block. Additionally, 0.2 mL of contrast dye (Isovue-300) was injected to ensure localized spread and no vascular uptake of the injected fluid. For the RFA, similar sites were targeted with a 20-gauge radiofrequency cannula (10 or 15 cm in length depending on body habitus) with a 10 mm active tip. Before the procedure, sensory testing was done at 50 Hz from 0 to 1 volt and motor stimulation was done at 2 Hz from 0 to 2.5 volts to ensure optimal positioning of the ablation (ensuring good motor stimulation of the back with no radicular symptoms or paresthesia). Each site was infiltrated with 1 mL of block solution containing 4 mL of 0.5% bupivacaine and 4 mL of 2% lidocaine (both preservative-free) prior to the ablation of each site at 80°C for 90 seconds.

In accordance with hospital policy, insurance approval, and the literature guidelines at the time of the study, if the patient achieved at least 50% pain relief within 8 hours following their first diagnostic lumbar MBB, the block was considered positive and the patient was scheduled for a second lumbar MBB. If the patient achieved at least 50% pain relief from the second diagnostic MBB, they proceeded on to receive bilateral lumbar RFA. For those patients who received RFA after two successful diagnostic MBBs, a block was considered a false positive if the patient did not achieve at least 50% pain relief at 4 and 8 weeks following the therapeutic RFA procedure.

Notably, study patients remained consistent for both diagnostic blocks with whether or not they received sedation; for example, if a patient refused sedation for their initial diagnostic block, but requested sedation for their second diagnostic block, the patient was automatically withdrawn from the study. However, since this study did not investigate sedation during RFA, patients remained enrolled if they switched from the sedation to non-sedation arm – or vice versa – between their second diagnostic block and RFA.

Patients enrolled in the study were given a diary to record their pain using the 11-factor Numeric Rating Scale (NRS-11), rate their functionality using the Oswestry Disability Index (ODI), and rate their satisfaction with the procedure using the 7-item Patient Global Impression of Change (PGIC) (24-26). Baseline NRS-11 pain and ODI scores of patients were collected prior to the procedure. Patients recorded hourly NRS-11 pain scores for the first 8 hours after the procedure in their pain diary. The PGIC and ODI was assessed once on the day after the procedure. The NRS-11, PGIC and ODI scores were recorded in the same way for the second lumbar MBB, as well as at 4 weeks and 8 weeks after the lumbar RFA. All responses were documented by the study team in an electronic REDCap database.

The primary outcome evaluated was the difference between baseline NRS-11 pain scores and the lowest reported score in the 8 hours following the MBB. A secondary outcome was the frequency of positive MBB results in sedated versus nonsedated patients. If the lowest NRS-11 pain score reported in the patients' 8-hour pain diary was at least 50% lower than the baseline score, this was considered a positive result. If there was less than a 50% reduction from the baseline NRS-11 score after the first diagnostic block, this was considered a failed block and the patient did not proceed to the second lumbar diagnostic block. If there was less than 50% relief recorded from the baseline NRS-11 score after the second diagnostic block, this was considered a failed block and the patient did not proceed to lumbar RFA. Patients only proceeded to receive the RFA after 2 MBBs with positive results.

For patients who proceeded to the RFA, the frequency of false positive blocks was evaluated. A patient was considered to have a false positive outcome when they had two positive diagnostic MBBs and a failed RFA result (less than 50% pain relief). This was assessed using the NRS-11 pain scores collected at 4 weeks and 8 weeks after RFA treatment.

Sociodemographic data, anthropometric measurements, and details regarding the etiology of the patients' lower back pain were also collected for each patient.

Data Analysis and Statistical Considerations

The NRS-11 pain, ODI, PGIC scores were compared

between the patients who received sedation and those who did not receive sedation. Numerical variables were summarized into the mean and standard deviation, or the median and interquartile range (IQR) and compared using the t-test or Wilcoxon rank sum test. Categorical variables were summarized into frequency and proportion and compared using the chi-square test or Fisher exact test. The 2-sample t-test or Wilcoxon rank sum test were used to compare the difference in pain scores including: the difference between the baseline pain score and the lowest score within 8 hours post-MBB for each diagnostic block, as well as the difference between the baseline pain score and scores reported 4 and 8 weeks post-RFA, and between the sedated and non-sedated groups. All statistical tests were performed using SAS 9.4 and were 2-sided, with a *P*-value less than 0.05 considered statistically significant.

An a-priori power size calculation indicated that a sample size of 26 for each group (52 patients in total) would be sufficient for at least 90% power to reject the null hypothesis of equal change in pain scores of both groups when the population mean difference is 2.0 with a standard deviation for both groups of 2.5, and a significance level (alpha) of 0.05 using a 2-sided, 2-sample, equal-variance t-test. Accounting for a 30% drop-out rate, 72 patients were enrolled in this study.

Results

Enrollment in this study took place for over 15 months, from June 2020 to September 2021. There were a total of 95 patients enrolled in the study, with a final analysis of 27 patients in the nonsedation group and 26 in the sedation group. A study flow-chart is provided in Fig. 1. The mean age of the patients was 60.3 ± 1.5, with 66% being women. The mean baseline NRS-11 pain scores for the study population were 7.1 ± 1.7 for a mean duration of 61.7 ± 90.1 months. 51% of patients were Caucasian, 43% African-American, and 6% classified as another category. The mean baseline ODI scores were 24.8 ± 15.2. There were no significant side effects reported by patients. Baseline demographic characteristics showed that the nonsedated patients were significantly older than the sedated patients (Table 1).

When comparing the absolute difference in pain scores before and after the MBB procedure, there was no significant difference between the sedated and non-sedated group after MBB-1 (*P* = 0.167) and MBB-2 (*P* = 0.6145) (Table 2). The absolute difference was calculated using the baseline NRS-11 pain score and the lowest reported score in the 8 hours following the diagnostic MBB. For sedated patients, 0.5-2.5 mg of midazolam was administered; for MBB-1, the mean quantity was 1.64 mg of midazolam, while for MBB-2, the mean quantity was 1.75 mg of midazolam. For both diagnostic blocks, the median quantity of midazolam

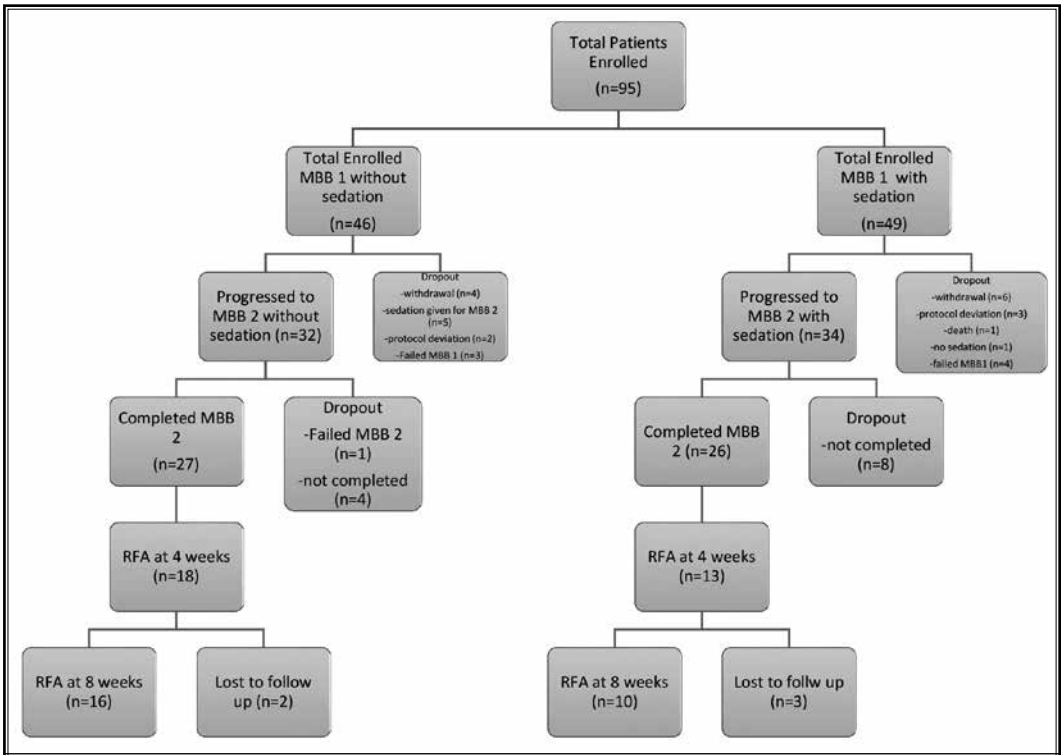

Fig. 1. *Flow chart displaying the number of patients at each stage of the study.*

was 2 mg. In both MBB-1 and MBB-2, 19.2% (5 out of 26) patients received 1 mg midazolam and 61.5% (16 out of 26) received 2 mg of midazolam.

When the frequency of positive MBBs in the patients who received sedation were compared to those who did not receive sedation, there were no significant differences between the 2 groups following MBB-1 (P = 0.1495) or MBB-2 (P = 0.1003), or after 2 positive MBBs (P = 0.5604) (Fig. 2). Although a higher frequency of patients in the sedation group had a positive response after MBB-1 compared to MBB-2, this difference was not significant (P = 0.4189).

When comparing the frequency of false positive MBBs in sedated and nonsedated patients, there were no significant differences between these groups at 4 weeks post-RFA (P = 0.7178) or 8 weeks post-RFA (P = 1.0) (Table 3, Fig. 3). Overall, 64.5% of patients were considered false positives at 4 weeks post-RFA, which increased to 73.1% at 8 weeks post-RFA. At 4 weeks, 60% of the sedated patients were false positives compared to 50% of nonsedated patients. Similarly, 70% of sedated patients were considered false positives after 8 weeks, compared to 75% of nonsedated patients. When patients were grouped according to their baseline NRS-11 pain scores, those with a lower baseline NRS-11 pain score (< 7) had higher frequencies of 81.8% of false positives at 4 weeks post-RFA, compared to 55% of patients with a higher baseline NRS-11 pain score (≥ 7). This was observed in both sedated and nonsedated patients. There was also a higher frequency of false positives at 8 weeks post-RFA in patients with lower baseline pain (88.9% in patients with baseline pain < 7 compared to 64.7% in patients with baseline pain ≥ 7). However, this trend was not observed in sedated patients at 8 weeks post-RFA, since patients in this group who had a lower baseline pain of < 7 had a lower incidence of false positives (66.7%) compared to patients who had a higher baseline pain of ≥ 7 (71.4%).

Overall satisfaction with the procedure was measured using the 7-point PGIC scale for 8 hours following each diagnostic block, and at 4 weeks and 8 weeks after RFA (Fig. 4). Following the diagnostic MBB-1 and MBB-2, majority of the patients responded that they experienced a change following the procedures. After

Table 1. *Demographic characteristics.*

		Non-Sedated Patients (n = 27)	Sedated Patients (n = 26)	*P*-value
Race n (%)	American Indian/Alaska Native	1 (4%)	0 (0%)	0.3413
	Black	9 (33%)	14 (54%)	
	White	16 (59%)	11 (42%)	
	Do Not Know	1 (4%)	1 (4%)	
Race Group n (%)	Black	9 (33%)	14 (54%)	0.3938
	White	16 (59%)	11 (42%)	
	Other	2 (7%)	1 (4%)	
Gender n (%)	Male	12 (44%)	6 (23%)	0.1006
	Female	15 (56%)	20 (77%)	
Age	n Mean (SD), Median (min-max)	27 65.9 (10.1), 69.0 (42.0-79.0)	25 54.3 (9.9), 53.0 (37.0-72.0)	0.0002
Pain Duration	n Mean (SD), Median (min-max)	24 55.2 (91.2), 24.0 (1.0-360.0)	23 68.4 (90.5), 36.0 (3.0-400.0)	0.3005
NRS Baseline score	n Mean (SD), Median (min-max)	27 6.7 (1.9), 7.0 (4.0-10.0)	26 7.5 (1.3), 7.0 (5.0-10.0)	0.0872
ODI Baseline score	n Mean (SD), Median (min-max)	24 22.5 (16.5), 21.0 (0.0-80.0)	26 27.0 (13.9), 26.0 (8.0-74.0)	0.0508

Table 2. *Absolute difference in pain score following MBB-1 and 2.*

		n	Mean	Std Dev	Median	Minimum	Maximum	*P*-value
MBB-1	Nonsedated	27	5.0	2.9	5.0	0.0	10.0	0.167
	Sedated	26	5.9	2.2	6.0	0.0	10.0	
MBB-2	Nonsedated	27	5.7	2.4	5.0	2.0	10.0	0.6145
	Sedated	26	5.7	2.3	6.5	0.0	10.0	

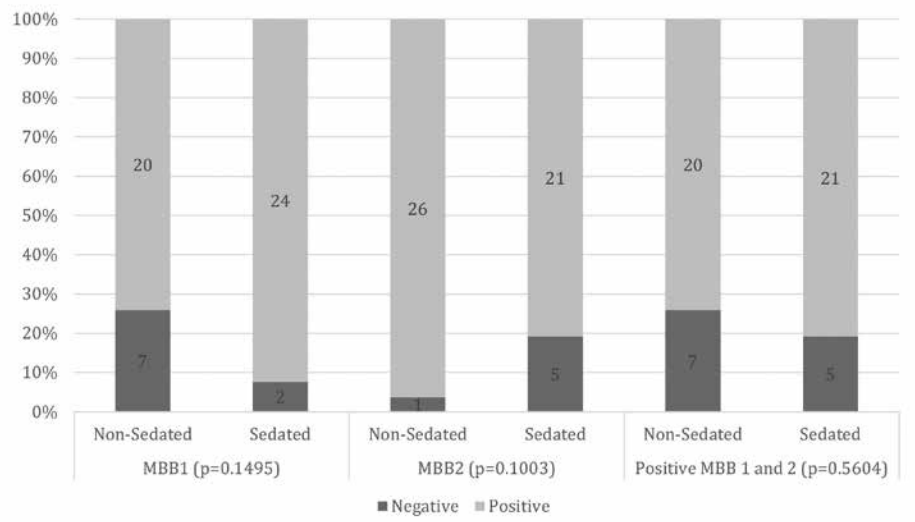

Fig. 2. *Frequency of positive MBBs in sedated and nonsedated patients after MBB-1, MBB-2, and a positive MBB-1 and 2.*

Table 3. *False positive rate at 4 weeks and 8 weeks post- RFA. False positive rate at 4 weeks and 8 weeks post- RFA when grouped according to baseline NRS-11 pain scores of ≥7 or <7.*

	Total	Non-Sedation	Sedation	*P*-value
False positives at 4 weeks post-RFA	64.5% (20/31)	61.1% (11/18)	69.2% (9/13)	0.7178
False positives at 4 weeks post-RFA (baseline NRS pain score **≥ 7)**	55% (11/20)	50% (5/10)	60% (6/10)	1.000
False positives at 4 weeks post-RFA (baseline NRS pain score **< 7)**	81.8% (9/11)	75% (6/8)	100% (3/3)	1.000
False positives at 8 weeks post-RFA	73.1% (19/26)	75.0% (12/16)	70.0% (7/10)	1.000
False positives at 8 weeks post-RFA (baseline NRS pain score **≥ 7)**	64.7% (11/17)	60% (6/10)	71.4% (5/7)	1.000
False positives at 8 weeks post-RFA (baseline NRS pain score **< 7)**	88.9% (8/9)	100% (6/6)	66.7% (2/3)	0.333

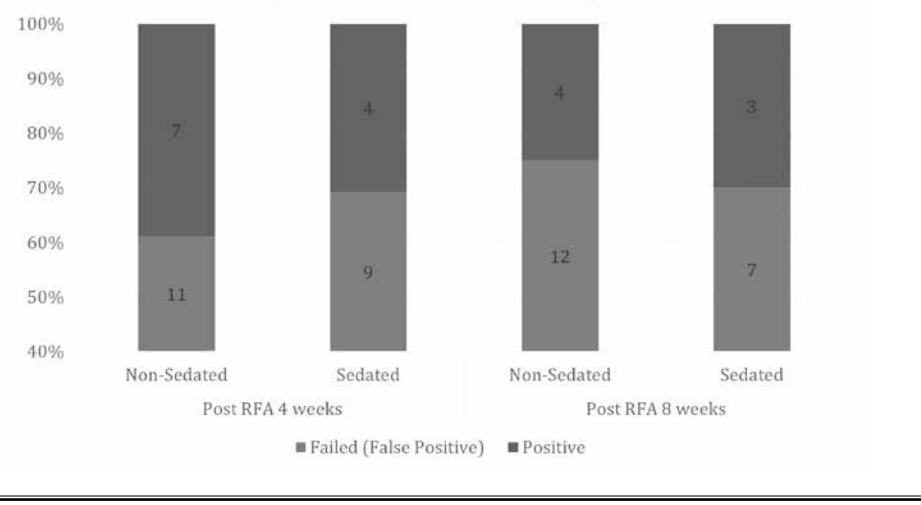

Fig. 3. *Frequency of false positive MBBs after 4 weeks and 8 weeks post-RFA.*

MBB-1 21% of patients responded with "no change" or "hardly any change" and after MBB-2 25% of patients reported the same. At 4 and 8 weeks post-RFA, there was a higher proportion of patients (40% and 50% of patients respectively) who felt that there was "no change" or "hardly any change" after their procedure. Patient functionality was evaluated using the ODI at baseline, 4 weeks, and 8 weeks post-RFA. The mean

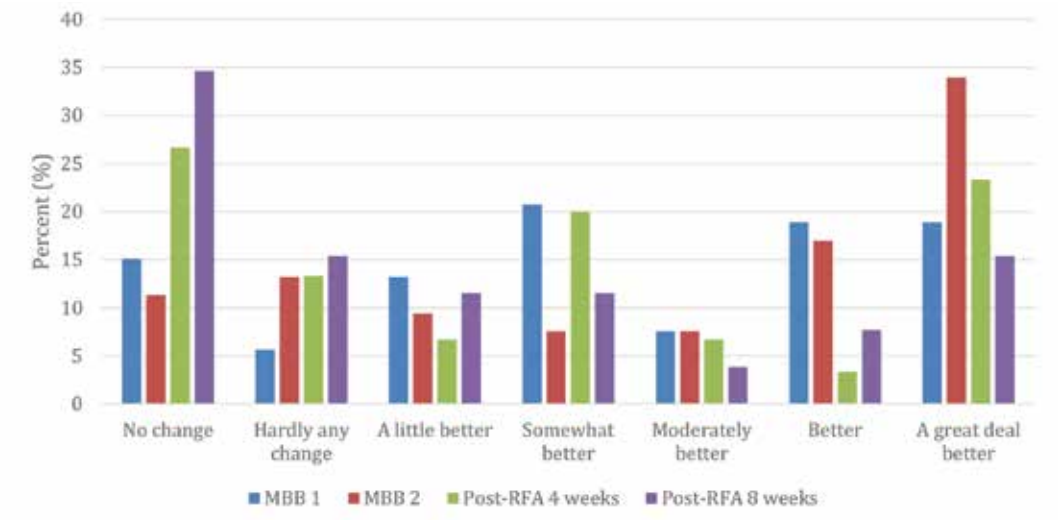

Fig. 4. *PGIC after MBB-1, MBB-2, and at 4 weeks and 8 weeks post- RFA.*

ODI score at 8 weeks (n = 15, mean = 2.8 ± 9.7) was higher than at 4 weeks (n = 18, mean = 1.7 ± 13.6), however this difference was not significant ($P = 0.8$).

Discussion

The findings of this study did not indicate that midazolam sedation affects perceived pain relief and false positive rates in patients who receive diagnostic MBBs and subsequent RFA to treat their lumbar spondylosis. The hypothesis was not supported by the results of this study, as there was no significant difference in the NRS-11 pain scores of patients who received midazolam sedation as compared to those who did not. Additionally, there was no significant difference in the frequency of positive MBBs between the sedated and non-sedated patients. For patients who proceeded to RFA, the results demonstrate that midazolam sedation was not associated with higher rates of false positive MBBs. These findings contribute to our understanding of the factors that impact the efficacy of diagnostic blocks and can guide the use of sedation during the treatment of chronic lower back pain.

Data Interpretation and Clinical Significance

Rates of chronic low back pain continue to increase in the United States, with an estimated lifetime adult prevalence of 65% to 80% (21). Back pain is linked to restrictions in mobility, interference with daily activities, anxiety, depression, and an overall reduction in quality of life (27). Thus, it is critical to develop methods that allow for more expedient identification of the source of pain. While lumbar MBBs are widely accepted as the gold standard for diagnosing facet joint pain, these diagnostic injections are prone to false positive blocks in 17-47% of patients. Transient pain relief from diagnostic lumbar MBB(s) suggest that the patient's pain is originating from the facet joint. However, in the case of false positive blocks, subsequent RFA procedures do not offer patients appreciable pain relief, causing delays in their diagnosis and/or treatment (28). In this study, clinicians moved forward with the curative RFA procedure if patients reported at least 50% pain relief from diagnostic blocks one and 2; "appreciable pain relief" from corresponding RFAs were defined as at least 50% pain relief at weeks 4 and 8 post-procedure. Thus, false positive MBB results occurred in cases where patients received at least 50% pain relief from diagnostic blocks one and 2 but did not experience at least 50% pain relief from the RFA.

In investigating the role of sedation on rates of false positive MBB results, the findings of this study indicate that midazolam does not significantly impact the difference between NRS-11 pain scores at baseline and up to 8 hours post-injection, nor does midazolam increase the relative frequency of false positive MBB results. However, the results of this study do indicate a high false positive trend following RFA in both sedated and non-sedated patients.

Comparison to Other Studies

A comprehensive evaluation of existing literature regarding false-positive diagnostic blocks yields conflicting data. A prospective study by Dreyfuss et al (11) evaluated 51 sedated patients and 51 non-sedated patients and found that intravenous sedation does not interfere with diagnostic pain relief after cervical, thoracic, and lumbar interlaminar epidural corticosteroid injections. In the sedated group, 27% of patients reported > 80% relief of axial pain and 22% reported > 80% relief of limb pain, compared to the non-sedated group in which 25%and 23% of patients reported > 80% axial and limb pain relief, respectively. Thus, there was no significant difference in pain scores between the treatment groups.

In contrast, a randomized, crossover study by Cohen et al (9) evaluated 73 patients, undergoing diagnostic sacroiliac blocks or sympathetic blocks, who either received sedation or no sedation for their initial block. Patients that experienced significant pain relief for 3 months from the initial diagnostic block underwent another injection, this time in the crossover arm. They found that blocks given with sedation, compared to blocks given without sedation, resulted in significantly reduced pain diary scores, reduced procedure-related pain, and a higher proportion of subjects with greater than 50% pain relief. These findings indicated that the use of sedation during diagnostic injections may increase the rate of false-positive MBBs.

Both studies have limitations that undermine their clinical applicability. In the Dreyfuss et al. study, a larger proportion of patients received a cervical block compared to lumbar blocks (11). Their findings may not be translated to real life practice, since most patients needing diagnostic blocks present for lumbar issues. Furthermore, the study design involved the use of steroids. The anti-inflammatory and analgesic effects of steroids can contribute to perceived pain relief and a false positive diagnostic block result, which is why it is important to only use local anesthetics during diagnostic interventions. A limitation with the Cohen et al. study was the lack of consistency in the type of sedation that was provided. Some patients were heavily sedated with opioids and other patients were only lightly sedated with benzodiazepines (9).

The results of this study were consistent with the findings of Dreyfuss et al (11), as sedation did not have an effect on postprocedural NRS-11 scores. It is important to note that the diagnostic injections were limited to lumbar MBBs in this study, as compared to cervical blocks in the study by Dreyfuss et al. The findings of this study contradict with the results of Cohen et al., as our study did not find any significant reduction in pain dairy scores or increased pain relief (greater than 50%) in the sedation group compared to the nonsedation group. Furthermore, Cohen's study focused on sacroiliac pain and sympathetic blocks, which is different from pain originating from the lower back (9).

Results from a prospective, randomized study by Manchikanti et al (14) in 2004 suggested that sedation (using midazolam or fentanyl) could be a confounding factor in the diagnosis of lumbar facet joint pain. The authors described that 93% of patients who received 1-5 mg of midazolam reported increased levels of relaxation compared to 40% of the patients who received 1-5 mL NaCl solution who reported the same. However, the proportion of patients reporting significant pain relief post-diagnostic block (using both an 80% and 50% relief threshold) was similar across groups. While Manchikanti et al's study provided a useful framework for the current study, it was not generalizable since their methodology followed a strict protocol including invoking specific movements to measure pain (14). The current study measured pain relief using patients' reported scores up to 8 hours post-procedure; further, pain scores from both diagnostic blocks as well as corresponding RFAs were recorded to develop a more longitudinal picture of the effect of midazolam on perceived pain.

In addition, it has historically been suggested that false positive rates following diagnostic block procedures may be due to a placebo response – to either the lumbar MBB or to sedation itself. In Manchikanti et.al's 2005 study, researchers found that "in patients undergoing interventional procedures, sodium chloride solution, midazolam, and fentanyl produced placebo effects in 13% to 15%, 15% to 20%, and 18% to 30% of patients respectively", moreover, a small proportion of patients also reported a nocebo response (15). Although the results of this randomized placebo-controlled study suggest that midazolam can produce placebo responses, Manchikanti's study compares early and late patient experience after a single, therapeutic facet joint nerve block. On the other hand, the current study examines diagnostic, or predictive, MBBs and defines pain relief using corresponding RFA pain scores (15).

It is important to interpret the response to MBB and RFA with respect to the chronic pain model rather than the acute pain model as described by Manchikanti

et al (29). Unlike acute pain, which mainly involves nociception, chronic pain is multidimensional – having complex psychosocial interactions. This can often explain the varying responses of different patients to the same local anesthetic and sedation although the pharmacodynamics of the individual drugs remains the same.

In summary, consensus guidelines from ASRA Pain Medicine and ASIPP shows that there is level II evidence (moderate) supporting the utility of benzodiazepines without opioid analgesics during facet joint interventions (17,21). In addition, different organizations suggest using different relief thresholds for describing a block as positive. For instance, ASIPP guidelines suggest using an 80% or greater pain relief as a criterion for positive facet block to reduce significant confounding effects that may be seen if the criteria of 50% or greater pain relief is used (17). However, the studies cited in the guidelines used criteria of previously painful movements being less painful, as opposed to our study which looked at overall pain scores while patients were carrying out their daily life activities. In addition, high pain relief cutoffs may be difficult to achieve as chronic pain patients may have multiple areas of pain that are overlapping and multi-factorial. For instance, facet degeneration may occur in combination with degenerative disc disease and myofascial pain syndrome, such that blocking the medial branch nerves may not provide pain relief in adjacent structures.

Study Limitations and Future Recommendations

There were several limitations to this study. Physicians, patients, and investigators were all aware of whether a patient was part of the experimental (midazolam sedation) group or the control (nonsedation) group. Still, efforts were made to mitigate bias. Investigators introduced the study to the patient and obtained consent only after the decision to use sedation was made. This was intended to eliminate bias in decision-making and to replicate real-life clinical situations. This study was also subject to the inherent limitations of using self-reported data, which can be particularly complicated when evaluating pain scores. Finally, the investigators acknowledge that there was a margin of variability in the volume of sedation provided to each patient and in the anatomical location of the injection site, with slight differences in the injection technique utilized between interventionalists. Another limitation was the limited number of patients who proceeded to receive RFA. Even after having positive MBB-1 and MBB-2 results, many patients were lost to follow-up and did not return to receive RFA for unknown reasons. This led to a fairly small sample size of patients who received the RFA, limiting the statistical power of the analysis of false positive rates. Finally, we are aware that there is variation in the cutoff to proceed to MBB-2 from MBB-1 and to the RFA from MBB-2, as some clinicians utilized 50% pain relief as the threshold, while others had looser criteria. This could have resulted in the discrepancy seen between the patients, several of who proceeded to MBB-2 and RFA even without achieving 50% pain relief. A possible explanation for this could be that patients reported subjective improvement in pain scores for instance with activity, movement, and functionality, which prompted the clinician to proceed to the next procedure phase.

In addition, the results of this study should be interpreted with caution as it may not relate to other institutions standard of positive MBB with at least 80% reduction in pain scores. Furthermore, our local anesthetic of choice was 0.5% bupivacaine because it is longer acting compared to lidocaine. Pain scores were collected for a duration of 8 hours after MBB which allowed us to evaluate the patients pain improvement as they gradually resumed their normal functional activities. Lidocaine may be an acceptable alternative to bupivacaine, but effects in pain scores and functionality may not be translatable to this study.

The results of this study may serve to guide the use of sedation medication during diagnostic blocks and inform treatment options for chronic pain. Midazolam sedation does not appear to be the cause of high false positive rates for lumbar facet blocks. Future investigation is necessary to evaluate other potential factors that may contribute to false positive rates, such as the placebo response or the spread of injectate into nearby structures (23). Additionally, it is important to seek ways to improve the predictive value of diagnostic blocks to allow for earlier intervention. More accurate, reliable, and faster diagnoses will result in earlier treatment and improved quality of life of patients suffering from chronic low back pain.

Conclusions

The results of this study indicated no significant differences in the NRS-11 pain scores of patients who received midazolam sedation during diagnostic lumbar MBBs compared to patients who did not receive seda-

tion. The frequent occurrence of false positive MBB results in this study underlines the fact that further clinical studies are necessary to evaluate other potential contributing factors.

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