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The Impact of Contrast Spread Patterns to Clinical Outcomes of Cervical Interlaminar Epidural Steroid Injection: An Observational Study

Ekim Can OZTURK[1], Rekib SACAKLIDIR[2], Savas SENCAN[2], Gulhan ERTAN[3], Osman Hakan GUNDUZ[2]

[1]Istanbul Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Department of Physical Medicine and Rehabilitation, Pain Medicine Section, Istanbul, Turkey
[2]Marmara University, School of Medicine, Department of Physical Medicine and Rehabilitation, Pain Medicine Section, Istanbul, Turkey
[3]Istanbul Medipol University, Department of Radiology, Istanbul, Turkey

Corresponding author: Ekim Can OZTURK ✉ ekimtrilogy@gmail.com

ABSTRACT

AIM: To investigate the relationship between epidural contrast spread patterns, and the treatment success of cervical interlaminar epidural steroid injection (CIESI) for cervical radicular pain.

MATERIAL and METHODS: A total of 76 patients aged between 20 and 60 years who had neck and unilateral upper limb pain due to a single-level disc herniation at C5-C6 or C6-C7 were included. Severity of pain and disability were assessed with Numerical Rating Scale (NRS-11) and Neck Pain Disability Scale (NPDS) at baseline, three weeks, and three months after the treatment. Contrast dispersion prior to injection of the medication was graded in anteroposterior fluoroscopic view. Treatment success was defined as a ≥50% improvement at three months in the NRS-11 scores compared to baseline.

RESULTS: A significant improvement in pain and disability scores was observed at three months compared to baseline ($p<0.001$). Treatment success was observed in 57% of the patients. The multivariate binary logistic regression analysis revealed that high initial NPDS scores, severe foraminal and central stenosis, Grade 1 contrast spread pattern were negative predictors of response to CIESI.

CONCLUSION: Lateral contrast spread toward the dorsal root ganglion (DRG) and spinal nerve root of the target level was associated with more favorable clinical responses. Clinicians performing CIESIs should exert effort to administer the injectate around the DRG and spinal nerve root at the target level.

KEYWORDS: Cervical epidural injection, Contrast medium, Epidurogram, Injectate, Spread pattern

ABBREVIATIONS: AP: Anteroposterior, **BMI:** Body mass index, **CDH:** Cervical disc herniation, **CIESI:** Cervical interlaminar epidural steroid injection, **CTFESI:** Cervical transforaminal epidural steroid injection, **DRG:** Dorsal root ganglion, **ESI:** Epidural steroid injection, **MRI:** Magnetic resonance imaging, **NPDS:** Neck Pain Disability Scale, **NRS:** Numerical Rating Scale, **SD:** Standard deviation, **TF:** Treatment failure, **TS:** Treatment success

Ekim Can OZTURK : 0000-0002-0987-0876
Rekib SACAKLIDIR : 0000-0001-6786-5306
Savas SENCAN : 0000-0001-8150-0581
Gulhan ERTAN : 0000-0002-0742-1305
Osman Hakan GUNDUZ : 0000-0002-3214-803X

INTRODUCTION

Cervical radiculitis is characterized with neck and arm pain radiating in a dermatomal distribution. The pain is often accompanied by weakness, numbness, altered reflexes in upper limbs. It affects 1 in 1,000 adults per year, leading to socioeconomic burden and decreased functionality. Cervical disc herniation (CDH) and spondylosis are the most common causes of cervical radiculitis, and C6 or C7 roots are affected in 80% of the cases (4,5,13,18).

The use of cervical epidural steroid injections (ESIs) has been increasing to manage cervical radiculitis-related pain which is unresponsive to conservative treatments (22). Interlaminar route is the first-line choice rather than transforaminal route thanks to its ease of application and safety profile (19). Regardless of the disc herniation level, cervical interlaminar ESI (CIESI) is usually performed at C7-T1 where epidural space is wider than higher spinal levels; however, recently some authors have reported similar complication rates with injections above C7-T1 (27). The effect of CIESI is influenced by several factors. Some retrospective studies have shown that the severity of neural foraminal or central canal stenosis, level of disc herniation, and duration of symptoms may play a role in the treatment outcomes (3,26).

Epidurographic contrast flow patterns have been a major issue among physicians performing epidural injections. Ventral contrast spread during lumbar interlaminar ESIs have been shown to be related with more favorable clinical improvements (10). On the other hand, there is a limited number of studies investigating the relationship between contrast dispersion patterns during cervical epidural injections and clinical outcomes. Previously two studies failed to find a correlation between contrast dispersion and therapeutic response to cervical transforaminal ESI (CTFESI) (6,23). On the other hand, Kim et al. reported that the restricted spread of contrast medium in central canal was associated with poor response to CIESI (15). However, relevant research had a retrospective design and lacked functional evaluation. Other studies examined the relationship between contrast spread patterns and volume of injectate or depicted a three-dimensional analysis of contrast dispersion without concerning clinical outcomes (8,16,20,26). Since the interlaminar route is not as target specific as the transforaminal route, it is of paramount importance to understand whether there is a correlation between contrast dispersion and clinical response to CIESI. Therefore, in the present study, we aimed to investigate the relationship between epidural contrast spread patterns and the treatment success of CIESI implemented for cervical radicular pain. Our secondary objective was to identify predictors of clinical outcomes after CIESI.

MATERIAL and METHODS

Study Design and Study Population

This single-center, prospective study was conducted at the Pain Management Center of a tertiary care center between January 2022 and March 2023. Initially, 82 patients suffering from cervical radicular pain who underwent fluoroscopy-guided CIESI were included. Prior to study, all patients were informed about the nature of the study and a written informed consent was obtained. The study was approved by the institutional Ethics Committee (No: 09.2020.41) and conducted in accordance with the principles of the Declaration of Helsinki.

Patients aged between 20 and 60 years who had neck and unilateral upper limb pain with a Numerical Rating Scale (NRS-11) score of ≥5 due to a single-level CDH at C5-C6 or C6-C7 were included in the study. Exclusion criteria were as follows: 1) severe motor weakness (≤3/5) in upper limb; 2) rheumatic diseases that may affect cervical spine such as rheumatoid arthritis and ankylosing spondylitis; 3) neurological disorders that may affect central or peripheral nervous system; 4) psychiatric illness; 5) malignancy; 6) contraindications to perform CIESI such as known allergy to ingredients of the injectate given during CIESI, bleeding diathesis, or active infection; 7) history of cervical ESI within the past six months; and 8) history of cervical spine surgery. The CIESI was performed only to patients who could not adequately relieved (NRS-11≥5) despite at least four weeks of conservative treatment including physical therapy and oral analgesics (*i.e.*, non-steroidal anti-inflammatory drugs, weak opioids, or combination therapy).

Data Collection and Assessment

The clinical and demographic data of the patients including age, sex, body mass index (BMI), and duration of symptoms were recorded. The NRS-11 score, and Neck Pain and Disability Scale (NPDS) were used for the assessment of pain intensity and functional status, respectively. The NRS-11 is a widely used scale to measure the severity of pain between 0 to 10. The NPDS is an easily applicable, 20-item instrument which measures the severity of neck pain and its effect on activities of daily living in cervical radiculopathy patients. The validity and reliability study of the NPDS was conducted in the Turkish population (2). The patients were evaluated at three different time points: before the procedure, at three weeks, and at three months after the procedure. Treatment success was defined as a ≥50% reduction in the NRS score at three months of follow-up. The patients were divided into two groups as the treatment success (TS) group and treatment failure (TF) group.

Radiological Assessment

Radiological assessment for grading central canal and neural foraminal stenosis was performed by a single neuroradiologist using sagittal and axial T2-weighted magnetic resonance imaging (MRI) scans, respectively. The presence of neural foraminal stenosis is divided into three categories according to the grading system of Kim et al. (Grade 0: normal; Grade 1: the narrowest width of the neural foramen is 51-100% of the width of the extraforaminal nerve root; Grade 2: neural foramen width is same or less than 50% of the extraforaminal nerve root width) (17). In the present study, Grades 0 and 1 were classified as mild stenosis, while Grade 2 neural foraminal stenosis was classified as severe stenosis. Similarly, central canal stenosis was graded into four categories according to

the system developed by Kang et al. (14) (Grade 0: absence of central canal stenosis; Grade 1: obliteration of more than 50% of subarachnoid space without spinal cord deformity; Grade 2: central canal stenosis with spinal cord deformity but no signal change in spinal cord; Grade 3: increased signal intensity of spinal cord close to the level of stenosis). We classified Grade 0 and 1 as mild, and Grade 2 as severe canal stenosis. Grade 3 patients were consulted to the neurosurgery department and not scheduled for a CIESI.

In the anteroposterior (AP) views, the extent of contrast medium spread was graded by dividing the causative level into two stages: Grade 1 indicated medial contrast spread restricted to the medial foramen (Figure 1) and Grade 2 indicated additional lateral contrast spread extending beyond the lateral border of the medial foramen (Figure 2). This grading system was adapted from the study of Kim et al. (15). Lateral fluoroscopy images were not assessed for contrast distribution, as the true ventral contrast spread on lateral images was rarely documented in previous studies (8,15). Contrast dispersion patterns were evaluated by the performing physician of the procedures who was not involved in the follow-up assessments.

Procedure

All procedures were carried by a pain physician having 10 years of experience in fluoroscopy-guided interventions. In the prone position, 2% prilocaine was administered under sterilized conditions to provide skin anesthesia. The C7–T1 interspace was visualized in an AP view to ensure a paramedian approach. Then, the C- arm was adjusted to a contralateral oblique angle and an 18-gauge Tuohy needle was advanced through C7–T1 interlaminar space under intermittent fluoroscopic imaging. The loss of resistance technique was utilized to confirm that the needle was in the epidural space. A 0.5 mL of contrast medium was given to check non-vascularity and epidural flow. If an appropriate flow was obtained, an additional 2.5 mL of contrast medium was given to grade epidural spread in the AP view. Otherwise, the needle was withdrawn a few centimeters and readjusted. Grading of the epidural spread pattern on the AP view is followed by an injection of a mixture of 12 mg of dexamethasone, 1 mL of 2% lidocaine hydrochloride, and 1 mL of 0.9% saline. The patients were observed for 2 hours in case of any adverse reactions and discharged to be evaluated at Week 3.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0 software (IBM Corp., Armonk, NY). Continuous variables were expressed in mean ± standard deviation (SD) and median (interquartile range), while categorical variables were expressed in number and frequency. The chi-square test was used to compare categorical variables. The Shapiro-Wilk test was used to analyze the distribution of quantitative data. The Mann–Whitney U test was performed for the comparison of non-normally distributed data, while the independent t-test was used to compare normally distributed data. Multivariate binary logistic regression analysis was carried out without any adjustments to calculate the odds ratio (OR) and 95%

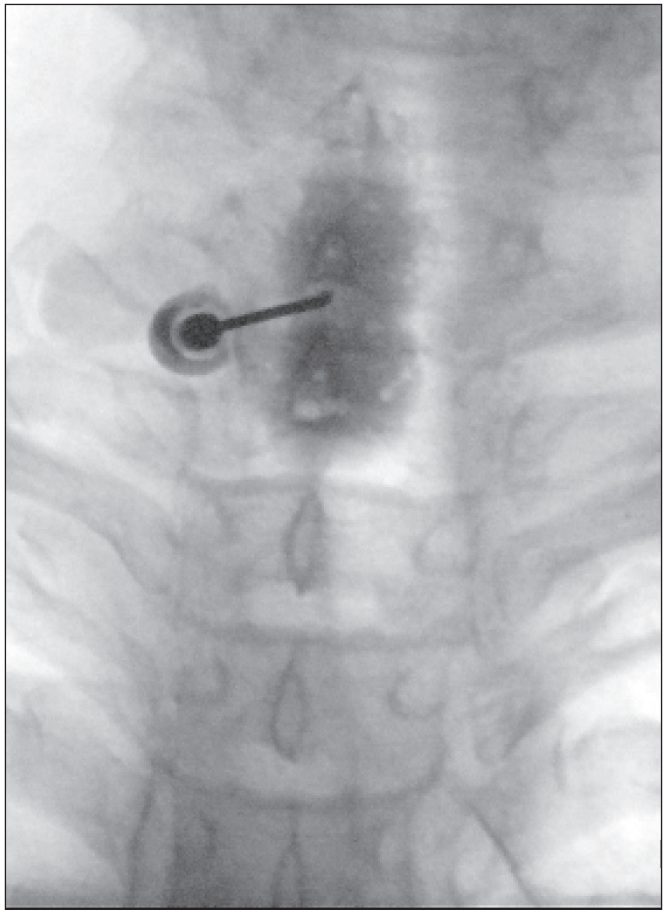

Figure 1: Grade 1 contrast spread.

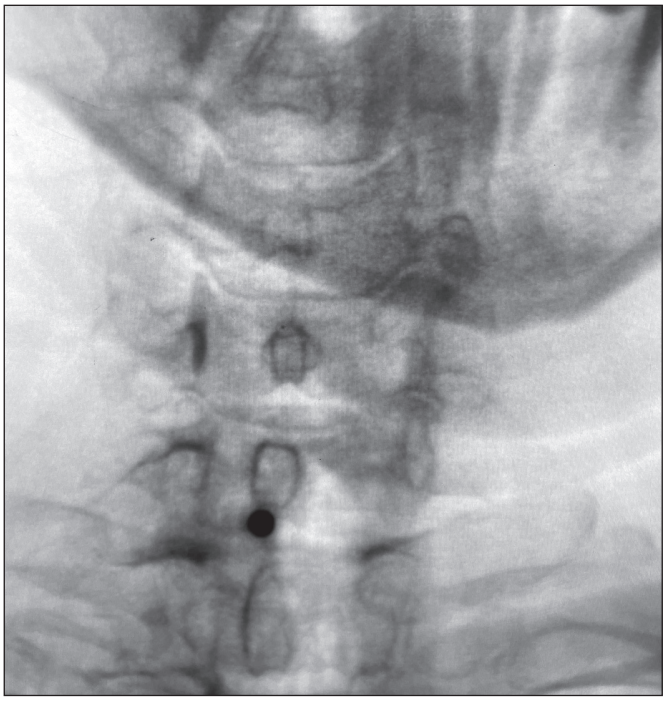

Figure 2: Grade 2 contrast spread.

confidence interval (CI). A p value of <0.05 was considered statistically significant.

RESULTS

Of a total of 82 patients, six were excluded, as they did not attend their appointments in the outpatient setting. Finally, 76 patients were included in the analysis. Of the patients, 40 (52.6%) were female and the mean age of the patients was 40.36 ± 7.42 years. The mean duration of symptoms was 13.62 weeks. The NRS-11 scores before CIESI and three months after treatment were 7.41 ± 0.94 and 3.72 ± 1.67, respectively (p<0.001). A similar improvement in functionality was observed in the NPDS scores which were 59.26 ± 11.05 before CIESI and 39.47 ± 13.88 3 months after CIESI (p<0.001). Thirty-nine patients (51.3%) had disc herniations at the C5-6 level and 37 had (48.7%) at the C6-C7 level. Grade 1 and Grade 2 contrast spread patterns were found in 51 (67.1%) and 25 (32.9%) patients, respectively. In terms of foraminal and central stenosis, 57 patients (75.0%) had mild stenosis and 19 (25.0%) had severe stenosis (Table I).

Table I: Demographic and Clinical Characteristics of All Patients

Variables		Value (n=76) n (%)
Sex	Male	40 (52.6)
	Female	36 (47.4)
Age (years) (mean ± SD)		40.36 ± 7.42
BMI (kg/m^2) (mean ± SD)		26.46 ± 2.07
Symptom duration (weeks)		13.62 (4-22)
NRS-11 (mean ± SD)	Pre-treatment	7.41 ± 0.94
	Post-treatment, 3rd week	3.15 ± 1.61
	Post-treatment, 3rd moth	3.72 ± 1.67
NPDS (mean ± SD)	Pre-treatment	59.26 ± 11.05
	Post-treatment, 3rd month	39.47 ± 13.88
Contrast spread pattern	Grade 1	51 (67.1)
	Grade 2	25 (32.9)
Herniation level	C5-6	39 (51.3)
	C6-7	37 (48.7)
Foraminal stenosis	Mild	57 (75.0)
	Severe	19 (25.0)
Central stenosis	Mild	57 (75.0)
	Severe	19 (25.0)

BMI: *Body mass index,* ***NPDS:*** *Neck pain and disability scale,* ***NRS-11:*** *Numeric rating scale.*

There was no significant difference between the two groups (TS group and TF group) in terms of age, sex, BMI, initial NRS-11 score, initial NPDS score, and disc herniation level. However, symptom duration, severity of foraminal and central stenosis, NRS-11 and NPDS scores at three months were significantly higher in the TF group (p <0.05), while Grade 2 contrast spread pattern was significantly higher in the TS group (p=0.01) (Table II). The multivariate regression analysis revealed that baseline NPDS score, NRS-11 score at three weeks, grade of contrast spread pattern, severity of foraminal and central stenosis were significant factors affecting treatment success of CIESI (Table III).

DISCUSSION

In the current study, we investigated the effect of epidural contrast dispersion on treatment success of CIESI. Lateral contrast spread toward the dorsal root ganglion (DRG) and spinal nerve root was associated with more favorable clinical responses. Besides, high baseline disability scores, severe foraminal, and central stenosis were correlated with inadequate pain relief.

To date, there is only one study examining the direct relationship between contrast medium dispersion and CIESI outcomes. In their retrospective study, Kim et al. showed that if contrast spread was solely within the central canal and did not reach around the DRG, pain relief after CIESI was likely to be poor (15). The authors also speculated that severe central canal stenosis could be the reason of limited diffusion of contrast medium. However, our study indicated that the severity of central canal and foraminal stenosis were similar between Grade 1 and Grade 2 contrast dispersion groups. Accordingly, it can be speculated that contrast medium spread pattern is an independent factor affecting treatment outcomes of CIESI.

Epidural space has a heterogenous nature with distinct anterior, posterior, and lateral compartments. Several factors such as disc displacement, spinal stenosis, aging, scar tissues, administered volume, anatomical variance may affect diffusion of the injectate in the epidural area (29). Levin et al. demonstrated that final needle tip position could also affect the contrast flow during CTFESIs (21). Other studies have explored contrast dispersion patterns in a manner to establish the optimal volume of injectate to be used in CIESIs (16). Park et al. reported that a 3 mL of contrast dye was sufficient to observe an appropriate spread to target lesions (24). On the other hand, Goel et al. concluded that the degree of neck flexion or volumes of injectate less than 4 mL had no clear effect on diffusion of the contrast dye (9).

Ventral epidural contrast spread during lumbar interlaminar injections has been shown to be associated with more favorable clinical improvements (10). However, cervical epidural space has different characteristics than the lumbar epidural space. In a three-dimensional analysis of Gill et al., no true ventral spread was encountered during 24 CIESI procedures. In the current study, we did not assess lateral fluoroscopy images in terms of ventral epidural spread (8).

Table II: Comparison of Demographic and Clinical Variables Between Treatment Success and Treatment Failure Groups

		Treatment success group (n=44)	Treatment failure group (n=32)	p-value
Age (years) (mean ± SD)		39.38 ± 8.36	4.76 ± 8.69	0.241
BMI (kg/m^2) (mean ± SD)		26.41 ± 2.01	26.53 ± 1.72	0.810
(weeks) (mean ± SD)		12.61 ± 3.90	15.03 ± 3.54	**0.007**
PreNRS-11 (mean ± SD)		7.27 ± 0.82	7.65 ± 1.07	0.108
PostNRS-11; 3rd week (mean ± SD)		2.70 ± 1.42	3.78 ± 1.67	**0.004**
PostNRS-11; 3rd moth (mean ± SD)		2.59 ± 0.87	5.28 ± 1.17	**<0.001**
PreNPDS (mean ± SD)		57.78 ± 10.76	61.30 ± 11.28	0.173
PostNPDS; 3rd moth (mean ± SD)		31.70 ± 9.45	50.15 ± 11.78	**<0.001**
Sex; n (%)	Male	20 (45.5)	20 (62.5)	0.108
	Female	24 (54.5)	12 (37.5)	
Contrast spread pattern; n (%)	Grade 1	21 (47.7)	4 (12.5)	**0.001**
	Grade 2	23 (52.3)	28 (87.5)	
Herniation level; n (%)	C5-C6	21 (47.7)	18 (56.3)	0.308
	C6-C7	23 (52.3)	14 (43.7)	
Foraminal stenosis; n (%)	Mild	40 (90.9)	17 (53.1)	**<0.001**
	Severe	4 (9.1)	15 (46.9)	
Central stenosis; n (%)	Mild	39 (88.5)	18 (56.3)	**0.002**
	Severe	5 (11.5)	14 (43.7)	

BMI: *Body mass index,* ***NPDS:*** *Neck pain and disability scale,* ***NRS-11:*** *Numeric rating scale.*

Table III: Factors Associated with Treatment Success of Cervical Interlaminar Epidural Steroid Injection according to Multivariate Binary Logistic Regression Analysis

	OR	p-value	95% CI lower to upper
Age (years)	1.005	0.938	0.887 – 1.138
BMI (kg/m^2)	0.798	0.446	0.447 – 1.426
Sex	8.648	0.084	0.749 – 99.810
Symptom duration (weeks)	1.238	0.142	0.931 – 1.641
PreNRS-11	1.290	0.132	0.949 – 1.529
PostNRS-11; 3rd week	0.296	**0.034**	0.096 – 0.913
PreNPDS	0.698	**0.039**	0.496 – 0.982
Contrast spread pattern	0.018	**0.024**	0.001 – 0.591
Herniation level	0.558	0.635	0.050 – 6.158
Foraminal stenosis	0.003	**0.025**	0.000 – 0.479
Central stenosis	0.033	**0.028**	0.002 – 0.699

BMI: *Body mass index,* ***CI:*** *Confidence interval,* ***NPDS:*** *Neck pain and disability scale,* ***NRS:*** *Numeric rating scale,* ***OR:*** *Odds ratio.*

Dorsal root ganglia play an important role on acute nociception and the maintenance of chronic pain (25). In a retrospective study investigating the relationship between the contrast spread pattern and pain reduction, Han et al. reported that cervical epidural neuroplasty with a contrast runoff pattern (out from the neural foramen flowing past the DRG) was associated with a higher success rate (11). Similarly, the results of our study highlight the importance of DRG in cervical epidural procedures. Contrast dispersion toward the DRG and compressed spinal nerve root may ensure the beneficial effects of ESIs on ischemic neuritis.

Furthermore, previous studies have addressed some of the aforementioned predictors of treatment success of CIESI, such as the presence of severe foraminal and central stenosis (3,15). However, the present study is the first to elucidate the relationship between high baseline disability scores and poor clinical effect of CIESI. A reasonable explanation may be the co-occurrence of high disability scores with other poor prognostic factors including depression, anxiety, and pain catastrophizing which were not addressed in the current study (1,7). Additionally, severe disability may be the sign of severe chemical neuritis. In an observational study, Hong et al. showed that patients with higher baseline disability scores required surgery after CTFESI (12). The authors recommended CTFESIs for patients suffering from cervical degenerative disease with moderate-to-high disability scores (a Neck Disability Index score between 15-35). Also, our previous study revealed that high level CDHs were associated with inadequate response to CIESI (26); therefore, we included only the most common levels of CDHs (C5-C6 and C6-C7) (28) to provide a homogeneous population that is most likely to benefit from CIESI.

Limitations

Nonetheless, there are certain limitations to this study. First, as mentioned in previous reports, contrast medium dispersion may not accurately estimate the extent of injectate diffusion (6). Therefore, well distribution of contrast medium does not always warrant the well distribution of injectate and a favorable therapeutic response. Second, *albeit* we attempted to eliminate most of the confounding factors, patients were allowed to take analgesics during the study. Comparing TS and TF groups with respect to the need for analgesics after CIESI could have strengthened our results. Third, the single-center design with a relatively short follow-up period precludes the generalization of our results. Nonetheless, to the best of our knowledge, this the first study to identify a direct relationship between contrast spread patterns and outcomes after CIESI. The main strengths of this study are the inclusion of patients only with low-level CDH, assessing contrast dispersion at the causative level, and implementing functional evaluation.

CONCLUSION

In conclusion, contrast medium dispersion restricted to the central canal and medial foramen, high baseline disability scores, and severe central canal and foraminal stenosis are associated with treatment failure after CIESI. Delivering injectate close to the affected area may enhance the therapeutic effect of the procedure. Based on these findings, physicians performing CIESIs should exert effort to administer the injectate around the DRG and spinal nerve root of the target level. Patients with poor prognostic factors should be treated with CIESI cautiously. Further multi-center, large-scale studies with longer follow-up are needed to draw more reliable conclusions on this subject.

AUTHORSHIP CONTRIBUTION

Study conception and design: ECO, SS, OHG
Data collection: ECO, RS, SS, GE
Analysis and interpretation of results: RS, ECO, OHG, GE
Draft manuscript preparation: ECO, RS, OHG, SS
All authors (ECO, RS, SS, GE, OHG) reviewed the results and approved the final version of the manuscript.

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