Původní sdělení | Original research article

The clinical and angiographic impact of intravascular ultrasound guided stenting of unprotected left main and proximal left anterior descending coronary artery. A prospective randomized controlled study in Egypt

Noha Hassanin Hanboly[a], Yasser Mohamed Kamel Baghdady[a], Mostafa Mokhtar Mostafa[a], Assem Abdelaziz Fahmy Hashad[a], Yasser Ahmed Sadek[b]

[a] *Cardiovascular Department, Faculty of Medicine, Cairo University, Cairo, Egypt*
[b] *Cardiovascular Department, Faculty of Medicine, Helwan University, Egypt*

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Nechráněný kmen levé věnčité tepny
Proximální levá přední sestupná větev

SOUHRN

Kontext: Koronarografické vyšetření má pro řádné vyhodnocení lézí na koronárních tepnách jisté limitace. Použití intravaskulárního ultrazvuku (intravascular ultrasound, IVUS) před perkutánní koronární intervencí (PCI) může odhalit významné stenózy, pomáhá zvolit vhodný stent a může upozornit na možné komplikace. Cílem studie bylo hodnotit důsledky použití IVUS na klinické a angiograficky potvrzené výsledky revaskularizace nechráněného kmene levé věnčité tepny (unprotected left main, ULM) nebo proximální levé přední sestupné větve (left anterior descending, LAD) pomocí stentu při ischemické chorobě srdeční (ICHS).
Materiály a metody: Byla provedena prospektivní randomizovaná kontrolovaná studie s 60 pacienty se stabilní anginou pectoris nebo s akutním koronárním syndromem bez elevací úseku ST. Koronarografické vyšetření provedené na katetrizačním pracovišti egyptského Národního ústavu zdraví odhalilo významné ischemické postižení kmene levé věnčité tepny nebo proximální LAD. U pacientů byla indikována revaskularizace formou PCI. Perkutánní koronární intervence navigovaná koronárním IVUS byla provedena u 30 pacientů (skupina A), zatímco ve skupině B nebyl při PCI koronární IVUS použit. Účastníci studie byli sledováni po dobu šesti měsíců s cílem analyzovat primární nebo sekundární sledované parametry.
Výsledky: Navigace pomocí IVUS byla spojena se statisticky významně větším minimálním průsvitem cév po implantaci stentu potvrzeným kvantitativní koronarografií (quantitative coronary angiography, QCA) (p = 0,001), větším průměrem stentu (p = 0,001) a další dilatací (p = 0,02). Srovnání obou skupin prokázalo, že navigace pomocí IVUS byla spojena se statisticky významně nižším výskytem trombózy stentu v cílových lézích, nefatálního infarktu myokardu ve vztahu k počtu cílových lézí, s nižšími počty revaskularizačních výkonů na cílových lézích i s nižšími celkovými počty závažných nežádoucích srdečních příhod (major adverse cardiac events, MACE) během šestiměsíčního sledování (p = 0,038 pro všechny uvedené parametry).
Závěry: Provádění PCI s implantací stentu do ULM a proximální LAD, navigované pomocí IVUS, zlepšuje klinický výsledný stav se statisticky významně nižším výskytem MACE do 6 měsíců díky významně nižšímu riziku revaskularizace cílové léze a trombózy stentu. U pacientů s ischemickým postižením ULM nebo proximální LAD doporučujeme rutinní používání navigace pomocí IVUS při revaskularizaci implantací stentu.
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ABSTRACT

Background: Coronary angiography has some limitations in the proper assessment of coronary artery lesions. Intravascular ultrasound (IVUS) before percutaneous coronary intervention (PCI) can identify significant stenosis, select the appropriate stent and detect complications.
The study aimed to evaluate the impact of intravascular ultrasound on clinical and angiographic outcomes after revascularization by stenting for patients with unprotected left main (ULM) or proximal left anterior descending (LAD) coronary artery disease (CAD).
Materials and methods: A prospective randomized controlled study that was carried on sixty patients presented with stable angina or non-ST elevation acute coronary syndrome. Coronary angiography that was carried out at cardiac catheterization laboratory at the National Heart Institute in Egypt revealed significant left main or proximal LAD coronary artery disease. Patients were scheduled for revascularization by PCI.

Adresa pro korespondenci: Ass. Prof. Noha Hassanin, Cardiovascular Department, Faculty of Medicine, Cairo University, Cairo, Egypt, e-mail: Noha.Ali@kasralainy.edu.eg
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Percutaneous coronary intervention guided by coronary IVUS was done in thirty patients (Group A). Whereas, Group B included 30 patients in which PCI was not guided by IVUS. The patients were followed for six months to detect any primary or secondary endpoints.

Results: IVUS guidance was associated with a significant higher post-stent minimal lumen diameter as found by quantitative coronary angiography (QCA) ($p = 0.001$), stent diameter ($p = 0.001$), and adjunct post--dilatation ($p = 0.02$). By comparing both study groups it was found that IVUS guidance was associated with significant lower rates of stent thrombosis in target lesions, non-fatal myocardial infarction related to target lesions, target lesion revascularization and all cause major adverse cardiac events (MACE) within 6 months of follow-up (p-value 0.038, for all).

Conclusions: IVUS guided PCI during ULM and proximal LAD coronary artery stenting improves clinical outcome with significant lower rates of MACE at 6 months which is due to significant lower risk of target lesion revascularization and stent thrombosis. We recommended routine use of IVUS during revascularization by stenting in cases of ULM or proximal LAD CAD.

Keywords:
Coronary artery stenting
Intravascular ultrasound
Proximal left anterior descending artery
Unprotected left main coronary artery

Introduction

Contrast angiography is the most important imaging method used to diagnose and guide therapy for coronary artery disease (CAD). Recently, intravascular ultrasound (IVUS) evolved as important adjunctive to coronary angiography in diagnosis and management of CAD. IVUS was developed not only for informative and geometrical imaging of atherosclerotic plaque but also for detailed study of histology, morphology, and pathology of CAD.[1–3]

The images of IVUS systems are produced by performing a series of pulse sequences or vectors in which an acoustic pulse is emitted and the subsequent reflections from the tissue are detected.[4] Properties of the ultrasound image, such as the resolution, depth of penetration and attenuation of the acoustic pulse by tissue are dependent on the geometric and frequency properties of the transducer. Frequencies used by IVUS catheters ranged from 20 MHz to 40 MHz.[4]

After the routine administration of heparin and intracoronary nitroglycerin, the coronary artery is cannulated selectively. The operator advances or retracts the imaging device over the wire, recording images on videotape or CD for further analysis. Although many centers use a motorized pullback device to withdraw the catheter at a constant speed (between 0.25 and 1 mm/s; most frequently 0.5 mm/s) a single pullback, even when controlled by a motor, may be insufficient for a complete diagnostic examination.[5]

Although it was postulated that IVUS use was limited by its cost, a recent study in Australia evaluated the cost-effectiveness of PCI guided by IVUS compared with angiography-guided PCI in patients undergoing drug--eluting stent implantation. The study compared costs, life-expectancy, and quality-adjusted life years for both treatment groups.

The study found that cost-effectiveness of IVUS may be greatest among patients with left main and complex coronary lesions.[6]

Moreover, according to the latest guidelines IVUS or optical coherence tomography (OCT) should be considered in selected patients to improve stent implantation.[7]

It was found that left main coronary artery disease (LMCAD) constituted higher prognostic risk as a result of the large myocardial territory at risk, ranging from 75% to 100%, depending on the dominance of the left coronary circulation.[8] Regardless of the symptomatic status or the associated ischemic burden the current guidelines recommended revascularization for all patients with ≥50% stenosis of the LMCAD.[9]

Functional assessment of lesion severity using the coronary pressure-derived fractional flow reserve (FFR) is the standard of care for patients with intermediate LM stenosis.[10]

Many studies demonstrated a survival benefit of coronary artery bypass graft surgery (CABG) in patients with CAD and LM or three-vessel disease, particularly when the proximal LAD was involved.[11]

The **NOBLE** (Nordic-Baltic-British Left Main Revascularization Study) trial compared CABG with percutaneous coronary intervention (PCI) in 1201 patients with significant LM disease and SYNTAX score of 23. At a median follow-up of 3.1 years, the study found that the primary endpoint of death, non-procedural myocardial infarction, stroke and repeat revascularization happened more frequently in the PCI than the CABG group.[12]

On the other side, CABG for noncritical LM lesions may be deleterious because of low graft patency rates and enhanced obstruction of bypassed native coronary vessels, which makes the subsequent PCI of native vessels technically difficult if needed for relief of symptoms.[13]

Noninvasive high-risk features suggestive of significant LM disease are Duke treadmill score ≤11, stress-induced sustained ventricular tachyarrhythmia, exercise LV ejection fraction ≤35%, large reversible anterior perfusion defect, stress-induced LV dilation or increased lung uptake in the setting of moderate perfusion defect or large fixed perfusion defect and echocardiographic wall motion abnormality involving more than two segments developing at a low-dose dobutamine.[14]

The hemodynamic significance of clinically ambiguous LM lesions can be obtained invasively by IVUS imaging or physiologically with pressure wire assessment of FFR. In the multicenter **LITRO** study of intermediate LM stenosis between 25% and 60%, postponing revascularization of LM lesions with minimal luminal area (MLA) of ≥6 mm^2 was safe and associated with better outcomes at 2 years of follow-up.[15] According to the latest guidelines IVUS may be considered for the risk stratification of patients with intermediate LM stenosis.[16] In patients with distal LM lesions IVUS can ensure adequate expansion and apposition of stents after LM PCI (Fig. 1).[17]

Although current guidelines continued to recommend CABG surgery as class I indication for myocardial revascu-

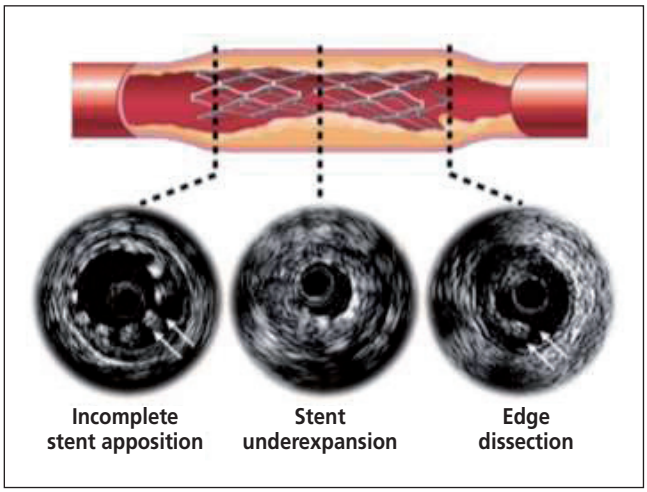


Fig. 1 – Stent-related complications after stent deployment.[18]

larization, recent trials and registry studies in LM CAD support PCI as a reasonable alternative in patients with less complex LM anatomy.[8]

The current guidelines are against PCI in patients who are good candidates for surgical bypass with coexisting complex multivessel disease defined by high SYNTAX score ≥33.[10] The SYNTAX score is used to grade the complexity of coronary artery disease.[19]

Comparing double kissing (DK) crush technique with provisional stenting for LM distal bifurcation lesions, lower rates of target lesion failure and stent thrombosis with DK crush technique was found.[20]

Proximal LAD coronary artery disease is considered as a high-risk feature because of the large area of myocardium it supplies. Patients with stable CAD and isolated proximal LAD disease have similar survival rates whether treated with CABG or PCI.[21,22]

A heart team discussion in patients with stable CAD and proximal LAD disease is recommended by the current revascularization guidelines and conferred a class I indication level of evidence A to both percutaneous and surgical treatment strategies.[10]

Although PCI can be performed with good results in proximal LAD CAD, in the presence of complex bifurcation lesions involving a large first diagonal branch, involvement of the distal LM coronary artery, ostial location or adjacent circumflex ostial disease, CABG should be considered. The current guidelines recommended revascularization to improve the prognosis for significant proximal LAD disease described as any lesion with more than 50 percent stenosis and documented ischemia or fractional flow reserve ≤0.80 for angiographic diameter stenoses <90 percent.[23]

Heart team approach is recommended to discuss the options of PCI versus CABG as well as a preference for CABG if SYNTAX score is above 22 with low surgical risk.[23]

We aimed to study the clinical and angiographic results of IVUS guided revascularization in patients with ULM or proximal LAD coronary artery disease by following the patients after the procedure for 6 months to detect the occurrence of any major adverse cardiac events (MACE).

Materials and methods

A prospective study lasted for two years and included sixty patients presented with stable angina or non-ST elevation acute coronary syndrome. Coronary angiography study was done for all patients and revealed significant LM or proximal LAD CAD eligible for revascularization by PCI.

A written consent was taken from all participants. The study protocol was approved by the local ethics committee at the Faculty of Medicine Cairo University and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

The study included two groups. PCI guided by coronary IVUS was done in thirty patients (Group A). Whereas, Group B included 30 patients in which PCI was not guided by IVUS.

The patients with severe left ventricular dysfunction defined as ejection fraction less than 30%, cardiogenic shock, ST elevation myocardial infarction, prior CABG and those who refuse to participate in the study were excluded.

All patients were subjected to history taking and risk factor assessment. Diabetes mellitus was defined as fasting blood glucose ≥126 mg/dl or a two-hour post glucose challenge value ≥200 mg/dl.[24]

Systemic hypertension was diagnosed if the average of two or more properly measured readings as systolic blood pressure ≥140 mmHg or diastolic ≥90 mmHg. Patients who were taking antihypertensive medications were defined as having hypertension regardless of their observed blood pressure.[25]

Dyslipidemia was defined as elevation of cholesterol level (≥200 mg/dl) and triglycerides level (LDL ≥150 mg/dl, HDL ≤40 mg/dl) or within normal level on statin therapy.[26]

Body mass index (BMI) was used as a measure of body fat in adult men and women based on height and weight. BMI = weight (kg) / height (m)^2.[27]

General, cardiac examination, twelve leads surface electrocardiogram and laboratory tests including cardiac enzymes, kidney function tests and lipid profile were done for all patients.

Coronary angiography was done to all patients. Femoral sheath was introduced. CAD was defined as the presence of at least more than 50% stenosis of major coronary arteries (left anterior descending, left circumflex, or right coronary arteries) or their major branches (diagonal, obtuse marginal, posterior descending, or posterior left ventricular arteries).

Visual assessment of lesions severity: Operators visually assessed the percent diameter stenosis and determined their severity. Detected stenosis was viewed in two orthogonal projections.

Quantitative coronary analysis (QCA) was performed by validated and automated edge-detection CAAS software (Cardiovascular Angiography Analysis System, Pie Medical Imaging) in all patients in two orthogonal views. Using the contrast-filled catheter for calibration, measured parameters were calculated as the mean of the values obtained from the 2 projections in end diastolic images.

Parameters obtained through QCA were defined as minimal lumen diameter (defined as the smallest dia-

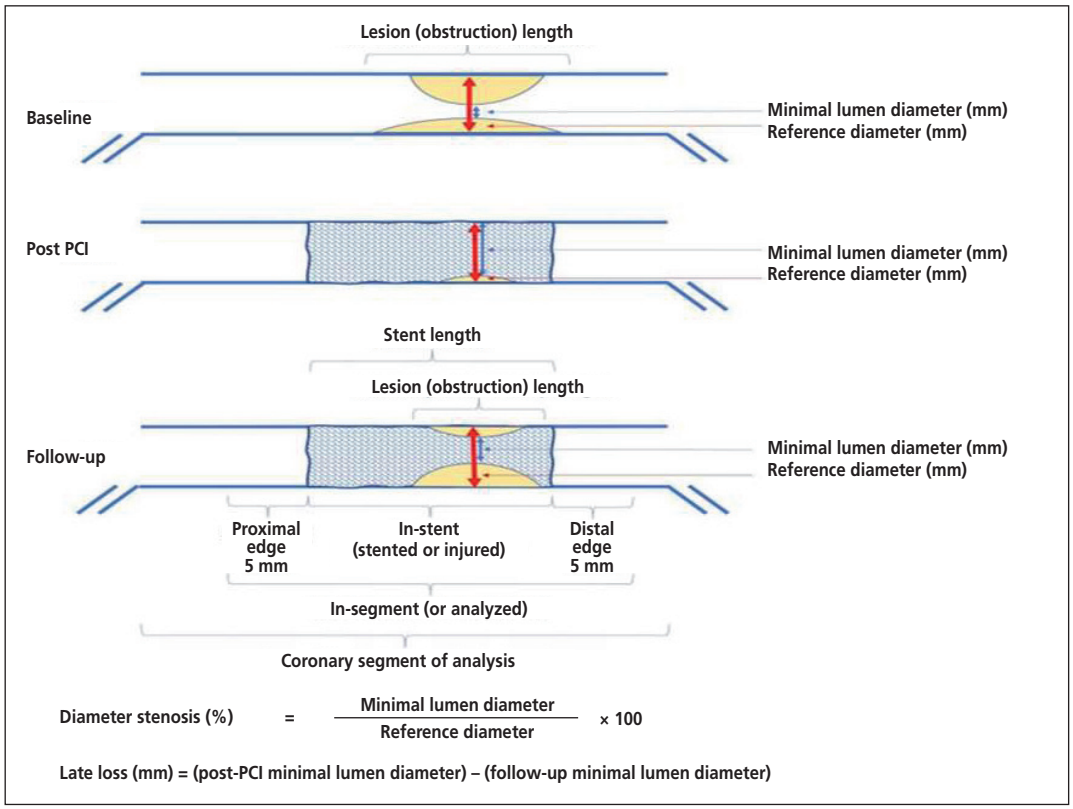


Fig. 2 – Standard scheme of measurement data.[28] PCI – percutaneous coronary intervention.

meter of the lumen), reference diameter (defined as the average diameter of the lumen assumed without atherosclerotic disease), obstruction length (the QCA software automatically recognized the two borders between the normal and diseased vessel by detecting the directional change in the contour of the coronary artery.[28]

Moreover certain formulas were used to study the outcome of interventional procedure, e.g. acute gain defined as post-PCI minimal lumen diameter – baseline minimal lumen diameter, late loss defined as post-PCI minimal lumen diameter – follow-up minimal lumen diameter (Fig. 2).[28]

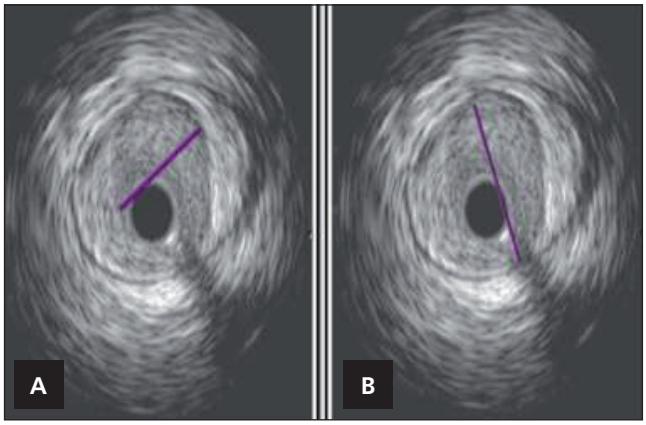
Patients were randomized into two groups: Group A (IVUS guided group) which included 30 patients in which PCI was guided by the IVUS findings in addition to the standard angiography and Group B (non-IVUS guided group) which included 30 patients in which PCI was guided by the angiography findings only.

IVUS technique: Both iLab™ System 1.2 Ultrasound Imaging System Boston Scientific Corporation–USA and VOLCANO S5™ System PHILIPS–USA were used. Imaging was performed using a 40 MHz, 6 F compatible catheters (ATLANTIS SR Pro) and a 20 MHz, 5 F compatible catheters (Eagle Eye). Probes were inspected for fractures or kinks that may affect the image quality. Flushing was done using heparinized saline for the ATLANTIS SR Pro catheters. Probes were connected to console and motor drive unit.

Intracoronary infusion of nitroglycerine to minimize vasospasm was done and then the rapid exchange IVUS catheter was introduced in the coronary over a standard 0.014" guide wire. The IVUS catheter was advanced guided by the fluoroscopy for approximately 10 mm distal to the anatomical landmark (i.e., side branch) and then retracted slowly to straighten the catheter shaft.[29]

After imaging acquisition the lumen-intima and media-adventitia interfaces were traced at the point of worst stenosis of the lesion. IVUS analysis was performed by 2 independent observers blinded to the QCA information. Minimal luminal area was defined as the area bounded by the luminal border while the maximal luminal diameter was defined as the longest diameter through the center point of the lumen (Fig. 3).[30]

Other qualitative and quantitative IVUS analyses were performed. Lumen cross-sectional area (CSA) was quantified by tracing the leading edge of the blood-intima acoustic interface. The outer vessel border (external elas-



A) Minimal luminal diameter **B) Maximal luminal diameter**

Fig. 3 – Minimal and maximal luminal diameter by IVUS.[31]

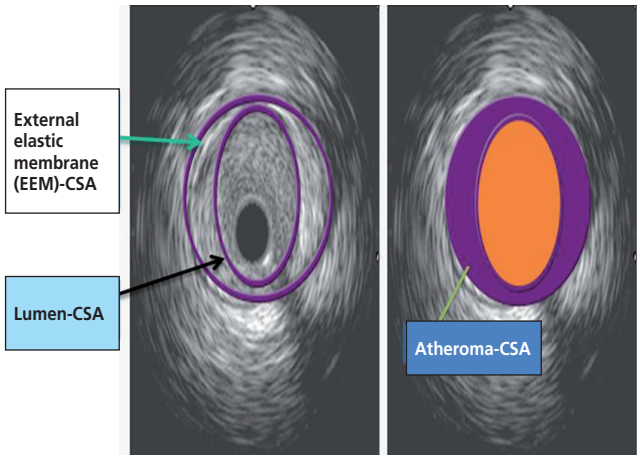


Fig. 4 – Atheroma-CSA (area in purple) was calculated as the difference between EEM-CSA and lumen-CSA.

tic membrane [EEM] CSA) was detected as the interface between media and adventitia. Atheroma-CSA was calculated as the difference between EEM-CSA and lumen--CSA.[32] Plaque burden was defined as atheroma CSA divided by the EEM CSA (Fig. 4).[33]

If EEM area increases during atheroma development, the process is termed positive remodeling. If the EEM decreases, the process is termed negative remodeling.[32]

Remodeling was assessed by the remodeling index expressed as lesion site EEM area divided by the reference EEM area. Positive remodeling was defined as remodeling index ≥1.05 and negative remodeling if the index was ≤0.95.[34]

Moreover, plaques were classified by IVUS to soft plaque with lesion echogenicity less than the surrounding adventitia, fibrous plaque with intermediate echogenicity between soft plaque and highly echogenic plaques and calcified plaque which had higher echogenicity than the adventitia.[3]

Percutaneous coronary intervention was done according to latest guidelines.[10] Floppy guide wire was passed and positioned distally in the diseased vessel. Single or multiple dilatations were done at the lesion site .A suitable sized stent was deployed at the lesion site at adequate pressures. Control injections were done after stenting to assess the Thrombolysis in Myocardial Infarction (TIMI) flow and possible complications. Good stent apposition was defined as close contact to prevent blood flow between the strut and the underlying vessel wall.[35]

The standard medications were given according to the patient condition including nitroglycerin, dual anti-platelet therapy (DAPT), anticoagulation, statins, and beta blockers unless contraindicated. Patients were followed up for six months to detect any primary or secondary endpoints. Target lesion revascularization was defined as any repeated intervention (by coronary artery bypass graft or PCI) performed to treat a stenosis or thrombosis inside the implanted stent or within the 5mm segments adjacent to the stent.[10]

Statistical analysis was performed using a commercially available software program (SPSS 19; SPSS, Chicago, IL, USA). Qualitative values were presented as number and percentages. Chi-square test was used to compare categorical data. For outcome results the hazard ratio, its 95% confidence interval, and the value of risk reduction were also calculated. Numerical data were presented at mean and standard deviation. Independent t test was used for comparison of numerical data between both groups. The level of significance was set at $p \leq 0.05$.

Results

A prospective randomized controlled study that was carried on sixty patients presented with stable angina or non-ST elevation acute coronary syndrome. Coronary angiography was carried out at cardiac catheterization laboratory National Heart Institute, Egypt.

Patients were randomized into two groups, Group A (IVUS guided group) included 30 patients in which PCI was guided by the IVUS findings in addition to the standard angiography and Group B (non-IVUS guided group) that included 30 patients in which PCI was guided by the angiography findings only. Table 1 showed the baseline characteristics of the study groups.

Table 1 – Baseline characteristics of the study groups

	IVUS guided (n = 30)	Non-IVUS guided (n = 30)	*P*-value
Age (years)	64.6±7.6	64.5±7.2	0.958
Gender	Male: 26 (86.7%) Female: 4 (13.3%)	Male: 23 (76.7%) Female: 7 (23.3%)	0.317
Hypertension	20 (66.7%)	18 (60.0%)	0.592
Diabetes mellitus	11 (36.7%)	13 (43.3%)	0.598
Current smoking	15 (50%)	14 (46.7%)	0.796
Dyslipidemia	17 (56.7%)	14 (46.7%)	0.483
Family history of CAD	5 (16.7%)	8 (26.7%)	0.347
Renal insufficiency	1 (3.3%)	1 (3.3%)	1
Previous PCI	5 (16.7%)	7 (23.3%)	0.519

Age was expressed as mean ± standard deviation. CAD – coronary artery disease; IVUS – intravascular ultrasound; n – number; PCI – percutaneous coronary intervention.

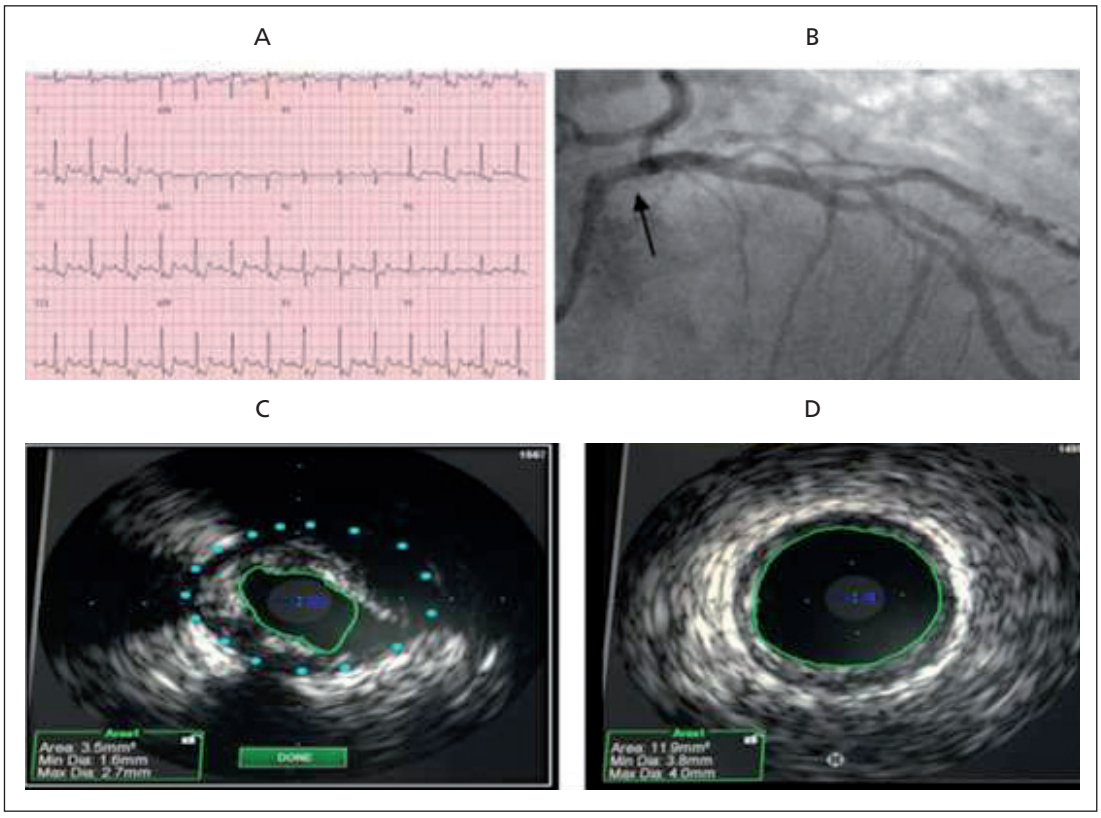


Fig. 5 – A 68-year-old male patient, hypertensive, smoker presented with prolonged typical chest pain. (A) Twelve lead electrocardiogram of the patient, (B) coronary angiogram showed left main coronary artery disease, intravascular ultrasound guided pre- (C) and post-procedure (D). Procedure was successful with no complications.

Moreover, there was no statistically significant difference between both groups regarding the clinical presentations (Table 2).

Table 3 showed the coronary angiographic data of the study groups including number of diseased vessels, number of significant lesions, percentage of diameter stenosis, pre- and post-stent minimal lumen diameter, stent diameter, stent length, percentage of complete revascularization and medical treatment used during and after the procedure. IVUS guidance was associated with a significant higher post-stent minimal lumen diameter (MLD) by QCA (p = 0.001), stent diameter (p = 0.001) and adjunct post-dilatation (p = 0.02).

Table 4 showed the IVUS findings in Group A. Fibrotic lesion was seen in 100% of patients, while calcific lesions occurred in 30% of patients. Mean minimal lumen area (MLA) (mm^2) was 3.7±1.1 and mean external elastic membrane cross section area (EEM CSA) (mm^2) was 16.5±5.01. Mean plaque burden (%) was 12.8±4.4, while mean percent area stenosis (%) was 64.6±9.1. Positive remodeling occurred in 36.7%, while negative remodeling occurred in 63.3%.

Comparing Group A to Group B, it was found that IVUS guidance was associated with significant lower rates of stent thrombosis in target lesions, non-fatal myocardial infarction related to target lesions, target lesion revascularization and all cause major adverse cardiac events within 6 months of follow up **(**none in Group A versus 13.3% in Group B, p-value = 0.038 for all). Figure 5 illustrates the angiographic and IVUS findings of one of the enrolled patients in Group A.

Table 2 – The clinical presentation of the study groups

	Group A (n = 30)	Group B (n = 30)	*P*-value
Stable angina	9 (30%)	10 (33.3%)	0.781
NSTE-ACS	21 (70%)	20 (66.7%)	0.781
Heart failure	2 (6.67%)	2 (6.67%)	1
LVEF (%)	49.4±9.5	52.3±10.5	0.272

LVEF% was expressed as mean ± standard deviation. LVEF – left ventricle ejection fraction; n – number; NSTE-ACS – non-ST elevation acute coronary syndrome.

Discussion

IVUS because of its good imaging quality provided important information that is supportive to the conventional coronary angiography regarding lumen and vessel dimensions, plaque burden, and composition.[36] Moreover, IVUS identified the lesions in which revascularization can safely be deferred, guided therapeutic strategy in lesions requiring PCI and assessed the stent deployment.[36]

This study aimed to investigate the impact of IVUS guided revascularization by stenting for patients with ULM or LAD coronary artery disease. This study was carried out on sixty patients admitted with stable angina or non-ST elevation acute coronary syndrome .The coronary angiography revealed significant LM or proximal LAD coronary artery

Table 3 – The angiographic and procedural characteristics in both study groups

		Group A (n = 30)	Group B (n = 30)	*P*-value
Number of diseased vessels	1	3 (10%)	3 (10%)	0.422
	2	14 (46.7%)	10 (33.3%)	
	3	13 (43.3%)	15 (50%)	
	4	0 (0%)	2 (6.7%)	
Number of significant lesions	1	8 (26.7%)	9 (30%)	0.750
	2	14 (46.7%)	12 (40%)	
	3	8 (26.7%)	8 (26.7%)	
	4	0 (0%)	1 (3.3%)	
Ostial LM lesion		2 (6.7%)	2 (6.7%)	1
Mid-segment LM lesion		4 (13.3%)	1 (3.3%)	0.161
Distal LM lesion		10 (33.3%)	5 (16.7%)	0.136
Proximal LAD lesion		29 (96.7%)	30 (100%)	0.313
Pre-stent minimum lumen diameter by QCA (mm)		0.84±0.35	0.68±0.34	0.165
Reference lumen diameter by QCA (mm)		3.17±0.36	3.09±0.37	0.127
Percentage of diameter stenosis by QCA (%)		73.8±9.85	81.53±10.87	0.359
Length of lesion by QCA (mm)		23.47±8.91	25.5±9.13	0.386
Post-stent MLD by QCA		3.65±0.32	3.27±0.33	**0.001***
Diffuse morphology lesion (without IVUS)		13 (43.3%)	16 (53.3%)	0.438
Stent length (mm)		27.4±9.2	27.4±8.27	1
Stent diameter (mm)		3.54±0.35	3.27±0.33	**0.003***
Direct stenting		12 (40%)	12 (40%)	1
Pre-dilatation		18(60%)	18(60%)	1
Adjunct post-dilatation		28 (93.3%)	21 (70%)	**0.02***
Successful PCI		30 (100%)	30 (100%)	1
Unsuccessful PCI		0 (0%)	0 (0%)	1
Complete revascularization		23 (76.7%)	18 (60%)	0.165
GpIIb/IIIa inhibitor		4 (13.3%)	6 (20%)	0.488
DAPT in the whole follow-up duration		30 (100%)	30 (100%)	1

DAPT – dual antiplatelet therapy; GpIIb/IIIa – glycoprotein IIb/IIIa; IVUS – intravascular ultrasound; LAD – left anterior descending; LM – left main; MLD – minimal lumen diameter; PCI – percutaneous coronary intervention; QCA – quantitative coronary analysis. * Significant *p*-value ≤0.05.

Table 4 – IVUS findings in Group A

Variable	Value
Fibrotic lesion (with IVUS)	30 (100%)
Calcific lesion (with IVUS)	9 (30%)
EEM CSA (mm^2)	16.55±5.01
MLA (mm^2)	3.70±1.14
Plaque burden (%)	12.8±4.5
Percent area stenosis (%)	64.6±9.1
Positive remodeling	11 (36.7%)
Negative remodeling	19 (63.3%)

EEM CSA – external elastic membrane cross section area in mm^2; MLA – mean minimal lumen area in mm^2.

disease eligible for PCI. The patients were divided into two groups according to the IVUS guidance during PCI.

The main finding in this study was that IVUS guidance significantly decreases incidence of adverse events in patients undergoing unprotected LM or proximal LAD stenting compared to conventional angiography guidance alone.

In our study, we found that IVUS guidance was associated with a significant 13.3% reduction in incidence of major adverse cardiac events (MACE) compared to non-IVUS guidance within 6 months of follow up ($p = 0.038$). This effect was driven by a significant (13.3%) reduction in incidence of stent thrombosis ($p = 0.038$) that led to a significant (13.3%) reduction in incidence of both non-fatal myocardial infarction and target vessel revascularization ($p = 0.038$).

No cardiac death, in-stent restenosis or new signs of heart failure occurred in both groups (*p*-value = 1). As for the angiographic findings, IVUS guidance was asso-

ciated with a significant higher post-stent MLD by QCA (p = 0.001), stent diameter (p = 0.001), and adjunct post--dilatation (p = 0.02).

Although our study was limited by small study population, our results were concordant with the meta-analysis named Intravascular Ultrasound-Guided Implantation of Drug-Eluting Stents to Improve Outcome, which included 24,849 patients (11,793 IVUS-guided and 13,056 angiography-guided).

The study found that IVUS-guided PCI was associated with significantly lower rates of myocardial infarction (p <0.001), target vessel revascularization (p = 0.01) and stent thrombosis (p = 0.002). But in addition to our study, IVUS-guided PCI was also associated with significantly lower rates of mortality.[37]

Moreover, another study found that among patients requiring long coronary stent implantation, the use of IVUS-guided everolimus-eluting stent implantation compared with angiography-guided stent implantation resulted in a significantly lower rate of major adverse cardiac events at one year primarily due to lower risk of target lesion revascularization.[38]

On the other side, the **MAIN-COMPARE** registry which included patients with LM coronary artery stenosis who underwent elective stenting under the guidance of IVUS (756 patients) versus the conventional angiography (219 patients) found that IVUS guidance was significantly associated with a lower three-year death incidence compared to angiography guidance while the risk of myocardial infarction or target vessel revascularization was not associated with the use of IVUS guidance.[39]

In the same way, in a pooled analysis of four registries named Clinical Impact of Intravascular Ultrasound Guidance in Drug-Eluting Stent Implantation for Unprotected Left Main Coronary Disease in which a total of 1,670 patients were included with 505 patients (30.2%) underwent drug eluting stent implantation under IVUS guidance, found that IVUS-guided revascularization was an independent predictor for MACE in the overall population of this study with a lower incidence rate of MACE in the IVUS group compared to the non-IVUS group (p = 0.04). But in contrast to our study, there was a reduced incidence of death (p = 0.01) .However, the incidence of myocardial infarction and target vessel revascularization was not significantly different between the two groups (p = 0.4) and (p = 0.7), respectively.[17]

Reduction in stent thrombosis with IVUS guidance may be due to a better resolution of IVUS (100 microns) compared to coronary angiography (150–200 microns), its ability to identify stent edge dissections and incomplete stent apposition which cannot be detected by conventional coronary angiography.[40]

Many studies showed a better outcome and a reduction of MACE with IVUS guided PCI. But the differences between them were in the effect of IVUS on the different components of MACE. IVUS evaluations of stent under--expansion, incomplete lesion coverage, small stent area, and large residual plaque have been found to predict stent thrombosis.[18]

In our study, the reduction in MACE in the IVUS-guided group was attributed mainly to the reduction in stent thrombosis which led to a reduction in non-fatal myocardial infarction and target vessel revascularization.

Another trial showed that the clinical benefit of IVUS-guided drug eluting stent implantation was due to the post--procedural larger minimal lumen diameter and the more frequent adjunct post-dilation in the IVUS-guided group.[38]

Same findings were found in our study in which IVUS guided group showed larger mean post-stent minimal lumen diameter (3.65±0.32 versus 3.27±0.33mm in Group B; p-value: 0.001), higher incidence of adjunct post-dilation (93.3% versus 70% in Group B; p-value: 0.02) and larger stents diameter (3.54±0.35 versus 3.27±0.33 mm in Group B; p-value: 0.003) . Accordingly our study found better outcome in IVUS guided group due to these findings.

Recent study revealed that pre-stent IVUS assessment in chronic total occlusion PCI provides important information on vessel morphology and size. Angiography-based stent size prediction for the proximal and distal vessels was frequently underestimated, IVUS use demonstrated larger vessel diameter, resulting in a significantly larger implanted stent diameter.[41]

Since our study was limited by a small population we recommended many multi-center studies with a larger sample size and a longer period of follow up to investigate the benefit of IVUS guided PCI.

Conclusions

IVUS guidance during unprotected LM and proximal LAD coronary artery stenting improves clinical outcome with significant lower rates of MACE at 6 months which is primarily due to a significant lower risk of target lesion revascularization and stent thrombosis. The study recommended routine use of IVUS during stenting of ULM and proximal LAD coronary artery.

Conflict of interest

The authors declare that they have no conflict of interest.

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