Transforaminal Steroid Injection After Dorsal Root Ganglion Pulsed Radiofrequency (DRG-PRF): Impact on Pain Intensity and Disability

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ABSTRACT

Introduction: Dorsal root ganglion pulsed radiofrequency (DRG-PRF) is frequently used for the treatment of chronic lumbar radicular pain with good outcomes in terms of pain management. Transforaminal epidural steroid injection (TFESI) is often administered immediately after DRG-PRF to increase the anti-inflammatory effects, but support for the synergic mechanism is lacking in the literature. The aim of this study was to investigate the potential role of TFESI immediately after DRG-PRF and its possible role on pain intensity and patient disability.

Methods: A database of patients who underwent DRG-PRF with or without TFESI immediately after DRG-PRF was retrospectively analysed; propensity score matching was applied to the analysis to reduce possible bias. Pain intensity (numerical rating scale [NRS]) and Oswestry disability index (ODI) were recorded pre-operatively and at the 1- and 3-month follow-up in the two groups of patients.

Results: A total of 252 patients were included in this retrospective analysis, 126 patients in the DRG-PRF+TFESI group and 126 patients in the DRG-PRF group after propensity score matching. Both groups displayed a significant reduction in pain intensity (NRS score reduction; $p < 0.0001$) and improvement in the ODI ($p < 0.0001$) from baseline at the 3-month follow-up. Interestingly, the use of TFESI after DRG-PRF was not associated with any clinical benefit as no difference in NRS and ODI was found between the two groups at the 1- and 3-month follow-ups.

Conclusions: Our study revealed a significant pain reduction and disability improvement after DRG-PRF in patients with lumbar radicular pain. Interestingly, no positive role of TFESI immediately after DRG-PRF was observed. These findings suggest that DRG-PRF provides substantial

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pain relief, and no added benefit is obtained with subsequent steroid injection. Future prospective studies with expanded follow-up periods are needed to confirm these findings.

Keywords: Low back pain; Radicular pain; Pulsed radiofrequency; Dorsal root ganglion; Transforaminal; Steroid injection

Key Summary Points
Why carry out this study?
Transforaminal epidural steroid injection (TFESI) is frequently administered immediately after dorsal root ganglion pulsed radiofrequency (DRG-PRF) to increase the anti-inflammatory effects of PRF
However, this supposed synergic mechanism has not been confirmed and no definitive results have supported this strategy
The aim of this study was to investigate the potential role of TFESI immediately after DRG-PRF and its possible effects on pain intensity and patient disability
What was learned from the study?
DRG-PRF effectively reduces pain and improves disability in patients with chronic lumbar radicular pain
TFESI administered immediately after DRG-PRF does not demonstrate additional clinical benefits in terms of pain intensity or patient disability
Propensity score matching ensures reduced bias in comparing the outcomes of DRG-PRF alone versus DRG-PRF with TFESI, enhancing the reliability of the study findings
Prospective studies with longer follow-up periods are warranted to validate these findings and further explore the efficacy of DRG-PRF and TFESI in managing lumbar radicular pain

INTRODUCTION

Chronic spinal pain is a leading cause of disability among adults worldwide with detrimental effects on quality of life and burdensome costs for healthcare systems [1]. Lumbar disc herniations and degenerative spine conditions (stenosis, osteoarthritis, listhesis, scoliosis and vertebral compression fractures) are common conditions involved in low back pain and lumbosacral radicular pain [2]. The main components of the pathophysiology of chronic radicular pain are nerve root compression, inflammation and glial activation [3, 4]. Transforaminal epidural steroid injection (TFESI) is a common interventional option for the treatment of these conditions [5], and although a significant pain reduction has been reported by many published studies with the use of TFESI [6, 7], the efficacy is generally time-dependent and effectiveness in reducing radicular pain is often transient [8, 9].

In the last 25 years, pulsed radiofrequency (PRF) has emerged as a percutaneous, minimally invasive technique that uses an electrical current to achieve medium to long-term pain reduction, especially for neuropathic pain [10]. The procedure was originally described in 1998 for radicular lumbar pain but its application has since been been expanded to include different pain conditions [11].

The dorsal root ganglion (DRG) is a common target of PRF when the aim is to effectively control lumbar radicular pain [12–17]. This technique relies on the intermittent administration of high-frequency, short-duration current at a temperature below 42 °C to induce an electrical neuromodulation without structural damage [18]. The PRF current comprises alternatively repeated electromagnetic waves with a frequency of 500 kHz and pulse width of 20 ms with 480 ms resting phase [19].

Recently, different therapeutic mechanisms have been reported to explain PRF-induced pain relief. The C-fiber long-term depression was the first described mechanism of pain signalling inhibition [20]. Many other mechanisms were subsequently reported, including microglia downregulation [21], increased levels

of endogenous opioid messenger RNA [22], enhancement of noradrenergic and serotonergic descending pain inhibitory pathways [23] and microscopic damages of membranes, mitochondria, microfilaments and microtubules [24]. Recent studies have highlighted the anti-inflammatory effects of PRF as a result of a reduction of proinflammatory cytokines [25, 26], along with an increase of nestin and matrix metalloproteinase-2 expression at the level of the DRG [27].

TFESI is frequently used immediately after DRG-PRF to increase the anti-inflammatory effects of PRF [28]. However, the supposed synergic mechanism has not been confirmed, and no definitive results have supported this strategy. Notably, steroid injections can cause possible severe adverse effects, such as an increase in blood sugar levels, especially in patients with diabetes [29], epidural lipomatosis, spinal cord infarct, menstrual changes, adrenal suppression, Cushing's syndrome, osteoporosis and steroid myopathy [30, 31].

The aim of this study was to investigate the potential role of TFESI immediately after DRG-PRF and its possible effects on pain intensity and patient disability.

METHODS

Study Population

The data of consecutive patients with low back pain and radicular pain who underwent DRG-PRF at our Interventional and Surgical Pain Centre, Guglielmo da Saliceto Hospital, Piacenza, Italy, from January 2019 to December 2021 was entered into a retrospective database specifically created for this study. This study was approved by the local Ethics Committee (747/2023/DISP/AUSLPC) and performed in accordance with the principles of the Declaration of Helsinki.

The inclusion criteria consisted of patients with chronic low back pain, radicular pain, no response to medical and physical treatments and with transitory response to previous epidural or transforaminal steroid injections. Patients with incomplete clinical data and those who were pregnant were not entered into

the database. Patients with localized infection, haemorrhagic diathesis, spinal pathologies (e.g. tumours), vertebral fractures, instability, central canal stenosis, clinical signs of motor palsy, uncontrolled diabetes, heart failure or comorbid psychiatric condition were not included.

Data Collection

Electronic medical records were reviewed to collect demographic and clinical data. Pre- and intra-operative variables such as age, gender, body mass index (BMI), pain duration, level of DRG-PRF, single or dual level (L4L5 + L5S1) DRG-PRF, pain intensity (numerical rating scale [NRS]) and Oswestry disability index (ODI) were collected. The ODI score was calculated from a 10-item questionnaire to assess patients' pain and its impact on daily life activities. This score ranges from minimal disability (0–20), moderate disability (21–40), severe disability (41–60), crippled (61–80) and bed-bound (81–100).

Due to the limited sample size, patients who underwent lumbar (L) spine DRG-PRF at L1, L2 and L3 were not included in the present study. NRS and ODI were collected at 1 and 3 months after DRG-PRF to evaluate the outcome of the procedure. All of the included patients underwent a previous transforaminal injection with lidocaine 1% to confirm radicular involvement. The last transforaminal injection was performed at least 1 month prior to DRG-PRF.

DRG-PRF Procedure

Patients were placed in the prone position with a pillow under the lower abdomen to reduce the physiological lordosis and to provide an easy approach to the intervertebral foramen. A conscious sedation with midazolam 0.05 mg/kg was induced and a 20G, 10-cm radiofrequency cannula with a 10-mm curved active tip was placed near the DRG under fluoroscopic guidance and strict aseptic conditions. Sedation was administered, if necessary, to certain patients to alleviate discomfort and anxiety associated with the procedure. We opted for a curved-tip needle to enhance needle mobility in

cases of foraminal stenosis or bone hypertrophy, as its design allows it to be rotated for easier passage beneath the pedicle. However, these are merely personal impressions, and well-designed studies are necessary to confirm these considerations. The DRG is typically located in the dorsal-cranial quadrant of the intervertebral foramen on lateral fluoroscopic view and in the middle of the pedicle in the anteroposterior view [32]. The position of the cannula was confirmed by contrast injection to exclude a vascular placement and to evaluate the dye distribution along the medial and lateral border of the root and around the thecal sac [33]. The final location of the cannula was checked with sensory and motor stimulations. For the sensory stimulation at 50 Hz, a ≤ 0.4 V threshold was considered and confirmed by paraesthesia onset in the usual distribution of radicular pain. A motor stimulation (2 Hz) threshold greater than 1.5- to twofold the sensory threshold was considered appropriate to ensure the proper position of the cannula away from the ventral root and close to the DRG [34]. An impedance < 400 Ω was also required. The stylet of the cannula was consequently replaced by the radiofrequency probe and a PRF current was applied at 45 V with 20-ms pulse width and 2-Hz pulse rate for a duration of 360 s. The choice of a 360-s duration for PRF was based on prior studies demonstrating efficacy and safety within this timeframe [35–37]. Additionally, a recently published in vitro study suggests a potential effect of PRF on sensitized DRG neurons by reducing central sensitization biomarkers, such as phosphorylated extracellular signal-regulated kinase (pERK) and Ca^{2+} influx when PRF is performed at 2 Hz, 20 ms for 360 s [38]. Increasing the length of the PRF period ensures that each patient receives the precise amount of current necessary to achieve optimal therapeutic effects. However, it is important to note that no definitive protocol exists regarding the optimal PRF settings for clinical effectiveness. The maximum target temperature was 42 °C. However, as previously reported, it is possible for PRF to produce bursts of heat, causing the temperature to briefly exceed this limit around the radiofrequency electrodes by microseconds [39]. This brief increase in temperature is carefully controlled, and during these short periods, the machine will not deliver current to prevent any potential tissue damage while maintaining the therapeutic effects of the treatment.

Immediately after DRG-PRF, 1 ml of 1% lidocaine mixed with 40 mg triamcinolone was injected at the DRG level in the DRG-PRF+TFESI group. The decision to perform a TFESI immediately after DRG-PRF was based only on physicians' choice and personal experience, and no randomization was done. This important issue was adequately addressed in the statistical analysis to avoid possible bias.

Statistical Analysis

Continuous variables are reported as the median and interquartile range (IQR) while categorical data are reported as the relative number and percentage. A propensity score was calculated using different statistical techniques with the use of frequentist and machine learning approaches. Logistic regression, random forest, generalized boosted model (GBM) and covariate balance propensity score (CBPS) were used to estimate propensity scores and for covariate weighting. The best overlap of the distribution of propensity scores (common support) was obtained with the logistic regression model, which was consequently used for the final analysis. Age, gender, BMI, pain duration, level of DRG-PRF, dual level DRG-PRF, basal NRS and basal ODI were considered as covariates. Different calipers (from 0.05 to 0.50) with 0.10 increase were tested for the matching. The standardized mean difference (SMD) was used as covariate balance measurement before and after propensity score matching. As previously recommended, a 0.10 SMD distance between covariates after the propensity score matching was the cut-off value [40]. The best propensity score matching was obtained with exact matching, caliper = 0.30, 1:1 ratio, with no replacement. Therefore, a database with matched patients was implemented, and the average treatment effect (ATE) related to NRS and ODI at 1 and 3 months after DRG-PRF was estimated with the Holm–Šídák correction for

multiple comparisons. Statistical significance was set at a two-tailed *p* value<0.05. R software v4.2.2 (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org) was used for the analyses.

RESULTS

A total of 158 patients in the DRG-PRF+TFESI group and 150 patients in the DRG-PRF group were initially considered for the study; of these 61 patients were excluded due to incomplete or missing data. After the propensity score matching, 126 patients in the DRG-PRF+TFESI group and 126 patients in the DRG-PRF group were matched. Consequently, 32 patients in the DRG-PRF+TFESI group and 24 patients in the DRG-PRF group were discarded due to covariate imbalance. As previously reported, the best overlap between propensity score values (common support) was obtained after logistic regression estimation (Fig. 1).

All of the covariates were also adequately balanced after propensity score matching (Fig. 2). Ppatients' covariates before and after propensity score weighting are summarized in Table 1. The median age of the included patients was 61

(IQR 52–69) years in the DRG-PRF+TFESI group and 62 (IQR 52–69) years in the DRG-PRF group (SMD - 0.0506). The majority of patients in each treatment group were female (59% and 61% in the DRG-PRF+TFESI and DRG-PRF group, respectively). The median BMI was 26.2 (IQR 23–28.4) kg/m^2 in the DRG-PRF+TFESI group and 25 (IQR 23–28) kg/m^2 in the DRG-PRF group (SMD 0.0147). Pain duration at the time of the intervention was 3.1 (IQR 1.5–4.7) years and 3.4 years (1.8–4.6 IQR) (SMD 0.0887), baseline NRS was 7.9 (IQR 7.6–8.4) and 8 (IQR 7.4–8.4 IQR) (SMD -0.0201) and ODI was 53 (IQR 49–57) and 53 (IQR 49–58) (SMD - 0.0542), in the DRG-PRF+TFESI and DRG-PRF groups, respectively. DRG-PRF was mainly performed at the L4-L5 level (57.3% of patients in the DRG-PRF+TFESI group, 58.2% in DRG-PRF group).

No difference was found between baseline NRS (*p*=0.87) and ODI values (*p*=0.95) in the DRG-PRF and DRG-PRF+TFESI groups (*p*=0.87). The ATE of the TFESI in the matched dataset revealed no difference between the DRG-PRF+TFESI and DRG-PRF groups in terms of NRS (NRS DRG-PRF+TFESI group: 4.3±2.3; NRS DRG-PRF group: 4.4±2.2; *p*=0.88) and ODI (ODI DRG-PRF+TFESI group: 20±7.9; ODI DRG-PRF group: 22±7.8; *p*=0.95) at the 1-month follow-up after DRG-PRF. The same results were
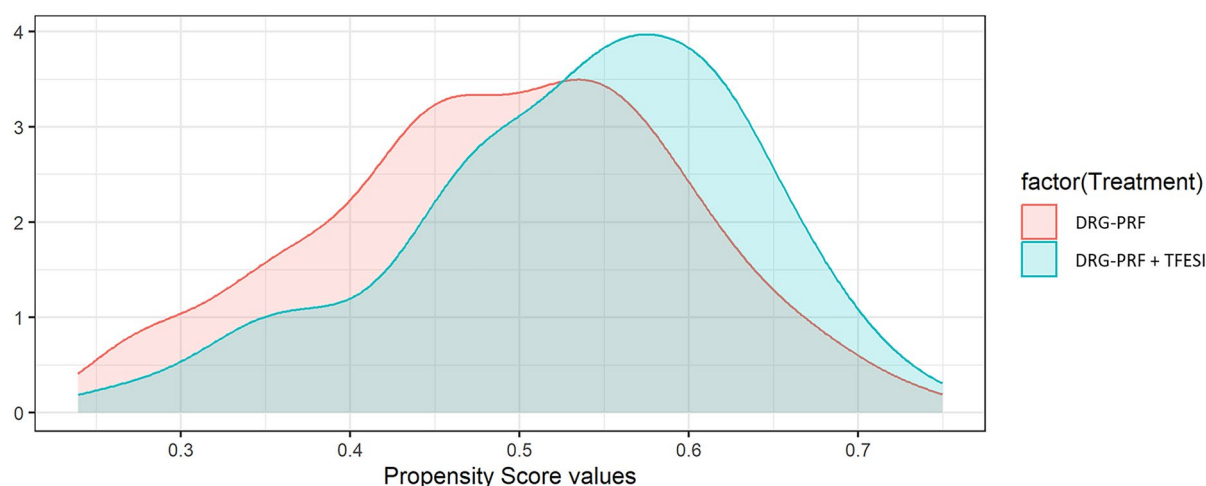
Fig. 1 Best overlap of propensity score values (common support) across the two treatment groups (DRG-PRF and DRG-PRF+TFESI) after propensity score estimation with logistic regression. In addition to overlapping,

the propensity score values have a similar balanced distribution. *DRG* dorsal root ganglion, *PRF* pulsed radiofrequency, *TFESI* transforaminal epidural steroid injection
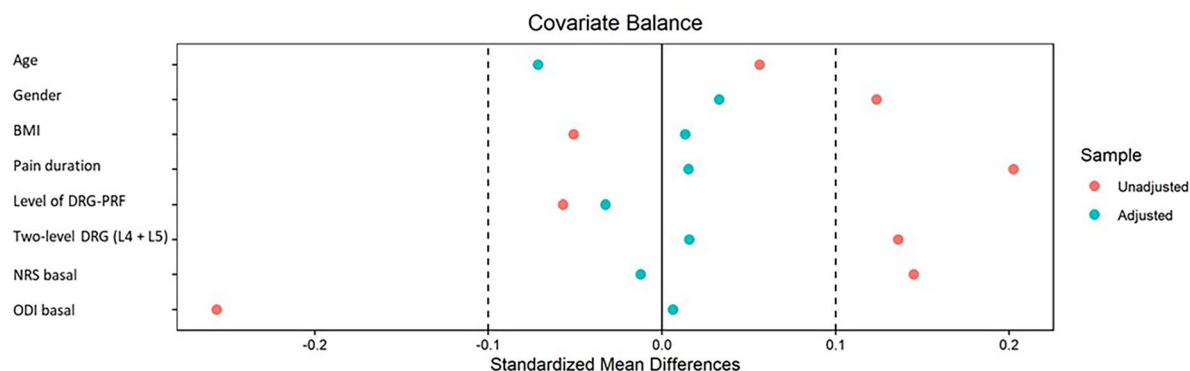
Fig. 2 Covariates standardized mean differences before (unadjusted) and after (adjusted) propensity score matching. All covariates were below the cut-off value of 0.10. *BMI* Body mass index, *DRG* dorsal root ganglion, *NRS* numerical rating scale, *PRF* pulsed radiofrequency, *ODI* Oswestry disability index

Table 1 Baseline covariates of patients unweighted and weighted by propensity score

Baseline covariates	All patients (*n* = 308)	Unweighted			Propensity score weighted		
		DRG-PRF + TFESI group (*n* = 150)	DRG-PRF group (*n* = 158)	SMD	DRG-PRF + TFESI group (*n* = 126)	DRG-PRF group (*n* = 126)	SMD
Age, years	62 [53–73]	62 [51–73]	62 [55–71]	0.05	61 [53–70]	62 [52–74]	− 0.07
Gender				0.12			0.03
Male	186 (60.4%)	86 (57.3%)	100 (63.3%)		50 (41%)	48 (39%)	
Female	122 (39.6%)	64 (42.7%)	58 (36.7%)		72 (59%)	74 (61%)	
BMI, kg/m²	25.7 [23–28]	25.4 [23.5–27.8]	26.1 [22.5–28.4]	− 0.05	26.4 [23–28]	25.4 [23–27]	0.01
Pain duration, years	3.2 [1.6–4.7]	3.4 [1.6–5]	3.1 [1.5–4.4]	0.20	3.1 [1.5–4.7]	3.2 [1.6–4.5]	0.02
Level of DRG-PRF				0.06			− 0.03
L4-L5	181 (58.8%)	86 (57.3%)	95 (60%)		78 (62%)	76 (60%)	
L5-S1	127 (41.2%)	64 (42.7%)	63 (40%)		48 (38%)	50 (40%)	
Two-level DRG-PRF	136 (44%)	75 (50%)	61 (39%)	0.14	56 (44.4%)	55 (43.6%)	0.02
NRS basal	7.9 [7.5–8.4]	8 [7.6–8.4]	8 [7.3–8.4]	0.15	7.9 [7.5–8.4]	8 [7.4–8.4]	− 0.01
ODI basal	53 [49–58]	53 [48–57]	54 [50–58]	- 0.26	53 [49–57]	53 [49–58]	0.006

Values in table are presented as the median with the interquartile range in square brackets or as the number with the percentage in parentheses

BMI Body mass index, *DRG* dorsal root ganglion, *L* lumbar spine, *L5-SI* lumbosacral joint, *NRS* numerical rating scale, *PRF* pulsed radiofrequency, *ODI* Oswestry disability index, *SMD* standardized mean difference, *TFESI* transforaminal epidural steroid injection

obtained at the 3-month follow-up for NRS (NRS DRG-PRF + TFESI groups 4.8 ± 2.6; NRS DRG-PRF group: 4.2 ± 1.6; $p = 0.80$) and ODI improvement (ODI DRG-PRF + TFESI group: 27 ± 11; ODI DRG-PRF group: 27.6 ± 10; $p = 0.96$). Compared to baseline, the NRS was significantly reduced in both groups at the 1-month ($p < 0.0001$) and 3-month follow-ups ($p < 0.0001$), while the ODI score was similarly improved at the 1-month ($p < 0.0001$) and 3-month follow-ups ($p < 0.0001$) (Fig. 3).

DISCUSSION

In this study the use of TFESI (DRG-PRF + TFESI group) immediately after DRG-PRF was not associated with any clinically significant benefit. In fact, no difference in pain intensity (NRS scale) and disability index (ODI scale) was found at the 1- and 3-month follow-ups after DRG-PRF regardless of whether TFESI was administered or not. Significant pain relief and ODI improvement were maintained for up to 3 months in both groups.

DRG-PRF is frequently used with good results for the treatment of refractory radicular pain in patients with disc herniations, lumbar stenosis or persistent spinal pain syndrome (PSPS) [41]. The neuromodulatory and anti-inflammatory effects are the key elements of DRG-PRF but, as previously cited, other therapeutic mechanisms have been reported. Unfortunately, a complete description and a full understanding of all these complex mechanisms are still unavailable [42]. Various DRG-PRF protocols have been published, and analytical problems arise when attempting to compare different studies in a meta-analysis [43, 44]. In addition, DRG-PRF can be applied
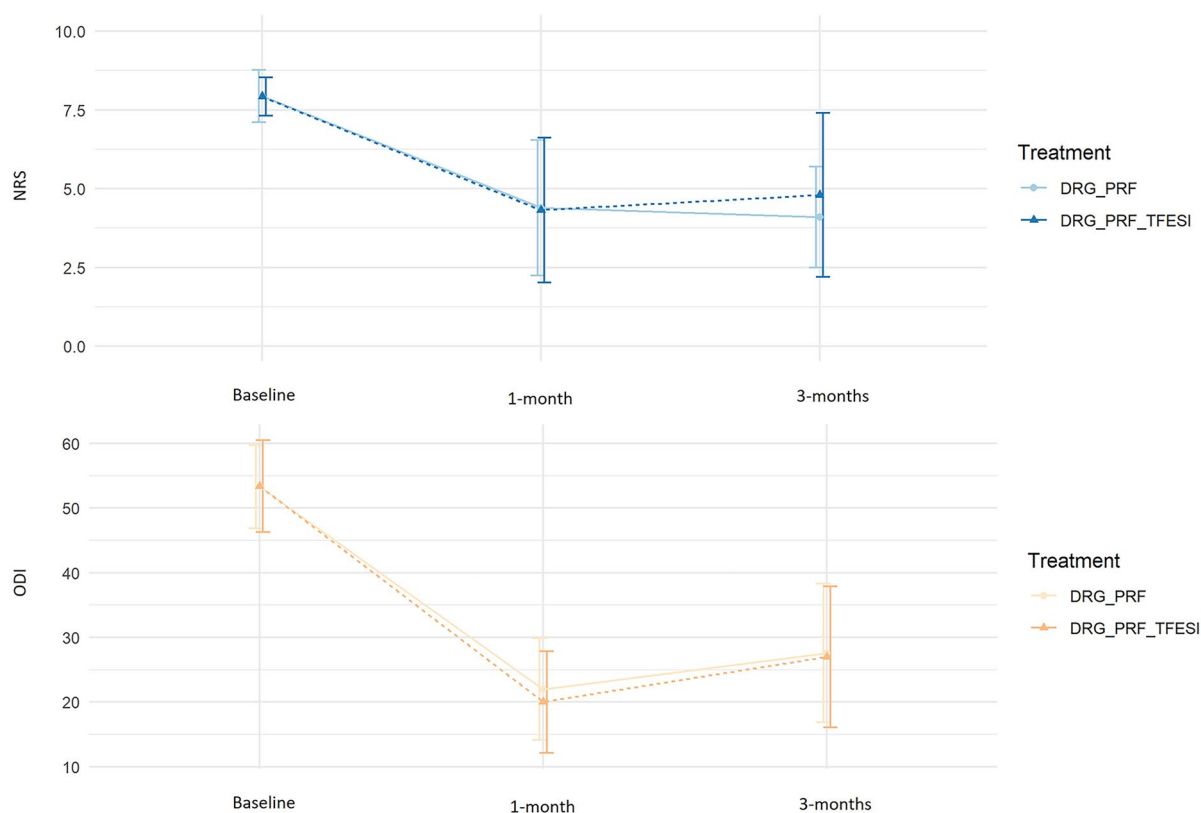
Fig. 3 Changes in pain scores (NRS) and disability index (ODI) during the follow-up, after DRG-PRF in the two groups (DRG-PRF and DRG-PRF + TFESI). *DRG* Dorsal root ganglion, *NRS* numerical rating scale, *PRF* pulsed radiofrequency, *ODI* Oswestry disability index, *TFESI* transforaminal epidural steroid injection

whether transforaminal or epidural, and the selection of the appropriate technique has not been adequately addressed. The same problems can be found in preclinical animal studies where the ideal voltage, number of cycles, pulse duration and optimal electrode distance are still far from being clarified [45]. All of these issues should be addressed in future studies for a better indication of the application of PRF for pain management. Indeed, the authors of a previously published review concluded that while there may be a convincing role of DRG-PRF for the treatment of cervical radicular pain, the evidence for PRF efficacy in treating lumbar radicular pain has yet to be confirmed by further studies, largely due to the absence of standardization of PRF parameters and enrolment criteria [46]. Moreover, as reported by Van Zundert et al., in the setting of a randomized controlled trial PRF treatment of the cervical DRG showed promising pain relief outcomes, indicating potential efficacy in patients with chronic cervical radicular pain [47].

In the present study, DRG-PRF was performed at 45 V with 20-ms pulse width and 2-Hz pulse rate, for a duration of 360 s, as previously suggested by many authors for the treatment of lumbar radicular pain [48–50]. High-voltage PRF has recently been proposed as a new method to increase the efficacy of the procedure and has been extensively studied for the treatment of herpes zoster-related pain [51–53]. However, the first encouraging results of high-voltage PRF [54, 55] were not confirmed in a recently published double-blind randomized control trial [56]. Taking all of these elements into account, high-voltage PRF cannot currently replace PRF performed at 45 V, and new evidence is needed to support the use of high-voltage PRF. Hopefully, the results of this ongoing trial will provide more information on this topic [57]. We believe that unresolved questions about the optimal "PRF dose", including the voltage and duration of energy delivery, may significantly contribute to conflicting results in some studies and should be thoroughly addressed in future research. Finally, it is important to note that our results should be interpreted as strictly linked to the DRG-PRF protocol used and cannot be generalized.

TFESIs are frequently used with good short-term results for the management of radicular pain [58]. Steroids can reduce the inflammatory cascade by inhibiting the synthesis and the release of pro-inflammatory cytokines [59, 60]. When injected trasforaminally, they can potentially act at the anterior epidural space, where higher concentrations of substance P and glutamate are present [61, 62]. Adding steroids to PRF treatment has the potential to enhance the efficacy of this treatment by reducing inflammation. Steroids are known for their anti-inflammatory properties, which may complement PRF's mechanism of action. However, as we previously noted, there are potential local (epidural lipomatosis and spinal cord infarct) and systemic (increase in blood sugar levels, menstrual changes, adrenal suppression, Cushing's syndrome, osteoporosis and steroid myopathy) negative effects to consider. Moreover, steroids could attenuate some of the intended effects of PRF by altering the physiological response at the DRG level or potentially affecting the healing process.

A direct correlation with clinical improvement was found when an anterior epidural spread of the medication was obtained [63]. Although PRF was superior to TFESI and associated with positive results in previous studies for the treatment of radicular pain [64, 65], some authors have reported no difference in patients who received PRF or sham treatment [14, 66]. A recent retrospective study by Yang et al. [67] showed a 60% median pain reduction at the 1-month follow-up in patients with disk herniation, spinal stenosis or PSPS after DRG-PRF combined with TFESI, while no control group without steroids was considered. Our findings are in line with this publication. Indeed, our DRG-PRF + TFESI group showed a 46% NRS reduction at the 1-month follow-up. Unfortunately, it is not possible to fully compare the two studies since Yang et al. analysed only pain intensity and no ODI data were reported. Moreover, it is possible to argue that some patients in the Yang et al. study [67] underwent more than one DRG-PRF before the 1-month follow-up, since the number of DRG-PRF procedures performed is higher than the number of enrolled patients and DRG-PRF application

at multiple spinal levels was not allowed by the protocol.

The same findings were reported in a subsequent study on the use of DRG-PRF with TFESI in 42 patients with different spine-related, pain-associated diagnoses [28]. If we consider only the lumbar spine group, DRG-PRF was able to reduce the NRS by 53% and 52% at the 1- and 3-month follow-ups, respectively. Notably, the authors were also able to show a 64% reduction in the NRS at 1 week after DRG-PRF, and a general decrease in the use of analgesics at 3 months after the procedure. Although this study highlights a number of important elements, such as the earlier follow-up and the decrease in analgesic use after DRG-PRF, the limited sample size and a possible covariate imbalance among the included patients prevents a possible comparison with our data and data from other studies.

To the contrary, in another published study PRF was considered to be an adjuvant treatment in conjunction with TFESI to increase the efficacy and the response rate of the injected steroid [14]. In this randomized controlled study, the authors reported a better pain relief at 2 and 3 months after DRG-PRF+TFESI when compared to TFESI alone while no difference was found at the 1-month follow-up, thus demonstrating a possible short-term role of TFESI. However, it is important to note that the results of this study should be interpreted cautiously since the primary outcome (pain reduction) was underpowered due to loss to follow-up and possible change of concomitant analgesic medication use, as allowed by the protocol. Consequently, is not possible to rule out that TFESI, PRF and analgesic medications can interact over the observed outcome.

In a retrospective study, 135 patients with lumbar radicular pain were treated with TFESI alone, DRG-PRF alone or TFESI combined with DRG-PRF [68]. All of the patients experienced an early analgesic effect, but only the second and third group obtained a more prolonged period of pain relief up to 3 months, as compared to patients treated with TFESI alone. Interestingly, at the 1-month follow-up, the lowest pain intensity and ODI improvements were obtained by patients in the TFESI + DRG-PRF group. In contrast, our data did not show any difference at the 1-month follow-up between the DRG-PRF+TFESI and DRG-PRF groups. This apparent difference could be related to the enrolled patients: in their retrospective study Ding et al. [68] enrolled a more heterogeneous group of patients with axial (non-radicular) or radicular chronic low back pain without a subgroup analysis, while we considered only selected patients with only radicular pain. Moreover, Ding et al. [68] also used 1 mg of vitamin B12 as an adjuvant in TFESI. Another study compared the use of TFESI in combination with DRG-PRF to TFESI alone in patients with lumbar or cervical radicular pain due to disc herniation [69]. Although pain intensity was significantly reduced in both groups after the treatment and the NRS score was lower in the DRG-PRF group, no statistically significant difference was found during the 12-week follow-up period.

To the best of our knowledge, no previously published studies comparing DRG-PRF+TFESI and DRG-PRF exist. The results of our study confirm that DRG-PRF does not require the injection of steroids to increase its efficacy for the treatment of radicular pain. DRG represents a key aspect due to its unique neuroanatomical structure and function on pain transmission [70, 71], along with a possible role as rescue therapy in patients with spinal cord stimulation failure [72]. All of these elements underline the crucial importance of DRG in radicular pain. This is the first study that directly compares pain reduction and ODI improvements in patients with radicular pain treated with DRG-PRF with and without TFESI immediately after PRF.

Although our study showed no clear advantages for the use of steroids after DRG-PRF in patients with radicular pain, additional prospective studies are needed to confirm these results and to expand on the clinical role of DRG-PRF in radicular pain. Moreover, it is important to consider our results as being strictly linked to the DRG-PRF protocol that was used. Another future area of research includes the development of well-constructed DRG-PRF outcome prediction models with a validation process. Indeed, as was recently outlined, different results can be obtained when a validation analysis is carried

out to evaluate the strengths and weaknesses of the models [73, 74].

This study has several limitations. First, it is a single-centre, retrospective study. However, this potential weakness is counterbalanced by a significant sample size and the use of a propensity score-based analysis. In retrospective studies a wide distribution of observed covariates can be observed, and this can lead to biased estimates of the treatment's effect. The propensity score has been used to reduce this bias. Indeed, as previously suggested, it could be considered comparable to a randomized trial [75, 76]. No data were collected regarding previous spine surgery; recently published data suggest that PRF is more effective in patients with disc herniation and spinal stenosis compared to patients with PSPS [12, 77]. However, these findings were not confirmed by Yang et al. [67]. We are not able to confirm these findings since data on the occurrence of previous lumbar surgery were collected in only a small number of patients and the required minimum sample size to be analysed and matched was not reached. Moreover, it was not possible to systematically collect the concomitant analgesic medications used by our enrolled patients. This is related to inaccuracies and failures in reporting these data during follow-up visits.

Other possible covariates, such as lifestyle habits (e.g. smoking, physical activity) or psychological factors (depression, anxiety and pain catastrophizing), were not studied, although all of these elements can certainly affect the observed results. Even if radicular pain was the leading symptom in these patients, it was not possible to rule out the presence of other minor contributing factors (e.g. facet or sacroiliac joints pain, muscular pain, postural imbalance) that could have influenced the DRG-PRF outcome.

In our study, only 1- and 3-month follow-up data were collected, and no data on early follow-up (e.g. 1 and 2 weeks) were available. This is related to our internal organization since patients are normally reassessed 1 month after an interventional procedure. Due to the retrospective nature of this study, these data cannot be documented. Consequently, a possible short-term benefit after steroid injection cannot be ruled out. Future studies with early follow-up, ranging from a few days post DRG-PRF to the first 2 weeks after treatment, are needed to clarify the potential role of steroid injection during the early period following DRG-PRF.

CONCLUSIONS

Our propensity scores matching analysis revealed a significant pain reduction and disability improvement after DRG-PRF in patients with lumbar radicular pain. Interestingly, no positive role of steroid injection immediately after DRG-PRF was observed. These findings would suggest that DRG-PRF does not require the injection of steroids to increase its efficacy. Future prospective studies with earlier and longer follow-up are needed to confirm our findings.

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presentation of the research, manuscript, or abstract in any form has occurred.

Data Availability. The dataset used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. All the authors (Matteo Luigi Giuseppe Leoni, Fabrizio Micheli, David Michael Abbott, Marco Cascella, Giustino Varrassi, Pasquale Sansone, Roberto Gazzeri, Monica Rocco and Marco Mercieri) have nothing to disclose regarding the topic of this article. They have no affiliation with, or involvement in any organization or entity with any financial or non-financial interest in the subject matter discussed in this manuscript. Giustino Varrassi is an Editor-in-Chief of *Pain and Therapy*. Giustino Varrassi was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

Ethical Approval. This study was approved by the Local Ethics Committee (747/2023/DISP/AUSLPC) and performed in line with the principles of the Declaration of Helsinki.

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