Původní sdělení | Original research article

Near-infrared spectroscopy derived indexes as a potential predictor of plaque burden volume progression after unprotected left main coronary artery intervention

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ARTICLE INFO

Article history:
Submitted: 26. 11. 2024
Revised: 27. 12. 2024
Accepted: 19. 1. 2025
Available online: 3. 2. 2025

Klíčová slova:
Intravaskulární zobrazovací metody
IVUS
Kmen levé věnčité tepny
LCBI
MaxLCBI4mm
NIRS
Objem plátu
Progrese plátu

SOUHRN

Úvod: Ischemická choroba srdeční (ICHS) je celosvětově hlavní příčinou úmrtí, což je jedním z důvodů významných technologických pokroků intervenční kardiologie v posledních dekádách. Kombinace intravaskulárního ultrazvuku (IVUS) a infračervenému spektru blízké spektroskopie (NIRS) nabízí detailní pohled na morfologii koronárních tepen a složení aterosklerotických plátů. Tyto pokročilé zobrazovací technologie umožňují přesnější hodnocení ICHS a zlepšují terapeutické strategie.
Cíl: NIRS dokáže detekovat a určitým způsobem kvantifikovat obsah lipidů v aterosklerotickém plátu pomocí indexů LCBI (Lipid-Core Burden Index) a maxLCBI4mm (Maximal Lipid Core Burden Index ve 4mm segmentu). V této studii jsme zkoumali vztah mezi těmito indexy a progresí aterosklerotického plátu v období 9–12 měsíců od perkutánní koronární intervence (PCI) s implantací lékového stentu v kmeni levé koronární tepny.
Metody: Jednalo se o prospektivní, monocentrickou studii zahrnující 27 pacientů s významnou stenózou kmene levé věnčité tepny, kteří podstoupili IVUS-NRS vedenou PCI. Sériově byly hodnoceny LCBI, maxLCBI-4mm a objem plátu (PV) před PCI, bezprostředně po PCI a v rámci kontrolního vyšetření za 9 až 12 měsíců u 18 pacientů.
Výsledky: Průměrný věk pacientů dosahoval 72,7 roku, přičemž převládali muži (88 %). Průměrný LCBI před PCI byl 128,9 ± 122,0, zatímco maxLCBI4mm byl 263,7 ± 172,0. Volumetricky pomocí IVUS měřený PV po PCI byl 418,7 ± 203,3 mm³, při kontrole se zvýšil na 454,5 ± 209,4 mm³ (p = 0,105). Analýza neodhalila významnou korelaci mezi rozdílem PV (po PCI a při kontrole) a výchozími hodnotami LCBI, resp. maxLCBI4mm (p = 0,626, resp. 0,786).
Závěr: Výsledky neprokázaly statisticky významnou korelaci mezi počátečními hodnotami LCBI, resp. maxLCBI4mm a progresí PV v kmeni levé věnčité tepny. Korelační grafy však naznačují trend ke snížení PV u pacientů s vysokými výchozími hodnotami LCBI a maxLCBI4mm jako možný efekt vysoce intenzivní statinové terapie.

Keywords:
Intravascular imaging
IVUS
LCBI
Left main
MaxLCBI4mm
NIRS
Plaque progression
Plaque volume

ABSTRACT

Background: Coronary artery disease (CAD) is the leading cause of death worldwide, which has driven significant advances in the field of interventional cardiology. The combination of intravascular ultrasound (IVUS) and near-infrared light spectroscopy (NIRS) offers a detailed view of coronary artery morphology and plaque composition. This advanced imaging capability facilitates a more accurate assessment of CAD and enhances therapeutic strategies.

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DOI: 10.33678/cor.2025.010

Please cite this article as: Hudec M, Kaňovský J, Brázdil V, et al. Near-infrared spectroscopy derived indexes as a potential predictor of plaque burden volume progression after unprotected left main coronary artery intervention. Cor Vasa 2025;67:6–15.

Objective: NIRS can detect and quantify lipid content in atherosclerotic plaque using the Lipid Core Burden Index (LCBI) and the Maximal Lipid Core Burden Index in a 4 mm segment (maxLCBI4mm). In this study, we examined the relationship between these indices and atherosclerotic plaque progression in the crucial area of the left main coronary artery (LM) during a follow-up period of 9 to 12 months after percutaneous coronary interventions (PCI).

Methods: A prospective, single-centre study was conducted involving 27 patients with significant left main stenosis who underwent IVUS-NIRS guided PCI. Serial assessments of the LCBI, maxLCBI4mm, and IVUS-derived plaque volume (PV) were performed at baseline, immediately post-PCI, and during follow-up at 9 to 12 months in 18 patients.

Results: The mean age of the study population was 72.7 years, with a predominance of male patients (88%). The average LCBI of the LM coronary artery before PCI was 128.9 ± 122.0, while maxLCBI4mm was 263.7 ± 172.0. The IVUS-measured PV post-PCI was 418.7 ± 203.3 mm³, increasing to 454.5 ± 209.4 mm³ at follow-up (p = 0.105). Analysis revealed no significant correlation between the difference in PV and baseline LCBI or maxLCBI4mm, with p-values of 0.626 and 0.786, respectively.

Conclusion: This study found no significant association between initial LCBI and maxLCBI4mm segment values and subsequent changes in PV in the left main coronary artery. However, correlation graphs indicate a trend toward decreased PV in patients with high initial LCBI and maxLCBI4mm.

Introduction

Coronary artery disease remains the leading cause of death worldwide, according to recent data from the World Health Organization.[1,2] This fact is one of the reasons why interventional cardiology research has made significant advances over the last few decades. The use of intravascular imaging (IVI) has already become standard in contemporary clinical practice.

IVI provides more information about the vessel than conventional coronary angiography (CAG). The two most widely used methods of IVI are intravascular ultrasound (IVUS) and optical coherence tomography (OCT).[3] Both methods can be used to plan, guide and optimise the final result of percutaneous coronary interventions (PCI), in addition to stratifying the patient's future risk based on coronary data analysis. IVUS relies on the analysis of backscattered ultrasound signals, while OCT analyses the backscattering of light waves. Each of these methods presents certain advantages and disadvantages based on their underlying principles. Generally, IVI characterizes the morphological features of the coronary arteries before and/or after coronary interventions.[4,5]

A detailed analysis of the characteristics of vessel wall tissue regarding the presence of lipids and calcifications has been challenging until recently. In 2013, the FDA approved a new method – near-infrared light spectroscopy (NIRS). This system is typically coupled with IVUS and provides real-time analysis of the composition of atherosclerotic plaques, identifying the likelihood of lipid presence – known as lipid core plaque (LCP).[6]

The use of IVI is already established in European and American guidelines for myocardial revascularization. Clinical scenario in which the use of IVI is recommended includes PCI of the left main (LM) bifurcation, where IVUS is typically employed.[7,8] The LM bifurcation represents a critical area within the coronary system. A long-term successful outcome in this region necessitates not only an impeccable intervention guided by IVUS, ideally performed at a high-volume catheterization centre,[9] but also a comprehensive understanding of all factors influencing the vessel's post-intervention condition. NIRS can detect and quantify lipids in atherosclerotic plaques within coronary arteries. The probability of their presence is coded in different colours. Thus, NIRS may also be valuable in predicting the progression of atherosclerosis following PCI of the LM.

Near-infrared spectroscopy

NIRS is a catheter-based intravascular imaging tool. The fundamental principle of this method involves spectroscopic analysis to determine the unknown chemical composition.[10] The spectrometer emits radiation of a known wavelength into the sample, with a range of 780–2500 nm, which is classified as near-infrared light radiation. This wavelength range is advantageous because it does not interact with haemoglobin or water, unlike optical coherence tomography (OCT), and therefore does not require the use of contrast agents for blood clearance.[11–13]

Within the sample, the radiation is partially scattered and absorbed, based on the presence and concentration of specific chemical bonds.[14] The altered radiation is then returned to the spectrometer, where it is analysed to produce a graph of absorbance for each wavelength. Each chemical substance interacts uniquely with the wavelength, producing a distinct graph of absorbance. This allows for the identification of chemical composition within the analysed segment of the coronary artery.[10,15]

The qualitative results are represented by chemogram and block chemogram, while the quantitative analysis is expressed through Lipid Core Burden Index (LCBI) and LCBI for the most affected 4 milimetres (maxLCBI4mm).[16] NIRS provides a two-dimensional graphical representation of the analysed coronary artery segment. The technique conducts a detailed analysis every 1 mm, assessing up to 1300 points per millimetre. Each point in the analysed section is assigned a colour indicating the probability of lipid presence, ranging from red (indicating a low probability of lipids) to yellow (indicating a high probability of lipids).[17,18] The quantitative expression of NIRS results is labelled as the Lipid Core Burden Index (LCBI). This index serves as a numerical representation of the chemogram, providing a dimensionless value. It quantifies the number

of points within the analysed segment that exhibit a lipid presence probability greater than 0.6, multiplied by 1000. MaxLCBI4mm is the highest automatically determined LCBI value within any 4 mm segment, indicating the area with the most significant lipid-core plaque presence.[19,20]

Methods

Design

This prospective, single-centre study was designed to investigate the relationship between near-infrared spectroscopy (NIRS)-derived indexes (Lipid Core Burden Index [LCBI] and maxLCBI4mm of the left main coronary artery [LM]) and the volumetrically assessed plaque volume (PV) of the LM. The aim was to predict atherosclerosis progression following percutaneous coronary intervention (PCI) with the latest generation drug-eluting stent (DES). The study followed the Declaration of Helsinki, was approved by the local Ethics Committee and all patients signed the informed consent.

Sub-analysis of the cohort includes assessment of atherosclerosis progression according to statin dose – group of high intensity dosage of statin (HDS) and moderate intensity dosage of statin (MDS). High intensity dosage of statin includes patients with dose of atorvastatin 40 mg and more or dose of rosuvastatin 20 mg and more.[21]

Patients with coronary artery disease (CAD) underwent baseline IVUS-NIRS-guided PCI of the LM bifurcation, followed by serial IVUS-NIRS examination of the LM at follow-up catheterization between 9 to 12 months after baseline procedure. During both procedures, NIRS--derived LCBI and maxLCBI4mm of the LM, as well as IVUS--derived volumetric analysis of the LM, were obtained at baseline, immediately post-PCI, and during the follow-up catheterization.

Additionally, a clinical follow-up was conducted at 1, 3, 6, and 12 months post-index procedure for all enrolled patients. We were aiming to clinical events such as death, rehospitalization due to cardiovascular reasons, acute myocardial infarction (AMI), repeated coronary angiography (CAG), and target or non-target lesion revascularization (TLR or NTLR).

NIRS analysis

The NIRS analysis was conducted using a 3.2-French dual-modality intracoronary catheter (DualPro™; Infraredx Inc.). NIRS analysis was specifically restricted to the segment of the left main coronary artery (LM), identified by the proximal edge (ostium in the aorta) and the distal part (the last frame before the LM divides into the left anterior descending artery [LAD] and the left circumflex artery [RCx]). The software automatically calculated the Lipid-Core Burden Index (LCBI) and the maxLCBI4mm for this segment, as previously described.

Data were collected at three key stages: baseline (prior to PCI), immediately post-PCI, and during follow-up catheterization. These data helped in assessing the progression of atherosclerosis and the effectiveness of the PCI.

Figures are included to illustrate the NIRS analysis: **Figure 1** presents a simplified scheme of NIRS analysis of the coronary artery, **Figure 2** demonstrates the application of NIRS in clinical practice, and **Figure 3** compares images from coronary angiography (CAG), intravascular ultrasound combined with NIRS (IVUS-NIRS), and optical coherence tomography (OCT).

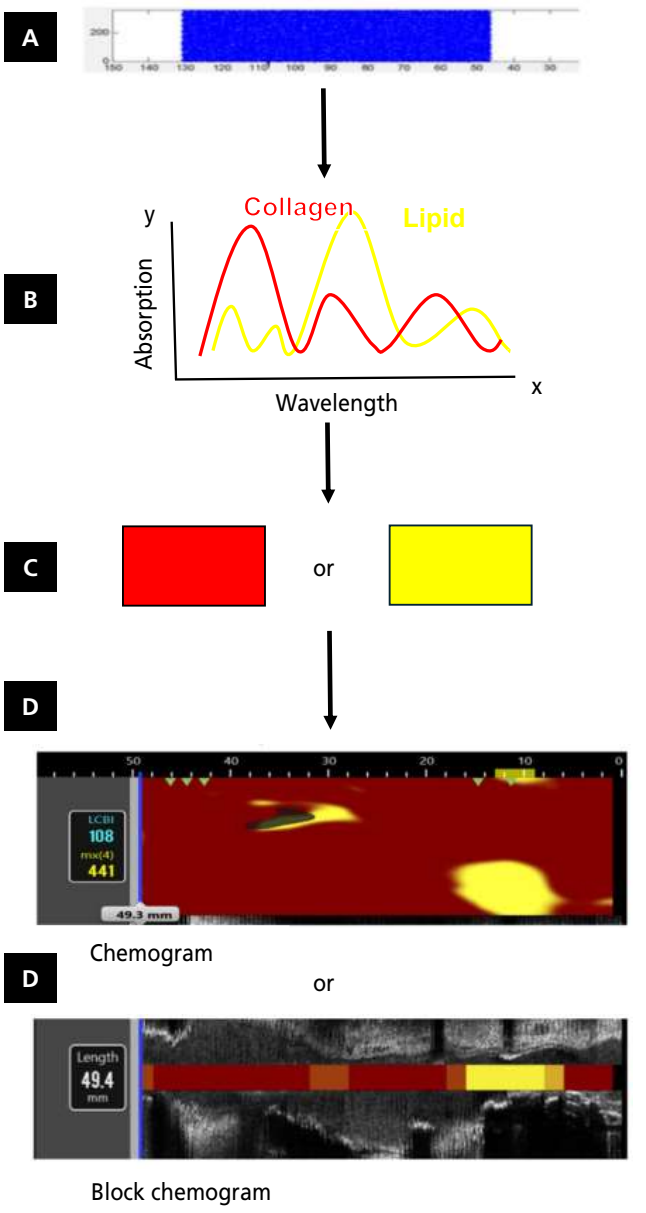

Fig. 1 – Simplified scheme of NIRS analysis of the coronary artery. (A) Section of the analysed coronary artery (x-axis shows the artery longitudinally, y-axis shows the transverse section). The section where the chemical analysis was carried out, point by point, is shown in blue. (B) Simplified graph of absorbance of different wavelengths for cholesterol and collagen (the shape of the curves does not correspond to the real curves of absorbance for the collagen and lipids). (C) According to the probability of the presence of lipids, each of the analysed points is assigned a value of 0–1, which corresponds to a colour scale from red to yellow. (D) Resulting chemogram with LCBI and maxLCBI4mm values and block chemogram with the length of the analysed section.

IVUS analysis

Intravascular ultrasound (IVUS) data were recorded simultaneously using the same dual-modality intracoronary

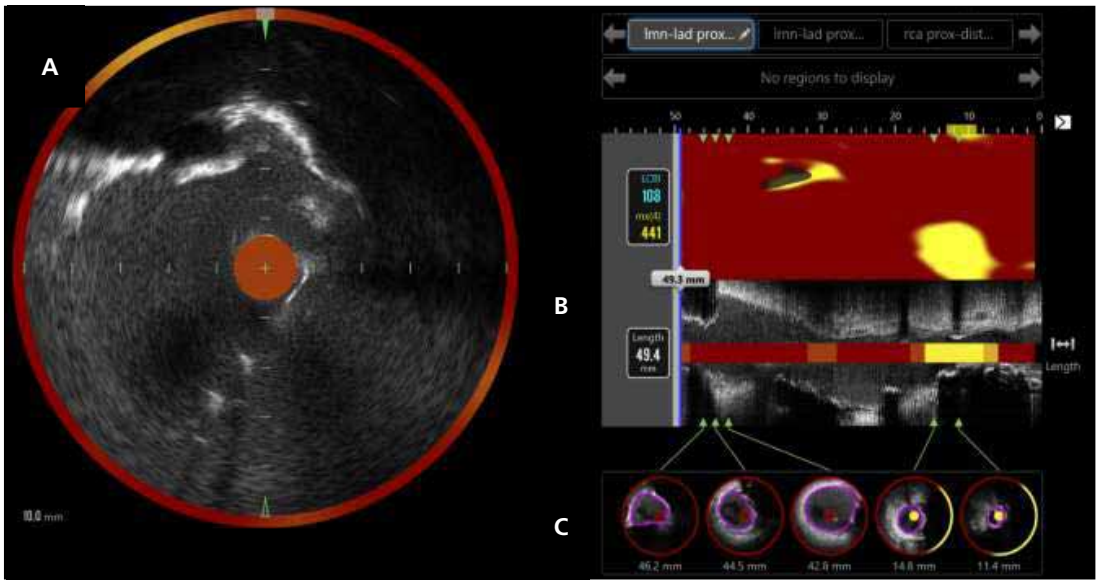

Fig. 2 – Combined imaging of the examined section from the latest version of IVUS-NIRS (Makoto Intravascular Imaging System™) in real practice. (A) Sagittal view in the distal part of the examined coronary artery segment. This is a co-registered IVUS and NIRS recording. Black and white IVUS image in the central part. Along its perimeter, a coloured bar expressing the chemogram in the adjacent section (according to the probability of cholesterol presence from red to yellow). In the very centre of the image, a coloured circle – expressing the block chemogram in this frame. (B) Chemogram and block chemogram of the entire examined part. By moving the cursor, you can select individual sections in the IVUS pull-back record. (C) Examples of 5 sections through the investigated vessel showing a high probability of the presence of cholesterol plaques in last images.

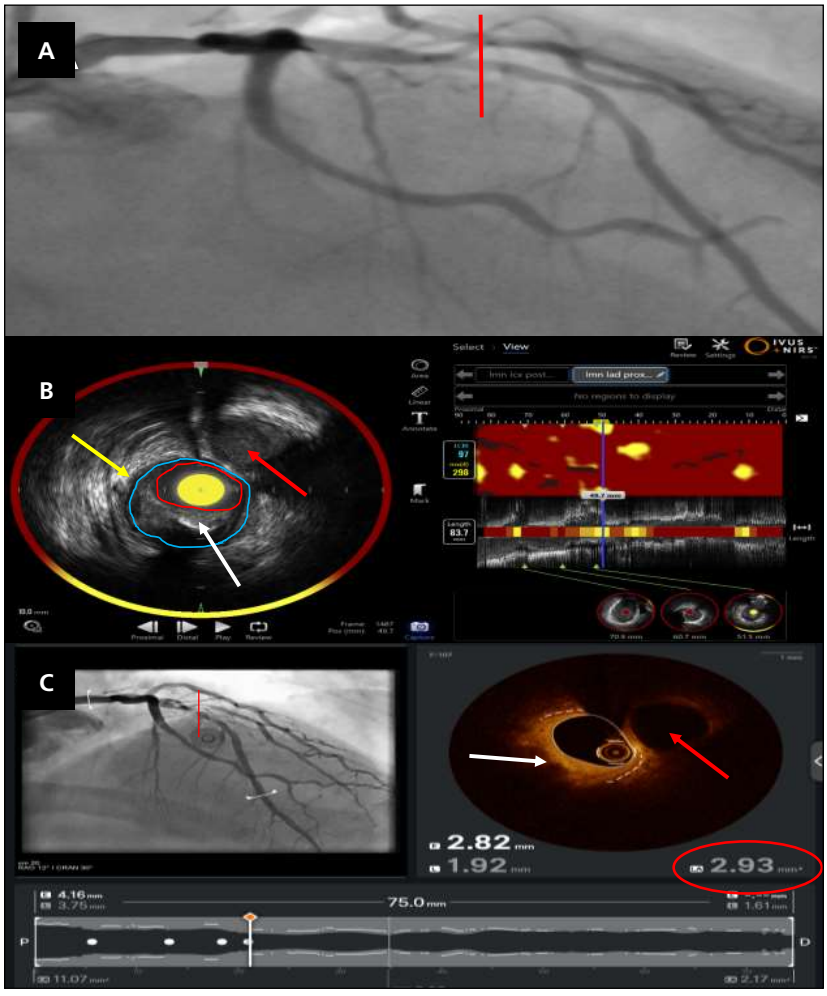

Fig. 3 – Comparison of CAG, IVUS-NIRS and OCT images from the same part of the artery. (A) CAG focused on the left coronary artery – middle part of the left anterior descending (LAD), just behind origin of the diagonal branch. The red line shows the segment further analysed by IVUS-NIRS and then OCT. (B) IVUS-NIRS analysis of the middle part of the LAD (mentioned above). In the left part of the figure, black and white sagittal IVUS section through the artery (yellow arrow – LAD, red arrow – side branch, blue circle – shows the external elastic membrane, red circle – shows the lumen of the artery, white arrow – fibrotic plaque with calcifications). Around perimeter, a coloured bar represents the chemogram of the adjacent section and in the middle a coloured circle represents the cumulative block chemogram in that section. On the right there is the chemogram and block chemogram of the entire analysed LAD with LCBI 97 and maxLCBI4mm 298. (C) OCT analysis of the identical segment. In the left part co-registered view with CAG. White brackets show the entire length of the analysed segment (75 mm totally), red line shows the currently analysed segment. In the right part of the figure OCT image. The white circle indicates the LAD area with a centrally placed OCT catheter, from which a dark shadowing bar emits. The red arrow points to the lateral diagonal branch, the white arrow to the fibrotic plaque with calcifications with maximum arterial involvement between 4 and 12 o'clock, the red circle highlights the lumen area of the segment.

Table 1 – Demographic characteristics of analysed sample	
Number of patients (enrolled/excluded)	27/9
Excluded patients	9 (33.3%)
Died	3 (33.3%)
Covid-19	2 (22.2%)
Incomplete data	4 (44.4%)
Male sex	15 (88%)
Age (years)	72.7 (± 5.5)
Acute myocardial infarction	7 (38.8%)
Chronic coronary disease	11 (61.1%)
Body mass index (kg/m^2)	27,9 (± 4.2)
Diabetes mellitus	8 (44%)
If yes: insulin-dependent	4 (50%)
Hypertension	17 (94.4%)
Chronic kidney disease (CKD)	3 (16.6%)
If yes: CKD G2	1 (33.3%)
If yes: CKD G3	2 (66.6%)
Dyslipidaemia	18 (100%)
If yes: atorvastatin 80 mg	2 (11.1%)
If yes: atorvastatin 40 mg	7 (38.9%)
If yes: atorvastatin 20 mg	5 (27.8%)
If yes: atorvastatin 10 mg	1 (5.6%)
If yes: rosuvastatin 40 mg	2 (11.1%)
If yes: rosuvastatin 20 mg	1 (5.6%)
High intensity dosage of statin*	12 (66.6%)
Moderate intensity dosage of statin*	6 (33.3%)
Current smoker	0 (0%)
History of CAD	8 (44%)
If yes: in target lesion	1 (12.5%)
2 and more stent technique of PCI	14 (77.8%)
P2Y$_{12}$ inhibitor	18 (100%)
Clopidogrel	15 (83.3%)
Ticagrelor	3 (16.6%)

* High intensity dosage of statin includes patients with dose of atorvastatin 40 mg and more or dose of rosuvastatin 20 mg and more.

catheter. The pullback speed was set at 0.5 mm per second. IVUS analysis was conducted in accordance with the criteria set forth by the American College of Cardiology consensus statement on IVUS.[22] Both baseline and follow-up IVUS images were evaluated by experienced analysts.

The external elastic membrane (EEM) and lumen were assessed at intervals of every 0.2 mm. The cross-sectional area defined by the EEM is referred to as the cross-sectional EEM area (EEM CSA), while the area defined by the lumen/stent is known as the cross-sectional minimal lumen/stent area (MLA/MSA CSA). The plaque burden area (PB) is calculated as the difference between the EEM CSA and the MLA/MSA CSA, expressed in square millimetres, alongside the entire length of LM in each timepoint of the analysis. Simpson's rule was applied to generate a volumetric model of the lumen and calculate the total plaque volume (PV) of the left main coronary artery in cubic millimetres.[23] The analysis was performed at three key stages: baseline (prior to PCI), immediately post-PCI, and during follow-up catheterization.

Statistical analysis

Basic characteristics of patients were divided into categorical variables and continuous variables. Continuous variables were described by mean and standard deviation, categorical variables were presented as frequencies and relative frequencies. The lumen area and plaque volume were evaluated as the sum of the volumes of the truncate cone between two measurements. Changes of lumen area or plaque burden volume were calculated as a difference between values before PCI and after PCI and after PCI and in the follow-up.

Statistical significances of plaque volume change in all dataset and in groups of statin dose were tested by Wilcoxon signed-rank test. The differences of plaque volume change between groups of statin dose were tested by Mann–Whitney U test. Relationship between PV change and LCBI index was tested by Spearman's correlation coefficient. Change of parameter analysis was performed using SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.)

Results

Patient characteristics

Between May 2016 and July 2022, a total of 27 patients with significant left main stenosis were enrolled in the study after providing informed consent. All patients underwent baseline IVUS-NIRS-guided PCI. Prior to the final statistical analysis of the NIRS and IVUS data, nine patients were excluded for various reasons: three patients died before the scheduled IVUS-NIRS follow-up, two patients declined the follow-up IVUS-NIRS due to the COVID-19 pandemic, and for four patients, the data were deemed unevaluable due to technical issues or poor imaging quality. As a result, complete NIRS-IVUS data from both baseline and follow-up were available for 18 patients. The NIRS and IVUS data for these patients were analyzed and statistically evaluated. Clinical follow-ups, conducted as outpatient visits or by phone at 1, 3, 6, and 12 months after the index procedure, focused on major cardiovascular clinical events including death, rehospitalization due to cardiovascular reasons, acute myocardial infarction, and target or non-target lesion revascularization. The clinical follow-up was completed in all patients.

Population with complete data

The mean age of the patients was 72.7 ± 5.5 years, with 15 patients (83.3%) being male and a mean body mass index (BMI) of 27.9 ± 4.2. The indication for baseline PCI was acute myocardial infarction in 7 patients (39%), while the remainder underwent PCI due to chronic coronary disease. The mean left ventricular ejection fraction in the population was 53 ± 13%. Eight patients (40%) had dia-

Table 2 – Clinical characteristic of complete group	
Clinical follow-up control (at least 2 controls)	27 (100%)
Month 1	18 (66.7%)
Month 3	18 (66.7%)
Month 6	22 (81.5%)
Month 12	24 (88.9%)
Clinical events	15 (55.5%)
Death	3 (20%)
Cardiovascular reason	0
Acute myocardial infarction	1 (6.7%)
Rehospitalization	8 (53.3%)
Cardiovascular reason	2 (25%)
Target lesion revascularization	1 (6.7%)
Non-target lesion revascularization	2 (13.3%)

Table 3 – Basic IVUS-NIRS characteristics of patients	
	Mean ± SD
LM LCBI before PCI (mean)	128.9 ± 122.0
maxLCBI4mm before PCI (mean)	263.7 ± 172.0
LM LCBI post-PCI (mean)	48.1 ± 35.1
maxLCBI4mm post-PCI (mean)	129.6 ± 101.6
LM LCBI follow-up (mean)	57.6 ± 50.9
maxLCBI4mm follow-up (mean)	133.7 ± 136.7
Lumen volume before PCI (mean)	121.8 ± 68.4
Lumen volume post-PCI (mean)	184.3 ± 96.9
Lumen volume follow-up (mean)	195.9 ± 119.4
Lumen volume: difference between before PCI and post-PCI	62.5 ± 79.4; 61.6 (–29.0; 228.6)[1];*
PV baseline	368.1 ± 214.2
PV post-PCI	418.7 ± 203.3
PV follow-up	454.5 ± 209.4
PV difference between follow-up and post-PCI	35.7 ± 91.1; 20.3 (–70.0; 205.2)[1]
PV difference between follow-up and post-PCI according to statin dosage:	
High intensity dosage of statin	42.4 ± 102.5; 14.5 (–85.1; 209.3)[1]
Moderate intensity dosage of statin	22.5 ± 43.5; 30.5 (–45.8; 73.1)[1]
Average number of analysed cross sections per a patient	35.4 ± 15

[1] Parameter was described by mean with SD and median with 5th and 95th percentile.
* Statistically significant difference of change of lumen.

betes mellitus, and 3 patients (17%) had chronic kidney disease (CKD) at stage 2 or worse. A history of previously treated coronary artery disease (CAD) was present in 8 patients (44%), and no patients were active smokers at the time of enrolment.

A double stent technique was used in 8 patients (44%), and clopidogrel was utilized as the $P2Y_{12}$ inhibitor in the dual antiplatelet therapy strategy for 15 patients (83%). Patients were treated with the maximum tolerated statin dose: 12 patients (66.6%) received high intensity dosage of statin and 6 patients (33.3%) received moderate intensity dosage of statin. The baseline characteristics of the analyzed population are detailed in **Table 1**.

Clinical events in complete population

Clinical follow-up was conducted for all 27 patients, with at least two clinical assessments performed either via phone or outpatient visits. During the follow-up period, 3 patients (11%) died from non-cardiovascular causes, 1 patient (4%) experienced an acute myocardial infarction (AMI), and 2 patients (7.5%) were rehospitalized due to cardiovascular reasons. Target lesion revascularization (TLR) occurred in 1 patient (4%), while non-target lesion revascularization (NTLR) occurred in 2 patients (7.5%). Detailed clinical follow-up characteristics of the complete population are provided in **Table 2**. Statistical significance for differences in clinical events was not calculated, as this was not a primary endpoint of the study and the number of events was small.

IVUS and NIRS data

Mean length of the analysed segment – LM – was 11.9 ± 4.5 mm. The average LM LCBI before PCI was 128.9 ± 122.0, maxLCBI4mm 263.7 ± 172.0. Compared with baseline values, both indices showed a decrease after PCI and at follow-up. Mean values after PCI were LCBI 48.1 ± 35.1; maxLCBI4mm 129.6 ± 101.6 and at follow-up were LCBI 57.6 ± 50.9; maxLCBI4mm 133.7 ± 136.7. The mean plaque volume (PV) as measured by IVUS was 418.7 ± 203.3 mm³ post-PCI and 454.5 ± 209.4 mm³ at follow-up. The mean difference in PV between follow-up and post-PCI was 35.7 ± 91.1 mm³, with a median difference of 20.3 mm³ (range: –70.0 to 205.2), which was not statistically significant ($p = 0.105$).

The analysis also included the difference between mean lumen volume at baseline (121.8 ± 68.4 mm³) and post-PCI (184.3 ± 96.9 mm³), showing a mean difference of 62.5 ± 79.4 mm³. The median of this difference was highly statistically significant (range: 61.6 to –29.0, 228.6) with a p-value of 0.001. Detailed results are presented in **Table 3**. Spearman's correlation coefficient was used to analyse the relationship between PV change (post-PCI PV versus follow-up PV) and LCBI before PCI (–0.122; $p = 0.626$), maxLCBI4mm PCI (–0.069; $p = 0.786$) respectively. No statistically significant correlations were found. These analyses are detailed in **Figures 4** and **5**.

Effect of statin therapy

Patients were treated with the maximum tolerated statin dose – 15 patients (83%) with atorvastatin (in the dose of 38 ± 20 milligrams) and 3 patients (17%) with rosuvastatin (in the dose of 26 ± 21 milligrams). PV difference between follow-up and post-PCI according to dosage of statin was analysed. In HDS the mean difference in PV between follow-up and post-PCI was 42.4 ± 102.5 and in MDS the mean difference was 22.5 ± 43.5 mm³. There was not a statistically significant difference between HDS and MDS in PV difference. Detailed results are presented in **Table 3**.

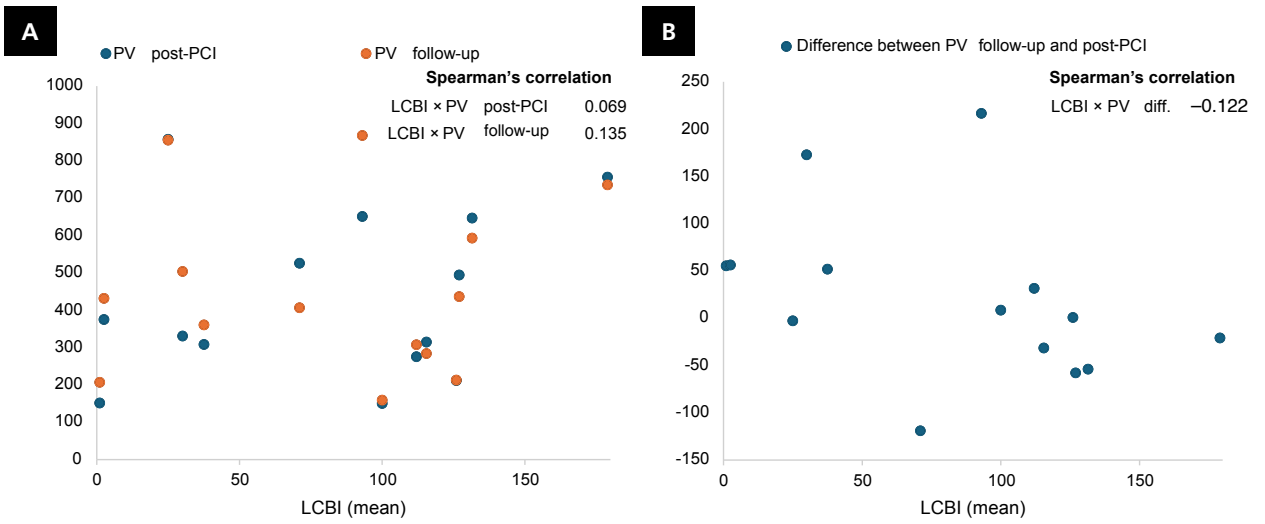

Fig. 4 – (A) Relationships between PV post-PCI and in follow-up and LCBI. (B) Relationship between difference of PV follow-up and post-PCI and LCBI.

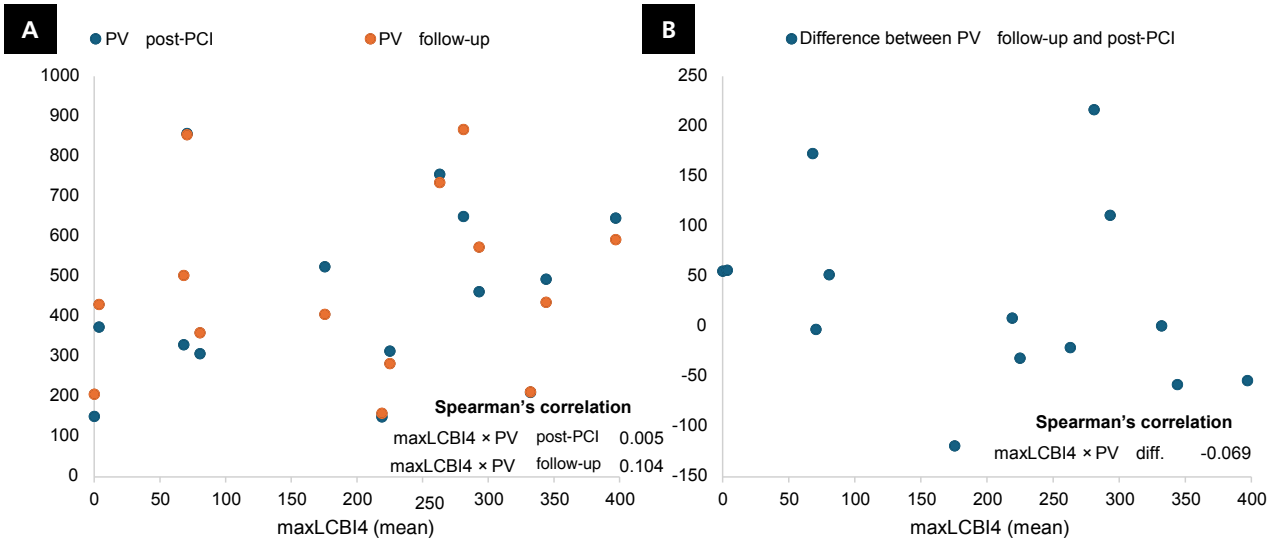

Fig. 5 – (A) Relationships between PV post-PCI and in follow-up and maxLCBI4mm. (B) Relationship between difference of PV follow-up and post-PCI and maxLCBI4mm.

Discussion

Although the patient cohort is relatively small, the presented data can be considered unique. To our knowledge, this is the first study to explore the relationship between baseline LCBI or maxLCBI4mm values and plaque volume (PV) progression. Previous studies have utilized NIRS data to assess PV, but not as a predictor of its progression after PCI.[24,25] Moreover, the coronary artery segment analysed is the left main of the left coronary artery, a critical area in the coronary system. According to current information, a similar analysis of the LM using NIRS data has not been published.

Our objective was to predict the relationship between NIRS-derived indexes (LCBI and maxLCBI4mm) and atherosclerotic plaque progression in the unique LM area over a 9- to 12-month follow-up period after percutaneous coronary interventions (PCI). Our data did not reveal a significant correlation between initial LCBI or maxLCBI4mm and PV progression during the follow-up. Despite a slight increase in PV observed during the control examination, the change was not statistically significant. This result suggests the potential excellent effect of high/moderate intensity lipid-lowering therapy.

We utilized NIRS as an intravascular tool to analyse atherosclerotic plaque. Although NIRS is predominantly used on an experimental basis in interventional cardiology, its routine clinical application remains limited. Nonetheless, NIRS has been shown to be an important tool across a wide range of recent studies.

One of the persistent complications in PCI is the occurrence of periprocedural acute myocardial in-

farction (PAMI), which affects 3–15% of all PCI procedures.[26] The likely mechanism involves distal embolization of lipid-rich material from the target lesion into the peripheral coronary vessels. NIRS has been employed to identify high-risk lesions that predispose patients to slow-flow or no-flow phenomena post-PCI. In the COLOR registry, lesions with an LCBI of 500 or greater were identified as being at risk for PAMI.[14] Similarly, the CANARY study identified lesions with an LCBI of 600 or greater as at risk for PAMI.[27] Identifying these high-risk lesions before PCI could assist in preventing complications, and it suggests that rigorous antithrombotic preparation of the patient prior to the procedure might be beneficial.

The ability to identify and quantify lipid materials using NIRS has been instrumental in evaluating the effects of antilipidemic therapies. In the YELLOW study, maximum doses of rosuvastatin were shown to decrease the maxLCBI4mm in non-intervened arteries, highlighting its effectiveness.[28,29] Recent findings from the PACMAN-AMI trial demonstrated incremental regression of coronary plaque, reduction of the lipid core, and plaque stabilization with the use of PCSK9 inhibitors in patients with acute coronary syndrome.[30] We are still awaiting the results of the FITTER study, which is evaluating the effect of evolocumab on the coronary lipid plaque component in non-culprit lesions.[31]

Finally, several studies have focused on the stratification of coronary lesions based on LCBI and maxLCBI4mm values. The most relevant studies include the LRP and PROSPECT II trials. Both of which assess lesion vulnerability in non-culprit arteries (NC) and the relationship between NIRS index values and the incidence of major cardiovascular events in these arteries (NC-MACE). In the LRP study, over 1500 patients with non-obstructive coronary artery disease (CAD) were evaluated. The study found a statistically significant association between maxLCBI4mm and NC-MACE within 24 months of assessment. Specifically, patients with a maxLCBI4mm of ≥400 had an 89% higher risk of NC-MACE (hazard ratio 1.89; *p*-value = 0.0021).[32] The PROSPECT II study explored the incidence of NC-MACE in patients following AMI over a 4-year period. Vulnerable lesions in this study were defined as those with maxLCBI4mm ≥325. Notably, most of these lesions were initially classified as non-significant angiographically.[33]

Our results corroborate previous studies demonstrating that LCBI and maxLCBI4mm decrease following coronary stent implantation. The observed reduction in LCBI can be attributed to several factors. First, microembolization of the lipid core may occur due to the disruption of the lipid cap during stent implantation, leading to the release of lipid material and subsequent micro-embolization to distal segments of the coronary vessels.[14,34] Additionally, stent implantation can result in the compression of the lipid core, causing a shift of lipid content towards the distal and proximal ends of the stent, as observed in the analyzed segment.[35,36] Finally, the structural design of the stent may reflect the NIRS catheter beam, partially obstructing analysis of the segment. Consequently, the LCBI value may be underestimated.[34]

Correlation graphs indicate a trend of decreased PV in patients with high initial LCBI and maxLCBI4mm. This decrease in PV may be attributed to plaque redistribution following PCI. These findings corroborate results from previous studies that have examined plaque redistribution after coronary stent implantation, verified through IVI.[35] Furthermore, the longitudinal redistribution of plaque is influenced by its composition. T. Roleder et al. demonstrated that in lesions characterized by a high lipid burden (HLB), defined as maxLCBI4mm >265, the decrease in PV is more pronounced compared to lesions with a lower lipid burden. HLB lesions are more susceptible to compression and are likelier to protrude through the stent struts.[36] Moreover, intensive lipid-lowering therapy may significantly contribute to the reduction of PV, particularly in lesions with a high lipid burden. Future studies should explore whether intensive lipid-lowering therapy is more effective in lesions presenting with elevated NIRS indices.

Limitations of the study

The study enrolled a relatively small group of patients, primarily due to the specific anatomical focus on the left main coronary artery. During the follow-up period, 33% of patients were excluded from the study either due to declined serial invasive examinations, due to the COVID-19 pandemic or due to insufficient image quality of the baseline examination recordings.

The identification of the external elastic membrane (EEM) and lumen could be enhanced with the use of artificial intelligence software, which is already implemented in some OCT and IVUS systems. However, current NIRS-IVUS systems lack this capability. As mentioned in the discussion, lipid detection using NIRS may be inaccurate when analysing plaque located behind stent strings. Therefore, we used before PCI indices for the final statistical analysis. Additionally, the authors identified a potential source of error stemming from the inability to co-register angiography with IVUS-NIRS data. This limitation complicated the manual analysis and accurate delineation of the proximal and distal edges of the left main coronary artery compared to co-registered systems.

Conclusion

Our trial did not demonstrate a significant correlation between initial LCBI or maxLCBI4mm and the development of plaque volume during the follow-up period in the left main coronary artery. However, correlation graphs indicate a trend toward decreased PV in patients with high initial LCBI and maxLCBI4mm, which aligns with findings from previously published studies. The potential favourable effect of high-intensity lipid-lowering therapy in high lipid burden (HLP) lesions warrants further investigation in subsequent studies.

Competing interest
The authors have no relevant financial or non-financial interests to disclose.

Funding
The study was supported by Ministry of Health, Czech Republic – conceptual development of research organization (FNBr, 65269705).

Author contributions
All authors contributed to the study conception and design. Data collection (Martin Hudec, Jan Kaňovský, Vojtěch Brázdil, Martin Poloczek, Otakar Boček, Petr Jeřábek, Roman Štípal, Petr Kala), IVUS and NIRS data analysis (Martin Hudec, Ivona Kask, Kristýna Hochmanová, Radka Smitalová), statistical data analysis (Simona Littnerová, Jiří Jarkovský, Klára Benešová), review and editing (Jan Kaňovský) and supervision (Petr Kala). The first draft of the manuscript was written by (Martin Hudec), and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval
The study protocol was approved by the local ethics committee (Faculty Hospital Brno, EK610062015, 10th June 2015). The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate
All patients provided written informed consent prior to enrolment.

Data availability statement
Dataset available in request from the authors.

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