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In Vivo Quantification of the Deformations of the Femoropopliteal Segment: Percutaneous Transluminal Angioplasty vs Nitinol Stent Placement

Can Gökgöl, MSc[1], Steffen Schumann, PhD[1], Nicolas Diehm, MD, MBA[2], Guoyan Zheng, PhD[1], and Philippe Büchler, PhD[1]

[1]Institute for Surgical Technology & Biomechanics, University of Bern, Switzerland

[2]Clinical and Interventional Angiology, Vascular Institute Central Switzerland, Aarau, Switzerland

Corresponding Author:

Assoc. Prof. Dr. Philippe Büchler, Institute for Surgical Technology and Biomechanics (ISTB), University of Bern, Stauffacherstrasse 78, CH-3014 Bern, Switzerland. Email: philippe.buechler@istb.unibe.ch

Abstract

Purpose: To quantify the deformations of the femoropopliteal (FP) segment in patients undergoing endovascular revascularization and to compare the post-treatment deformations caused by primary nitinol stent implantation to those produced by percutaneous transluminal angioplasty (PTA).

Methods: Thirty-five patients (mean age 69±10 years; 20 men) scheduled for endovascular therapy were recruited for the study. During endovascular interventions, angiographic images were acquired with the legs straight and with a hip/knee flexion of 20°/70°. Image acquisition was performed before PTA for all patients, after PTA in 17 patients receiving this treatment only, and after primary stent implantation in the remaining 18 patients. A semi-automatic approach was used to reconstruct the 3-dimensional patient-specific artery models from 2-dimensional radiographs. Axial shortening and curvature changes in the arteries in vivo were calculated for the calcified, dilated, and stented regions, as well as the regions that were distal and proximal to the diseased and treated segments.

Results: Leg flexion resulted in shortening of the artery in all investigated FP segments. The dilated arteries exhibited greater shortening compared to their stented counterparts (post-PTA 7.6%±4.9%, post-stent 3.2%±2.9%; $p=0.004$). Leg flexion also led to an increase in the curvatures of all the sections of the FP segment. While stented arteries had significantly higher curvature values than PTA within the regions proximal to the treated sections, the choice of the treatment method did not affect the curvature of the other segments. Despite this, 40% of the stented arteries exhibited kinking during leg flexion.

Conclusion: The choice of the treatment method affects the post-interventional axial deformations of the FP segment but does not influence the curvature behavior. While PTA results in a more flexible artery, stents restrict the arteries' shortening capabilities. Depending on the anatomical position of the stents, this axial stiffening of the arteries may lead to chronic kinking, which may cause occlusions and, consequently, impact the long-term success of the procedure.

Keywords

artery deformation, axial deformation, balloon angioplasty, curvature, 2D/3D reconstruction, endovascular revascularization, femoropopliteal segment, kinking, leg flexion, nitinol stent, percutaneous transluminal angioplasty, peripheral artery disease, popliteal artery, superficial femoral artery

Introduction

For over a decade, endovascular therapy has been the primary treatment method for most patients with peripheral artery disease (PAD).[1] The main challenge with this treatment has been to overcome comparatively high restenosis rates in the femoropopliteal (FP) segment and the need for target lesion revascularization (TLR). The implantation of nitinol stents following percutaneous transluminal angioplasty (PTA) using conventional uncoated balloons improved restenosis rates[2–5] but led to a new set of problems, such as arterial wall damage through stent-artery interactions,[6–8] loss of primary patency due to neointimal hyperplasia or stent fractures,[9–11] or restriction of the natural deformation behavior of the FP tract.[12,13] The invention of drug-eluting nitinol stents, along with improved stent designs, partially solved these issues.[14–16] The remaining occurrences of restenosis are hypothesized to have a mechanical origin and to be caused by the stent’s effects on arterial deformation during leg flexion.[12,13]

With the advent of drug-coated balloons, bioresorbable stents, and atherectomy devices, the state of the art in the endovascular treatment of FP lesions is moving away from stent placement and toward the so-called "leave nothing behind" strategy.[17,18] The motivation behind this approach is to completely resolve the problems caused by the presence of permanent metal scaffolds. A limited number of nonrandomized clinical trials addressed the efficacy of this technology, and initial results showed superior outcomes vs both balloon angioplasty and uncoated stents, as well as similar primary patency and TLR rates compared with drug-coated stents.[16,18,19] However, contradictory outcomes among different devices suggest that the technology needs further advancements before it can be considered the gold standard among the available endovascular treatments.[16,19,20] Furthermore, stent placement will continue to be utilized for cases in which PTA fails to provide optimal revascularization. Therefore, there is a need to improve the long-term outcomes of stent implantation in the FP segment. To reduce the risk of restenosis, current stent designs should be adapted to conform to the dynamic mechanical environment in the FP segment.

In order to observe whether PTA provides better arterial flexibility compared to stent placement, axial deformation and bending behavior of the FP segment following both approaches need to be investigated. While several publications reported the in vivo deformations of healthy and calcified arteries in both living subjects and cadavers,[21–27] only 2 studies examined the arterial deformations of patients who underwent stent placement.[28,29] However, both studies had limitations that impacted the significance and interpretation of their results. The study from Nikanorov et al[28] considered only a single nitinol stent, and the measurements were performed on single 2-dimensional (2D) radiographs, overlooking the 3-dimensional (3D) nature of the vessel deformations. On the other hand, Ganguly et al[29] mainly focused on the methodology and validation behind the deformation analyses and provided limited information concerning the flexion angle, stent types, and lesion locations, thereby making it difficult to interpret their findings. Additionally, the implications of conventional balloon angioplasty on the deformation behavior of the FP segment are currently not known. Therefore, the objective of this work was to quantify the in vivo FP segment deformations of patients undergoing primary nitinol stent implantation compared with PTA alone. In addition, by comparing the post-PTA deformation behavior with the deformations following stent implantation, recommendations could be made to improve existing stent designs to overcome current shortcomings.

Methods

Study Design and Data Acquisition

Thirty-five patients (mean age 69±10 years; 20 men) scheduled for endovascular therapy were recruited to undergo 2D radiographic imaging of their lower limbs. All patients were classified with Fontaine stage IIb ischemia and had a mean lesion length of 69±9 mm. Information about lesion locations, as well as the calcification levels, are presented in Table 1. This study was approved by the local ethics committee, and each patient signed a consent form for inclusion in the study and use of anonymized data outside the clinical environment.

The method of treatment for each patient was decided during endovascular therapy. All patients underwent initial PTA, in which the balloon was expanded to ~10 atmospheres. Based on a qualitative evaluation of lesion behavior and artery recoil, primary stent implantation was deemed necessary for 18 patients. Three patients received 2 stents for a total of 21 self-expanding nitinol stents (Table 1): 6 Pulsar 18 (Biotronik AG, Bülach, Switzerland); 1 Xpert (Abbott Vascular, Santa Clara, CA, USA); 5 Zilver PTX (Cook Medical Inc., Bloomington, IN, USA); and 9 Protégé EverFlex (Medtronic/Covidien, Mansfield, MA, USA). Stents were sized to overlap ~5 mm into the healthy proximal and distal segments surrounding the lesions. Among the remaining 17 patients who underwent solely PTA, only 2 patients were treated with drug-coated balloons, and all were subjected to subsequent balloon expansion until an adequate lumen diameter was reached. Patients were followed with oscillometry, ankle-brachial index measurement, and duplex sonography at 3, 6, and 12 months following the endovascular procedure.

All angiographic images were acquired with a Philips Allura FD 20 Xper X-ray system with Clarity Upgrade (Philips Medical Systems, Best, the Netherlands). Contrast material was diluted by 50% with saline and injected via the sheath. Prior to the acquisitions, a lightweight calibration phantom was attached to the patient’s thighs using a strap. The initial acquisition was performed first with the leg straight and then with a hip/knee flexion of 20°/70° both before and after treatment. At each configuration, a set of 2 images was acquired, separated by an average view angle of 45° to 60°. The images were stored on the workstation as subtraction angiography and cine images.

3D Reconstruction of the Vessel Centerline

The calibration phantom was required to reconstruct the 3D centerline of the arteries from 2D images. The phantom consisted of 16 radiopaque spherical fiducials that were projected onto the angiographic images as black circular spots. The particular 2D fiducial positions, together with a priori 3D information on the fiducial locations, were used to calibrate each angiographic image.[30] The resulting calibration parameters provided accurate information on the spatial relationship of the acquired images. Based on this spatial relationship, corresponding 2D image locations could be triangulated to a unique 3D position. This triangulation concept was used to retrieve the 3D information of the centerline.[31]

The vessel boundary was defined by picking 2D image points along its projected outline. After defining the artery boundary in 1 image, the beginning and the end of the vessel were represented on the second view in terms of 2 epipolar lines, which were used as a guide to outline the boundary of the vessel in the respective other view. The defined boundary points were further interpolated, and pairs of opposing boundary points were used to compute respective center points. The set of 2D center points from both views were then triangulated to retrieve the centerline in 3D. A validation involving the mean forward and backward projection errors confirmed the accuracy of the reconstruction methodology.[31]

In order to identify the corresponding vessel locations on the straight and flexed knee images, certain landmarks were placed at the stent/balloon ends and at corresponding side branches between each image using the epipolar constraint. Furthermore, to make sure that the same vessel regions were being considered between pre- and post-treatment images, the landmarks at the stent/balloon ends were projected onto the pre-PTA images to accurately identify the lesion ends. All the landmarks were extracted as 3D points.

Artery Deformations

A previously established methodology was adopted to estimate vessel deformations.[32] The calculations were directly performed on the reconstructed centerlines, which were each divided into 3 sections defined by the landmarks that were used to identify the corresponding locations on the straight and flexed images (ie, proximal to lesion, lesion center, and distal to lesion for the pretreatment measurements and proximal to treated region, stented/dilated region, and distal to treated region for post-treatment measurements). The sample sizes for each section of the FP segment are reported in Table 2.

The deformations investigated in this study were the changes in length and curvature due to flexion of the leg. The lengths of the individual vessel sections were estimated by calculating the total linear distance between the landmarks defining the boundaries of each section. As such, the axial deformation was defined as the change in length between flexed and straight positions divided by the undeformed length in the straight position.

The curvature at a single location was measured by fitting a circle to 3 consecutive points on the centerline.[32] The distance between each consecutive point corresponded to the average vessel diameter and was updated with respect to the investigated FP region. The curvature was defined as the inverse of the radius of the circle. Moving this circle along the entire centerline provided the complete curvature profile of a vessel section. Both the mean and maximal curvature changes were then calculated as the difference between the curvature profiles in the straight and flexed positions.

Statistical Analysis

Statistical significance regarding the effects of leg flexion, as well as the influences of stent implantation and PTA on deformations, was assessed using paired *t* tests. The threshold of statistical significance was $p<0.05$. Based on the follow-up data, the rate of symptomatic restenosis within 6 months of the procedure was calculated. Additionally, associations between restenosis and nonphysiological FP deformations including kinking were explored using logistic regression analyses. The outcomes are reported as the odds ratio and risk ratio, respectively, with the 95% confidence interval. Statistical analyses were performed using Matlab (version 7.13; The Mathworks Inc., Natick, MA, USA).

Results

Prior to endovascular treatment, the vessel sections of all samples shortened with leg flexion (Table 2). Within the lesion, the average shortening was higher for the stent group (–6.4%±3.4%) than the PTA group (–4.6%±3.0%). However, this difference was not statistically significant (p=0.11). Furthermore, it was not possible to make a relevant comparison in the proximal regions as there was data from only 1 patient for the pre-stent proximal group.

Regardless of the treatment method, the shortening behavior was preserved for all sections after the operation. For the patients treated with PTA only, the average shortening within the treated regions (–7.6%±4.9%) increased compared to the diseased regions (5.0%±2.3%). On the other hand, patients who received stents showed a statistically significant decrease in the average shortening within the stented regions as opposed to their pretreatment counterparts (post-stent –3.2%±2.9% vs pre-stent –6.4%±3.4%, p=0.005). Consequently, a statistically significant increase in the axial flexibility of the treated artery section was observed when the treatment did not involve primary stent implantation (post-PTA vs post-stent p=0.004).

The mean and maximal curvatures of all the vessel sections increased with leg flexion. For both the diseased and treated regions, the average curvature values nearly doubled with flexion (Table 2). Prior to the treatment, there were no statistically significant differences between the curvature behaviors of the stent and PTA groups, either within the lesion or distal to the lesion. Likewise, the average curvature values in these regions were similar before and after treatment (Table 2). However, similar statements for the proximal regions could not be made due to limited data in the pre-stent proximal group.

Within the regions proximal to the treated segments, the mean and maximum curvature values in the flexed positions were significantly higher with stented arteries than when only PTA was performed (mean curvature p=0.008; maximum curvature p=0.02). For the remaining vessel sections, the average curvature values did not show any significant differences between different treatment methods. Despite this, stent implantation resulted in notable kinking in

7 patients (Figure 1). The kinking almost always occurred within 1 cm of the distal stent end when the stents were implanted toward the popliteal artery. The only exception was 1 patient who had the stent implanted along the full length of the popliteal artery, which caused the kinking to occur in the distal superficial femoral artery (SFA), 1 cm from the proximal end of the stent. There was no visible evidence of kinking in the arteries treated with PTA.

With regard to the different anatomical sections along the FP segment, the average maximal curvature change in the popliteal artery (pre-PTA 0.32±0.18 cm^{-1}, post-PTA 0.29±0.13 cm^{-1}, post-stent 0.34±0.16 cm^{-1}) was always significantly higher than both the distal SFA (pre-PTA 0.11±0.08 cm^{-1}, post- PTA 0.07±0.02 cm^{-1}, post-stent 0.16±0.16 cm^{-1}) and mid SFA (pre-PTA 0.07±0.05 cm^{-1}, post-PTA 0.07±0.07 cm^{-1}, post-stent 0.12±0.11 cm^{-1}). No significant differences were found in the bending behaviors between the distal and mid SFA. Finally, there was no statistically significant difference in the deformations caused by the 3 different stent designs.

Clinically, 1 of the 35 patients died within 10 months of the procedure and was not available for a routine follow-up. Among the remaining patients, 7 experienced FP reobstruction as documented by duplex ultrasound: 2 patients within 30 days and 5 patients within 6 months. Of note, 4 of these patients had exhibited kinking with leg flexion immediately after the treatment. According to the regression analyses, this distribution of data resulted in a risk ratio of 5.0 (95% CI 1.48 to 17.86, p=0.01) and an odds ratio of 10.0 (95% CI 1.57 to 72.67, p=0.02), suggesting that the possibility of restenosis increases with the presence of kinking.

Discussion

The main drawback of endovascular therapy in the FP segment is the risk of restenosis.[1,5] Recent clinical trials reported the long-term restenosis rates in that challenging FP segment to be 17% with drug-eluting stents[15] and 20% with drug-coated balloons.[16] While these numbers are an improvement over the long-term outcomes obtained with uncoated devices,[4,18] they also further underline the hypothesis that the persisting restenosis rates can be attributed to the mechanical deformations of the FP segment.

The deformations in healthy SFA and popliteal arteries have been the subject of numerous studies.[21,23–26] However, comparisons between these studies (ie, old vs young patients, living subjects vs cadavers) show that the deformations are heavily dependent on the composition of the arteries.[25,26] As such, these studies can present only limited information to improve current treatment methods and devices. To this end, it is crucial to analyze the deformations of arteries with PAD prior to and after endovascular treatment. A recent study from Ní Ghriallais and colleagues[27] was a first step toward achieving this goal as they reported FP deformation data pre/post stenting using cadaver limbs removed from patients with PAD. Studies such as this would not only provide information on the vessel deformations of the target population, but also on the mechanical state of the artery resulting from different treatment modalities. The aim of our study was to estimate the in vivo deformations of 35 diseased FP segments prior to endovascular treatment and immediately after PTA or primary stent implantation.

For all FP segments, the lengths of the arteries shortened and their mean and maximum curvatures increased as the leg moved to a flexed position. This general deformation behavior was similar before and just after stent implantation and balloon angioplasty. Furthermore, both the axial deformation and curvature behaviors within the lesion showed no significant differences between the pre-stent and pre-PTA groups, which suggests that the choice of the treatment method was not influenced by the deformations of the diseased arteries.

The treatment had a statistically significant effect on the axial deformation behaviors of the diseased segments due to leg flexion. Performing PTA resulted in increased axial shortening, while primary stent implantation led to decreased axial compressibility. On the other hand, both procedures had a limited impact on the axial deformations of the regions distal to the diseased sections. Similarly, PTA had no effect on the axial behavior of the artery in the proximal regions.

Stented arteries had a significantly higher mean and maximum curvature values compared to the arteries that underwent only PTA in the regions proximal to the treated sections. However, there was only one 1 subject with data in the segment proximal to the lesion in the pre-stent group. As a result, it is not clear if the statistically significant differences observed between the mean and maximum curvatures of stented and dilated arteries were already present prior to the treatments or were caused by the different treatment methods. Within the treated and distal to the treated sections, the average bending behavior of the FP segment due to leg flexion was similar between the 2 treatment methods. However, 40% of the patients who received stents exhibited kinking either distal or proximal to the stent ends immediately after the procedure (Figure 1). In contrast, arteries that were treated with PTA only were not associated with kinking, and in 1 patient the procedure was even found to resolve an identified case of kinking observed before treatment, resulting in a smoother bending behavior (Figure 2).

Our results suggest that the restrictions imposed by the stents on the axial shortening capabilities of the arteries are liable to produce extreme deformations. Due to the FP segment's posterior location to the knee joint, the overall length of the FP segment is expected to decrease during flexion. If the vessel is not able to compress axially, the additional tissue would either form a curve of its own or join a pre-existing curve, resulting in an increased curvature profile and, possibly, kinking. This is especially true for the cases in which stent implantation occurs in the sections of the FP segment that undergo greater deformation with leg flexion, such as the distal SFA and the popliteal artery.[23,28,29,31] The comparisons between the 2 treatment methods further support the relation between kinking and increased axial stiffness due to stent placement.

Previous clinical studies have suggested that chronic kinking may disrupt natural blood flow, leading to restenosis or reocclusions.[12] In our study, 4 of the 7 patients with restenosis exhibited kinking with leg flexion following treatment, supporting the assumption that kinking is associated with restenosis. Based on this observation, the "leave nothing behind" strategy could be considered the optimum treatment approach, as performing only PTA helped restore the natural deformation behavior of the SFA and popliteal arteries. However, bailout stenting will continue to be utilized for arteries that are dissected or suboptimally dilated. Therefore, to decrease the possible restenosis rates caused by stent implantation, future stents would benefit from designs that enable axial shortening during leg flexion. Another, albeit more controversial, solution would be to place an additional stent into the arteries that experience kinking. This would help smooth the transition from the mechanical stiffness of the stented segment to the adjacent bare artery. The major risk with this approach concerns the formation of stenosis due to stenting a healthy artery, which may be inhibited to a certain extent by using drug-eluting stents.

Due to the limited number of studies and the differences in their designs, a direct comparison of our results with previous publications is difficult. In a previous preliminary study, 3D rotational angiography was used to measure the popliteal artery deformations in 5 patients with PAD.[22] The average axial shortening and mean and maximum curvatures from that study compare favorably with our current pre-PTA measurements within the lesion. Nikanorov et al[28] measured the axial elongation, bend radius, and deflection angle on 17 patients who received the Absolute (Abbott Vascular) self-expanding stent. With a 70°/20° knee/hip flexion, the authors reported a mean axial compression of 2.4%±0.4% in a combined segment of the SFA/proximal popliteal (2 patients) and a mean curvature of 0.1 cm^{-1} in the popliteal artery (6 patients). Finally, Ganguly et al[29] reported a mean axial shortening of 4%±3% and a mean curvature change of 0.05 cm^{-1} in the stented femoral arteries (unknown stent types) of 13 patients with an unknown degree of leg flexion. The results from both studies compare favorably with our observations. The differences can be attributed to the number of patients included in the study, to the different stent designs implanted in the patients, and to the different methods used to perform the measurements.

Limitations

The main limitation of the present study concerns the reconstruction of the 3D models from only two 2D radiographic images. Due to the sparse number of views, the identification of corresponding side branches was not possible in most cases. Besides changes to the artery's length and curvature, leg flexion also caused twisting of the SFA and popliteal arteries. However, the twist angle could not be measured as it required accurate positions of the side branches and their deviation from the main branch. Due to mismatched field of views between the angiographic images, the severity of the calcifications and, in some instances, the lengths of the lesions, it was not always possible to identify the proximal and distal regions, leading to varying reductions in the sample sizes of these subgroups. However, with the exception of 1 subgroup, the inclusion was above 80%, thereby providing a sufficient number of datasets to allow relevant statistical evaluations.

All the calculations were performed on 2 static positions, so the measurements actually represent the deformations at a single point that is found during the walking cycle rather than considering a dynamic walking situation, which includes the effect of muscle contraction on vessel shape. Finally, a follow-up study is needed to further support the hypothesis that kinking significantly increases the risk of restenosis.

Conclusion

The current study showed the different effects of the available endovascular treatment methods on FP segment deformations. In this context, PTA was observed to help in recovering the natural deformation behavior of the arteries. On the other hand, stent implantation limited the artery's axial compressibility during leg flexion, which led to kinks when the stents were implanted in the sections of the FP segment that are normally subject to large deformations. Assuming kinking is associated with restenosis and reocclusion, our results would favor the "leave nothing behind" approach to FP revascularization. However, for arteries that require stent implantation, the current stent designs should be improved to allow for greater shortening with leg flexion.

Declaration of Conflicting Interests

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Legends

Figure 1. Angiographic images of the femoropopliteal (FP) segments from 3 patients acquired prior to balloon angioplasty (A, C, E) and following primary stent implantation (B, D, F) during hip/knee flexion of 20°/70°. For all cases, the placement of the stents in the higher deformational sections of the FP segment increased the curvature compared to the pretreatment phase, leading to extreme deformations, such as kinking, with leg flexion.

Figure 2. Angiographic images of the femoropopliteal (FP) segment acquired during hip/knee flexion of 20°/70° prior to (A) and following (B) balloon angioplasty. Dilation resolved the kinking observed in the pretreatment phase and returned the segment to a more natural deformation behavior.

Table 1. Patient Characteristics and Procedure Details.

Age, y	69±10
Men	20
Fontaine stage	IIb
Calcification	
Moderate	23
Severe	12
Lesion length, mm	119±105
Pre-PTA group	71±53
Pre-stent group	168±120
Total occlusions	18
Region of the lesion	
CFA to mid/distal SFA	1
Proximal to mid SFA	2
Proximal to distal SFA	3
Mid SFA	5
Mid to distal SFA	11
Distal SFA	6
Distal SFA to popliteal artery	1
Popliteal artery	6
Patients treated with PTA	17
Uncoated balloons	15
Drug-coated balloons	2
Patients treated with stents	18
Pulsar-18	6
EverFlex	9
Zilver PTX	5
Xpert	1
Stent length, mm	168±131

Abbreviations: CFA, common femoral artery; PTA, percutaneous transluminal angioplasty; SFA, superficial femoral artery.

Table 2. Axial Deformation and the Curvatures of the Femoropopliteal Segment During Hip/Knee Flexion Before and After Percutaneous Transluminal Angioplasty.

	N	Axial Deformation, %	Curvature, cm^{-1}							
			Mean				Maximum			
			Straight	Flexed	Δ	p	Straight	Flexed	Δ	p
Pre-PTA	17									
Proximal to lesion	14	–5.0±2.3	0.05±0.02	0.07±0.02	0.02±0.01	0.031	0.10±0.03	0.14±0.05	0.08±0.05	0.041
Lesion	17	–4.6±3.0	0.07±0.02	0.12±0.08	0.05±0.07	0.028	0.13±0.05	0.26±0.17	0.18±0.16	0.025
Distal to lesion	14	–11.5±4.0	0.06±0.02	0.17±0.16	0.11±0.15	0.060	0.11±0.04	0.30±0.25	0.24±0.25	0.038
Pre-stent	18									
Proximal to lesion	1	–8.0	0.06	0.17	0.11	—	0.11	0.34	0.28	—
Lesion	18	–6.4±3.4	0.05±0.02	0.09±0.04	0.04±0.03	0.004	0.12±0.04	0.19±0.08	0.12±0.04	0.008
Distal to lesion	15	–12.9±3.6	0.06±0.02	0.16±0.05	0.10±0.06	0.005	0.13±0.05	0.33±0.12	0.28±0.14	0.004
Post-PTA	17									
Proximal to treated region	14	–4.4±3.6	0.04±0.02	0.06±0.01	0.01±0.02	0.097	0.08±0.02	0.11±0.03	0.05±0.05	0.036
Lesion	17	–7.4±5.3	0.07±0.02	0.13±0.07	0.06±0.06	0.003	0.13±0.03	0.25±0.15	0.19±0.12	0.005
Distal to treated region	15	–11.6±4.3	0.06±0.02	0.20±0.18	0.15±0.17	0.120	0.11±0.04	0.29±0.23	0.25±0.21	0.130
Post-stent	18									
Proximal to treated region	14	–8.7±8.7	0.05±0.02	0.13±0.09	0.08±0.10	0.094	0.10±0.04	0.24±0.19	0.18±0.19	0.082
Lesion	18	–3.2±2.9	0.06±0.02	0.09±0.05	0.03±0.04	0.003	0.11±0.05	0.21±0.16	0.16±0.14	0.004
Distal to treated region	15	–9.3±6.7	0.07±0.02	0.16±0.08	0.09±0.07	<0.001	0.13±0.04	0.30±0.16	0.24±0.18	<0.001

Abbreviation: PTA, percutaneous transluminal angioplasty.