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Is the Interfascial Space a Potential Target for Neuromodulation in Pain Management?

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ABSTRACT

Objective: Interfascial space blockade is a common method for treating acute and chronic pain. This involves opening fascial adhesions and providing local anti-inflammatory and anaesthetic activity to relieve pain. Neuromodulation, which has rich nerve innervation, may enhance the effectiveness of this treatment. This study investigates the therapeutic effect of integrating neuromodulation with pulsed radiofrequency (pRF) into erector spinae plane (ESP) blockade.

Materials and Methods: This study was a single-blind, randomized controlled trial that included 56 patients with upper back pain caused by myofascial pain syndrome. One group received ESP block, while the other group received ESP block and pRF. Pain improvement was monitored using the visual analog scale (VAS) before and 30 min after treatment, as well as at 2, 4, and 12 weeks.

Results: Improvement was observed in both groups with treatment at all times (Friedman; Group Block $p=0.001$, Group Block+pRF $p<0.001$). The block and pRF group had lower VAS scores at weeks 4 and 12 compared to the block only group (Mann-Whitney U; week 4 $p=0.002$, week 12 $p<0.001$).

Conclusion: At the 12-week follow-up, both ESP block and pRF treatments added to ESP block were effective in relieving upper back myofascial pain. However, the addition of pRF significantly increased the effectiveness and duration of the treatment. The interfascial space presents a potential new target for pain management through neuromodulation.

Keywords: Erector spina plane block, Neuromodulation, Pain treatment, Pulsed radiofrequency, Upper back myofascial pain

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INTRODUCTION

Myofascial pain syndrome (MPS) is a frequent cause of chronic musculoskeletal pain due to the presence of myofascial trigger points. Although the incidence rate is on average 85%, it is more common in young- and middle-aged women.[1] The erector spinae plane (ESP) block is a used treatment for chronic pain caused by MPS.[2-5] It is a fascial block that has gained significant interest since its description in 2016 and is now used to treat both acute and chronic pain. The ESP block is carried out by accessing the fascia between the transverse process of the vertebra and the erector spinae muscle.

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Fascial blocks are considered to be effective by dissolving fascial adhesions by hydrodissection, anti-inflammatory effect by steroid injection, and modulation of peripheral and central sensitization by blocking free nerve endings with local anesthetic.[6,7] In the literature, the efficacy of ESP block in myofascial pain has typically been followed for an average of 6–8 weeks. The most emphasised mechanism of analgesic efficacy is drug diffusion. The drug spreads to the paravertebral area through the intertransverse connective tissue and to the epidural area through the intervertebral foramen. It then spreads to the erector spinae muscle and ultimately to the dorsal rami nerve endings within the muscle.[8]

The histological section of the trapezius muscle after the interfascial block revealed numerous nerve branches in the interfascial section. The text mentions the mechanism of myofascial pain relief through the effect of local anaesthetic on the nerve endings in this interval.[9] Currently, the mechanism of pain relief with fascial blocks is primarily attributed to the volume and content of the drug injected into the area. However, is this area open to neuromodulation due to its dense nerve network? Is pulsed radiofrequency (pRF), which is frequently used in chronic pain treatment, effective in this area? pRF works through a complex mechanism of action. It elicits electric field effects that result in changes in neural cellular substrates.[10]

Recent immunohistochemical studies suggest that the fascial network contains approximately 250 million nerve endings, making it the largest sensory organ after the skin.[11,12]

Furthermore, current research has highlighted the topic of cellular communication, which occurs faster than nerve conduction through quantum tunneling. The magnetic field generated by electrons in the cell membrane directly affects other cells, regardless of receptor stimulation. There is discussion of a communication speed that exceeds that of nerve conduction.[13]

It is possible that the pRF current, generated by an electric field, can create neuromodulation in the peripheral and central nervous system via a retrograde pathway from free nerve endings with cellular adaptation. However, there are few studies on this subject in the literature. Therefore, we investigated whether fascial neuromodulation is a viable treatment option for chronic pain. We investigated whether adding pRF treatment to the ESP block would extend the duration of pain relief in patients with upper back myofascial pain.

MATERIALS AND METHODS

This was a single-blind, randomized, controlled trial. Ethics committee approval was obtained from the ethics committee of Dışkapı Yıldırım Beyazıt Training and Research Hospital on July 04, 2022 (Decision no: 141/16). The study was conducted in accordance with the Declaration of Helsinki.

Randomization and Blinding

We used a computer-assisted randomization program to allocate patients into groups. We assigned patients sealed envelopes marked group 1 (block group)-group 2 (block+pRF group). The investigators who assessed the patients at the 3-month follow-up were blinded.

Participants

A total of 85 patients with upper back myofascial pain were evaluated and 60 individuals who met the inclusion criteria were included in the study from August 2022 to August 2023. Power analysis was performed using G*Power software to determine the required sample size for our study. Our initial data used for the power analysis included an effect size of 0.985, a significance level of $\alpha=0.05$, a desired power of $(1-\beta)=0.95$ and a total sample size of 56. These values were based on preliminary 12-week visual analog scale (VAS) mean and standard deviation (SD) data from 10 patients. The power analysis indicated that a sample size of 56 would be required to detect a significant effect with the specified parameters.

Inclusion Criterias

Individuals aged between 18 and 65 years, experiencing pain that is not restricted to a single dermatome or myotome, and exhibiting tight bands and one or more identifiable trigger points in the erector spinae muscles. Pain must be present when pressing the tender point on the erector spinae, assessed as ≥6 points on the VAS. Pain should be in the upper thoracic levels, tenderness should be detected by palpation, especially around the 3-4-5th thoracic vertebrae.

Exclusion Criterias

Patients undergo internal medicine, pulmonology, physiotherapy and rheumatology controls as a routine practice of our clinic and the following reasons were determined as exclusion criteria: upper back pain not due to malignancy, cervical or thoracic disc disease, not accompanied by rheumatological diseases that may cause chronic pain, not accompanied by severe depression or somatisation disorder, not associated with pregnancy or interventional procedure, not associated with bleeding diathesis or use of blood thinners.

The study design is depicted in Figure 1.

Treatment

ESP Block

All procedures were performed under sterile conditions and monitoring. All procedures were performed by the same physician with at least 5 years of experience in ultrasound (USG) and interventional procedures. The patient was placed in the prone position. The thoracic spinous processes and costae

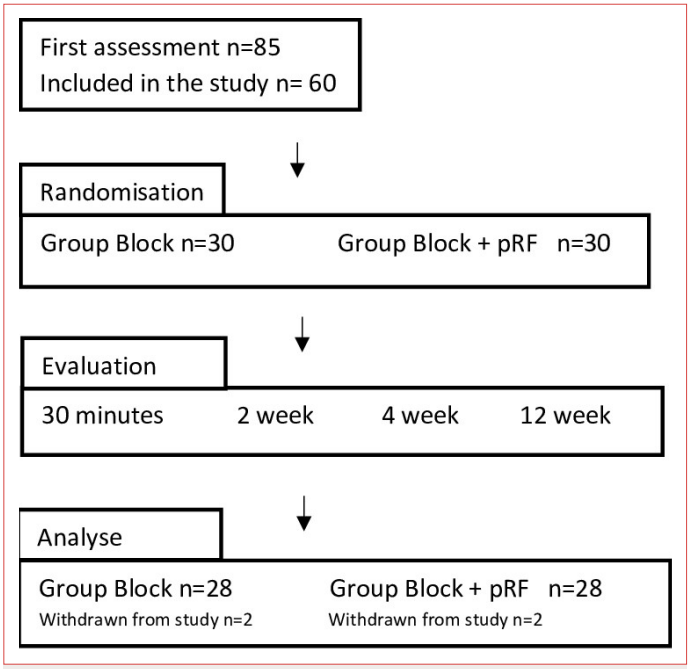

Figure 1. Flow chart diagram.

were scanned with a linear USG probe. Once the transverse processes were visualised, the spinal needle was inserted into the cephalic end of the transverse process using the inplane technique. Procedures were applied to the upper thoracic vertebrae (thoracic levels 3–5). Each patient was injected with 2 cc of dexamethasone, 8 cc of 0.5% bupivacaine, and 10 cc of saline in a volume of 20 cc. Patients were observed for 2 h for possible complications.

ESP Block + pRF

All procedures were performed under sterile conditions and monitoring. The patient was placed in the prone position. The spinous processes of the thoracic vertebrae and the costae were scanned with a linear USG probe. After visualisation of the transverse processes, a 10×10 cm cannula electrode was inserted into the cephalic end of the transverse process using the in-plane technique. 4 cc of saline was injected.

A radiofrequency generator (TOP Lesion Generator -10) and a 22-gauge 10 cm 5 mm active hybrid electrode (Equip, FIAB SPA, Italy) were used. A pRF current was applied for 8 min (5 Hz at 45 V, 5 ms at a temperature of 42°C). Each patient was then injected with 2 cc of dexamethasone, 8 cc of 0.5% bupivacaine and 6 cc of saline in a volume of 16 cc (A total of 20 cc was reached with 4 cc of saline injected before pRF). Patients were observed for 2 h for possible complications, (Fig. 2).

The white arrow symbolizes both the block needle and the radiofrequency cannula.

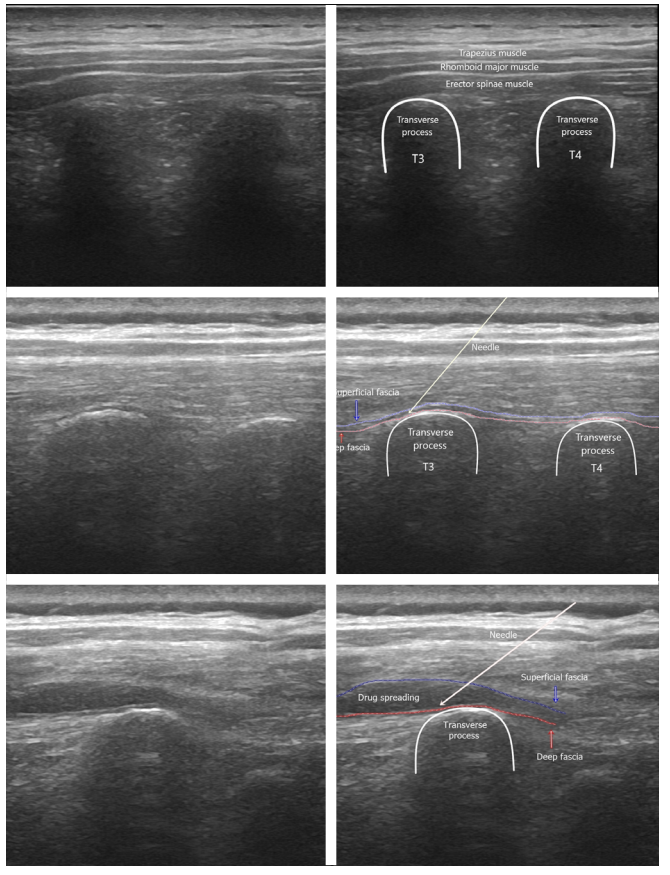

Figure 2. Intervention of erector spinae plane block and pulsed radiofrequency.

Outcome Assessment

We assessed all patients using the VAS scores before and 30 min, 2–4–12 weeks after treatment. Our primary objective was to ascertain the impact of treatment on pain intensity using VAS scores. Our secondary aim was to examine the side effects of treatment. For the VAS, a score of 0 indicated no pain and 10 represented the highest pain experienced during the most severe pain.

Statistical Methods

All analyses were conducted using Jamovi Project (2022, Jamovi Version 2.3, Computer Software). The findings of this study are expressed as frequencies and percentages. Normality analysis was performed using the Shapiro–Wilk test, skewness, kurtosis, and histograms. Normally distributed variables are presented as means and SD. Categorical variables were compared using the Chi-square test. Numerical dependent variables were compared between the groups using an independent sample t-test and Mann-Whitney U test. Repeated measures were analyzed using the Friedman and Wilcoxon test. Statistical significance was set at $p<0.05$.

RESULTS

There was no difference in age or gender between groups. There was no difference between pre-treatment, 30 min post-treatment, and week 2 VAS scores. The block + pRF group had statistically significantly lower VAS scores at weeks 4 and 12 compared to only block group (Mann-Whitney U test; p=0.002, p<0.001), (Table 1).

The groups were evaluated within themselves. In the Block group, a statistically significant decrease was observed at all time points after treatment compared to baseline VAS measurements (Wicoxon test; basal-30 min p<0.001, basal-2w p<0.001, basal-4w p<0.001, basal-12w p=0.005). In the block group, there was a statistically significant decrease in change over 12 weeks (Friedman test; p=0.001).

In the block + pRF group, a statistically significant decrease was observed at all times after treatment compared to the baseline VAS measurement (Wicoxon test; basal-30 min p<0.001, basal-2w p<0.001, basal-4w p<0.001, basal-12w p<0.001). The pRF + Block group showed a statistically significant decrease over 12 weeks (Friedman test; p<0.001), (Table 2 and Fig. 3).

No significant side effects that required treatment were observed during the procedure. Three patients experienced nausea and hypotension after the injection, but they recovered within half an hour and were kept under observation.

Table 1. Demographic characteristics and group comparisons

	Group Block		Group Block+pRF		test st.	p
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)		
Age	50.93±11.81	52.5± (25–72)	36.36±10.17	40 (10–50)	0.774	0.442[a]
Gender						
Female (%)	23 (46)		27 (54)			0.084[b]
Male (%)	5 (83)		1 (17)			
VAS basal	8.75±1.14	9 (7–10)	8.46±1.81	9 (4–10)	390	0.973[c]
VAS 30 minutes	4±2.38	4.5 (1–9)	3.75±2.59	3.5± (1–10)	352.5	0.510[c]
VAS 2 week	3.32±2.38	2.5 (1–9)	3.14±1.6	3 (1–6)	395.5	0.953[c]
VAS 4 week	4.29±2.57	4 (1–9)	2.21±1.39	2 (1–6)	203.5	0.002[c]
VAS 12 week	6.86±2.69	7.5(1–10)	3.46±2.8	2 (1–10)	165	<0.001[c]

[a]: Independent samples t test; [b]: Chi-square test; [c]: Mann–Whitney U test; VAS: Visual analog scale; pRF: Pulsed radiofrequency. SD: Standard deviation.

Table 2. Change in VAS between all-time points and within 12 weeks

VAS	Basal	30 min	2 week	4 week	12 week	test st.	p*
Group block							
Mean±standard deviation	8.75±1.14	4±2.38	3.32±2.38	4.29±2.57	6.86±2.69	66.853	0.001
Mean rank	4.5	2.23	1.86	2.61	3.8		
p**		<0.001	<0.001	<0.001	0.005		
Group pRF+block							
Mean±standard deviation	8.46±1.81	3.75±2.59	3.14±1.6	2.21±1.39	3.46±2.8	60.98	<0.001
Mean rank	4.84	2.86	2.7	1.89	2.71		
p**		<0.001	<0.001	<0.001	<0.001		

p*: Friedman test; p**: Comparison with baseline VAS by Wilcoxon test; VAS: Visual analog scale; Min: Minutes; pRF: Pulsed radiofrequency.

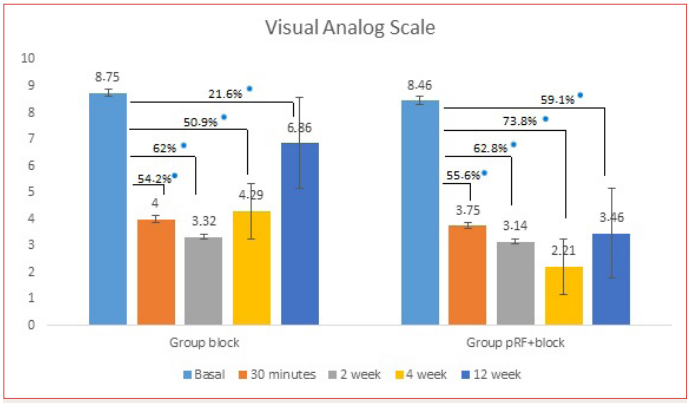

Figure 3. Temporal change of visual analog scale scale.

Blue spot: Between two time point P<0.05; pRF: pulsed radiofrequency.

DISCUSSION

The results of this study indicate a statistically significant improvement in both groups at the 12-week follow-up. Additionally, the group that received pRF in addition to ESP block had lower VAS scores at 4 and 12 weeks, with statistically significant differences compared to the only block group (p=0.002, p<0.001). Pain relief with fascial neuromodulation is more effective than blockade alone for up to 12 weeks. The pain improvement levels of the ESP block group were similar to the literature data; it will be discussed below in terms of interfascial pRF application in myofascial pain.[2-5]

The fascial continuum is recognized as adipose tissue with its innervation, specialised for each region where it is located. Adipose tissue serves as a source of energy, heat, and secreted biochemical substances. It also acts as a mechanical tension attenuator, interacting with metabolism through paracrine and autocrine modes. Fascial layers are structurally and functionally separated, as shown by macroscopic, three-dimensional microscopic examinations and immunohistochemical studies. Fascia has a dual phylogeny from mesoderm and ectoderm, as seen in embryological development.[14]

The fasciatome is a term used to identify the deep fascia layer supplied by the same nerve root and determine the main directions of movement. It is similar to the dermatome, which is a mapping method resulting from the rich innervation of the skin. Pain corresponding to the fasciatome is clinically recognized as radicular pain because it originates from the same nerve root.[15]

In MPS, the fascial system can be a source of pain due to its extensive nerve organization. This is not only because it is a tissue through which nerves pass but also because the connective tissue that forms the fascia is innervated and contains mechanoreceptors. Recent immunohistochemical studies on superficial and deep fascia have revealed this rich nerve network.

The superficial fascia has more autonomic and sensory nerve fibres, whereas the deep fascia has more proprioceptive and nociceptive fibres. Fede et al.[11] state that the superficial fascia is the most innervated tissue in the body after the skin. (skin>-Sup Fascia>Deep Fascia>Deep Adipose Tissue>Superfiscial Adipose Tissue). Larsson et al.[16] stated that superficial fascia acts as a mechanoreceptor, causing mechanical allodynia due to its dense autonomic fibres. These studies highlight the rich autonomic innervation of the superficial fascia. They suggest that stress, trauma, or sudden temperature changes can cause sympathetic activation not only in the skin but also in the superficial fascia. This mechanism also explains how external factors such as heat or manual therapy can improve fascial sensitivity and reduce pain.[17-19]

A review of immunohistochemical features of muscular/deep fascial innervation found that the thoracolumbar fascia is the most innervated fascia in both rats and humans. The study measured nerve fibre lengths and diameters of deep fascia containing proprioceptors and nociceptors, and the results showed an increase in both length and diameter of these fibres in pathological conditions. It has been reported that nociceptor density increases in inflamed fascia, also known as pathological fascia. Fascial nociceptors are part of the pain generator that can be predisposed by chemical and mechanical stimuli. From this perspective, chronic MPS may be hypothesized to result from fascial peripheral sensitization causing central sensitisation, which in turn causes chronic pain. Therefore, myofascial pain may be a problem of fascial origin rather than muscular origin.[12]

In another review examining the role of deep fascia in chronic pain, the main factor causing chronic pain in MPS is pathological fascia. As a result of immunohistochemical studies, an increase in both collagen and myofibroblast activity was observed in the tissue defined as pathological fascia. This increase is characterised by tissue stiffness and causes changes in the signalling of proprioceptive nerve endings located in the deep fascia. Another innervation change is the increased density and sensitivity of nociceptive nerve fibres. This has been associated with an increase in markers of inflammation, such as pro-inflammatory cytokines and immune cells. In summary, pain from deep fascia is probably due to a combination of increased nerve density, sensitivity, and chronic nociceptive stimulation, either physical or chemical.[20]

Can the rich neural network of deep and superficial fascia layers be a target tissue for neuromodulation with pRF? Can the fascial area be effectively used for pRF? pRF is a neuromodulation technique that generates an electric field to decrease pain

expression in the central nervous system through a series of reactions occurring in the neural substrates.[10,21,22]

The mechanism of action of pRF is not clear, although it acts through biological pathways. Modification mechanisms of pRF have been implicated in nociceptive signalling. This modification occurs through a variety of mechanisms, including neurotransmitters, ion channels, postsynaptic receptors, immune activity, microglial markers, inflammatory cytokines, and intracellular proteins.[21] pRF is effective in treating chronic pain in various anatomical locations and pain syndromes.[23-26] However, there is limited literature on pRF data in MPS. Bevacqua and Tamimi reported pain improvement in MPS patients with pRF applied to trigger points in case reports. Niraj found that 8 out of 12 patients experienced pain relief lasting 6 weeks after trigger point injection and pRF.[27-29]

Two studies compared pRF and block in the interfascial area. In the first study, conducted by Park in an MPS, one group received interfascial PRF to the gastrocnemius, and the other group received interfascial block. The pain scores of the PRF group remained lower for a longer period compared to the block-only group, with 50% pain relief in 2–4 weeks. It is worth noting that the pain scores measured immediately after the treatment were lower in the block group. The reason for this may be that the Prf group did not receive an injection of local anesthetic or steroid. The results indicate that interfascial blockade is more effective than pRF in the acute period.[30]

The other study conducted in the trapezius muscle in MPS involved two groups. One group received only interfascial block, while the other group received only pRF. Cho et al.[31] found that the recovery time was longer in the pRF group. Patients in both groups showed a significant decrease in Numeric Rating Scale (NRS) scores at 2, 4, and 8 weeks after treatments. Two weeks after each treatment, the decrements of NRS scores were not significantly different between the two groups. However, 4 and 8 weeks after the procedures, they found that the NRS score was significantly lower in the PRF group than in the block group.

We obtained similar results to the above studies, with a longer-lasting improvement in the pRF + block group compared to the block group. The decrease in VAS score between 30 min, 2–4–12 weeks before and after treatment was 54.2%, 62%, 50.9%, and 21.6% in the block group, respectively. pRF+block group showed 55.6%, 62.8%, 73.8%, and 59.1%, respectively. As can be seen, while both groups were similar at the first two measurements, pain scores continued to decrease in the pRF group at week 4. At week 12, there was still more than a 50% improvement.

In Park and Cho's studies, patients undergoing pRF were not injected with local anaesthetics or steroids in the interfascial space.[30,31] Park found that patients' pain scores were significantly higher in the pRF group than in the block group immediately after the study.[30] According to our results, the pain scores measured after 30 min were similar in both groups and statistically significantly lower than before treatment. In our opinion, the combination of local anesthetic and/or steroid injected into the interfascial area after pRF application provides patients with more comfort and less pain in the acute phase.

We gave each patient 4 cc of saline before the pRF application. Our aim was both to confirm that we were in the fascial area and to increase the electric field formation of pRF waves in a liquid medium. pRF achieves its main effect by creating an electric field.

Cellular transmission of the electromagnetic field through the cell membranes, known as quantum tunneling, takes place more easily in liquid media, and the synchronicity of this phenomenon is so great that as cellular functionality increases, the speed of information transfer is faster than the speed of nerve conduction. The expanding electromagnetic field spreads to other cells, keeping the whole body in communication.[13,32-34]

Based on all this information, we can form some ideas about how pRF produces a long-lasting activity. The rich fascial nerve network, especially the nociceptors located in the deep fascia, communicates with the central nervous system via A-delta and C fibres. These nociceptors contain large amounts of substance p and calcitonin gene-related peptides (CGRP).[35] Substance P and CGRP are important mediators in pain generation and trigger the onset of pain signalling. pRF modulates pain generation from the periphery to the central nervous system in a first step by etching these free nerve endings. This provides a longer-lasting improvement than interfascial blockade.

Study Limitations

The limitations of the study were that the follow-up period was limited to 12 weeks, and there was no third control group in which only pRF was applied. Another limitation was that we could not evaluate the effect of interventions on drug consumption, and there was no functionality scoring. The last restriction may be the uniqueness of the torasic levels used. For a more homogeneous application procedure, a treatment procedure applied at a single level could have been investigated.

CONCLUSION

Combined block with pRF applied to the ESP interfascial area has a longer-lasting effect than block alone. Local anesthesia and/or steroid injection after pRF application is beneficial for patient comfort and early pain improvement. There is a need for further studies and largeron neuromodulation of fascial areas in the treatment of chronic myofascial pain.

DECLARATIONS

Ethics Committee Approval: The study was approved by Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (No: 141/16, Date: 04/07/2022).

Informed Consent: Written informed consent was waived because of the retrospective nature of the study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Authorship Contributions: Concept – GRGP; Design – GRGP; Supervision – GRGP; Fundings – GRGP; Materials – GRGP; Data collection &/or processing – TA; Analysis and/or interpretation – TA; Literature search – TA; Writing – TA; Critical review – TA.

Peer-review: Externally peer-reviewed.

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