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ORIGINAL RESEARCH

Efficiency of the Guide Extension Catheter-Facilitated Tip-in Technique in the Recanalization of Coronary Chronic Total Occlusion

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Background: The tip-in technique, which involves advancing an antegrade microcatheter cross the lesion over a retrograde guidewire, is an elaborated maneuver in the recanalization of coronary chronic total occlusion (CTO). We seek to assess the efficiency of a guide extension catheter-facilitated tip-in technique in comparison to the traditional retrograde approach, which is accomplished by an externalization wire.

Methods: Thirty-three CTO patients successfully revascularized using guide extension catheter-facilitated "tip-in" were included and matched with another 33 patients by J-CTO score and operators, whose CTO was recanalized using an externalized wire. The manipulation time from the first retrograde wire entering the antegrade guide to the first antegrade balloon inflation in the occlusion was calculated.

Results: Compared with the wire-externalization group, the manipulation time in the tip-in group was significantly shortened [389s; interquartile range (IQR), 272–478 vs 706s; IQR, 560–914; $p < 0.001$]. There was a trend in decreasing total operation time and radiation dose, but it did not reach statistical significance.

Conclusion: Guide extension catheter-facilitated tip-in is an efficient method to achieve the recanalization of CTO in a retrograde way, which would be pivotal when the retrograde microcatheter could not be advanced into the antegrade guide catheter.

Keywords: chronic total occlusion, extension guide catheter, tip-in, retrograde

Introduction

With the innovation of equipment and techniques, the success rate of recanalization of coronary chronic total occlusion (CTO) via percutaneous coronary intervention (PCI) has been improved dramatically over the years.[1] The retrograde approach played an indispensable role in crossing the occlusion, which could be accomplished by wire externalization, tip-in and rendezvous.[2,3] Both wire externalization and rendezvous require retrograde crossing of a microcatheter, which could be impossible in tortuous and severely calcified lesions. Under such circumstances, tip-in would be the most suitable way to accomplish the procedure.

The tip-in technique involves inserting a retrograde wire into an antegrade microcatheter, most commonly in the distal curve of the antegrade guide catheter.[4] Tip-in could avoid retrograde advancement of microcatheters cross the lesion and hold unique values in CTO PCI. However, we noticed that the maneuver to intubate the retrograde wire could be challenging in some cases, such as non-coaxial alignment of the guide catheter and coronary ostium. Hence, we adopted

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a guide extension catheter-facilitated tip-in technique, in which the antegrade extension catheter was added and could be used for three purposes: (1) "pick up" the retrograde wire within the coronary artery to assist the entry into the guide catheter; (2) Narrowing the lumen to facilitate the convergence of the retrograde wire and antegrade microcatheter; (3) Increase coaxial alignment and antegrade support if necessary.

We enrolled 33 CTO patients successfully revascularized by guide extension catheter-facilitated tip-in, who were matched 1:1 with another 33 CTO patients treated by wire externalization during the same period. This study aimed to assess the efficiency of this guide extension catheter-facilitated tip-in technique and assist in its application in clinical practice.

Methods

Population and Data Collection

Between March 2021 and October 2022, 33 consecutive patients with CTO lesions successfully recanalized using guide extension catheter-facilitated tip-in were included in Zhongshan hospital, Fudan University. Another 33 CTO patients, who were treated by externalized wire during the same time interval, were 1:1 matched by J-CTO score and operators. Of note, none of the patients in the externalization group have tip-in attempted. Demographic and procedural data were prospectively collected through electronic medical record system and analyzed retrospectively. This study was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (No.: B2021-726R) and conducted in accordance with the guidelines of the Declaration of Helsinki. All participants were given written informed consent at the time of index hospitalization.

Study Definitions

CTO was defined as 100% occlusion with Thrombolysis in Myocardial Infarction (TIMI) 0 flow for a presumed or documented duration of ≥3 months.[5] Occlusion duration was determined based on prior angiogram, the onset of ischemic symptoms, prior history of myocardial infarction, or typical angiographic features (such as no thrombus, no staining at the proximal cap, and presence of mature collaterals).

Angiographic assessment of a collateral connection (CC) was based on Werner's classification: CC0, no continuous connection between the donor and recipient artery; CC1, thread-like continuous connection (<0.4 mm); and CC2, continuous branch-like connection (≥0.4 mm).[5] The perfusion of the occluded artery segment was assessed using the Rentrop classification: 0, none; 1, filling of side branches of the occluded artery without visualization of the epicardial segment; 2, partial filling of the epicardial segment via collateral channels; 3, complete filling of the epicardial segment of the artery.[6]

The J-CTO (Multicenter CTO Registry in Japan) score was calculated by assigning 1 point to each of the following factors: blunt proximal cap, presence of calcification, bend >45°, occlusion length ≥20 mm, and previously failed attempt.[7]

Tip-in is achieved by intubating the retrograde wire with an antegrade microcatheter, usually in the distal curve of the antegrade guide catheter. In this study, this technique was adapted by adding an antegrade extension catheter, which was used to facilitate the retrograde wire to enter the antegrade guide catheter as well as the microcatheter (Figure 1). Wire externalization used a dedicated externalization wire (RG3, Asahi Intecc), which entered the retrograde microcatheter and ran through the occlusion into the antegrade guide catheter to allow the conversion to an antegrade approach.

Statistical Analysis

The continuous and categorical variables were summarized as median (interquartile range [IQR]) and n (%), respectively. Comparison between categorical groups was conducted by χ^2-test or Fisher's exact test, as applicable. Student's *t*-test and the Mann–Whitney *U*-test were used to assess differences between groups in normally and nonnormally distributed continuous variables, respectively. A two-sided p value of less than 0.05 was considered statistically significant. Analysis was performed with SPSS for Windows, release 25.0 (IBM SPSS, Inc., Chicago, IL, USA).

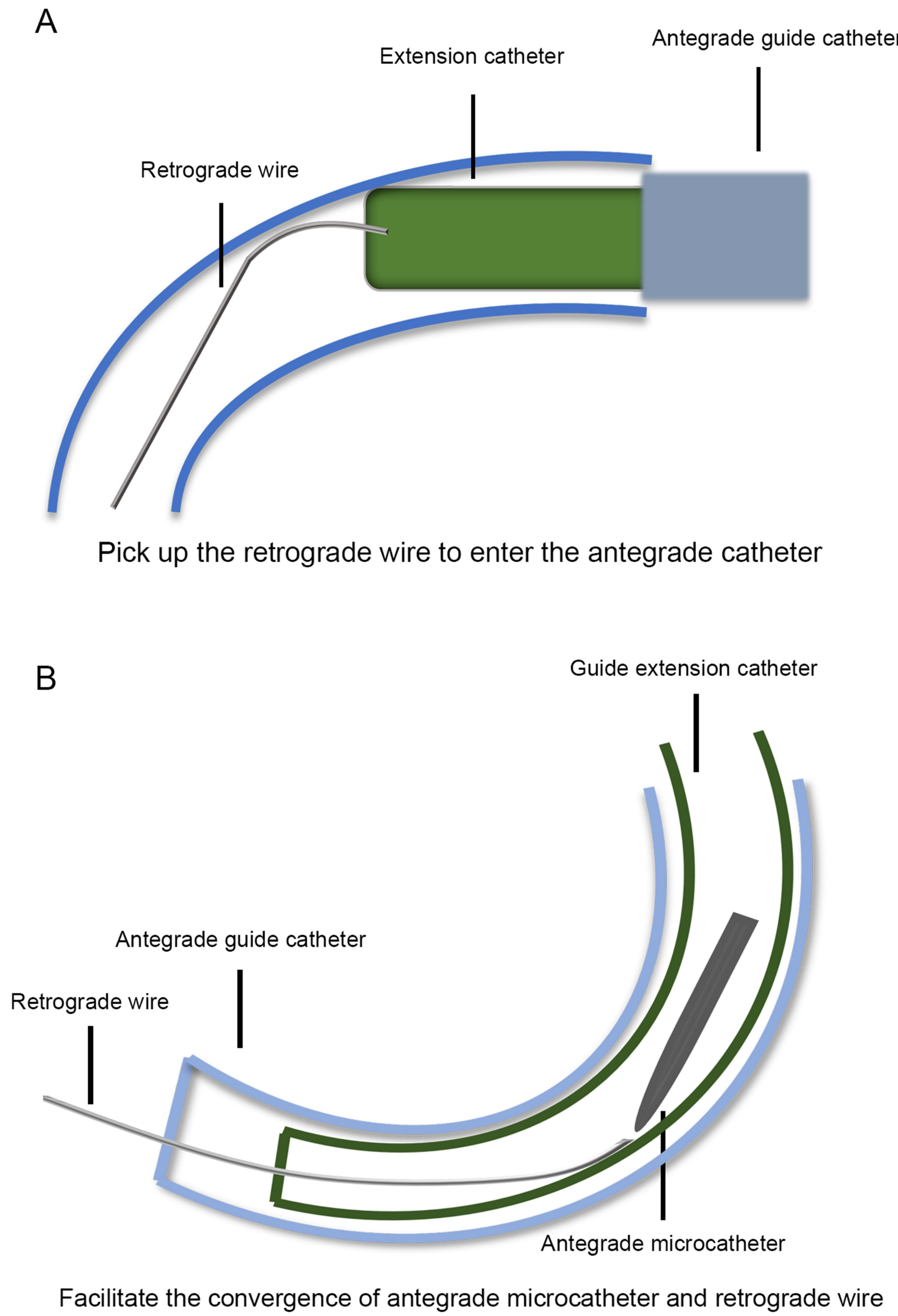

Figure 1 Depiction of guide extension catheter-facilitated tip-in technique. (**A**) The guide extension catheter could advance into the coronary artery to "pick up" the retrograde wire. (**B**) The guide extension catheter narrowed the lumen which facilitated the entry of retrograde wire into the antegrade microcatheter.

Results

Baseline characteristics are summarized in Table 1. The median age of the population was 56 years old [interquartile range (IQR), 47–66]. About 90.9% of the patients were male. Forty-six patients (69.7%) had hypertension and 23 (34.8%) had diabetes. Eighteen patients had previously failed attempts to recanalize the target CTO. There was no significant difference in clinical features between the tip-in and wire externalization group (Table 1).

Table 1 Demographic and Clinical Characteristics

	Total (n=66)	Tip-in (n=33)	Wire Externalization (n=33)	p value
Age (years)	56 (47–66)	56 (46–65)	56 (48–67)	0.837
Male	60 (90.9)	31 (93.9)	29 (87.9)	0.392
Hypertension	46 (69.7)	20 (60.6)	26 (78.8)	0.108
Diabetes mellitus	23 (34.8)	12 (36.4)	11 (33.3)	0.796
Smoking history	32 (48.5)	16 (48.5)	16 (48.5)	1.000
OMI	18 (27.3)	10 (30.3)	8 (24.2)	0.580
Prior PCI	49 (74.2)	25 (75.8)	24 (72.7)	0.778
Prior CABG	1 (1.5)	0 (0)	1 (3.0)	1.000
Prior attempts of the target CTO	18 (27.3)	8 (24.2)	10 (30.3)	0.580
Laboratory and auxiliary examinations				
Creatinine (mg/dl)	85 (75–97)	90 (73–103)	84 (75–95)	0.457
eGFR (mL/min/1.73m^2)	85 (70–97)	81 (65–100)	87 (72–96)	0.501
hs-CRP (mg/L)	0.8 (0.5–2.4)	1.6 (0.5–2.9)	0.7 (0.4–1.3)	0.120
White Blood Cell Count (x10^9/L)	6.22 (5.18–8.08)	6.04 (5.19–7.48)	6.27 (5.18–8.55)	0.202
Platelet (x10^9/L)	201 (158–253)	184 (156–232)	222 (170–264)	0.059
Hemoglobin (g/L)	140 (131–150)	138 (132–150)	140 (130–151)	0.663
NT-proBNP (pg/mL)	151.0 (69.4–350.1)	179.2 (81.2–487.0)	131.0 (64.0–205.0)	0.135
Cardiac troponin T (ng/mL)	0.012 (0.009–0.017)	0.015 (0.009–0.025)	0.011 (0.009–0.013)	0.051
Total cholesterol (mmol/L)	3.18 (2.71–3.87)	3.18 (2.86–3.58)	3.28 (2.61–3.87)	0.818
Low density lipoprotein (mmol/L)	1.38 (1.10–1.87)	1.37 (1.08–1.98)	1.46 (1.10–1.82)	0.918
Triglyceride (mmol/L)	1.60 (1.21–2.45)	1.86 (1.24–2.45)	1.48 (1.11–2.61)	0.603
High density lipoprotein (mmol/L)	0.90 (0.80–1.05)	0.89 (0.80–1.04)	0.90 (0.80–1.06)	0.969
Lp(a) (mmol/L)	28 (11–70)	33 (19–79)	23 (9–70)	0.696
Uric acid (μmol/L)	376 (326–427)	378 (333–427)	371 (325–428)	0.793
Ejection fraction (%)	62 (51–66)	62 (47–66)	64 (57–67)	0.066
Ejection fraction < 40%	6 (9.1)	5 (15.2)	1 (3.0)	0.199

Note: Data are shown as median (interquartile range) or n (%).
Abbreviations: CABG, coronary artery bypass grafting; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; hs-CRP, high-sensitivity C-reactive protein; Lp(a), lipoprotein (a); NT-proBNP, N-terminal pro-B-type natriuretic peptide; OMI, old myocardial infarction; PCI, percutaneous coronary intervention.

Procedural details are displayed in Table 2. There was no significant difference in Syntax score, J-CTO score and the condition of collateral vessels (Rentrop classification and Werner's classification), which we believed could infer that the complexity of the procedure was comparable between two groups. The targeted vessel with total occlusion was similar between the tip-in group and the wire externalization group. The operators most often chose the septal artery as the retrograde route (86.4%). Of note, most operators used Instantpass (APT) as the antegrade microcatheter in the tip-in group. It was probably due to the fact that the relatively larger size of the tip (1.9F) of this microcatheter would be easier to intubate the retrograde guidewire. Besides, the top two wires used to enter the antegrade microcatheter were Ultimate Bro 3 (Asahi) and Gaia 3rd (Asahi) (76.8% and 6.1%, respectively. Data not shown).

Compared with wire externalization, tip-in saved the time to advance the retrograde microcatheter and convert to a dedicated externalization wire. The critical step of tip-in was the convergence of the antegrade microcatheter and the retrograde wire, which could be time-consuming in some cases, for example, when large antegrade guide catheter (≥7F) was used. The antegrade extension catheter with narrowed lumen (mostly 5/6F) was used to further fasten this process (Figure 1). In order to assess the efficiency of guide extension catheter-facilitated tip-in technique, we calculated the manipulation time from the retrograde wire first entering the antegrade guide catheter to the first inflation of an antegrade balloon in the occlusion. The manipulation time was significantly shortened in the tip-in group (389s; IQR, 272–478 vs

Table 2 Lesion and Procedural Features

	Total (n=66)	Tip-in (n=33)	Wire Externalization (n=33)	p value
Syntax score	19.0 (12–22.5)	20.0 (13.5–23.4)	16.0 (11.0–21.5)	0.072
J-CTO score	2 (2–3)	2 (2–3)	2 (2–3)	0.533
Retrograde route				0.473
Septal	57 (86.4)	27 (81.8)	30 (90.9)	
Epicardial	9 (13.6)	6 (18.2)	3 (9.1)	
Rentrop classification				0.296
2	22 (33.3)	13 (39.4)	9 (27.3)	
3	44 (66.7)	20 (60.6)	24 (72.7)	
Werner's classification				0.597
CC1	21 (31.8)	12 (36.4)	9 (27.3)	
CC2	45 (68.2)	21 (63.6)	24 (72.7)	
Target vessel				
LAD	24 (36.4)	14 (42.4)	10 (30.3)	0.306
LCX	1 (1.5)	1 (3.0)	0 (0)	1.000
RCA	41 (62.1)	18 (54.6)	23 (69.7)	0.205
Antegrade guide catheter size				0.282
6F	9 (13.6)	3 (9.1)	6 (18.2.)	
7F	57 (86.4)	30 (90.9)	27 (81.8)	
Retrograde guide catheter size				0.186
6F	45 (68.2)	25 (75.8)	20 (60.6)	
7F	21 (31.8)	8 (24.2)	13 (39.4)	
Antegrade microcatheter				
None	5 (7.6)	0 (0)	5 (15.2)	0.053
Corsair (Asahi)	20 (30.3)	5 (15.2)	15 (45.5)	0.007
Instantpass (APT)	39 (59.1)	28 (84.8)	11 (33.3)	<0.001
KDLC (Kaneka)	2 (3.0)	0 (0)	2 (6.1)	0.492
Retrograde microcatheter				
Corsair (Asahi)	36 (54.5)	18 (54.5)	18 (54.5)	1.000
Instantpass (APT)	27 (40.9)	15 (45.5)	12 (36.4)	0.453
Finecross (Terumo)	2 (3.0)	0 (0)	2 (6.1)	0.492
Retrograde extension catheter				0.641
Guidezilla (6F, Boston Scientific)	5 (7.5)	2 (6.1)	3 (9.1)	
Expressman (5F, APT)	61 (92.5)	31 (93.9)	30 (90.9)	
Retrograde crossing technique				
Wire escalation	25 (37.8)	15 (51.6)	10 (24.2)	0.205
Reverse CART	39 (59.1)	16 (42.4)	23 (75.8)	0.080
Parallel wire	2 (3.0)	2 (6.1)	0 (0)	0.490
PTCA without stenting	6 (9.1)	2 (6.1)	4 (12.1)	0.669
Stent length (mm)	67.8±35.1	62.0±33.2	73.7±36.5	0.052
Contrast volume (mL)	310 (240–410)	315 (235–405)	310 (240–410)	0.949
Manipulation time# (second)	493 (376–720)	389 (272–478)	706 (560–914)	<0.001
Operation time (minute)	150 (108–190)	141 (106–170)	159 (124–201)	0.079
Radiation dose (mGy)	2706 (1879–3605)	2363 (1701–3873)	2771 (2192–3605)	0.223

Notes: Data are shown as median (interquartile range), mean ± standard deviations or n (%). #The time interval from the first retrograde wire entering the antegrade guide to the first antegrade balloon inflation in the occlusion was calculated.
Abbreviations: CART, controlled antegrade and retrograde subintimal tracking; LAD, left anterior descending artery; LCX, left circumflex artery; PTCA, percutaneous coronary angioplasty; RCA, right coronary artery.

706s; IQR, 560–914; $p < 0.001$). Besides, we noticed the trend in shorter total operation time (141min; IQR, 106–170 vs 159min; IQR 124–201; $p = 0.079$) and less radiation exposure (2363mGy; IQR 1701–3873 vs 2771mGy; IQR, 2192–3605; $p = 0.307$) in the tip-in group, which had not reached statistical significance yet.

Discussion

In this study, we evaluated the efficiency of guide extension catheter-facilitated tip-in technique. Compared with the conventional wire externalization method, the modified tip-in could significantly decrease the time to convert to an antegrade approach after retrograde wire entering the antegrade guide catheter.

With the constant improvement of techniques and equipment, CTO PCI could be currently achieved with a high success rate of 80–90%.[8,9] The frequency of use of the retrograde approach was 30–40%, which would be even higher in complex CTO.[9,10] In order to convert to an antegrade approach after retrograde lesion crossing, several candidate strategies can be considered contemporarily, such as wire externalization, rendezvous, tip-in and antegrade microcatheter probing.[11]

Among these techniques, a retrograde crossing of the microcatheter was mandatory except tip-in. A dedicated wire >300cm was also required in wire externalization. However, advancing a retrograde microcatheter into the intended location may not always be possible, especially when the lesion was calcified, torturous or within a stent.[12] Besides, the microcatheter could impair the blood flow from collateral channels and the perfusion of the occluded territory. Long time deposition of the microcatheter in the collaterals may be intolerable for patients with profound heart failure. In such cases, tip-in would be the most appropriate strategy to accomplish the revascularization. Compared with other techniques, tip-in could maximally reduce the manipulation of the retrograde microcatheter.

The key step of tip-in was to advance the retrograde wire into the antegrade microcatheter, which could be occasionally time-consuming. Firstly, inserting the wire into the antegrade guide catheter could be challenging if the guide could not coaxially engage with the coronary ostium or the proximal segment of the artery was tortuous. Second, operators tended to use larger antegrade guiding catheters to increase the support and facilitate equipment delivery. As shown in Table, 7F antegrade guide catheters were most often used in our study. Meanwhile, in other reports, 8F catheters maybe the primary choice.[13] This increased the difficulty to insert the wire into the microcatheter. Therefore, we adapted the traditional tip-in technique by adding an antegrade extension catheter. The extension catheter could improve the efficiency of tip-in from three aspects. (1) It could be advanced into the coronary artery to pick up the retrograde wire, which we called "active greeting technique" (AGT). (2) The extension catheter reduced the lumen to 5/6F, which facilitated the convergence of the wire and microcatheter. As mentioned above, the extension catheter-facilitated tip-in significantly decreased the manipulation time after the retrograde wire entered the antegrade guide catheter. (3) The extension catheter could also increase the antegrade support to assist in microcatheter advancement and equipment delivery if needed.

Even though 33 patients in the tip-in group were all successfully recanalized, there were 3 patients excluded in whom tip-in failed during the recruitment phase of this study. In order to increase the success rate of extension catheter-facilitated tip-in, certain tips are as follows. First, adequately dilate and modify of the lesion if reverse controlled antegrade and retrograde subintimal tracking (CART) is used. A balloon over 2.0mm in diameter is recommended if possible. Second, if resistant CTO is anticipated, choose a coiled type of microcatheter with tapered tip. Third, insert the retrograde wire into the antegrade microcatheter as far as possible or insert the back end of an extra-guidewire into the antegrade MC, as introduced by Giuseppe Venuti etc.[14]

In this study, the overall procedural time and radiation dose showed a trend to decrease in the tip-in group but it had not reached statistical significance yet. Even though the wire externalization process costs more time, externalized wire provides substantial support that may facilitate and expedite other parts of the procedure. With our experience, the manipulation time to convert to an antegrade approach after retrograde wire engagement could be further reduced if full preparation was made and proper equipment chosen (as we mentioned above). Moreover, in some cases, extra non-CTO lesions were treated in the meantime, so it was not feasible to concisely define the time spent on CTO. This could influence the final results concerning the total operation time and radiation dose. In addition, even the use of an externalization wire still, we believe guide extension catheter-facilitated tip-in is an efficient and promising retrograde approach to revascularize CTO in experienced hands.

This study had several limitations. This was a single-centered retrospective study. Although patients in the two groups were 1:1 matched and showed no significant difference in baseline characteristics, there may be bias due to unrealized factors. Besides, the strategies of PCI were chosen at the discretion of the operators and there was no universally standardized protocol. Third, the sample size was relatively small and as mentioned above, non-CTO lesions may be treated in the same operation. Fourth, the effect of failed tip-in technique on the manipulation or procedural time was not assessed due to limited cases. These limitations will be taken into account in our further clinical researches and prospective studies.

Conclusion

The guide extension catheter-facilitated tip-in is an efficient technique in retrograde CTO PCI with unique advantages. Further multicenter prospective randomized trials are needed to confirm our findings.

Data Sharing Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approvement

This study was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (No.: B2021-726R) and conducted in accordance with the guidelines of the Declaration of Helsinki. All participants provided written informed consent at the time of index hospitalization.

Author Contributions

Hao Lu and Juying Qian are corresponding authors. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

There are no conflicts of interest pertaining to this submission.

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