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Correlating SPECT-CT activity in cervical facet joints with positive response to cervical medial branch blocks

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A B S T R A C T

Introduction: Cervical facet arthritis is a significant source of neck pain and impaired function that is amenable to treatment with medial branch radiofrequency neurotomy (RFN). Identifying appropriate patients for this treatment requires integration of information from the history, physical exam and diagnostic imaging, but the current diagnostic standard for facet-mediated pain is positive comparative medial branch blockade (MBB). SPECT-CT has recently been evaluated as a potential predictor of positive medial branch blocks with mixed results. The purpose of this retrospective analysis was to determine if a relationship exists between increased uptake on SPECT-CT of a given cervical facet joint and a positive MBB.

Methods: A retrospective review was performed to identify all patients undergoing cervical MBB within 12 months after having a cervical SPECT-CT. Each procedure was categorized as either Concordant (all facet joints demonstrating increased ^{99m}Tc uptake on SPECT-CT were blocked) or Discordant (at least one facet joint demonstrating increased ^{99m}Tc uptake on SPECT-CT was not blocked or block was performed in a patient that had no increased uptake on SPECT-CT). Statistical analysis was performed to determine if concordance between facet joints demonstrating increased uptake on SPECT-CT and those undergoing MBB was associated with a positive block using cutoffs of 50% and 80% pain relief.

Results: A total of 43 procedures were analyzed (25% Concordant, 75% Discordant) and both groups demonstrated improvement in pain Numeric Rating Scale (NRS) scores. No significant association between concordance and positive MBB was identified at thresholds of 50% ($p = .481$) and 80% ($p = 1.000$) pain relief.

Conclusion: SPECT-CT findings do not accurately predict positive cervical MBB but may provide valuable information that can be considered with other factors when deciding which joints to treat.

1. Introduction

Neck pain is the fourth most burdensome disease as measured by years lived with disease. Disability-adjusted life years due to this condition have increased from 23.9 million to 33.6 million between 1990 and 2010 [1]. The 12-month prevalence of neck pain in the general population is between 30% and 50% and activity is limited in up to 11.5% of those patients [2]. Among patients with neck pain, the zygapophyseal joints are believed to be a contributor to pain in 25%–65% of cases, but among those seeking care in a pain clinic it is above 50% [3,4], with upper cervical levels being affected more often than lower levels [5,6].

Cervical facet-mediated pain typically presents as axial pain in the neck that worsens with movement and can be localized to well-established referral patterns [7,8]. Physical examination, however, has not been shown to be effective in accurately diagnosing painful facet joints [9]. Radiographs demonstrating signs of degeneration including sclerosis, bone hypertrophy, and osteophytes suggest underlying osteoarthritis, but conventional radiographs are insensitive in the detection of mild facet disease [10]. CT demonstrates similar findings, but with improved detail. MRI provides improved soft-tissue resolution and the ability to detect active synovial inflammation and facet joint effusions. However, many asymptomatic patients have abnormalities on CT and MRI making it difficult to rely on imaging alone to make clinical decisions [11–13]. Furthermore, CT and MRI imaging findings are unable to predict response to interventions including facet joint blocks and radiofrequency neurotomy (RFN) [14,15]. Thus, accurate identification of the most likely pain generator and response to interventions is

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challenging using clinical information and traditional imaging modalities alone. Current paradigms for establishing the diagnosis of facet-mediated pain focus on diagnostic medial branch blocks (MBBs) [16,17].

There has been recent interest in determining if Single-Photon Emission Computed Tomography (SPECT) in conjunction with CT scanning (SPECT-CT) can successfully identify painful zygapophysial facet joints and predict a positive response to targeted interventions. Some evidence suggests increased SPECT-CT activity may be helpful in identifying painful facet joints and the modality has been proposed as a potential tool to obviate the need for diagnostic injections [18,19]. However, a high level of discordance between increased activity on SPECT-CT and the level at which interventions are directed has also been identified, often because that location did not correlate with clinical findings, suggesting this may not be as valuable as others have proposed [20]. The ability of SPECT-CT to predict a positive response to diagnostic block of the cervical facet joint and ultimately RFN remains unknown. The purpose of this study was to determine through retrospective review if a relationship exists between increased uptake on SPECT-CT of a given cervical facet joint and a positive response to MBB. It was hypothesized that joints demonstrating increased levels of ^{99m}Tc uptake on SPECT-CT are correlated with a positive MBB.

2. Material and methods

2.1. Patients

Institutional Review Board approval was obtained for this retrospective analysis. The institutional imaging database was searched for all records of patients who underwent SPECT-CT of the cervical spine for pain between January 2016 and June 2020 and also underwent diagnostic cervical MBB. The search excluded patients with infection, tumors, or iatrogenic spine complications. Injections were also excluded if MBB was performed more than 365 days after the SPECT-CT, due to the increased likelihood of a new or different potential chronic pain generator. Finally, cases were excluded if there was incomplete pre-/post-injection NRS data. In cases where two MBBs were performed as comparative blocks only the first block was analyzed.

2.2. ^{99m}Tc medronate SPECT-CT examination

Within our large multispecialty tertiary referral spine center providers may choose to order a SPECT-CT as part of the diagnostic evaluation, if in their clinical judgment it is expected to add diagnostic clarity and influence their decision-making with respect to the plan of care. For all scans, ^{99m}Tc medronate injection (Tc-99 m MDP), 22 mCi was administered intravenously. After approximately 3 h, planar imaging of the spine in anterior and posterior projections was performed. SPECT/CT imaging of the spine was then performed. CT images were acquired using a low-dose protocol for attenuation correction and anatomical localization purposes.

2.3. Intervention protocol

After consultation with a board-certified pain management provider, if appropriate based on the integration of all available clinical and imaging information including reports and images for SPECT-CT, cervical MBBs were performed at levels determined by the clinical judgement of the assessing provider. Per institutional standards, all MBBs were performed under fluoroscopy. Once needles were confirmed to be in the appropriate position using AP and lateral images, nonionic iodinated high-osmolar radiopaque contrast media was injected. If no vascular flow was observed 0.5 cc of local anesthetic (0.5% bupivacaine or 2% lidocaine) was injected at each site. Every patient receiving diagnostic MBBs at our center is asked to self-report pre- and post-procedure pain using the Numeric Pain Rating Scale (NRS) by an independent collaborator, either a registered nurse or a pain medicine specialist one business day after the completion of the block with the patient keeping a written hourly diary to prevent recall bias. This information is then documented in the chart for physician review. Age, gender, race, laterality, and level of joints blocked and pre- and minimum post-procedural NRS during the anesthetic phase were collected from the electronic medical record. Maximal percent pain relief was calculated using pre- and post-procedural NRS values.

2.4. Image analysis

A retrospective chart review of diagnostic radiology reports for all SPECT-CTs was performed. The level and laterality of any facet joints reported as demonstrating increased ^{99m}Tc uptake were recorded. Then, each injection (defined as a single injection session in which one or more joints were blocked) was categorized as either Concordant or Discordant. Concordant injections were defined as those in which all facet joints demonstrating increased ^{99m}Tc uptake on SPECT-CT were blocked. Discordant injections were those in which at least one facet joint demonstrating increased ^{99m}Tc uptake on SPECT-CT was not blocked or those performed on patients that had no facet joints with increased uptake on SPECT-CT.

2.5. Statistical analysis

Categorical variables were described using absolute and relative frequencies, while continuous variables were described using means and standard deviations or medians and interquartile ranges. A Wilcoxon signed ranks test was used to compare pre-/post-procedure NRS scores in each group. Fisher's exact test was used to determine if there was a significant association between SPECT-CT concordance and positive cervical MBB using thresholds of both 50% and 80%. All analyses were performed using IBM SPSS Statistics (version 28.0.0.0 (190)).

3. Results

Between January 2016 and June 2020, a total of 64 patients were identified as having had both a cervical SPECT-CT and cervical MBBs on one or more joints on one or more occasions. Some patients underwent more than one distinct block, resulting in a total of 81 procedures being reviewed. Twenty-one were excluded for having SPECT-CT performed after the MBB, 12 were excluded for having the procedure more than 1 year after the imaging, 3 were excluded for having incomplete pre-/post-injection NRS data, and 2 were excluded for being the second in a series of 2 procedures in the same patient at the same level. A total of 43 distinct injections (defined as a single injection session in which one or more joints were blocked) among 40 unique patients were included in the final analysis. Twenty-five percent of injections were categorized as Condordant and 75% as Discordant. The demographic and baseline pain characteristics of these patients are summarized in Table 1.

A total of 74 cervical facet joints were treated percutaneously with

Table 1
Demographic and baseline pain characteristics by group.

	Overall	SPECT Concordant	SPECT Discordant
Number of unique patients (%)	40	10 (25%)	30 (75%)
Number of MBBs (%)	43	10 (23%)	33 (77%)
Average age in years (SD)	64.5 (9.9)	63.8 (8.1)	64.7 (10.5)
% male	47.5	50	46.7
% Caucasian	87.5	100	83.3
% Black	2.5	0	3.3
% Other or unknown	10	0	13.3
Median Baseline NRS (IQR)	7 (3)	6.5 (3)	7 (3)
Median Joints Per Procedure (SD)	1.72 (.876)	1.6 (.966)	1.8 (.792)

34 of those demonstrating increased uptake (Table 2). The most commonly treated cervical facet joints in order of decreasing frequency were C3/4, C2/3, C4/5, C5/6, C7/T1, and C6/7. The most common joints to display increased uptake on SPECT-CT in order of decreasing frequency were C3/4, C4/5, C2/3, C7/T1, C5/6 and C6/7 (Fig. 1). Overall and among Discordant procedures 2 joints were most commonly targeted, whereas in the Condordant group 1 joint was most commonly targeted (Fig. 2). Concordant patients had a significant decrease in NRS from pre- (median = 6.5) to post- (median = 3) treatment with MBB ($Z = -2.67$, $p = .007$). Discordant patients also had a significant decrease in NRS from pre- (median = 7) to post- (median = 3) treatment with MBB ($Z = -4.874$, $p < .001$).

Responder analysis was performed using thresholds of at least 50% and 80% improvement in pain. Using a threshold of at least 50% relief of pain, 26 (61%) blocks were positive and using a threshold of 80% pain relief, 7 (16%) blocks were positive. Proportions of patients achieving 50% and 80% relief by concordance is shown in Fig. 3. The results of the Fisher's exact test for thresholds of 50% ($p = .481$) and 80% ($p = 1.000$) do not indicate a significant association between Concordant injection and positive MBB.

4. Discussion

The results of this study demonstrate that both Concordant and Discordant procedures resulted in a significant decrease in pain with MBB. Over 75% of patients undergoing cervical MBBs had at least one discordant level and patients with concordance between SPECT findings and facet joints targeted with MBB were not more likely to have a positive response to MBB at thresholds of either >50% or >80% relief of pain following the procedure. Taken together, these results demonstrate that MBBs are effective in reducing pain in a subset of patients with axial neck pain, but given the large proportion of injections performed at areas without increased uptake, it appears other factors influence the clinician's decision-making process, which is sound practice given the lack of significant association between areas of increased SPECT-CT activity being injected and positive response to MBB.

The prevalence of facet arthritis differs by age, level of the spine, severity of morphologic changes, presence of symptoms, and technique used for identification. In this population, the highest number of joints demonstrating increased ^{99m}Tc uptake on SPECT-CT were found in the upper cervical spine (C2-3, C3-4, C4-5) with decreasing prevalence at more caudal levels. This is in agreement with MRI findings from a cohort of patients with neck pain (average age 61 years old) which found facet bone marrow edema at the C3-4 (34.7%), C4-5 (24.3%) and C2-3 (19.3%) levels with remaining segments demonstrating a lower prevalence (6%–9%) [5]. Of note, in this study, the second most common joint demonstrating increased uptake on SPECT-CT was C2-3 followed by C4-5 which had only one less joint demonstrating positive uptake. This may be within the expected error of this population but may also be a factor of referral patterns with a significant number of patients being referred by neurology for evaluation of cervicogenic headaches. Similar results were also found in 465 adult cadaveric spines of approximately the same age as this cohort which demonstrated the highest cervical facet edema prevalence in this age group at C3-4 (13.3%) followed closely by C2-3 (12.37%) and C4-5 (14.62%) [6]. When arthrosis was mild, C4-5 was most affected (11.72%); when moderate C3-4 (2.15%) and C4-5 (2.04%) were affected most; and when severe C2-3 (2.58%) and C5-6 (1.94%) were the two most commonly affected joints [6]. The results of this study differ from those in a study of asymptomatic individuals examined with CT in a matched age range which showed C2-3 was the least affected joint with a trend towards increasing prevalence at more caudal levels [11]. This may be due to differences in prevalence of imaging findings among symptomatic and asymptomatic individuals, however, proving imaging findings are the source of one's pain has remained elusive.

Table 2
Distribution of total number of facet joints with and without increased SPECT-CT uptake treated or not treated with MBB.

	Facet Joints Undergoing MBB (n = 74)	Facet Joints Not Undergoing MBB (n = 442)
Increased SPECT-CT Uptake Present (n = 80)	34	46
Increased SPECT-CT Uptake Not Present (n = 436)	40	396

One additional discrepancy of interest is that at C7-T1, 12 joints were identified as having increased uptake on SPECT-CT, but only 5 joints were addressed with MBB at that level with 3 of those demonstrating increased uptake. The relatively low proportion of joints undergoing MBB at this level, may be due to other clinical factors such as the distribution of pain weighing more heavily on the decision-making process of procedural level selection, or it could potentially represent a relative reluctance to perform blocks at this level due to technical difficulty. Although the total number of joints in this category is relatively low, the fact that 3 of 5 demonstrated increased SPECT-CT uptake may suggest that clinicians who decide to order MBBs at this level more often do so based on findings from the SPECT-CT. Further input from clinicians or a prospective study design would be necessary to further assess these theories.

Previous research has provided mixed results with the ability of SPECT-CT to accurately identify painful cervical facet joints on which interventional pain management treatments or surgery will be effective. One small study of seven patients demonstrated a mean improvement in disability by 40% and VAS by 4, 9 months after undergoing surgical treatment of painful cervical facet joints identified by SPECT-CT [19]. Similarly, another study of 25 patients with positive findings on SPECT-CT who underwent surgical treatment for their concordant symptoms had a decrease of 6.6 in self-reported VAS 6 months after the operation [18]. However, this study did not provide data for patients without increased uptake on SPECT-CT who did undergo surgery, and therefore comparisons between outcomes for patients with and without increased uptake on this modality could not be made. A larger study of 112 patients found that facet-targeting procedures were more successful at reducing pain by both 50% and 80% when areas of increased uptake on SPECT-CT were targeted [21]. Less encouraging results were found in a mixed population of patients with either neck or back pain who underwent intra-articular facet joint injection demonstrating no better immediate pain relief if the level injected matched the area of increased uptake on imaging [22]. Together, these results suggest there may be a benefit to choosing a treatment for suspected cervical facet pain based on findings on SPECT-CT, however, the data for percutaneous facet-targeting procedures remains sparse and results are mixed.

SPECT-CT has been shown to be useful in identifying pathology (facet arthropathy and other pain sources) in 92% of patients with chronic neck pain who had previously nondiagnostic MRI or CT results, suggesting a potential role in better localizing these patients' sources of pain [23]. However, up to 70% of facet joints selected for percutaneous treatment (intra-articular facet joint injection or MBB) have been shown to be discordant with those demonstrating increased uptake on SPECT-CT with this discrepancy being attributed to a lack of correlation between metabolically active facet joints and clinical findings in 35% of cases [20]. The results of this study are in agreement with these previous results in that SPECT-CT identified areas of increased uptake in 83 joints in 40 individuals, but nearly 3/4 of patients had procedures performed at levels that excluded at least one SPECT-positive facet joint. This may be due in part to the fact that there are no single pathognomonic historical symptoms or physical examination findings, nor findings on CT or MRI that can predict a positive response to cervical MBB [16]. As a result of this uncertainty, clinicians may "cast a wide net" and target more than the minimum number of joints in an effort to capture all

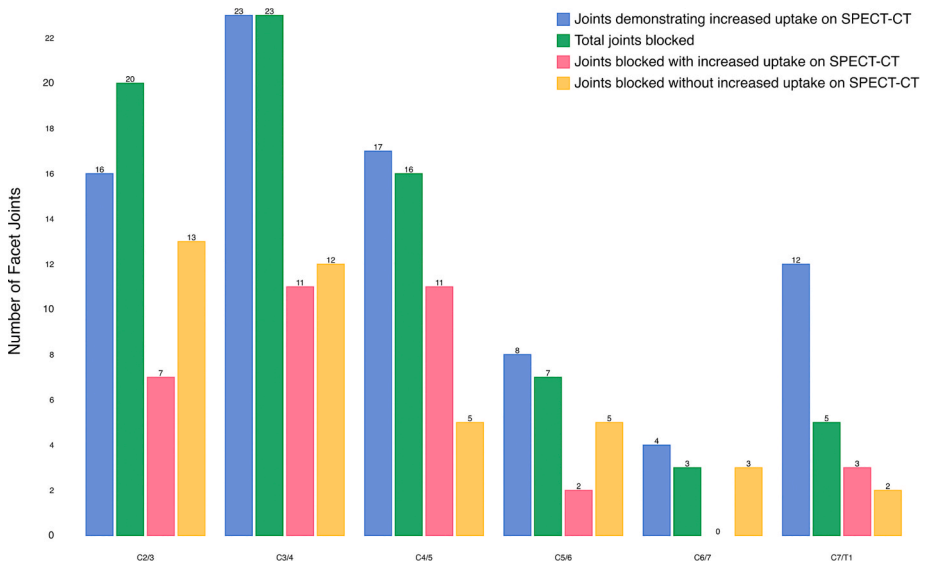

Fig. 1. Number of cervical facet joints per level with reported increased SPECT-CT uptake, total undergoing MBB at that level with breakdown of those undergoing MBB with and without increased uptake. The left and right facet joints are grouped at each level.

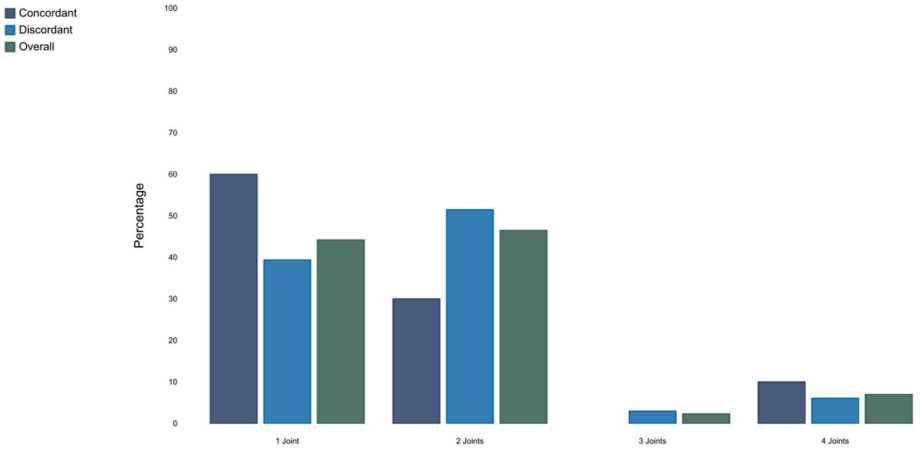

Fig. 2. Total number of facet joints blocked per procedure by level of concordance and overall.

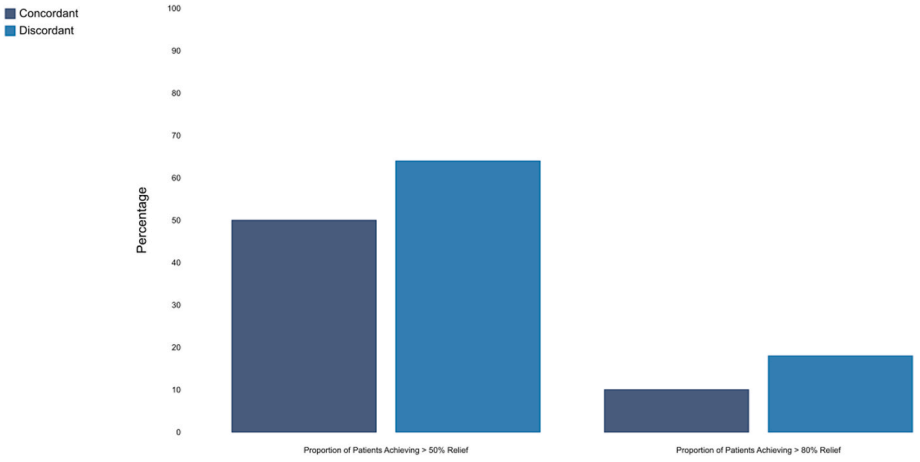

Fig. 3. Proportion of patients with positive MBB using thresholds of >50% and >80% improvement in NRS by level of concordance.

potential pain sources, obtain a positive result, and proceed with RFA with the hopes of achieving clinical improvement for the benefit of the patient.

However, typically only 1 or 2 joints were targeted per procedure. This may be due to the fact that pain referral patterns for the cervical spine are relatively well-defined [7,8] and that the laterality of pain is more easily defined than is typically the case in the lumbar spine negating the need for frequent bilateral procedures. When one joint was blocked, more patients had procedures categorized as concordant, but when two were blocked they were more likely to be discordant. This may simply reflect the fact that the more joints that are blocked, the more likely it is to include a location not showing increased uptake on SPECT-CT, but it is difficult to know how to fully interpret this without additional information about clinicians' thought processes at the time.

This study agrees with others that have shown SPECT-CT is not alone able to predict a positive response to MBBs [20,22], but fails to confirm the results of a recent methodically similar study that showed consistently more successful cervical facet joint injections and MBBs when performed at levels concordant with SPECT-CT uptake [21]. The reasons for this remain uncertain, but one key difference that may have influenced this was the exclusion of patients with no areas of increased uptake in the Nolan et al. study which would tend to bias the results towards a positive result. Another key difference is the inclusion of intra-articular facet joint injections in the Nolan et al. study. Positive response to MBBs was chosen as the criteria against which SPECT-CT findings were compared in this study because it is the recommended prognostic test to identify painful facet joints before proceeding to RFN [16,24,25], and the interval of expected detection of relief is on the order of hours which minimizes recall bias.

The inability of SPECT-CT alone to accurately predict which joints will respond to an interventional procedure is not unexpected, given that a small percentage of patients have normal SPECT-CT findings in the presence of characteristic facet pain [23]. Patients may in fact have facet-mediated pain, but the time-point at which imaging was performed may have been sub-optimal to detect an area of increased uptake correlating with their symptoms. SPECT-CT uses radionuclide bone scintigraphy to identify areas of increased osteogenic activity and skeletal blood flow, representing local inflammation or hyperemia [26,27]. Such inflammation typically occurs early in the degenerative facet cascade and is predictive of progressive degenerative radiologic anatomic abnormalities [28] typically seen later in the course of disease on MRI, but that does not necessarily correlate with areas of increased uptake on SPECT-CT [20]. Therefore, SPECT-CT may help identify patients during an early inflammatory period of facet disease before they have developed morphologic changes on other imaging modalities but may be negative later in the course of the disease. This may also have contributed to the disproportionate number of injections being categorized as Discordant. Given that our patient population has more chronic symptoms, they may be more likely to not have any increased uptake on SPECT-CT, yet still be recommended to undergo MBB based on other clinical criteria, disproportionately increasing the number of injections categorized as Discordant.

Interestingly, a relatively small proportion of patients (16%) in this study were considered to have a positive block using a threshold of 80% relief of pain. A review of the accuracy of medial branch blocks in diagnosing painful cervical facet joints reported a prevalence ranging from 54% to 67% [29]. This review only included prospective studies of placebo-controlled or comparative local anesthetic medial branch blocks performed under fluoroscopic guidance with less than 1 mL of injectate using a diagnostic criterion standard of 80% pain relief [29]. The reason for this discrepancy warrants further investigation. One possibility is that providers ordering MBBs in this study had more liberal criteria for ordering that procedure in a clinical setting compared to the likely more strict criteria utilized in prospective studies. As a result, the populations studied elsewhere in the literature may have excluded patients unlikely to respond to the planned intervention than would be the case in this retrospective analysis. Furthermore, each patient included in this study had a SPECT-CT completed, which are often ordered at our institution by clinicians when initial interventions fail or there is diagnostic ambiguity. Therefore, our study may have included a high proportion of patients unlikely to have a positive response to any further intervention. Additionally, the relatively small sample size in this study is prone to large fluctuations in calculated proportions.

There are several limitations to the methodology of this study. Given the retrospective nature, there was incomplete data in 6% of injections which subsequently had to be eliminated from the study which has potential to introduce information bias. Although MBBs were selected as the diagnostic test of choice to minimize the time between intervention and patient self-report of pain, the potential for recall bias still exists given any delay in query or report of this information. The NRS value chosen to calculate the maximal pain improvement could have been from a single timepoint and may not necessarily reflect a sustained positive response. Furthermore, this review relied on existing radiology reports to identify levels of increased uptake on SPECT-CT. Given multiple raters and a lack of a standardized grading scale that is used across the institution, there is inherent subjectivity and interrater variability in identifying facet joints with increased uptake. Additionally, due to practice variability many patients, particularly early in the period of review, had only one MBB available for review. In an effort to remain consistent across all patients, only the first medial branch block response was reviewed. Ideally dual comparative blocks would have been used to determine if individuals had a positive response.

In conclusion, this study suggests that performing MBB on facet joints demonstrating increased ^{99m}Tc uptake on SPECT-CT is not associated with achieving a positive block. Additional research is needed to determine what combination of clinical and imaging factors may best predict which subset of patients with axial neck pain will have a positive response to MBB. Future prospective studies using SPECT-CT in patients with and without pain undergoing intra-articular corticosteroid and MBBs at various stages of the facet degenerative process are also needed to fully characterize the potential benefit of this modality in identifying specific sources of pain in the cervical spine. Until additional evidence is available, determining the most appropriate cervical facet joints to target with a procedure will continue to depend upon integration of all available clinical data including SPECT-CT when available.

5. Conclusions

The results of this study do not demonstrate a significant association between MBBs being performed on facet joints demonstrating increased uptake on SPECT-CT and resulting in a positive block. Further research is needed to better understand the role of SPECT-CT in conjunction with other factors in helping clinicians determine which cervical facet joints are most likely the source of pain.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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