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CLINICAL RESEARCH
Interventional cardiology

Assessment of acute injuries and chronic intimal thickening of the radial artery after transradial coronary intervention by optical coherence tomography

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Aims Transradial coronary intervention (TRI) introduces a trauma to the radial artery (RA), possibly influencing quality as a bypass conduit if subsequently used. We sought to determine the acute and chronic effects of TRI on the RA by optical coherence tomography (OCT).

Methods and results Immediately after TRI completion, 73 RAs in 69 patients were examined. The sheath was pulled back 2 cm distal to the puncture site, and OCT imaging was performed. The acute injuries and intimal thickening were compared between first-TRI RAs and repeat-TRI RAs. Intimal tears were observed in 49 RAs (67.1%) and were more frequent in the distal than in the proximal RA ($P = 0.001$). Medial dissections were not uncommon (26 RAs, 35.6%). The frequency of acute injury was significantly higher in repeat-TRI RAs ($P < 0.001$). Intima/medial area, the maximum intimal thickness/medial thickness ratio, and per cent narrowing were all significantly greater in repeat-TRI RAs in the distal and proximal RA. Multivariate analysis revealed that a repeated TRI procedure was the only independent predictor of intimal thickening.

Conclusion Optical coherence tomography clearly demonstrated significant acute injuries and chronic intimal thickening of RA after TRI. Further study should evaluate the impact of these effects when TRI RAs are subsequently used as conduits, on long-term graft patency and on clinical outcomes after bypass surgery.

Keywords Revascularization • Artery • Bypass • Arteriosclerosis

Introduction

The radial artery (RA) has been widely used as an alternative access for coronary intervention, and recent advances in the miniaturization of devices have further facilitated the transradial approach as a routine technique in many centres. In addition to the reported benefits of transradial coronary intervention (TRI), including fewer bleeding complications and earlier ambulation, recent studies demonstrate that TRI is independently associated with a lower risk of death or myocardial infarction after percutaneous coronary intervention.[1,2]

In contrast, after the reports of excellent clinical and angiographic outcomes, RA has gained widespread use as an alternative arterial conduit for surgical coronary revascularization.[3–5] Since TRI induces a trauma to RA that could influence its suitability as a bypass conduit if subsequently used for myocardial revascularization, concern has been raised about the frequent use of the RA as an access and about bilateral RA use for TRI. There is a paucity of data demonstrating the nature and extent of the acute injuries and the chronic structural changes caused by TRI to the RA. Such data could help when considering whether the RA is suitable as a conduit after its use as an entry point in interventional procedures.

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Optical coherence tomography (OCT) is an emerging imaging technology capable of a resolution at ~10–20 μm and is suited for precise imaging of the luminal surface of blood vessels and wall structures in a way that is not possible using other imaging modalities. Previous reports demonstrate the feasibility of OCT imaging as an accurate tool to assess the quality of conduit vessels for coronary artery bypass grafting.[6,7] The histological validation of OCT imaging has been demonstrated by Kume *et al.*[8]

Acute RA injuries after TRI and chronic effects on RA morphology assessed by OCT have not been reported. Therefore, the purpose of the present study was to investigate the nature and the extent of the effects of TRI on RA morphology by OCT.

Methods

Patient population

From March 2009 to September 2009, 238 patients with a normal Allen test result underwent TRI at our institution. We excluded patients with severe heart failure, cardiogenic shock, serum creatinine >2.0 mg/dL, or important systemic disease, such as Raynaud's disease. Of the remaining patients, we studied 118 consecutive patients who underwent coronary OCT imaging (ImageWire, LightLab Imaging, Westford, MA, USA), which was used to examine RA after the completion of TRI. The indication for OCT imaging of coronary lesions was the assessment of angiographic or intravascular ultrasound findings of suspected plaque ruptures or thrombus. We further excluded 47 patients who had undergone a diagnostic catheterization through the RA, which was subsequently used for first-time TRI, and 2 patients who underwent TRI with the use of the 7F system. After excluding these patients, 73 RAs were investigated in the present study. In four patients, bilateral RAs were examined by OCT imaging during the study period. Therefore, the first-TRI RA group (RAs that were never cannulated, including access for diagnostic catheterization before first-time TRI) consisted of 42 RAs, and 31 RAs were included in the repeat-TRI RA group (RAs used for TRI at least twice). The patients' clinical characteristics are summarized in *Table 1*. The protocol was approved by the institutional review board, and all patients gave written informed consent.

Table 1 Clinical characteristics of the study patients

	First-TRI RA group (n = 42)	Repeat-TRI RA group (n = 31)	*P*-value
Age (years)	66.0 ± 13.1	63.6 ± 9.4	0.364
Male gender	32 (76.2%)	28 (90.3%)	0.137
Body mass index (kg/m^2)	24.9 ± 4.3	24.8 ± 2.5	0.892
Diabetes	21 (50.0%)	14 (45.2%)	0.683
Hypertension	34 (81.0%)	24 (77.4%)	0.774
Dyslipidaemia	27 (64.3%)	25 (80.6%)	0.191
Current smoking	13 (31.0%)	6 (19.4%)	0.295
Three-vessel disease	7 (16.7%)	13 (41.9%)	0.032
Creatinine	0.84 ± 0.33	0.88 ± 0.44	0.706
Total cholesterol	205.8 ± 38.5	172.3 ± 30.6	<0.001
LDL cholesterol	131.2 ± 31.5	98.9 ± 24.0	<0.001
HDL cholesterol	48.6 ± 12.7	44.0 ± 12.9	0.157
Triglyceride	139.3 ± 107.1	162.7 ± 82.7	0.318
HbA1c	6.08 ± 1.10	5.90 ± 0.85	0.474
Statin use	12 (28.6%)	22 (71.0%)	<0.001
Aspirin use	22 (52.4%)	31 (100%)	<0.001
Approach			
Right RA	29 (69.0%)	25 (80.6%)	0.295
History of TRI			
First	42 (100%)	0	
Second	0	20 (64.5%)	
Third	0	6 (19.4%)	
Fourth	0	4 (12.9%)	
Fifth	0	1 (3.2%)	

Data are presented as the mean value ± SD or absolute frequency (%) of patients. TRI, transradial coronary intervention; LDL, low-density lipoprotein; HDL, high-density lipoprotein; RA, radial artery.

Transradial coronary intervention

After local anaesthesia by lidocaine, the right or left RA was punctured using a 22-gauge needle. A 0.025 in. guidewire was introduced through the needle, followed by insertion of a sheath with an introducer (16 cm; TERUMO Co., Tokyo, Japan). The sheath size used in the present study was 6 F (external diameter 2.48 mm). With the sheath in place, 0.2 mg of nitroglycerin and 8000 U of heparin were introduced into the side port of the sheath. A 0.035 in. radifocus guidewire (TERUMO Co., Tokyo, Japan) with a guiding catheter was advanced through the sheath and the RA. Selection of the guiding catheter and TRI strategy were left to the operator's discretion. Immediately after the completion of TRI, an RA angiogram was performed with a radiopaque scale in place to locate the RA ostium, the tip of the sheath, and the puncture site. After administration of 0.5 mg isosorbide dinitrate, the sheath was extracted to a point that was 2 cm distal to the puncture site. This approach facilitated OCT examination from the RA ostium to 2 cm distal to the puncture site.

Optical coherence tomography imaging

The OCT system used in the present study has been described previously.[9,10] A 0.016 in. OCT catheter was inserted into a forearm and placed at the RA ostium through the sheath under fluoroscopic guidance. Imaging was performed using an upper-arm tourniquet while applying pressure that was 20–30 mmHg higher than systolic blood pressure and with continuous infusion of Ringer's solution through the sheath. After flushing with 7–10 mL of the solution, continuous infusion of the solution at 1.5–2.0 mL/s was sufficient to remove blood for OCT imaging. Automated pull-back imaging (2.0 mm/s) was repeatedly performed to examine RA from the ostium to the sheath tip, yielding sequential transverse views of the RA with a frame rate of 20 Hz and a slice width of 0.1 mm. The OCT probe's IR light transilluminated the vessel wall and the skin under dimmed lighting of the catheterization laboratory, which can be used as an exact registration of OCT findings with the guidance of a radiopaque ruler and fluoroscopy. The OCT images were digitalized and analysed using proprietary software (LightLab Imaging, Inc.) according to the principles of OCT imaging described elsewhere.[6] Current OCT systems have been designed for use in coronary arteries and thus are not optimal for use in the larger diameter peripheral vessels, such as the proximal portion of the RA. Further, because the catheter may rest against one side of the vessel wall, a portion of the vessel may be outside of the imaging range, preventing full cross-sectional visualization. In these cases, the assessment of acute injuries was performed on the visualized portion of the RA, and morphometric measurements were not performed. All analyses and assessments of RA were performed on vessel basis.

Image analysis of the acute injuries

The layered structure of the RA wall was observed in all cases in the present cohort by OCT. Based on previous studies with histological validations, the intima was defined as a signal-rich layer nearest to the lumen, and media was defined as a signal-poor middle layer. The internal elastic lamina was defined as a signal-rich band between the intima and media, and the external elastic lamina was defined as a signal-rich band between the media and adventitia. An intimal tear was defined as luminal surface discontinuity with or without an intimal flap that was restricted within the intima. Medial dissection was defined as a luminal surface disruption that extended into the media either in a radial or in a circumferential direction (*Figure 1*).

Localization of each injury was documented according to the following three portions of the RA divided on the basis of the sheath location during TRI: proximal: RA ostium to the tip of the sheath; mid: the tip of the sheath to the centre of the sheath; distal: the centre of the sheath to 2 cm distal to the puncture site (*Figure 2*). The presence of the thrombus was also examined, and detected thrombi were classified

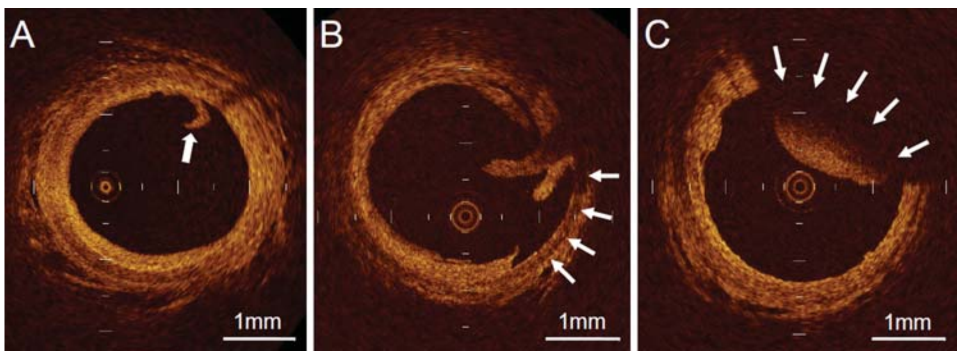

Figure 1 Representative cases of acute injuries in optical coherence tomography imaging. (*A*) Representative image of intimal tear (arrow) shows an intimal disruption restricted to the intima. (*B*) Representative image of medial dissection (arrows) shows a tear involving the intima–media border. (*C*) Representative image of thrombus (arrows) shows a high-signal protruding mass inside the lumen.

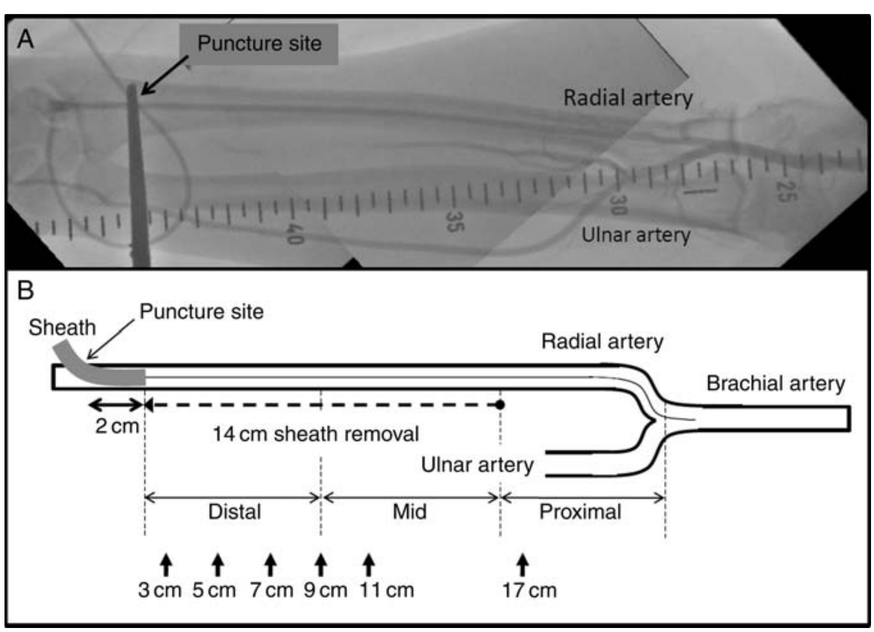

Figure 2 Schematic representation of optical coherence tomography analysis of the radial artery. (*A*) Radial artery angiogram was performed with a radiopaque scale to identify the location of radial artery ostium, sheath tip, and puncture site. A pair of Pean forceps is located at the puncture site. (*B*) The location of the acute injuries was reported according to the following three regions: distal—centre of the sheath to 2 cm distal to the puncture site; mid—tip of the sheath to the centre of the sheath; proximal—radial artery ostium to the tip of the sheath. Morphological measurements were performed at 3, 5, 7, 9, 11, 17 cm from the puncture site (short arrows at the bottom).

as a red or white thrombus. Red thrombus was defined as high-backscattering protrusions inside the lumen of the artery, with signal-free shadowing in the OCT image, and white thrombus was defined as low-backscattering projections in the OCT image on the basis of reported criteria.[11]

Image analysis of intima and media thickening

Optical coherence tomography morphometric measurements included intimal and medial area, intimal and medial thickness, external elastic lamina area, and lumen area. Morphometric measurements were performed at 3, 5, 7, 9, and 11 cm from the puncture site, and at 17 cm, representing the portion between the sheath tip and the RA ostium (*Figure 2*). Five consecutive cross-sectional OCT images at each site were analysed, and the mean value was used for further analysis. If the image showed an intimal tear, medial dissection, or insufficient image quality for the measurement, next closest measurable image slice without injuries was used. The OCT images were digitalized and analysed using automated contour-detection image-processing software (LightLab Imaging Inc.) with manual editing. Calculated measurements included the percentage of luminal narrowing (%LN), intimal thickness index (ITI: intimal area/medial area), and the ratio of the width of the intima to the width of the media at the maximum intimal thickness (IMR). Other investigators have suggested that the IMR is the most sensitive method available for grading atherosclerosis.[12,13] In the present study, three methods were used to evaluate the degree of intimal thickening and atherosclerosis: (i) %LN, (ii) ITI, (iii) IMR (*Figure 3*).

Intra- and interobserver reproducibilities

Two experienced observers who were blinded to the patient's identity performed OCT image analyses independently (interobserver variability). In the case of disagreement on the acute injuries, the two observers re-analysed the OCT images and reached a consensus diagnosis. The first observer repeated a blinded analysis after an interval of 1 week (intraobserver variability). Reproducibility of the acute injuries was determined by κ statistics. Linear regression analysis was used to verify the degree of agreement between the measurements of the two observers.

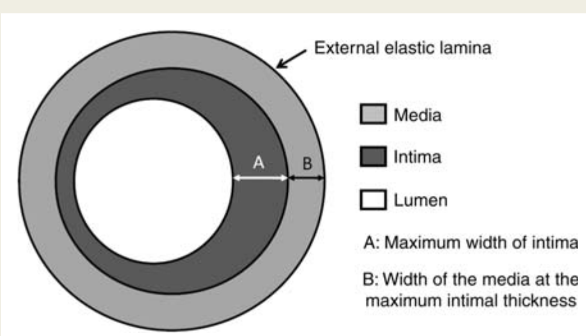

Figure 3 Schema depicting the indices used to evaluate the severity of intimal hyperplasia in the cross-sectional optical coherence tomography image of the radial artery. Morphological measurements included medial area, intimal area, lumen area, maximum width of the intima (*A*), and the corresponding width of the media (*B*). Calculated measurements included the percentage of luminal narrowing [(intimal area + medial area)/external elastic membrane area], intimal thickness index (intimal area/medial area), and the ratio of the width of the intima to the width of the media at the maximum intimal thickness (*A*/*B*).

Statistics

The Statistical Package for Social Science (SPSS) for Windows, version 13.0 (SPSS, Chicago, IL, USA), was used for all analyses. Categorical data are expressed as numbers and percentages and were compared using the χ^2 or Fisher's exact test, as appropriate. Continuous variables are expressed as the mean ± standard deviation for normally distributed variables and as median (25th–75th percentiles) for non-normally distributed variables. They were compared using a two-sided Student's *t*-test and Mann–Whitney *U* test, respectively. Pairwise tests were performed if the contingency table for all three acute injuries was significant. Multivariate linear regression analysis was performed to identify variables independently predicting IMR. A *P*-value <0.05 was considered statistically significant.

Results

Optical coherence tomography examinations

The mean length between the sheath tip and the RA ostium was 3.9 ± 1.4 cm. The mean length of examined RA by OCT was 15.9 ± 1.4 cm, and there was no significant difference between these values for the first-TRI RA and repeat-TRI RA groups. At 3, 5, and 7 cm, all images were measurable. Owing to the limitation of OCT signal range and/or the eccentric position of OCT probe, full cross-sectional visualization was not possible in two of the RAs in the repeat-TRI group and two of the RAs in the first-TRI group at 9 cm and one of the RAs in the first-TRI group at 11 cm. At 17 cm, three RAs in the repeat-TRI group and three in the first-TRI group were not measurable. Of the 438 examined sites, sufficient image quality for the measurements was obtained for 427 (97.5%) sites. At 17 cm from the puncture site, image acquisition was not suitable for measurements in 6 of 73 RAs (8.2%).

Clinical characteristics and catheterization procedures

The clinical characteristics and catheterization procedures are summarized in *Table 1*. In the repeat-TRI RA group, total cholesterol level and low-density lipoprotein cholesterol level were significantly lower, and the frequencies of statin and aspirin use were significantly greater than in the first-TRI RA group. The repeat-TRI RA group included 20 RAs with two TRIs, 6 RAs with three TRIs, and 5 RAs with more than four TRI procedures.

Assessment of acute injuries

The presence or absence of intimal tears and medial dissections was assessed in a total of 219 portions of 73 RAs. Intimal tears were detected in 70 portions (32.0%) and medial dissections in 35 portions (16.0%). Intimal tears and medial dissections were significantly more frequent in the repeat-TRI group than in the first-TRI group (intimal tear: 44.1 vs. 23.0%, $P = 0.002$; medial dissection: 24.7 vs. 9.5%, $P = 0.004$). *Figure 4* shows the frequencies of intimal tears and medial dissections in each portion of the RA. The frequency of intimal tears was significantly higher in the

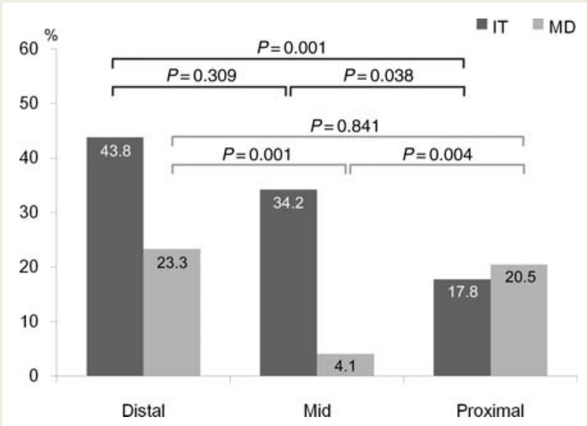

Figure 4 Frequencies of intimal tears and medial dissections. The frequency of intimal tears (dark grey) was greater in the distal than in the proximal portion of the radial artery (distal: 43.8%, mid: 34.2%, proximal: 17.8%). The frequency of medial dissections (light-grey) was significantly greater in the distal and proximal than in the mid portion (distal: 23.3%, mid: 4.1%, proximal 20.5%). IT, intimal tear; MD, medial dissection.

distal portion than in the proximal portion of the RA ($P = 0.001$). Medial dissections tended to cluster in the proximal and the distal portions. In 15 RAs (20.5%) of all 73 RAs, 3 red thrombi and 12 white thrombi were detected. There was no significant difference in frequency or localization of thrombi between the two groups.

Assessment of intima and media thickening

Optical coherence tomography findings in the first-TRI RA and repeat-TRI RA groups are presented in *Table 2*. Representative cases from the first-TRI RA group and repeat-TRI RA group are shown in *Figure 5*. Both intimal and medial areas were significantly greater in the repeat-TRI RA group for all examined sites. The lumen area in the repeat-TRI RA group was significantly smaller than that in the first-TRI RA group at 3, 5, and 7 cm from the puncture site. There was no significant difference in EEL area between the two groups at these sites, suggesting the absence of significant compensatory enlargement. The indices of %LN, ITI, and IMR showed significantly greater intimal hyperplasia in the repeat-TRI RA group. Multivariate linear regression analysis showed that repeat-TRI was the only independent predictor of IMR after controlling for other clinical variables (*Table 3*). Repeat-TRI was independently associated with more intimal thickening at all examined sites.

Intra- and interobserver reproducibilities of optical coherence tomography findings

High intraobserver agreement was obtained in the assessment of the acute injuries: 214/219 portions for intimal tear (97.7%; $\kappa = 0.95$), and 216/219 for medial dissection (98.6%; $\kappa = 0.95$). Interobserver agreement was also high: 207/219 (94.5%; $\kappa = 0.87$) for intimal tear and 216/219 (98.6%; $\kappa = 0.95$) for medial dissection, suggesting the accuracy of OCT-based assessment of the acute injuries. A highly significant correlation of measurements between pairs of observers was found (intraobserver: intimal area $r = 0.98$, $P < 0.001$; medial area $r = 0.97$, $P < 0.001$; interobserver: intimal area $r = 0.93$, $P < 0.001$; medial area $r = 0.94$, $P < 0.001$). The mean interobserver difference of intimal area measurements was 0.09 mm^2.

Discussion

To our knowledge, this is the first study reporting the use of OCT to evaluate the acute effects of TRI on the RA and chronic RA intimal thickening. The major findings of the present study are as follows. (i) Optical coherence tomography examination clearly demonstrated that TRI introduced acute injuries in a substantial portion of patients. (ii) Intimal tears and medial dissections showed different patterns of localization when using a 6 F, 16 cm sheath. (iii) Intimal thickening in the repeat-TRI group was significantly greater in both the distal and the proximal RAs. (iv) Repeat-TRI was an independent predictor of intimal thickening after adjusting for confounding factors.

Acute injuries

This study demonstrated that intimal tears were more frequently detected in the distal portion on the RA, suggesting an important role of the relationship between RA size and sheath size for acute injury. The outer diameter of the 6 F sheath was 2.48 mm, which is similar to the reported inner diameter of the distal RA[13–15] and the diameter observed in the present study (2.64 mm in the first-TRI group at 3 cm from the puncture site). However, more than half of the intimal tears were observed in the proximal portion of the sheath and the portion close to the RA ostium, suggesting the existence of another mechanism related to the intimal tears. The stretching effect of the sheath and the passage of the sheath itself might introduce intimal tears. Other factors, such as RA spasms, may also cause intimal tears when the sheath is introduced or removed, irrespective of RA diameter. Medial dissections showed a unique localization pattern of clustering in the proximal and distal RA. Medial dissections observed in the distal RA might have been introduced by a stretching effect from sheath insertion, whereas the proximal dissections close to the RA ostium were likely caused by catheter advancement or removal through the proximal RA where no sheath (16 cm length) protection existed. Our results might be interpreted as suggesting that potential refinement of the equipment may reduce acute proximal RA injuries by longer sheath application. Although no previous report has evaluated the acute injuries caused by TRI on the RA, Kamiya *et al.*[16] demonstrated that pre-operative transradial catheterization deteriorates early graft patency, suggesting adverse effects of TRI on graft quality.

The present findings of the acute injuries and the presence of thrombi may have important implications for surgeons considering the use of the RA as a conduit immediately after TRI. Injuries to the inner vascular layer are likely to directly influence the risk of early failure by hampering the anti-inflammatory and antithrombotic roles of the endothelium.[17] As the vascular endothelium is a major source of endogenous vasodilators, such as prostacyclin and NO, traumatic injuries may increase the risk of post-operative spasm for the RA graft.[18] Until a method is developed that reduces acute RA injuries by TRI, or we refute the hypothesis that post-TRI

Table 2 Morphometric measurements of radial arteries by optical coherence tomography

	Distance from the puncture site (cm)	First-TRI RA group	Repeat-TRI RA group	*P*-value
Intimal area (mm^2)	3	0.64 (0.56–0.77, *n* = 42)	1.72 (1.23–2.23, *n* = 31)	<0.001
	5	0.62 (0.54–0.81, *n* = 42)	1.26 (1.09–1.50, *n* = 31)	<0.001
	7	0.67 (0.55–0.80, *n* = 42)	1.28 (1.03–1.55, *n* = 31)	<0.001
	9	0.61 (0.50–0.80, *n* = 40)	1.01 (0.80–1.54, *n* = 29)	<0.001
	11	0.60 (0.48–0.76, *n* = 41)	0.90 (0.76–1.28, *n* = 31)	<0.001
	17	0.65 (0.54–0.75, *n* = 39)	1.17 (1.01–1.55, *n* = 28)	<0.001
Medial area (mm^2)	3	2.09 (1.74–2.62, *n* = 42)	2.36 (2.08–2.71, *n* = 31)	0.042
	5	1.91 (1.51–2.22, *n* = 42)	2.15 (1.95–2.68, *n* = 31)	0.007
	7	1.96 (1.54–2.49, *n* = 42)	2.17 (2.00–2.59, *n* = 31)	0.042
	9	1.92 (1.45–2.28, *n* = 40)	2.63 (2.05–2.92, *n* = 29)	<0.001
	11	1.99 (1.48–2.19, *n* = 41)	2.20 (1.93–2.45, *n* = 31)	0.010
	17	2.31 (2.05–2.87, *n* = 39)	2.88 (2.65–3.46, *n* = 28)	0.007
EEL area (mm^2)	3	8.13 (7.47–9.12, *n* = 42)	8.80 (7.35–9.75, *n* = 31)	0.320
	5	8.31 (7.13–10.52, *n* = 42)	8.07 (7.28–9.48, *n* = 31)	0.975
	7	8.38 (7.35–10.51, *n* = 42)	8.34 (7.64–9.81, *n* = 31)	0.918
	9	8.20 (7.31–9.89, *n* = 40)	9.13 (7.68–11.48, *n* = 29)	0.145
	11	8.67 (7.32–11.58, *n* = 41)	8.96 (8.35–11.58, *n* = 31)	0.477
	17	9.63 (8.28–13.26, *n* = 39)	12.44 (9.91–13.89, *n* = 28)	0.072
Lumen area (mm^2)	3	5.49 (4.92–6.18, *n* = 42)	4.81 (3.99–5.14, *n* = 31)	<0.001
	5	5.95 (5.03–7.38, *n* = 42)	4.82 (4.33–5.56, *n* = 31)	0.001
	7	6.11 (4.94–7.61, *n* = 42)	4.78 (4.28–5.71, *n* = 31)	0.002
	9	5.77 (5.09–7.44, *n* = 40)	5.04 (4.41–7.23, *n* = 29)	0.153
	11	6.24 (5.25–8.61, *n* = 41)	5.45 (5.03–8.56, *n* = 31)	0.105
	17	7.03 (5.32–10.45, *n* = 39)	8.05 (5.64–9.61, *n* = 28)	0.509
%LN	3	33.7 (27.8–38.2, *n* = 42)	48.8 (44.4–54.7, *n* = 31)	<0.001
	5	29.5 (26.0–32.8, *n* = 42)	42.3 (37.1–49.1, *n* = 31)	<0.001
	7	29.8 (25.7–34.1, *n* = 42)	42.4 (37.2–49.0, *n* = 31)	<0.001
	9	29.3 (25.8–32.7, *n* = 40)	40.2 (33.8–45.8, *n* = 29)	<0.001
	11	26.9 (22.7–31.0, *n* = 41)	35.3 (29.7–41.8, *n* = 31)	0.001
	17	29.3 (26.0–34.4, *n* = 39)	36.9 (30.3–40.9, *n* = 28)	0.003
ITI	3	0.33 (0.24–0.37, *n* = 42)	0.69 (0.51–0.87, *n* = 31)	<0.001
	5	0.34 (0.30–0.44, *n* = 42)	0.53 (0.43–0.74, *n* = 31)	<0.001
	7	0.35 (0.29–0.42, *n* = 42)	0.55 (0.46–0.65, *n* = 31)	<0.001
	9	0.33 (0.28–0.41, *n* = 40)	0.43 (0.32–0.67, *n* = 29)	0.006
	11	0.34 (0.28–0.38, *n* = 41)	0.42 (0.33–0.58, *n* = 31)	0.003
	17	0.28 (0.23–0.33, *n* = 39)	0.42 (0.33–0.54, *n* = 28)	<0.001
IMR	3	0.52 (0.42–0.73, *n* = 42)	1.22 (0.98–1.79, *n* = 31)	<0.001
	5	0.64 (0.49–0.85, *n* = 42)	1.19 (0.74–1.65, *n* = 31)	<0.001
	7	0.63 (0.44–0.75, *n* = 42)	1.03 (0.77–1.44, *n* = 31)	<0.001
	9	0.57 (0.45–0.64, *n* = 40)	0.85 (0.58–1.15, *n* = 29)	<0.001
	11	0.55 (0.47–0.69, *n* = 41)	0.76 (0.59–1.10, *n* = 31)	0.001
	17	0.46 (0.36–0.60, *n* = 39)	0.71 (0.54–1.16, *n* = 28)	<0.001

Data are presented as the median (IQR, number of measured RA).
IQR, inter-quartile range; TRI, transradial coronary intervention; RA, radial artery; %LN, per cent luminal narrowing; ITI, intimal thickness index; IMR, the ratio of the width of the intima and the width of the media at the maximum intimal thickness.

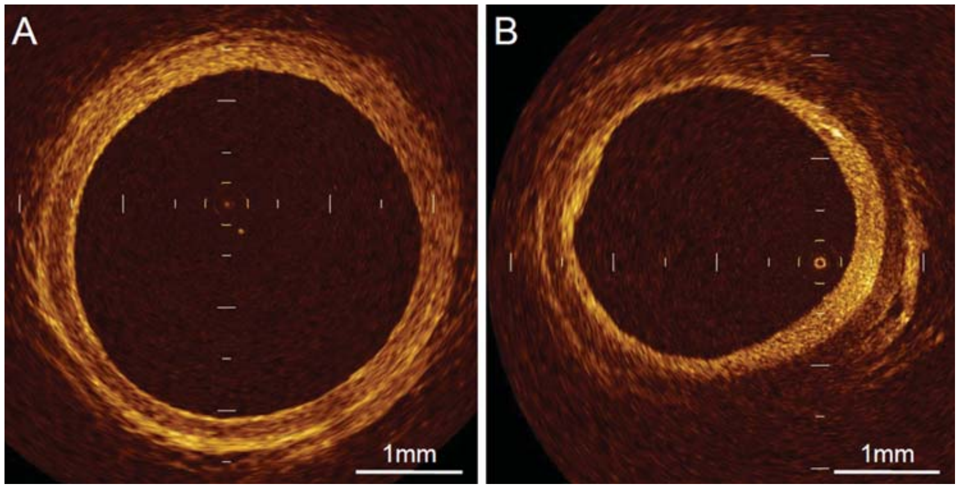

Figure 5 Representative cases of intimal hyperplasia observed by optical coherence tomography in the first-transradial coronary intervention group and the repeat-transradial coronary intervention group. (*A*) Representative optical coherence tomography image of the distal radial artery from the first-transradial coronary intervention group (58-year-old male). (*B*) Representative optical coherence tomography image of the distal radial artery from the repeat-transradial coronary intervention group (65-year-old male).

Table 3 Predictors of the ratio of intimal width to medial width at the maximum intimal thickness at 3 cm from the puncture site by multivariate linear regression analysis

	B	SE	t	P-value
Repeat-TRI	0.766	0.139	5.494	<0.001
Male gender	−0.235	0.177	−1.326	0.181
Age	−0.003	0.006	−0.457	0.739
Diabetes	−0.004	0.128	−0.031	0.949
Hypertension	0.071	0.164	0.434	0.889
Dyslipidaemia	−0.267	0.156	−1.712	0.415
Statin use	0.323	0.148	2.188	0.083

Adjusted $R^2 = 0.375$ for the model.
B, unstandardized coefficient; SE, standard error of coefficient.

RA injuries have an important impact on the long-term patency of the RA conduit or clinical outcomes after bypass surgery, the use of the RA as a conduit shortly after TRI might not be recommended because of acute vessel trauma and thrombus formation, which have been reported to be related to graft failure.

Chronic intima and media thickening

The findings in the present study agree with a previous ultrasound study,[14] which demonstrated a smaller lumen diameter and increased intimal thickening in the distal RA and compared the intima and media thickness, lumen diameter, and vessel area in repeat-TRI RAs with those in first-TRI RAs only for the distal 5 cm from the puncture site. The present study added further information and demonstrated that the intimal thickening was also significantly greater in the middle and proximal RA. Because the proximal portion of the RA is preferred for bypass surgery, this finding may be interpreted as suggesting that the whole length of the RA used for TRI, even when distal portions are discarded during conduit preparation, is affected by intimal hyperplasia.

As the present study did not provide serial observations of RA used for TRI, a causal relationship between acute injuries and chronic intimal thickening was not directly determined. Chronic intimal change might correlate with OCT-detected acute injuries and more minute endothelium denudation below OCT resolution because diffuse intimal thickening may not be explained solely by acute injuries reported in this study, and intimal changes seemed to be enhanced in the distal RA. Anatomic and histological studies demonstrate that the architecture of the RA varies along its course, and the muscular component of the media tends to be more represented in the distal RA.[19] Therefore, a hypothesis might be generated that the similar degree of acute injuries enhances the atherosclerotic response in the distal RA. No previous report had evaluated post-TRI RA medial changes, which were clearly detected in the present study. The %LN, ITI, and IMR were indices of comparing intimal disease in the present and previous studies. In using these indices, we assume that any thickening of the media occurs to the similar degree along the RA, from the puncture site to the RA ostium. This assumption may not be valid, as the greater thickness of the media in repeat-TRI RAs may invalidate these indices and potentially underestimate the intimal disease. Whether the significant medial thickening shown in the present study affects long term-patency in subsequent uses for bypass grafting remains to be determined.

Study limitations

This study was not a randomized comparison, so the possibility of bias exists. The present study did not provide serial RA observations and had no internal control group. We did not directly determine whether the chronic intimal thickening observed in the repeat-TRI group resulted from the accelerated progression of TRI-induced atherosclerosis, although multivariate analysis showed that repeat-TRI was an independent predictor of chronic intimal change. The sample size of 73 RAs in the study could be too small to perform multivariable modelling. This limitation could result in overfitting of the model. The RAs of the repeat-TRI group were examined at a mean of 11 months after the first TRI. It is not known if there was an ongoing process of atherosclerotic progression triggered by TRI at this point. Therefore, it remains to be clarified whether different results would have been obtained by examination at a later point. We did not evaluate the impact of the sheath size or the number of TRI procedures on the chronic intimal hyperplasia. Despite the significant difference in intimal and medial hyperplasia between first- and repeat-TRI RAs, the results should be considered as hypothesis-generating findings until the completion of a prospective study demonstrating whether these TRI-induced acute injuries and chronic intimal hyperplasia cause the RA graft failure.

Conclusion

We described the novel use of high-resolution OCT imaging to determine the nature and extent of the effect of TRI on the RA. Optical coherence tomography clearly demonstrated significant acute injuries and chronic intimal thickening of the RA after TRI. Efforts should be made to reduce these injuries by further miniaturization and sophistication of the devices and technical improvements or potential pharmacological interventions. The use of the RA following TRI should be avoided as a conduit in coronary bypass surgery until the long-term patency of the post-TRI RA has been demonstrated.

Conflict of interest: none declared.

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