

Peer Review File

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REVIEWER A

1. Regarding a 75-year-old gentleman treated by EVT, didn't he receive coronary angiography before EVT or at the same time frame? I want to know the information about coronary stenosis at that time.

Our response:

We conducted coronary angiography following the completion of EVT. In the revised manuscript, we modified this sentence on page 5, line 112-113 as follows;

Following the completion of endovascular treatment, coronary angiography was concomitantly conducted and it showed multiple moderate stenotic lesions.

2. It is about line 37, "which enabled to achieve very low LDL-C level ()". You leave brackets blank. Please fill in something.

Our response:

We added a value of LDL-C on page 3, line 70-71 as follows;

Due to his suboptimal control of LDL-C level with moderate intensity statin, high-intensity one (20mg atorvastatin) and 10mg ezetimibe were commenced, which enabled to achieve very low LDL-C level (50 mg/dL).

REVIEWER B

1. Line 49 LDL level is missing.

Our response:

We added a value of LDL-C on page 3, line 70-71 as follows;

Due to his suboptimal control of LDL-C level with moderate intensity statin, high-intensity one (20mg atorvastatin) and 10mg ezetimibe were commenced, which enabled to achieve very low LDL-C level (50 mg/dL).

2. Line 57 "this patient has not experienced" is better wording.

Our response:

We revised this sentence on page 4, line 80-81 as follows;

this case does not experience any cardiovascular events.

3. There is no need for the leg and prior PCI material in the supplement.

Our response:

We deleted Supplementary Figure I and II in the revised manuscript.

REVIEWER C

1. The serial changes of maxLCBI_{4mm} should be affected by multiple factors. For instance, since LCBI is a fraction of arc indicating lipid in any cross section, the wire/catheter bias could affect the size of arc (When the catheter located closer to the LRP in the vessel, the lipid rich arc derived from NIRS IVUS could be larger). Thus, the authors can not address pema fibrate as the only factor that made a serial changes of maxLCBI_{4mm} based on just a case.

Our response:

- We agree with the reviewer that the location of guidewire and NIRS catheter could be another factor affecting LCBI. However, the current technology is not capable of positioning the imaging catheter at exactly same distance from plaque surface every pullback. Further advanced technology will be required to sort out this issue.

- In the revised manuscript, we stated this in the Discussion section on page 9, line 182-184 and page 10, line 1-2 as follows;

The distance between NIRS imaging catheter and surface of plaque could affect maxLCBI_{4mm}. We conducted serial NIRS imaging in this case. However, NIRS imaging catheter was not necessarily positioned at the exactly same location relative to evaluated plaques every pullback. Further refinement of this imaging technique will be required for serial evaluation of maxLCBI_{4mm}.

2. The Table and figure 4 should be retouched. It is hard to see.

Our response:

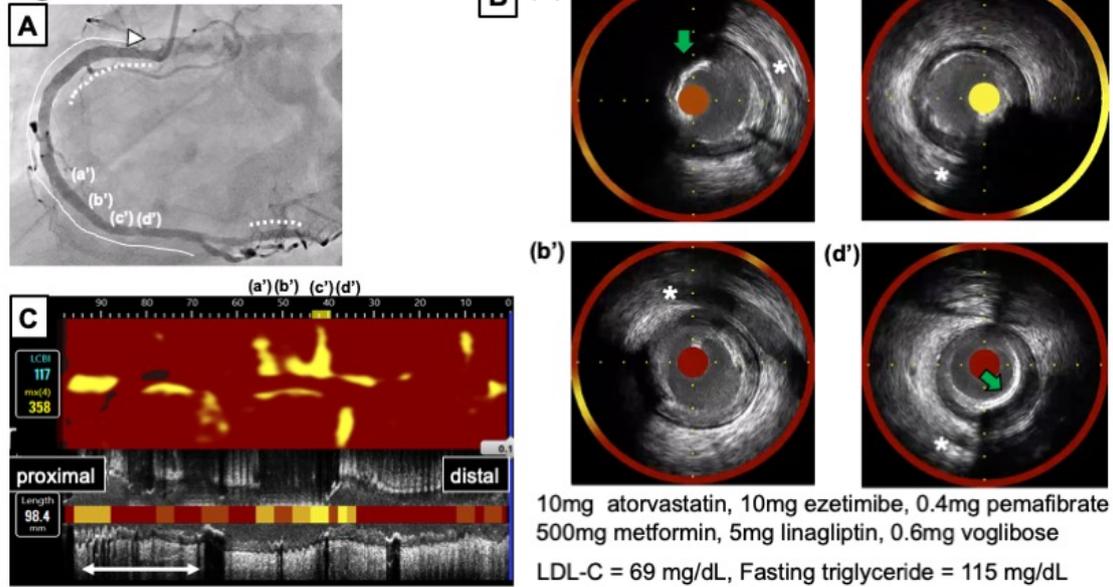
We uploaded the revised Table and Figure 4.

Table. Risk Factor Control and Medication Use

	2017	2018		2019	2021	2022
	EVT for PAD	NSTEMI (primary PCI)	Two months after PCI	uAP (PCI)	Follow-up coronary angiography	at the clinic
Risk Factor Control						
LDL-C	96 mg/dL	104 mg/dL	50 mg/dL	46 mg/dL	65 mg/dL	61 mg/dL
HDL-C	46 mg/dL	46 mg/dL	50 mg/dL	46 mg/dL	54 mg/dL	58 mg/dL
Triglyceride	283 mg/dL	274 mg/dL	278 mg/dL	248 mg/dL	106 mg/dL	141 mg/dL
Non-HDL-C	149 mg/dL	142 mg/dL	99 mg/dL	81 mg/dL	76 mg/dL	68 mg/dL
Apolipoprotein CIII	-	-	14.2 mg/dL	12.0 mg/dL	8.2 mg/dL	8.6 mg/dL
Remnant cholesterol	-	-	7.7 mg/dL	9.3 mg/dL	2.4 mg/dL	-
HbA1c	6.9%	7.1%	6.8%	6.5%	6.8%	6.7%
Medication Use						
Lipid-lowering therapy						
10mg atorvastatin						
20mg atorvastatin						
10mg ezetimibe						
0.2mg pema fibrate						

EVT = endovascular treatment, HbA1c = glycated hemoglobin, HDL-C = high-density lipoprotein cholesterol, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, uAP = unstable angina pectoris

Figure 4.

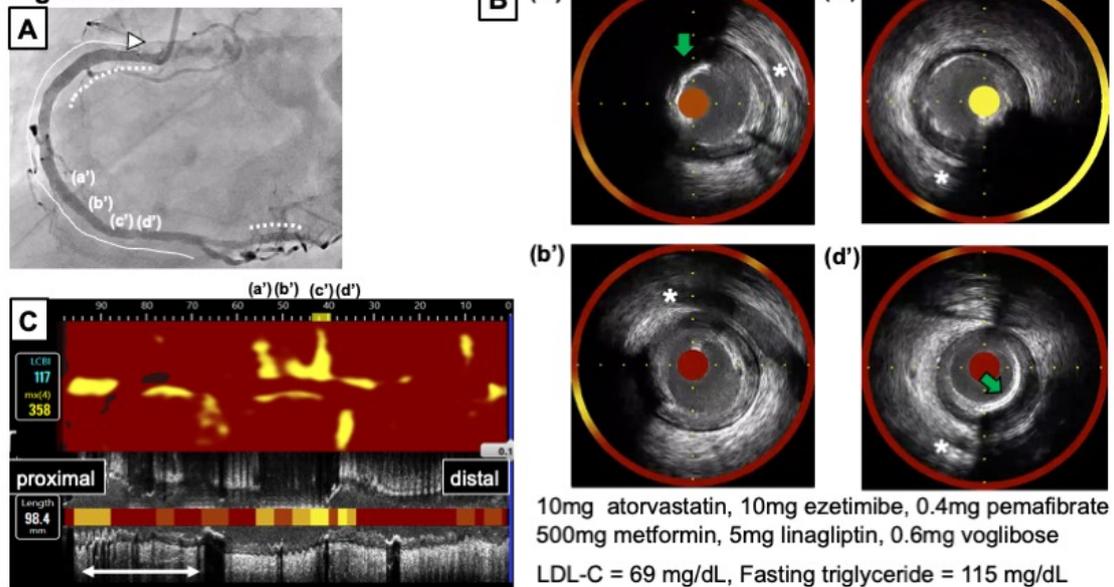


3. Is the section C' shown precisely? The C' seems to be located in the range of maxLCBI4mm in the longitudinal view (picture C), the chemogram shown in a cross section of C' (picture B) demonstrated no LRP in that section.

Our response:

The reviewer is correct. We found out that the submitted image C' was wrong one. We uploaded the revised Figure 4.

Figure 4.



4. The units used in the figures should be in accordance with those in the manuscript.

Our response:

We revised the units in Table 4.

Table. Risk Factor Control and Medication Use

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Remnant cholesterol	-	-	7.7 mg/dL	9.3 mg/dL	2.4 mg/dL	-
HbA1c	6.9%	7.1%	6.8%	6.5%	6.8%	6.7%
Medication Use						
Lipid-lowering therapy						
10mg atorvastatin						
20mg atorvastatin						
10mg ezetimibe						
0.2mg pemafibrate						

EVT = endovascular treatment, HbA1c = glycated hemoglobin, HDL-C = high-density lipoprotein cholesterol, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, uAP = unstable angina pectoris

5. Page6, Paragraph 1, line1 “Two years later”. The period from EVT to NSTEMI PCI seems just 1 year. Is it just a typo?

Our response:

We revised this sentence on page 6, line 126-127 as follows;

One year later, he presented non-ST-segment elevation myocardial infarction (troponin T level=0.016 ng/ml).

REVIEWER D

1. Please provide whether the reduction of LCBI was accompanied with the reduction of Plaque burden, MLA and Plaque Volume?

Our response:

- We analyzed the matched non-culprit middle and distal segment of RCA at baseline and follow-up timepoint (analyzed longitudinal length=56mm). As shown in the following Table, percent atheroma volume at follow-up imaging was numerically smaller, accompanied by a larger minimum lumen area.
- In the revised manuscript, we presented this data in the main text on page 8, line 153-155 and uploaded as Supplementary Table.

Serial changes in percent atheroma volume and minimum lumen area at the non-culprit middle and distal segments of RCA (analyzed longitudinal length of matched segment=56mm) were shown in Supplementary Table.

	Baseline	Follow-up	Absolute change
Percent atheroma volume	59.4%	57.3%	-2.1%
Minimum lumen area	5.53 mm	6.13 mm	+0.6 mm

2. I would rather conclude that pemafibrate administered together with the hypolipemic drugs has anti-atherosclerotic potential.

Our response: We revised this sentence in the Abstract on page 4, line 85-86 and main text on page 10, line 189-191 as follows;

This finding highlights potential anti-atherosclerotic benefit of pemafibrate use in patients receiving a statin.