ORIGINAL ARTICLE

Short Term Outcomes of Intravascular Ultrasound Guided Management of Patients with In-stent Restenosis in Comparison with Angiography Guided Management

Mansour M. M. Aref [a], Abd EL Hamid I. Abd EL Hamid [a], Abdelaal A. A. Alkhouly [b], Hazem A. Mahmoud [a,*]

[a] Department of Cardiology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt
[b] Department of Cardiology, Islamic Center of Cardiology, Al-Azhar University, Cairo, Egypt

Abstract

Background: ***Diameter stenosis of more than 50% within the stent or at its margins (five-millimeter segments next to the stent) on coronary angiography is commonly and arbitrarily used to define in-stent restenosis (ISR).***

Aim and objectives: ***The aim of this study was to compare the short-term outcomes of IVUS-guided management of patients with In-Stent restenosis with angiography-guided management.***

Patients and methods: ***Following authorization from our institution's ethical board, 60 patients undergoing revascularization at Al-Azhar University Hospital for ISR participated in this observational cohort study comparing outcomes from February 2023 to November 2024.***

Results: ***Compared to the angiography group, the IVUS group required much more time for the procedure and fluoroscopy. When comparing the IVUS and angiography groups, the contrast volume was noticeably lower in the former. While 3 patients (10%) in the angiography group and 1 patient (3.33%) in the IVUS group experienced restenosis, there was no statistically significant difference between the two groups.***

Conclusion: ***IVUS-guided interventions were associated with significantly reduced contrast volume and lower post-NC balloon dilatation requirements; however, they had longer procedure and fluoroscopy times compared to the angiography intervention. Both methods showed improvements in left ventricular ejection fraction over six months, indicating beneficial outcomes with both approaches.***

Keywords: In-stent restenosis; Angiography; Intravascular ultrasound

1. Introduction

While there have been advancements in the field, in-stent restenosis (ISR) remains the leading cause of failure after percutaneous coronary intervention (PCI). The incidence of ISR varies from 3% to 20% of patients, depending on the type of lesion, patient and lesion characteristics.[1]

Although the absolute number of ISRs has increased, the rate of ISRs has decreased in the drug-eluting-stent (DES) period due to the increased effectiveness of percutaneous coronary intervention (PCI) in treating more complex coronary artery disease.[2]

Angiographic in-stent stenosis (ISR) is usually arbitrarily and binaryly defined as a diameter stenosis of >50% in coronary angiography. This definition applies to both the stent itself and the 5-mm segments next to it.[3]

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* Corresponding author at: Cardiology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt. E-mail address: abulimar2023@gmail.com (H. A. Mahmoud).

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This approach offers simplicity while being grounded in the physiological importance of the degree of narrowing, demonstrating the optimal balance of sensitivity and specificity for predicting clinically driven target lesion revascularization (TLR), in contrast to other more precise yet less accessible thresholds.[4,5]

This study compares the short-term results of angiography-guided management vs intravascular ultrasonography (IVUS)-guided management for patients with in-stent restenosis.

2. Patients and methods

This observational cohort study was carried out on 60 patients with ISR

undergoing revascularization at Al-Azhar University Hospital, from February 2023 to November 2024, after approval of our institutional ethics committee.

Inclusion criteria:

Individuals who are between the ages of 18 and 80; both sexes; have CCS on GDMT prescribed for CA; Having target lesions in native coronary arteries via angiographic percent diameter stenosis (%DS) higher than 50% and one or more (up to three) ISR; in the IVUS group, have lesions that are either proliferative (expanding beyond the stent edges), focal (10 mm), multifocal (10 mm), or diffuse (10 mm); have only ever had DES implanted before; and know the diameter of the stent that was installed before.

Exclusion criteria:

The following conditions can prevent a patient from participating in the study: patient refusal, cardiogenic shock, severe left ventricular systolic dysfunction, cardiogenic shock, contraindications to cardiac catheterization, contraindications to dual antiplatelet therapy, moderate to severe renal impairment (creatinine clearance≤60 ml/min), hepatic disease (child B and C), severe valvular heart disease, and patients for whom follow-up is not possible.

Methods:

All patients in this study were subjected to the following:

After the participants were verbally informed of the study's goals and methods, their agreement was obtained. Age, sex, hypertension (HTN), diabetes mellitus (DM), dyslipidemia, smoking status, history of percutaneous coronary intervention (PCI), myocardial infarction (MI), cerebral vascular accident (CV), heart failure (HF), chronic kidney disease (CKD), ischemic heart disease (IHD), and medications were among the sociodemographic variables that were heavily recorded. Additionally, a general physical and a heart evaluation were conducted.

Routine laboratory investigations: complete blood count (CBC), serum urea and creatinine, serum cholesterol, triglycerides, and low-density lipoprotein (LDL) and high-density lipoprotein (HDL).

Resting 12-Electrocardiogram (ECG) leads:

Subjects' electrocardiograms were all performed. Every patient was monitored with a conventional 12-lead electrocardiogram (ECG) when they were admitted, using a paper speed of 25 mm/s and a standardization of 1 mV/10ˆmm.[6]

2D-Echocardiography:

The patient was evaluated with a two-dimensional transthoracic echocardiogram and Doppler assessment prior to discharge and 6months after. The parasternal projections were used to measure the LV dimensions using M-mode online. Left ventricular diameter during end-systole and end-diastole. During the patient's breath hold, M-mode, two-dimensional, and Doppler images were acquired. The apical 4- and 2-chamber views were utilized to delineate the end-systolic and end-diastolic volumes of the left ventricle for the assessment of its systolic function. The left ventricular ejection fraction (LVEF) was calculated using a biplane method. Irregularities in regional wall motion and Simpson's methodology.[7]

Coronary angiography:

The patient was divided into 2 groups randomly:

Group I (n=30): Intravascular ultrasound (IVUS) guided management and Group II (n=30): Angiographic guided management which classified in to four groups according to algorithm of angiographic classification of ISR16. Pie Medical Imaging's automated edge-detection algorithms (CAAS 5.7.1) were used to conduct quantitative coronary angiography (QCA) according to conventional protocols at Masstricht, The Netherlands. The presence of restenosis within the stented section was determined by measuring a diameter stenosis greater than 50%.

PCI and IVUS:

For the IVUS-guided management group. They used a phased-array catheter from Volcano Corp. in San Diego, CA, USA, and all IVUS images were taken after 200 mg of intracoronary nitro-glycerine was administered. The ultrasound machine used was a commercially available system, the Philips CX50 Extreme edition, and it had a high frequency probe with manual pull back.

Steps of IVUS:

A procedure for IVUS-guided treatment looks like this:

To compare the diameter of the reference vessel to that of the previously placed stent, an intravascular ultrasound scan (IVUS) must be performed before the intervention. If there is a large ISR, the minimal luminal area (MLA) can be measured. ISR pathology is classified according to Waksman's classification17. To find the length of

the stent, measure the distance between the two points of reference, one at the beginning and one at the end. Using the Waksman classification technique for ISR management. Using standard methods, insert a stent or DCB. Check the minimal luminal area (MLA) after the intervention by doing another IVUS. You can stop if the MLA is sufficient. Inflate the balloon to a higher pressure and try using a bigger one if the MLA doesn't cut it. We tried to meet the following success criteria that were set by IVUS after the procedure: stent minimal stent area (MSA) >80% of reference vascular area, acceptable apposition, and a symmetry index >70%.

Figure 1. Intravascular ultrasound (IVUS) machine.

Follow-up:

Clinical follow-up: It was ensured that the patient had clinical follow-up both during their hospital stay and at a subsequent visit six months after MACE treatment. Death, myocardial infarction, acute kidney injury (AKI) necessitating renal replacement therapy (RRT), cerebrovascular accident (CVA), severe bleeding necessitating blood transfusion, perforation, and pericardial effusion necessitating pericardiocentesis or surgical intervention (tamponade) are all examples of medical complications that can occur during a patient's hospital stay.

Angiographic follow-up: coronary angiography for all the patients to detect if there is evidence of ISR at six months.

The primary endpoint:

Cardiac mortality throughout the follow-up period.

The secondary endpoint:

Cardiovascular disease, myocardial infarction, and stent thrombosis, whether confirmed or suspected. Target lesion revascularization induced by ischemia (TLR).

Death from heart disease, MI, thrombosis in a stent, and revascularization of ischemia-driven target lesions were the main adverse cardiac events.

Ethical considerations:

Informed written consent was obtained from the patients. All patient data was protected, utilizing secret codes and individual files for each patient. All provided data were utilized solely for the present medical research. There are sufficient measures to ensure participant privacy and data confidentiality.

Statistical analysis

SPSS v26 (IBM Inc., Chicago, IL, USA) was used for statistical analysis. Shapiro-Wilk and histograms assessed data normality. For quantitative parametric variables like mean and standard deviation, an unpaired Student's t-test was used to compare groups. To examine qualitative variables, Chi-square or Fisher's exact tests were used on frequencies and percentages. Statistical significance is a two-tailed P-value below 0.05.

3. Results

Table 1. Demographic data of the examined groups.

		GROUP I (N=30)	GROUP II (N=30)	P-VALUE
AGE(YEARS)	Mean±SD	57.5±12.1	56.1±11.39	0.646
	Range	37-76	34-75	
SEX	Male	19(63.33%)	19(63.33%)	1.00
	Female	11(36.67%)	11(36.67%)	

Age and sex were insignificantly different between both groups, (Table 1; Figures 1&2).

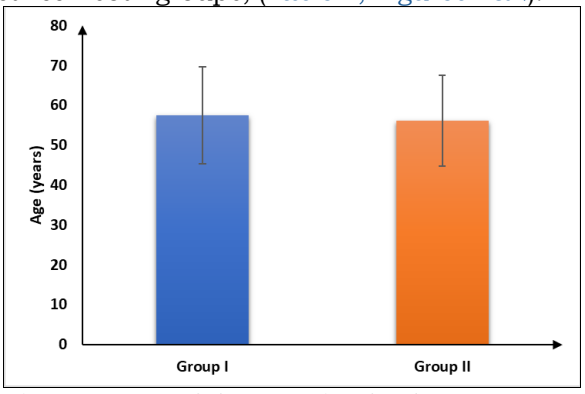

Figure 1. Age of the examined cohorts.

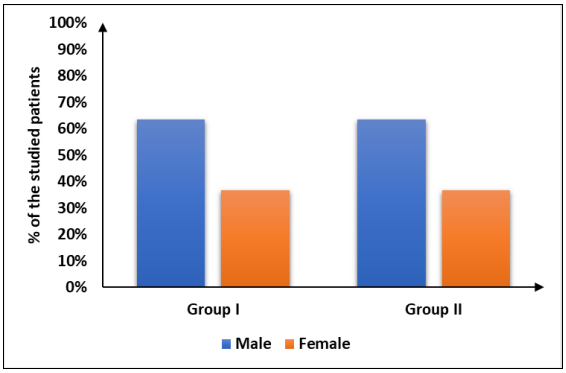

Figure (2): Gender of the examined cohorts.

Table 2. Procedural characteristics of the examined groups.

		GROUP I (N=30)	GROUP II (N=30)	P-VALUE
PROCEDURE TIME (MIN)	Mean±SD	56.57±8.02	34.6±7.32	<0.001*
	Range	43-75	22-45	
FLUOROSCOPY TIME (MIN)	Mean±SD	33.47±4.87	16.8±3.64	<0.001*
	Range	26-45	10-25	
CONTRAST VOLUME (ML)	Mean±SD	89.83±17.69	123.87±24.12	<0.001*
	Range	60-120	75-155	

*Significant as P-value≤0.05

Procedure time and fluoroscopy time were significantly higher in Group I than Group II(P-value<0.001). Contrast volume was significantly lower in Group I than Group II(P-value<0.001), (Table 2; Figures 3-5).

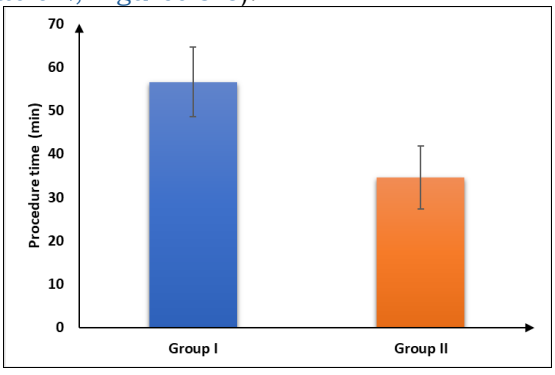

Figure 3. Duration of the procedure for the examined groups.

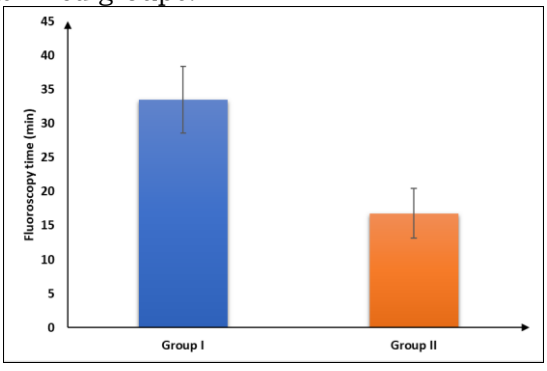

Figure 4. Fluoroscopy time of the examined groups.

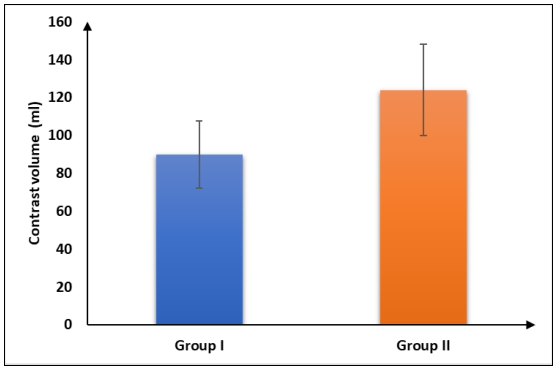

Figure 5. Contrast volume of the examined groups.

Table 3. Treatment strategy of the examined groups.

	GROUP I (N=30)	GROUP II (N=30)	P-VALUE
PRE-NC	30(100%)	30(100%)	----
POST-NC	7(23.33%)	18(60%)	0.004*
DES	17(56.67%)	18(60%)	0.793
DCB	10(33.33%)	12(40%)	0.592

*Significant as P-value≤0.05, NC:Non-compliant, DES:Drug-eluting stent, DCB:Drug-coated balloon.

Post-NC was significantly lower in Group I than Group II(P value=0.004). DES and DCB were insignificantly different between both groups, (Table 3; Figure 6).

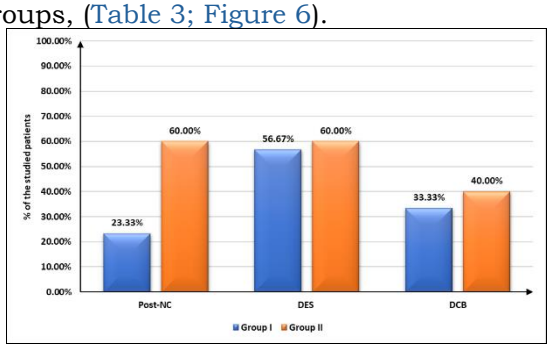

Figure 6. Treatment strategy of the examined groups.

Table 4. Clinical outcomes of the examined groups.

	GROUP I (N=30)	GROUP II (N=30)	P-VALUE
RESTENOSIS	1(3.33%)	3(10%)	0.301
MACE IN HOSPITAL			
DEATH	0(0%)	0(0%)	---
TARGET VESSEL MI	0(0%)	0(0%)	---
NON-TARGET VESSEL MI	0(0%)	0(0%)	---
ISCHEMIA-DRIVEN TLR	0(0%)	0(0%)	---
STENT THROMBOSIS	0(0%)	0(0%)	---
MACE AFTER 6 M			
DEATH	0(0%)	0(0%)	---
TARGET VESSEL MI	0(0%)	0(0%)	---
ISCHEMIA-DRIVEN TLR	0(0%)	0(0%)	---
STENT THROMBOSIS	0(0%)	0(0%)	---

MACE:Major adverse cardiac event, MI:Myocardial infarction, TLR:target lesion revascularization.

Restenosis was observed in 1 (3.33%) patient in Group I and in 3 (10%) individuals in Group II. Restenosis shown no significant difference between the two groups. Major adverse cardiovascular events (MACE) did not occur in any patients in either group during hospitalization or after six months, (table 4).

Table 5. Comparison between diameter of the previous deployed stent and reference luminal diameter as regards type of ISR of the examined group I.

		TYPE I (N=8)	TYPE II (N=17)	TYPE III (N=4)	TYPE V (N=1)
DIAMETER OF THE PREVIOUS DEPLOYED STENT (MM)	Mean±SD	3.2±0.34	3.2±0.2	2.9±0.14	---
	Range	3-4	3-3.5	2.75-3	3 - 3
REFERENCE LUMINAL DIAMETER (MM)	Mean±SD	3.7±0.44	3.3±0.21	3.2±0.21	---
	Range	3.3-4.7	3-3.6	3-3.4	2.9 - 2.9
P-VALUE		0.023*	0.164	0.055	---

*Significant as P-value≤0.05, ISR:In-stent restenosis.

Diameter of the previous deployed stent was significantly lower compared to reference luminal diameter in ISR Type I(P-value=0.023). There was no significant difference between diameter of the previous deployed stent and reference luminal diameter as regards ISR type II and III, (Table 5).

Table 6. IVUS MLA pre and post intervention of the studied group I.

		PRE	POST	P-VALUE
IVUS MLA (MM^2)	Mean±SD	3.1±0.43	7.1±0.35	<0.001*
	Range	2.6-4.9	6.7-8.6	

This is considered significant when the p-value is less than or equal to 0.05. IVUS is for intravascular ultrasonography, and MLA stands for minimum lumen area.

Post-intervention IVUS MLA considerably increased compared to pre-intervention (The p-value is less than 0.001), (Table 6 and Figure 7).

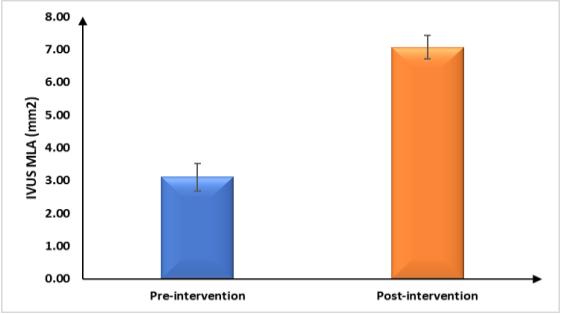

Figure 7. IVUS MLA pre and post intervention of the studied group I.

4. Discussion

The process of restenosis involves the constriction of the enlarged section of a coronary artery on multiple occasions. Recurrence of clinical symptoms of ischemia due to restenosis is known as "clinical restenosis," and it is often linked to the need for recurrent target lesion or vessel revascularization procedures (TLR/TVR)..[8,9]

Risk variables (diabetes mellitus, hypertension, dyslipidemia, and current smoking) were not substantially different between the two groups in this research. In terms of risk factors, 21 patients (or 70% of the total) in the IVUS group and 20 patients (or 66.67%) in the angiography group had diabetes mellitus, 15 patients (or 50% of the total) in the IVUS group and 19 patients (or 63.33%) in the angiography group had hypertension, 23 patients (or 76.67%) in the IVUS group and 24 patients (or 80% of the total) in the angiography group had dyslipidemia, and 11 patients (or 36.67%) in the IVUS group and 10 patients (or 33.33%) in the angiography group were current smokers.

In agreement with our findings, Lee et al.,[10] conducted a study on the IVUS versus angiography-guided PCI for acute myocardial infarction with cardiogenic shock. They showed that that the DM, HTN, dyslipidemia and current smoking were insignificantly different between IVUS and the angiography groups.

Neither group required much more time than the other to implant the stent and reach the target arteries, according to this study. Fluoroscopy and the operation took much longer in the IVUS group than in the angiography group. Compared to the angiography group, the IVUS group had much less contrast volume.

In the same line, Squiers et al.,[11] performed a retrospective review on 12,414 patients undergoing thoracic endovascular aortic repair; 5,121 patients were assigned to the group that received intravenous urea (IVUS), while 7293 patients were assigned to the group that did not receive IVUS. Using IVUS resulted in a significant decrease in contrast volume.

Concerning the post-noncompliant (NC) periods, the angiography group was significantly different from the IVUS group. Neither the drug-eluting stent (DES) nor the drug-coated balloon (DCB) group of patients showed any significant change. Both groups' left ventricular ejection fractions (LVEFs) before and after the 6-minute intervention were not significantly different from one another.

This agreed with Gao et al.,[12] who found that the DES was insignificantly different between the IVUS and the angiography groups.

This agreed with the findings of the meta-analysis conducted by Bavishi et al.,[13] who observed that there were no significant differences for stent thrombosis, cardiovascular death, or all-cause death between the IVUS and angiography.

Our results showed that the regarding the type

of ISR in the IVUS and angiography groups, type I was in 8(26.67%) and 16(53.33%) patients, type II in 17(56.67%) and 3(10%) patients, type III in 4(13.33%) and 11 (36.67%) patients, respectively, while type IV in 1(3.33%) patient in IVUS group and not present in the angiography group. Pre-NC was needed in all patients in both groups, post-NC in 7(23.33%) and 18 (60%) patients, DES was used in 17 patients (56.67%) and 18 patients (60%) in the IVUS group, whereas DCB was used in 10 patients (33.33%) and 12 patients (40%) in the angiography group. Compared to Type I, Type II, and IVUS contrast volumes were much larger.

Procedure time and fluoroscopy time were significantly higher in Type III than in Type I in the angiography group. IVUS minimal lumen area (MLA) was significantly higher post-intervention compared to pre-intervention. LVEF was significantly higher after 6 months compared to pre-intervention in both IVUS and angiography groups.

Pre-NC is often assessed in patients undergoing IVUS to ensure optimal stent deployment and vessel preparation. IVUS provides detailed images of the vessel, allowing clinicians to evaluate the vessel's condition, including plaque composition and distribution. This helps determine whether additional pre-dilation or vessel preparation is necessary to prevent issues like stent under-expansion or malposition. By addressing these factors before stent placement, IVUS helps improve the overall success and safety of the procedure, ensuring the stent conforms well to the vessel wall and reduces the risk of complications.[14,15]

In the same line, Sakai et al.,[16] discovered that the contrast volume was substantially lower in the IVUS-guided PCI group.

Supporting our study, Choi et al.,[17] found that intravenous urea stent usage was linked to a markedly reduced incidence of cardiac mortality.

4. Conclusion

IVUS-guided interventions were associated with significantly reduced contrast volume and lower post-NC balloon dilatation requirements; however, they had longer procedure and fluoroscopy times compared to the angiography intervention. Both methods showed improvements in left ventricular ejection fraction over six months, indicating beneficial outcomes with both approaches.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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