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ORIGINAL ARTICLE

From Compression to Closure: Efficacy and Safety of Vascular Closure Devices (VCD) Versus Manual Compression: A Comparative Analysis of Hemostatic Strategies of Obtura, Angioseal, and ProGlide VCD

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Abstract

Objective: **Use of vascular closure devices (VCDs) for femoral artery puncture site hemostasis has increased but their safety and efficacy have remained unclear. This study was designed to compare safety and efficacy of Obtura, Angioseal, and Proglide VCD to manual compression (MC) and also between for femoral artery haemostasis.**

Methods: **This was prospective, randomized controlled study where patients were randomly assigned on 1:1:1:1 basis. Primary endpoints were time to hemostasis (TTH) and ambulation time (AT) while secondary endpoints were deployment success, device related adverse events and technical success rate. ANOVA and Tukey HSD was conducted to draw significant difference between individual strategies. $P < 0.05$ was considered statistically significant.**

Results: **Total of 1000 patients (250 in each arm) who underwent transfemoral intervention at LPS Institute of Cardiology, Kanpur, India between January 2025 and March 2025 were evaluated. Sheath size, common femoral artery diameter and device size did not differ significantly across all the groups. Mean TTH was shortest for Angioseal (1.30 min) followed by Obtura (2.58 min), Perclose (3.97 min), and MC (17.61 min). Similarly, mean AT was shortest for Angio-Seal (123.06 min) followed by Perclose ProGlide (162.56 min), Obtura (185.42 min) and MC (743.23 min). Technical success in Angio-Seal, Obtura and Perclose ProGlide were 99.1%, 97.4% and 94.6% respectively. No access site complications (re-bleeding, infection, arteriovenous fistula, and transient access site nerve injury) were noted. There were 2(0.8%), 5(2%), 7(3.2%) and 12 (4.8%) cases of haematoma in Angio-Seal, Obtura, Perclose ProGlide and MC arm respectively. There were 2(0.8%), 2(0.8%), and 4 (1.6%) case of arterial pseudoaneurysm Obtura, Perclose ProGlide and MC arm respectively while none in Angio-Seal arm.**

Conclusion: **Vascular closure devices showed significantly faster haemostasis and shorter ambulation time compared to manual compression highlighting their clinical efficiency and Angio-Seal was superior safety and efficacy over Obtura and Perclose ProGlide.**

Keywords: Vascular closure devices, Haemostasis, Angioseal, Coronary angioplasty, Manual compression

1. Introduction

Transcatheter heart valve (THV) implantation and percutaneous coronary interventions (PCI) are still being most commonly performed through transfemoral access often requiring bigger sheath (>8Fr). Obtaining perfect hemostasis is of paramount importance as its failure is associated with increased mortality [1]. Various blueprints for preventing or minimizing bleeding, known as

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bleeding evasion maneuver, encompasses modification of antithrombotic strategies or usage of various types of vascular closure devices (VCDs) [2].

Manual compression (MC), although traditionally gold standard and cost-effective to secure hemostasis, carries a complication rate of 1−6% [3]. Not only it takes longer time of compression (15−20 min or more) to achieve hemostasis, its other drawbacks are local pain, tenderness, hematoma especially in obese, women, and those on anticoagulation, restriction of second procedure ipsilaterally, extended limb immobilization, delayed ambulation time (≥4 h), and decreased patient compliance [4,5]. Although these disadvantages of MC have been mitigated by introduction of VCDs thereby bringing remarkable decrease in hemostasis time leading to their early ambulation, faster recovery, enhancing comfort and quicker discharge, their usage are not being widespread because of cost, availability, and different regulatory issues [6].

The null hypothesis was that Obtura, Angio-Seal, Perclose ProGlide, and manual compression would not differ in time to hemostasis, and ambulation time (for primary outcomes) and technical success, and vascular access-related complications (for secondary outcomes) following transfemoral procedures.

2. Materials and methods

2.1. Study design and population

This was a prospective, stratified random control study comparing Obtura (Meril Lifescience, India), Angioseal (Terumo Inc, Tokyo, Japan), Perclose Proglide (Abbott Vascular Devices, Redwood City, CA, USA) versus standard MC. The study was conducted in accordance with Declaration of Helsinki, approved by Institutional ethical committee and written informed consent was obtained from all patients. Inclusion criteria were prospective patients ≥18 years undergoing either PCI or endovascular procedures through transfemoral access. Exclusion criteria were (a) patients having previous arterial access at same site within a month, (b) non-CFA access site, (c) fluoroscopically visible CFA calcium, (d) morbid obesity, (e) posterior wall puncture, (f) multiple punctures, (g) allergy to bovine materials, (h) access through vascular graft, and (i) pregnancy.

2.2. Study randomization

In this study, patients were randomized to 1:1:1:1 using permuted block method in either of four arms (Obtura, Angioseal, Perclose, MC) respectively.

Abbreviation

AT	Ambulation Time
CFA	Common Femoral Artery
MC	Manual compression
PCI	Percutaneous coronary interventions
TTH	Time To Haemostasis
THV	Transcatheter heart valve
VCD	Vascular closure devices

2.3. Device description and procedure

Obtura VCD comprises a bio-absorbable implant (bio-absorbable polymer anchor, Type-I bovine collagen sponge and bioabsorbable suture connecting anchor and collagen by self-tightening knot) and delivery component. It gets completely absorbed within 3 months and is available in 6 and 8F sizes which are compatible with 6F and 7F, and 8F delivery sheath respectively thereby does not require dedicated delivery sheath. On deployment, bioresorbable plug is released on external surface of the artery which helps in securing haemostasis by stretching in vicinity of puncture site [7].

Angioseal is collagen-based VCD which is deployed through a dedicated sheath which helps in depositing small, bioabsorbable collagen plug adjacent to puncture site. It brings out a mechanical seal by squeezing the puncture site between bioabsorbable anchor inside and collagen sponge outside the arterial wall. 6 and 8F devices are successful in bringing haemostasis up to 8 and 12 F arteriotomy sites respectively [8].

Perclose Proglide is basically a dedicated 6F VCD comprising single, ultrathin, monofilament, preformed, bioabsorbable suture with two needles capable of bringing haemostasis of 5−21 F arteriotomy sheaths. Minimum of two preplaced devices (either 11/1o′clock or 10/2 o'clock position) using pre-close technique are required for sheath sizes >16F with additional devices in case of inadequate arteriotomy closure [9,10].

Femoral access was taken under fluroscopic guidance in majority of patients and after gaining arterial aceess, contrast was injected and position of needle entry was checked in right and left anterior oblique projection. Only cases in which access were obtained through common femoral artery, were considered for VCDs mediated closure. In minority of population (n = 218; 22%), common femoral artery was accessed using ultrasound guidance. During procedure, unfractionated heparin (UFH) was used as anticoagulant and administered as per body weight (70−100U/Kg) to keep activated clotting time (ACT) as 250−300 s without glycoprotein

inhibitor or 200−250 s with its concomitant use. Following percutaneous coronary intervention, patients received dual antiplatelet (aspirin and clopidogrel/prasugrel/ticagrelor) and other drugs as per standard guideline. Manual compression was achieved after 6 h following the procedure keeping ACT below 180 s.

2.4. Study endpoints and definitions

The primary endpoints were composite of time to hemostasis (TTH), defined as time in minutes taken for achievement of complete hemostasis with or without need of light, non-arterial compression of ≤3 min and technical success. Technical success was defined as percentage of patients not requiring alternative therapy to achieve hemostasis for VCD arm while technical failure was defined as failure to deploy VCD correctly in spite of proper technique and requirement of MC to achieve haemostasis. Secondary endpoints were ambulation time (AT), and vascular closure related adverse events. AT was defined as time in minutes from achievement of hemostasis to patient's ambulation ≥20 ft without any physical assistance or re-bleeding [11]. Vascular closure related adverse events were re-bleeding following initial hemostasis, access site infection requiring extended hospitalization or intravenous antibiotics, local site hematoma, arterial pseudoaneurysm, transient access site-related nerve injury and arteriovenous fistula.

2.5. Statistical considerations

Categorical variables were expressed as numbers and percentages, and continuous variables as mean ± standard deviation. Categorical variables were compared using the chi-square test, while one-way analysis of variance (ANOVA) was used to evaluate differences among vascular closure strategies for sheath size, device size, CFA diameter, TTH, and AT. When ANOVA indicated statistical significance, post hoc pairwise comparisons were performed using Tukey's honestly significant difference test. A two-sided p value < 0.05 was considered statistically significant. Sample size estimation was based on previously published data by Devasia et al. [7], using the reported differences in time to hemostasis and ambulation time between vascular closure devices and manual compression as the primary effect size. The study was designed as a superiority, parallel-group randomized trial comparing three vascular closure devices (Obtura, Angio-Seal, and Perclose ProGlide) with manual compression. Assuming a two-sided α level of 0.05, 80% statistical power, and adjustment for multiple pairwise comparisons using Bonferroni correction, the minimum required sample size was 234 patients per group; allowing for a 5% dropout rate, 246 patients were required in each group. All statistical analyses were performed using SPSS software, version 20.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Baseline and demographic characteristics (Table 1)

In all four arms, majority of patients were males (74.4%) and had undergone PCI for acute coronary syndrome. Hypertension was the commonest risk factor (27.4%) followed by smoking (24.3%) and diabetes (23.2%). Other baseline characteristics of the all groups were similar..

3.2. Procedural variables

The descriptive analysis of data revealed significant differences across four closure techniques in terms of sheath size, device size, and common femoral artery (CFA) diameter (Table 2). For sheath size, mean ranged from 6.17 mm (Obtura) to 6.31 mm (MC), with maximum of 11F for Angioseal and Proglide. The relatively low standard deviations indicated consistent sizing across all techniques. Device size followed a similar pattern, with means ranging from 6.00 mm for Perclose (with no variability) to 6.36 mm for Angioseal. The CFA diameter were consistent across all groups (average - 7.03 mm), with minimal variation suggesting comparability in anatomical baseline conditions between groups.

One-way ANOVA demonstrated a small but statistically significant difference in sheath size among the four groups ($F(3, 996) = 3.426$; $p = 0.017$). Device size differed significantly across closure strategies ($F(2, 747) = 25.019$; $p < 0.001$), which was expected given the fixed device size of Perclose ProGlide. No significant difference was observed in common femoral artery diameter among groups ($F(3, 996) = 0.059$; $p = 0.981$).

Post-hoc analysis revealed significantly smaller sheath sizes for Obtura arm compared to Proglide ($p = 0.045$) and manual compression ($p = 0.029$) while no significant differences between Angioseal and other techniques ($p > 0.05$). Additionally, Proglide and MC did not differ significantly from each other ($p = 0.999$). These findings suggest that Obtura tends to employ smaller sheath sizes relative to other closure techniques, which may have procedural or clinical implications. Similarly, post

Table 1. Demographics, baseline and clinical characteristics of the study population (N = 1000).

Variables	Obtura (N = 250)	AngioSeal (N = 250)	ProGlide (N = 250)	MC (250)
Age (years)	58.9 ± 12.1	63 ± 7.2	62 ± 11.1	60.9 ± 14.2
Male/Female	189(76.90%)/61(24%)	177(71%)/73(29%)	191(77%)/59(23%)	187(75%)/63(25%)
BMI	23.78 ± 4.20	24.8 ± 2.2	23.8 ± 4.1	24.2 ± 5.1
SBP (mmHg)	127.3 ± 14.4	133.2 ± 11.2	139.3 ± 10.7	136.9 ± 17.2
DBP (mmHg)	79.5 ± 9.7	76.5 ± 10.3	80.2 ± 4.7	74.3 ± 13.6
ACS	211 (84%)	213 (84%)	209 (83%)	219 (87%)
CCS	33 (13%)	23 (9%)	31 (12%)	18 (7%)
Endovascular intervention	06 (2.4%)	14 (5.6%)	10 (4%)	13 (5.5%)
DM	52 (21%)	49 (19.6%)	62 (24.6%)	67 (26.81%)
HTN	76 (30.4%)	67 (26.8%)	71 (28.4%)	60 (24%)
Previous CABG	12 (2.4%)	4 (1.6%)	3 (1.2%)	08 (3.2%)
Smoking/Tobacco	61 (24.4%)	58 (23.25)	69 (27.6%)	55 (22%)
Medications				
a. Aspirin	250 (100%)	250 (100%)	250 (100%)	250 (100%)
b. Prasugrel	13 (5.2%)	10 (100%)	7 (100%)	6 (100%)
c. Ticagrelor	230 (92%)	230 (100%)	232 (100%)	231 (100%)
d. Clopidogrel	7 (2.8%)	10 (100%)	11 (100%)	13 (100%)
e. Statin	247 (98.8%)	249 (100%)	250 (100%)	245 (100%)
f. NOAC	10 (4%)	8 (3.2%)	3 (1.2)	4 (1.6%)
g. GPIIb/IIIa inhibitor	73 (29.2%)	79 (31.6%)	68 (27.2%)	83 (33.2%)
h. ACE I/ARB	198 (79.2%)	195 (78%)	211 (84.4%)	217 (86.8%)
i. BB/CCB	209 (83.6%)	215 (86%)	225 (90%)	219 (87.6%)
j. SGLTi	53 (21.2%)	47 (18.8%)	61 (24.4%)	57 (22.8)
k. MRA	67 (26.8%)	61 (24.4%)	70 (28%)	77 (30.8%)

BMI-Body mass index; SBP-Systolic blood pressure; DBP- Diastolic blood pressure; ACS-Acute coronary syndrome; CCS- Chronic coronary syndrome; DM- Diabetes mellitus; HTN- Hypertension; CABG- Coronary artery bypass grafting; NOAC- New oral anticoagulant; GP- Glycoprotein; BB-Beta blocker; CCB- Calcium channel blocker; SGLTI- Sodium glucose transport inhibitor; MRA-Mineralocorticoid receptor antagonist.

hoc analysis for CFA diameter revealed no significant differences among the closure techniques ($p > 0.95$) as mean differences between any two groups were minimal, with all confidence intervals including zero confirming that anatomical variability in artery size did not influence either procedural outcomes or technique selection.

3.3. Clinical outcomes

TTH showed marked variability as Angioseal was the fastest (mean = 1.30 min), followed by Obtura (2.58 min), Perclose (3.97 min), and MC (17.61 min), with a wide range (10.4–27.3 min). In terms of AT, Angioseal outperformed others with mean of

Table 2. Comparative descriptive analysis of procedural metrics by hemostatic strategies (N = 1000).

		N	*Mean ± SD*	*95% CI for Mean*	*Minimum*	*Maximum*
Sheath size	Obtura	250	6.17 ± 0.43	6.11–6.22	6	8
	Angioseal	250	6.23 ± 0.51	6.16–6.29	6	10
	Proglide	250	6.30 ± 0.68	6.22–6.39	6	10
	Manual compression	250	6.31 ± 0.65	6.23–6.39	6	8
CFA diameter (mm)	Obtura	250	7.05 ± 0.52	6.98–7.11	5.7	8.3
	Angioseal	250	7.03 ± 0.53	6.96–7.10	5.7	8.2
	Proglide	250	7.03 ± 0.54	6.97–7.10	4.2	8.2
	Manual compression	250	7.04 ± 0.52	6.98–7.11	5.7	8.2
Time to haemostasis (min)	Obtura	250	2.58 ± 0.16	2.56–2.60	2.2	2.9
	Angioseal	250	1.30 ± 0.12	1.28–1.31	1.1	1.5
	Proglide	250	3.97 ± 0.32	3.93–4.01	3.3	4.8
	Manual compression	250	17.61 ± 3.69	17.15–18.07	10.4	27.3
Ambulation time (min)	Obtura	250	185.42 ± 117.96	170.73–200.12	109	800
	Angioseal	250	123.06 ± 4.58	122.49–123.63	114	138
	Proglide	250	162.56 ± 8.41	161.52–163.61	144	180
	Manual compression	250	743.23 ± 23.06	740.36–746.10	529	889
Device size	Obtura	250	6.29 ± 0.70	6.20–6.38	6	8
	Angioseal	250	6.36 ± 0.77	6.26–6.46	6	8
	Proglide	250	6.00 ± 0.0	6.00–6.00	6	6
	Manual compression	0	–	–	.	.

123.06 min, followed by Proglide (162.56 min), Obtura (185.42 min) and MC (743.23 min) supporting VCDs in facilitating patient's early ambulation (Table 3). ANOVA showed highly significant differences among groups for time to hemostasis ($F(3, 996) = 4150.3$; $p < 0.001$) and ambulation time ($F(3, 996) = 5954.8$; $p < 0.001$).

Post hoc analysis demonstrated significant differences in time to hemostasis and ambulation time among all closure strategies ($p < 0.001$). Angio-Seal achieved the shortest time to hemostasis and was significantly faster than Obtura (mean difference −1.28 min) and manual compression (mean difference −16.31 min). Perclose ProGlide had a longer time to hemostasis than Angio-Seal but remained significantly faster than manual compression (mean difference −13.64 min). Manual compression resulted in the longest time to hemostasis, exceeding device-based strategies by more than 13−16 min (Table 3). Similarly, ambulation time was shortest with Angio-Seal, which was significantly faster than Obtura (mean difference −62.36 min) and manual compression (mean difference −620.17 min). Perclose ProGlide permitted earlier ambulation than manual compression but was significantly slower than Angio-Seal (mean difference +39.50 min). Manual compression was associated with the longest ambulation time, exceeding device-based techniques by more than 550 min (Table 3).

Technical failure was observed in 6 patients (2.4%) in the Obtura group, 2 patients (0.8%) in the Angio-Seal group, and 12 patients (4.6%) in the Perclose ProGlide group. Vascular closure−related adverse events occurred in 10 patients (4.0%) in the Obtura group, 4 patients (1.6%) in the Angio-Seal group, 12 patients (4.8%) in the Perclose ProGlide group, and 14 patients (5.6%) in the manual compression group. In the Obtura group, adverse events included minor bleeding (n = 3), pseudoaneurysm (n = 2), and hematoma (n = 5). In the Angio-Seal group, minor bleeding (n = 2) and hematoma (n = 2) were observed. In the Perclose ProGlide group, adverse events comprised minor bleeding (n = 4), pseudoaneurysm (n = 3), hematoma (n = 4), and local infection (n = 1). In the manual compression group, adverse events included minor bleeding (n = 4), pseudoaneurysm (n = 3), hematoma (n = 4), local infection (n = 2), and major bleeding (n = 1). Pseudoaneurysms were managed with prolonged ultrasound-guided compression, except for three cases that required surgical intervention. Local infections were treated with prolonged intravenous antibiotics, and major bleeding was managed with blood transfusion and fluid replacement.

4. Discussion

Manual compression had remained the gold standard to secure haemostasis for percutaneous femoral access for decades but after introduction of transcatheter heart valve and other endovascular procedures requiring large bore access, it was found deemed inappropriate. Impact of perfect arterial haemostasis has already been demonstrated in RIVAL trial as it impacts mortality [12]. VCDs not only offer faster and better haemostasis but also has 50−60% less complications compared to MC [13−15]. They are collagen based (Obtura, Angioseal), clip based (StarClose) plug based (MANTA), and suture based (Perclose, Prostar, Super Stitch). Our study is the first to compare Obtura, Angioseal, Proglide and MC in all comer real world patients.

Table 3. Post-hoc comparison of Sheath size, Common femoral artery diameter, Time to hemostasis and ambulation time according to hemostatic strategy using manual compression as the reference.

Outcome	Comparison vs MC	Mean difference	95% CI	p value
Sheath size	Obtura	−0.15	−0.28 to −0.01	0.03
	Angio-seal	−0.09	−0.22 to 0.05	0.37
	ProGlide	−0.01	−0.14 to 0.13	0.99
CFA diameter	Obtura	0.01	−0.11 to 0.13	0.99
	Angio-seal	−0.01	−0.13 to 0.11	0.99
	ProGlide	−0.06	−0.12 to 0.11	0.99
TTH (min.)	Obtura	−15.03	−15.46 to −14.60	<0.001
	Angio-seal	−16.31	−16.74 to −15.89	<0.001
	ProGlide	−13.63	−14.07 to −13.21	<0.001
AT (min.)	Obtura	−557.81	−571.68 to −543.93	<0.001
	Angio-seal	−620.17	−634.04 to −606.29	<0.001
	ProGlide	−580.67	−594.54 to −566.79	<0.001

Data are presented as mean difference (hemostatic device − manual compression), 95% confidence interval (CI), and p value. Manual compression served as the control group for all comparisons. Negative mean differences indicate shorter times compared with manual compression. MC -Manual compression; CFA- Common femoral artery; TTH-Time to hemostasis; AT- Ambulation time

Hemostasis was best achieved with Angioseal with least failure rate (0.8%) compared with Obtura (2.4%) and Proglide (4.6%). This may be attributed to design as its temper which helps in pushing the collagen plug is sturdy and strong compared to Obtura. In 3 cases, foot paddle of Obtura came out of the artery and in remaining 3 cases, it was inadequate to push the collagen plug sufficient enough to secure hemostasis. Although Devasia et al. reported 100% deployment success with Obtura [7], it was a small study (n = 134 patients) where all patients had undergone only angiography using only 6F sheath contrary to our study. Results with Obtura for bigger sheath and complex procedure might be different and has not been demonstrated till now. In case of Angioseal, vigorous pull led the suture to come out of the artery in one case and in another, plug could not be properly delivered. Higher failure rate with Proglide was attributed to its complex design. Knot failure in 5 cases, knot came out along with the device during attempted removal and could not be repositioned in 4 cases, thread breakdown in 3 cases and breakdown of plunger in 2 cases were reasons for its technical failure. Moreover, Proglide requires a learning curve. Our findings were consistent with 6.2% by Vinay et al. [10,15] 0.5% failure rate in CAP trial by Martin et al. [16]. Except breakdown of thread, remaining cases were managed with redeployment of another device after introduction of 0.035″ wire through wire port but former required manual compression as bail out. Underlying calcification, inadequate alignment, and failure of knot to properly abutting against the wall because of inadequate dissection through subcutaneous plane and presence of connective tissue might have been the contributing factors [17,18].

TTH in our study was consistent with findings reported by CAP trial [16], Uno et al. [19], and Vinay et al. [10]. It is a critical parameter influencing patient recovery and hospital workflow. Although Angioseal and Obtura are both collagen based VCD but better design and proper collagen placement were probably the reasons of superiority of Angioseal (1.3 min) over Obtura (2.58 min). Lower TTH of plug-based devices over Proglide have also been demonstrated by Ben-dor et al. [8], Chen et al. [9], and Martin et al. [16] attributed to simple design, faster hemostasis and deployment.

AT is pivotal for patient comfort, crucial for faster recovery, reducing hospital stay and making them self-reliant. Angioseal overscored the others with the shortest mean ambulation time (123.06 min) over Obtura (162.5min) and Proglide (185.4 min) which was consistent with findings from multiple trial and meta-analysis [10,19,20,21]. It assumes even more important role in situation where resource is limited as associated with shorter hospital stay.

In our study, hematoma was observed in 1.6% in VCD arm (Angioseal-1, Obtura-3, Proglide-8) compared with 4.3% in manual compression arm, consistent with findings from literature [15,22,23]. Most of patients were female and obese. Women contributed 24% population in our study and all three VCDs fared well which showed efficacy and safety among female population. They are more vulnerable to increased vascular complications because of small artery size and prone to overdosing of adjunct antithrombotic medications. In our study, no device related infection was observed in any of VCDs although its incidence in literature varies from 0.1 to 2% despite of complex population group including obese, female, elderly and diabetes. This may be attributed to shorter stay, faster ambulation, meticulous deployment technique and lack of long term follow up.

5. Conclusion

Adopting advanced vascular closure devices like Angioseal, Obtura and Proglide markedly improve procedural efficiency, thus bringing a paradigm shift toward device-based vascular closure techniques for vascular haemostasis. These are safe, effective and significantly reduce hemostasis and ambulation time in comparison to manual compression.

Limitation

Gender disparity (female only 24%), and shorter follow up were major limitations. Extended follow up of 3-month might have showed long term complications. Large sample size with uniform gender composition and longer follow-up would have been helpful in getting more reliable data.

Author contributions

Conception and design of Study: PS, KH, AM, SKS, PA, UP, NP. Literature review: PS, KH, AM, SKS, MS, AKS, RKV. Acquisition of data: PS, KH, MJJ, SKS, PA, NP, RKV. Analysis and interpretation of data: PS, KH, MJJ, SKS, MMR, NP, RKV. Research investigation and analysis: AM, MJJ, SKS, MMR, NP. Data collection: MJJ, SKS, MS, RKV. Drafting of manuscript: SKS, PA, MMR, UP, RKV. Revising and editing the manuscript critically for important intellectual contents: AM, MMR, MS, UP,

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Artificial Intelligence (AI) or Large Language Model (LLM) Use Declaration

The author(s) declare that no AI-assisted technologies were used in the writing, research, or content creation of this manuscript.

Conflict of interest

The authors certify that there is no conflict of interest with any financial organization regarding material discussed in the manuscript.

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