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Original Article

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Dexamethasone Injection Into Pterygomandibular Space Versus Sublingual Space on Post-Operative Sequalae of Lower Third Molar Intervention

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Abstract

Background: The surgical removal of lower third molar is still the most common surgical procedure that is done in oral and maxillofacial surgery field and creates the predictable post-operative sequelae such as pain, swelling, stiffness and difficulty in mouth opening. The purpose of this study is to compare pre-operative dexamethasone injection into pterygomandibular space (PGS) and sublingual space (SLS) in lower third molar intervention of post-operative pain, swelling, and limited mouth opening.

Methods: This study is the split-mouth, randomized crossover clinical trial in 30 healthy patients (mean age 21 years). These patients had similar bilateral lower third molar impactions. The patients were randomly divided into two groups receiving either 8-mg dexamethasone injection into SLS or PGS with the 4-week washout period intervention. Clinical assessment of facial swelling and maximum mouth opening was performed before operation and on day 2 and day 7 after operation. The post-operative pain was also measured by patients' response on pain visual analogue scale (VAS) on the first, second and third day after intervention.

Results: There is no significant difference between PGS group and SLS group in pain and swelling on the second and seventh day after operation. However, PGS group showed a greater degree of limited mouth opening than SLS group on the second day after operation.

Conclusions: This study showed that 8-mg dexamethasone injection into PGS or SLS was not different in reduction of pain, swelling, and limited mouth opening. This result suggests that dexamethasone injection into PGS or SLS is similarly effective.

Keywords: Lower third molar intervention; Dexamethasone injection; Sublingual space; Pterygomandibular space; Post-operative sequalae

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Introduction

The removal of mandibular third molar (MTM) is the most common surgical procedure that is done by oral and maxillofacial surgeons and is associated with predictable complications such as post-intervention pain, swelling, limited mouth opening [1]. The region of intervention is composed of loose connective tissue that contains blood and lymph vessels, and may cause post-operative sequelae. The post-operative pain begins when the effect of the local anesthesia subsides and reaches its maximum intensity during the first 12 h post-operatively. The large varieties of analgesics are available for management of post-operative pain. Limited mouth opening is a normal and expected outcome following third molar intervention, and usually reaches its peak on the third day and relieves in the first week [2]. This post-operative complication brought by MTM intervention usually causes discomfort feeling for patients that can impact their quality of life, which should be minimized as much as possible.

Post-operative events are usually treated with pharmacological strategy. Corticosteroid such as dexamethasone is known to reduce inflammation, fluid transudation and edema [3]. Dexamethasone has been used extensively in oral and maxillofacial surgery due to the glucocorticoid effects, absence of mineralocorticoid effects, and the least adverse effects on leukocyte chemotaxis [1, 4]. Glucocorticoids inhibit capillary

permeability, bronchoconstriction, and inhibit vascular and inflammatory responses [5]. Dexamethasone is being delivered for third molar intervention by many routes such as oral consumption, intravenous, intramuscular delivery in masseter, gluteal or deltoid region, sub-mucosal injection, endoalveolar powder and delivery into the potential space.

The previous studies mentioned the use of dexamethasone to reduce the complication following MTM intervention. The previous research of Grossi et al [6] studied the effect of submucosal injection of dexamethasone on post-operative third molar intervention. The study of Alcantara et al [7] also found that pre-operative dexamethasone in facial swelling control and limited mouth opening had better effect than 40 mg methylprednisolone. The previous research of Mojsa et al [8] also studied the effect of dexamethasone on three groups of facial swelling, post-operative pain and limited mouth opening following third molar intervention, and post-operative pain and limited mouth opening after removal of impacted lower third molar. The previous study of Antonio et al [9] mentioned that the oral administration and local injection in the masseter muscle of 8 mg dexamethasone proved effective in reducing post-operative pain, edema, and limited mouth opening following lower third molar intervention. The research of Chaurand-Lara and Facio-Umana [10] which studied the effect of administration of 20 mg methylprednisolone intramuscularly in masseter mentioned post-operative facial swelling and post-operative pain after surgical removal of impacted lower third molars. However, the previous study of Tiigimae-Saar et al [11] also found that a combination of a single dose of prednisolone and etorikoxib is suitable for treatment of post-operative pain, limited mouth opening, and swelling after third molar intervention.

The previous research of Tiwana et al [12] studied intravenous corticosteroids before third molar intervention without antibiotics in patients at high risk for delayed health-related quality of life and clinical recovery, and found intravenous corticosteroid administration had a limited, but beneficial effect on health-related quality of life outcomes. The previous article of Ehsan et al [13] found that 4 mg submucosal dexamethasone injection before surgical removal of MTM also significantly reduced post-operative swelling and limited mouth opening. The previous study of Bauer et al [14] found that the pre-emptive analgesia with ibuprofen was also insufficient to inhibit central sensitization, but dexamethasone was more effective to prevent post-operative pain in third molar intervention. The previous study of Baxendale et al [15] found that dexamethasone significantly reduced post-operative pain 4 h after MTM intervention and reduced the use of opioid analgesics, and dexamethasone could also reduce swelling significantly, but there was no effect on limited mouth opening. The study of Li et al [16] assessed the efficacy of dexamethasone in pericoronal injection for controlling post-operative swelling and limited mouth opening caused by impacted MTM intervention. Periodontal injection of 4 - 5 mg could control post-operative facial swelling and limited mouth opening following impacted MTM intervention. The previous article of Filho et al [2] showed that the administration of 4 mg versus 8 mg dexamethasone, and 8 mg dexamethasone was more effective to control post-operative swelling and limited mouth opening than 4 mg in mandibular impacted third molar intervention.

There are many routes of dexamethasone administration for research of mandibular impacted third molar intervention outcomes. The previous study of Latt et al [17] studied the efficacy of dexamethasone injection versus the saline injection (control group) on post-operative pain in lower third molar intervention. The previous study of Gozali et al [18] also mentioned the decreased post-operative pain using 8-mg dexamethasone injection into sublingual space (SLS) compared with the saline group in lower third molar intervention.

The benefit of the two routes is that no additional post-operative pain is caused to patient when injected after inferior alveolar nerve block, lingual nerve block and long buccal nerve block that is commonly done in dentistry of MTM intervention. This technique is simple and can be done easily for the dentist. Other techniques, such as intravenous or intramuscular delivery, require mastering additional techniques and cause post-operative pain to patient during injection.

On the other hand, there is no further study about dexamethasone injection into pterygomandibular space (PGS) versus into SLS. Therefore, this current research studied 8-mg dexamethasone injection into PGS versus SLS to control post-operative pain, facial swelling and limited mouth opening. The benefit of this study is to improve the patient's quality of life after intervention of MTM in simple lifestyle, safety, painless and less cost-effective therapeutic option.

Materials and Methods

The Oral and Maxillofacial Surgery Clinic of the Faculty of Dentistry, Mahidol University, Thailand is the address for this prospective randomized controlled split-mouth clinical crossover study. Every author of this study has ORCID iD and the protocol of this investigation was approved by the research ethics committee of Mahidol University Institutional Review Board (COA No. MU-DT/PY-IRB 2016/021.2303), and written informed consent (local language) was obtained from all the patients before intervention.

Sample size calculation

Sample size calculation has been performed by using G power 3.1.0 software, assuming α error is 0.05, power is 95% and estimated effect size is 0.4. After our pilot study we calculated our sample size following the related formula recommendations. Minimum sample size must be at least 25 adult patients and withdrawal of five patients. There was no withdrawal in this study, so this study included 30 patients. The patients have been informed of the procedures and objectives of the study and inform consent has been obtained.

This current research included 30 healthy patients (13 men, 17 women) on eligibility criteria selection as shown in Table 1, with an average age of 21 years (age range 16 - 31 years), with similar bilateral lower third molar and the same degree of positions (Table 2 and Fig. 1). The surgical removal

Table 1. Eligibility Criteria Selection of the Patients

Inclusion criteria selection of the patients
The patient has bilateral impacted lower third molars symmetrically positioned on both sides of the mandible of which surgical removal consists of flap operation, bone removal, and tooth section
Aged between 18 - 45 years
No history of allergy to dexamethasone, amoxicillin, or acetaminophen
No use of other medicine 1 month before and during the study period
The patient is able to understand and carry out the instructions given by the investigators
The patient has provided their consent for the study

Exclusion criteria selection of the patients
Pregnancy or current lactation
Patients with cardiovascular problems, renal and/or liver failure, or other serious medical conditions
Allergic to local anesthetics and other drugs that were used in this study
Patient with facial deformities that may interfere with the injections, surgery or evaluation
The existence of acute infection and/or swelling and pain at the time of surgery
Patients taking any medication during the previous 1 month prior to the surgery
Inability to follow the instructions or cooperate during the study
Duration of treatment more than 1 h

consisted of bone cut and tooth section. Patient had not used other medicines 1 month before the intervention, and had no history of allergy to drug used in this study.

This crossover research had spilt-mouth design by injection of 8 mg of dexamethasone into SLS and PGS on another side. Each patient appointed for two different surgical procedures by the same experienced surgeon (SLS injection and PGS injection). The washout period of the second appointment was 4 weeks after first intervention. The patients were blinded of 8-mg dexamethasone injection after inferior alveolar nerve block and were in a state of complete numbness [19-20], 8 mg of dexamethasone was injected, and then standard technique of lower third molar intervention was performed.

Table 2. Demographic Data of Patients in Study Groups

Data consideration	8 mg dexamethasone		Total	Percentage
	Pterygomandibular space injection	Sublingual space injection		
Number	30	30	60	100
Age				
16 - 25 years	28	28	56	93.3
26 - 32 years	2	2	4	6.6
Sex				
Male	13	13	26	43.3
Female	17	17	34	56.7
Position				
A	9	9	18	30
B	21	21	42	70
Class				
I	12	12	24	40
II	18	18	36	60

Position A: the part of the lower third molar is above the occlusal plane of the lower second molar; Position B: the highest portion of the lower third molar is between the occlusal plane and the cervical line of the second molar; Class I: there is sufficient space of accommodation of the mesio-distal diameter of the lower third molar; Class II: the space of accommodation of the mesio-distal diameter of the lower third molar is less than the mesio-distal diameter of the lower third molar.

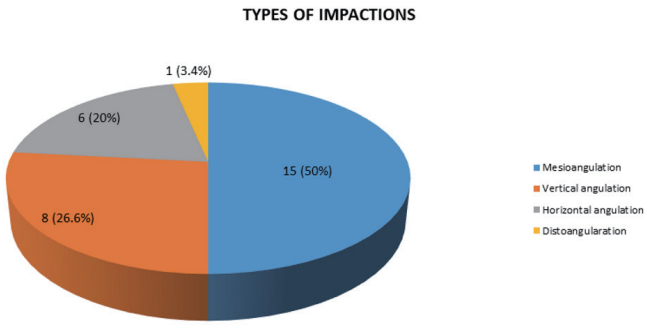

Figure 1. Types of impactions in the patients of this research study.

Eligibility criteria of patient's selection

Demographic data of each patient has been recorded (including name, sex, age, patient profiles, medical history, and dental history). Current and previous medical and dental history has been noted and compliance with the inclusion and exclusion criteria was established.

According to the withdrawal criteria, the patients can withdraw their participation in this research at any time depending on their own decision but no anyone withdrew.

Clinical measurements

Patient will be measured for post-operative pain, swelling and limit mouth opening on the day before intervention and on second and seventh day post-operatively with same technique as the pre-operative one by same examiner: 1) Post-operative pain assessment by visual analogue scale (VAS) scores [20-22] and the number of analgesic tablets required; 2) Facial swelling [17-18] was measured by facial contour by using three lines along the length of the face from the reference point, lateral corner of eye to angle of mandible, corner of mouth to border of earlobe, soft tissue pogonion to border of earlobe (Fig. 2); and 3) Limited mouth opening [17-18] was measured along the distance between incisal edge of maxillary and mandibular incisor (inter-incisal distance).

Statistical analysis of the data research

The Statistical Package for the Social Sciences (SPSS version 22, SPSS Inc., Chicago, IL, USA) was used to calculate the significance of differences between two groups. Descriptive statistical parameters (mean, standard deviation, and independent-sample *t*-test) were used to assess the significance of difference. $P < 0.05$ was considered significant.

Results

There were a total of 60 lower third molar removals involving 30 interventions with dexamethasone injection in SLS group and PGS group. Table 3 showed the duration of operation time

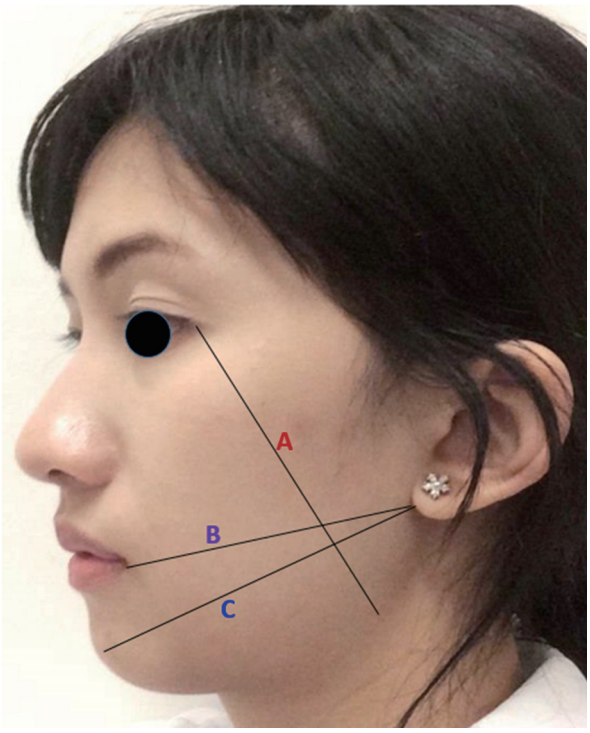

Figure 2. Three reference lines for facial length measurement. A: lateral corner of eye to angle of mandible; B: corner of mouth to border of earlobe; C: soft tissue pogonion to border of earlobe.

was 19.9 in PGS group and 20.5 in SLS group. There was no significant difference between duration of intervention. In this study, no post-operative complication was found in both groups.

The evaluation of post-operative pain based on 100-mm VAS was not significantly different in immediately intervention, day 1, day 2 and day 7 between both groups, and analgesic taking for post-operative pain was not significantly different on all post-operative days between control and test groups as shown in Table 4. Table 5 showed no significant increase in post-operative facial swelling on the second and seventh post-operative days compared with pre-operatively in both groups by measurement of tragus to commissure of mouth, tragus to pogonion, and gonial angle to lateral canthal of eye.

Measurements of limited mouth opening were significantly different ($P = 0.004$) on the second post-operative day and different between baseline and second post-operative day. Measurements of limited mouth opening were significantly different between two groups ($P = 0.004$). But on the seventh post-operative day there was no significant different (Table 6).

Discussion

MTM impaction is a common problem affecting a large proportion of population. The surgical removal of MTM is associated with many post-operative sequelae as post-operative facial swelling, post-operative pain and limited mouth opening. When the tissues are injured, the normal physiologic response

Table 3. Duration of Mandibular Third Molar Intervention of the Patients in Study Groups

Data consideration	8 mg dexamethasone		P value
	Pterygomandibular space injection (SD)	Sublingual space injection (SD)	
Duration of operation (min)	19.93 (2.71)	20.50 (2.77)	0.225

Table 4. Measurements of Post-Operative Pain (VAS in Millimeters and Number of Analgesic Taken in Number of Tablets) in Study Groups

Data evaluation	8 mg dexamethasone		P value
	Pterygomandibular space injection (SD)	Sublingual space injection (SD)	
VAS			
Day 0	21.57 (15.76)	20.90 (15.14)	0.840
Day 1	18.90 (14.96)	17.03 (14.23)	0.532
Day 2	14.17 (15.45)	13.90 (13.87)	0.935
Day 7	3.67 (10.15)	3.60 (8.25)	0.971
Number of analgesic taken			
Day 1	1.87 (1.04)	1.77 (0.97)	0.682
Day 2	2.67 (1.82)	2.53 (1.59)	0.742
Day 3	1.47 (1.47)	1.10 (1.29)	0.304

Day 0: immediate after operation; Day 1: first day after operation; Day 2: second day after operation; Day 3: third day after operation; Day 7: seventh day after operation.

Table 5. Swelling Measurements and Differences in Millimeters From Baseline Value in Study Groups

Data evaluation	8 mg dexamethasone		P value
	Pterygomandibular space injection, mean (SD)	Sublingual space injection, mean (SD)	
Tr-Com			
Baseline	115.10 (6.05)	115.03 (6.12)	0.326
Second day	118.83 (6.84)	118.66 (6.01)	0.724
Seventh day	116.56 (6.85)	116.53 (6.22)	0.926
Differences			
Second day-baseline	3.73 (2.42)	3.63 (2.44)	0.835
Seventh day-baseline	1.46 (2.14)	1.50 (1.50)	0.926
Tr-Pog			
Baseline	115.10 (6.05)	115.03 (6.12)	0.326
Second day	118.83 (6.84)	118.66 (6.01)	0.724
Seventh day	116.56 (6.85)	116.53 (6.22)	0.926
Differences			
Second day-baseline	3.73 (2.42)	3.63 (2.44)	0.835
Seventh day-baseline	1.46 (2.14)	1.50 (1.50)	0.926
Gn-Lc			
Baseline	106.86 (8.52)	105.6 (7.92)	0.99
Second day	110.83 (8.02)	109.53 (7.65)	0.177
Seventh day	108.56 (8.16)	107.26 (7.77)	0.115
Differences			
Second day-baseline	3.96 (2.57)	3.93 (2.11)	0.954
Seventh day-baseline	1.7 (2.56)	1.6 (2.13)	0.897

Tr-Com: tragus-commissure of mouth; Tr-Pog: tragus-pogonion; Gn-Lc: goial angle-lateral canthal of eye.

Table 6. Measurements of Limited Mouth Opening and Differences in Millimeters From Baseline Value in the Study Groups

Maximum incisal distance	8 mg dexamethasone		P value
	Pterygomandibular space injection (SD)	Sublingual space injection (SD)	
Baseline	46.36 (5.03)	46.36 (5.03)	1
Second day	33.83 (7.68)	36.96 (5.49)	0.004*
Seventh day	42.61 (5.11)	43.23 (4.88)	0.293
Differences			
Baseline-second day	12.53 (6.62)	9.40 (5.11)	0.004*
Baseline-seventh day	3.75 (3.74)	3.13 (2.62)	0.293

*P < 0.01.

Table 7. The Summary of Previous Studies of Dexamethasone

Authors	Year	Type of steroid	Administration	Parameter measurement	Results
Baxendale et al [15]	1993	8 mg dexamethasone	Oral	Post-operative pain: 4 h post-operative reduction	Significant reduction in pain 4 h post-operatively
Tiwana et al [12]	2005	NA corticosteroids and without antibiotics, no corticosteroids	Intravenous before surgery	Effect on health-related quality of life outcomes	IV corticosteroid administration had a limited, but beneficial effect on HRQOL outcomes
Grossi et al [6]	2007	4 and 8 mg dexamethasone	Submucosal injection before surgery	Post-operative edema	Significant reduction when 4 mg dexamethasone was given, but 8 mg provided no further benefit
Filho et al [2]	2008	4 and 8 mg dexamethasone	The consumption of 4 mg versus 8 mg before surgery	Swelling, trismus, pain	Better for swelling and trismus but not effective for pain
Mojsa et al [8]	2011	4 mg dexamethasone	4 mg injection, the "before" group, placebo group, the "after" group	Facial swelling, post-operative pain, trismus	Better control of pain, swelling, trismus
Antonio et al [9]	2011	8 mg dexamethasone	The oral administration, local injection in the masseter muscle	Pain, edema, limited mouth opening	Reducing post-operative pain, edema, trismus
Tiigimae-Saar et al [11]	2011	Single dose of 30 mg prednisolone, 120 mg etorikoxib	Prednisolone immediate before operation, etorikoxib 30 min before operation	Pain, facial swelling, trismus	Well-suited for treatment of post-operative pain, trismus, swelling, diminishing post-operative swelling of soft tissues
Chaurand-Lara and Facio-Umana [10]	2013	20 mg of methylprednisolone	Intramuscular in masseter and no administer	Swelling, pain	Decrease and an effective therapeutic reduction of swelling and pain
Bauer et al [14]	2013	NA ibuprofen or placebo, NA ibuprofen + dexamethasone, placebo	Pre-emptive analgesia	Post-operative pain	Pre-emptive analgesia insufficient to inhibit central sensitization, association with dexamethasone more effective
Li et al [16]	2013	4 mg and 8 mg dexamethasone	Injection of 4 - 5 mg in pericoronal injection	Post-operative swelling, trismus	Control facial swelling, trismus
Latt et al [17]	2016	Dexamethasone 8 mg, saline group	Pterygomandibular space injection	Post-operative pain	Decreased post-operative pain
Gozali et al [18]	2017	8 mg dexamethasone, saline group	Injection into sublingual area	Post-operative pain	Decreased post-operative pain

NA: unknown; HRQOL: health-related quality of life; IV: intravenous.

is inflammation, leading to post-operative pain and swelling. Experience of surgeons and difficulty of lower third molar surgery are recognized as significant factors in the incidence and severity of post-operative sequelae.

Corticosteroids have been shown to reduce level of lymphokine, prostaglandin, serotonin, bradykinin, cortisol, migratory inhibiting factor, and β-endorphin and are believed to decrease post-operative facial swelling and limited mouth opening [17-18]. Many previous literatures proved that preoperative dexamethasone injection had benefit in reducing post-operative complication in lower third molar intervention. All routes of administration lead to similar result because of systemic effect of steroid. All steroids must be administered before the infliction of tissue damage, not during or after intervention [23-25]. It caused peak level of bradykinin release occurring within 3 h after tissue trauma. Gersema and Baker [26] and Milles and Desjardins [27] concluded that steroid was unable to reduce the post-operative pain significantly.

Filho et al [2] administered 8 mg of dexamethasone, which was reported to be more effective than 4 mg. It is equal to the 200 mg of cortisol.

In the previous studies or research dexamethasone is being delivered for third molar intervention by many routes such as oral consumption, intravenous, intramuscular delivery in masseter, gluteal or deltoid region, sub-mucosal injection, and delivery into the potential space as shown in Table 7 [2, 6, 8-12, 14-18].

In this study, we injected dexamethasone into SLS and PGS as we believed that it is more convenient for the patient compared to intramuscular, intravenous delivery and deep intra-potential space injection, because patient will have numbness at this area after local anesthesia. The SLS is considered as superficial potential sites for drug administration. SLS injection is characterized by systemic administration, high permeability and rich blood supply.

Our project as the previous study of Gozali et al [18] found that 8 mg dexamethasone injected into SLS in lower third molar intervention offered several advantages: less post-operative pain (VAS pain score and analgesic consumption), wider maximum mouth opening, and less swelling compared to saline injection as compared to control group. However, the previous research of Latt et al [17] found that injection of 8 mg dexamethasone into the PGS also effectively reduced the post-operative swelling, limited mouth opening and post-operative pain in lower third molar intervention compared to the saline group.

In this split-mouth, crossover study, dexamethasone was injected into SLS and PGS after onset of local anesthesia. The duration of operation in this study was not significantly different between both groups, with same position and type of impacted lower third molar and by the same operator (Table 3). Post-operative facial swelling was evaluated by measuring three linear facial distances which was a non-invasive, simple, cost-effective and time-saving method. Post-operative pain was evaluated by VAS and number of analgesic taken, and limited mouth opening was measured by interincisal distance. This current study found that there is no significant difference between both groups because of the systemic effect of corticosteroid. Nonetheless PGS group showed a greater degree of limited mouth opening than SLS group on day 2 after operation because the technique of injection may cause trauma and maybe because of the large volume of drug injected, but it will improve on day 7 after operation. In this study, no post-operative complication was found in both groups.

In conclusion, significant dexamethasone injection in lower third molar intervention can decrease post-operative pain and swelling. This research studied PGS and SLS groups of dexamethasone injection. The injection in both groups had advantage that no pain appeared during dexamethasone administration, and there was no difference in post-operative pain and post-operative facial swelling, but PGS group had greater degree of post-operative limited mouth opening on day 2 after operation than SLS group. The suggestion from this study for the dentists is using 8-mg dexamethasone injection into both PGS and SLS.

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Financial Disclosure

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Conflict of Interest

The authors declare no conflict of interest.

Informed Consent

Written informed consent (local language) was obtained from all the patients before intervention.

Author Contributions

NW contributed to conceptualization; TC and WS contributed to methodology; PM contributed to validation and investigation; PM and WS contributed to formal analysis; WS contributed to resources; SK was involved in data curation; PM, WS and SK contributed to original draft preparation; BK and NW were involved in reviewing and editing of the manuscript; TC, NW and BK contributed to visualization and supervision; CV, NW and SK were involved in project administration.

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