Optical coherence tomography (OCT) vs intravascular ultrasound (IVUS) in diagnosing the mechanisms of in-stent restenosis in drug eluting stents

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Abstract

Background: In-stent restenosis remains a recognized complication of percutaneous coronary intervention (PCI). Conventional two-dimensional angiography is limited to visualization of the coronary lumen and provides inadequate assessment of in-stent restenosis mechanisms. In contrast, intracoronary imaging modalities such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT) enable detailed evaluation of in-stent restenosis, optimization of procedural outcomes, and improvement of long-term clinical results.

Aims: The aim of this study was to compare OCT and IVUS in detecting the mechanisms of in-stent restenosis and to evaluate their role in guiding management, whether through balloon angioplasty or repeat PCI with stent implantation.

Materials and methods: The study included 50 patients who had previously deployed stents presenting to our hospital, in the period from November 2022 to December 2024, with angina refractory to medical therapy. All of whom underwent comprehensive clinical evaluation including history, physical examination, ECG, echocardiography, and coronary angiography. Patients were divided randomly into two groups: Group 1 (n=25) underwent IVUS-guided PCI, while Group 2 (n=25) underwent OCT-guided PCI.

Results: OCT was significantly superior to IVUS in detecting mal-apposition (p = 0.015) and neo-atherosclerosis (p = 0.018) as mechanisms of in-stent restenosis. No statistically significant differences were observed between OCT and IVUS in detecting neointimal hyperplasia (p = 0.713), under-expansion (p = 0.077), or edge dissection (p = 0.269).

Conclusion: Intracoronary imaging is a valuable tool for identifying the mechanisms of in-stent restenosis, guiding tailored therapy, and improving clinical outcomes. OCT offers superior diagnostic capability compared with IVUS, particularly in detecting mal-apposition and neo-atherosclerosis.

Keywords

In-stent restenosis, percutaneous coronary intervention, intracoronary imaging, OCT, IVUS, balloon angioplasty, mal-apposition, neo-atherosclerosis.

Introduction

In-stent restenosis (ISR) is the leading cause of treatment failure following percutaneous coronary intervention.[1] It often manifests as an acute coronary syndrome and is linked to poorer long-term outcomes compared with interventions for de novo coronary artery disease.[2] ISR is defined angiographically as a recurrent diameter stenosis of more than 50% within the stented segment or its adjacent 5-mm edges.[3] Several classification systems exist to describe the severity of ISR, among which the Mehran classification provides a morphological framework for characterizing ISR lesions.[4]

In-stent restenosis (ISR) is a unique pathological process seen after balloon angioplasty with stent implantation. It develops through several mechanisms, including neo-intimal hyperplasia, neo-atherosclerosis, inadequate stent expansion, and other related complications.[5]

Coronary angiography has long been considered the gold standard for diagnosing coronary artery disease and guiding percutaneous coronary intervention (PCI). However, modern intravascular imaging (IVI) techniques have emerged as valuable adjuncts, providing detailed plaque characterization and enhancing PCI outcomes. IVI plays a role in pre-procedural lesion and vessel assessment, intraprocedural guidance for lesion preparation and stent placement, and post-procedural evaluation to confirm optimal results and rule out complications.[6]

Beyond intimal hyperplasia, other identifiable causes of restenosis include stent under-expansion (seen in about 18–40% of cases), stent fracture (<5%), and late neo-atherosclerosis, which typically develops more than one year after DES implantation. IVUS and OCT are effective for detecting under-expansion and stent fracture, while OCT more readily diagnoses neo-atherosclerosis.[7] Management should be tailored to the underlying OCT findings—for example, placing an additional stent for neo-atherosclerosis or performing post-dilatation for under-expansion or mal-apposition.[8]

Therefore, intracoronary imaging is an essential modality in diagnosing causes of in-stent restenosis. Among available modalities, OCT is the preferred technique for assessing in-stent restenosis and stent thrombosis.[8]

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Methods

This is a cross-sectional study conducted on 50 patients who had previously deployed stents, presenting with angina refractory to maximal medical therapy, in the period from November 2022 to December 2024; 25 patients underwent IVUS-guided PCI and the other 25 patients underwent OCT-guided PCI.

In this study, patients were randomly assigned to have either IVUS or OCT for the assessment of the mechanism of in-stent restenosis, and according to the results obtained from the IVI, treatment was formulated.

Inclusion criteria:

All patients included had previous history of PCI and presented with symptomatic chronic coronary syndrome (angina not responding to maximal medical treatment).

Exclusion criteria:

1) Patient with a history of coronary artery bypass graft surgery
2) Patient with cardiogenic shock
3) Patients had aorto-ostial lesions
4) Patients with hypothyroidism or hyperthyroidism
5) Patients with acute hepatic failure (hepatic encephalopathy, Coma with markedly elevated liver enzymes and ammonia levels in blood)
6) patients with acute renal failure (Elevated creatinine levels with oliguria or anuria)
7) Patients with malignancies, autoimmune diseases
8) Patients with congenital heart disease
9) Patients with acute or chronic pulmonary disease

All patients subjected to the followings:

1) Full history taking
2) Complete physical examination
3) 12-lead surface ECG
4) Echocardiography
5) Lab Investigation (CBC, serum creatinine), cardiac enzyme (in case of ACS).
6) PCI was done guided by Intracoronary Imaging (IVUS or OCT)

IVUS measurements in the study included cross-sectional areas of the external elastic membrane, lumen, stent, and neointimal hyperplasia (NIH). The findings highlighted the role of both NIH and chronic stent underexpansion as key mechanisms of ISR. A major limitation, however, was the inability to assess the prevalence of neoatherosclerosis, since grayscale IVUS is not the optimal modality for this purpose. IVUS is particularly useful in patients with severely impaired renal function undergoing PCI, where minimizing contrast use is crucial. In such cases—especially when multiple OCT runs would otherwise be required for vessel sizing or evaluation of stent expansion—IVUS offers a valuable alternative.[2]

Patients were randomly assigned to undergo either IVUS or OCT for the assessment of the implanted stents. This randomization was performed after diagnostic angiography.

Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 24. Qualitative data were expressed as frequency and percentage. Quantitative data were expressed as mean ±SD. Mean (average): the central value of a discrete set of numbers, specifically the sum of values divided by the number of values. Standard deviation (SD): is the measure of dispersion of a set of values. A low SD indicates that the values tend to be close to the mean of the set, while a high SD indicate that the values are spread out over a wider range.

The following tests were done:

Independent sample T test (T): when comparing between two groups.

Chi-square test: was used when comparing between non-parametric data.

Probability (P-value)

– P-value < 0.05 was considered significant.
– P-value < 0.001 was considered as highly significant.
– P-value > 0.05 was considered insignificant.

Results

Table 1 - Demographic data according to imaging method.

	OCT (N = 25)	IVUS (N = 25)	Stat. test	P-value
Age (years)	63.8 ± 10.01	64.4 ± 12.8	T = 0.16	0.874 NS
Sex	Male: 14 (56%) Female: 11 (44%)	Male: 13 (52%) Female: 12 (48%)	X^2 = 0.081	0.777 NS

T: independent sample T-test, X^2: Chi-square test, NS: non-significant (p > 0.05).

There was no statistically significant difference in age or sex distribution between the two groups.

Table 2 - Time since stent implantation.

	OCT (N = 25)	IVUS (N = 25)	P-value
<1 year	5	6	0.8
1-3 years	13	12	0.85
>3 years	7	7	0.72

No statistically significant differences were found between the groups regarding time since stent implantation.

Table 3 - Echocardiographic findings according to imaging method.

	OCT (N = 25)	IVUS (N = 25)	T	P-value
LVEDD (mm)	51.1 ± 6.8	54.1 ± 6.0	1.65	0.105 NS
LVESD (mm)	36.4 ± 7.7	39.7 ± 7.5	1.52	0.135 NS
EF (%)	54.7 ± 9.8	50.6 ± 9.5	1.51	0.137 NS

No statistically significant differences were observed in LVEDD, LVESD, or ejection fraction between the groups.

Table 4 - Culprit vessel according to imaging method.

Culprit Vessel	OCT (N = 25)	IVUS (N = 25)	X^2	P-value
LM	2 (8%)	5 (20%)	1.49	0.221 NS
LAD	15 (60%)	17 (68%)	0.34	0.556 NS
LCX	8 (32%)	3 (12%)	2.9	0.088 NS
RCA	2 (8%)	5 (20%)	1.49	0.221 NS

There was no statistically significant difference between the groups regarding the culprit vessel.

Table 5 - MLA and plaque burden according to imaging method.

	OCT (N = 25)	IVUS (N = 25)	T	P-value
MLA	2.35 ± 0.85	2.38 ± 0.77	0.12	0.904 NS
Plaque burden	78.6 ± 11.6	77.7 ± 11.4	0.28	0.779 NS

No significant difference was observed between the two groups in terms of MLA or plaque burden.

Table 6 - Cause of in-stent restenosis according to imaging method.

Cause of Stent Failure	OCT (N = 25)	IVUS (N = 25)	X^2	P-value
Malapposition	12 (48%)	4 (16%)	5.9	0.015 S
Under-expansion	6 (24%)	12 (48%)	3.12	0.077 NS
Edge dissection	6 (24%)	3 (12%)	1.22	0.269 NS
Neoatherosclerosis	13 (52%)	5 (20%)	5.55	0.018 S
Neointimal hyperplasia	4 (16%)	5 (20%)	0.13	0.713 NS

S: p-value < 0.05 significant; NS: non-significant.

Mal-apposition and neo-atherosclerosis were significantly more frequent in the OCT group, while no significant differences were found for under-expansion, edge dissection, or neointimal hyperplasia.

Table 7 - Management according to imaging method.

Management	OCT (N = 25)	IVUS (N = 25)	X^2	P-value
NC	5 (20%)	2 (8%)	1.49	0.221 NS
DCB	13 (52%)	9 (36%)	1.29	0.254 NS
DES	9 (36%)	14 (56%)	2.01	0.156 NS

No statistically significant differences were observed in management strategies between the groups.

Summary of results

Overall, there were no significant differences between OCT and IVUS groups in demographic data, hemodynamic parameters, echocardiographic findings, culprit vessel distribution, MLA, plaque burden, or treatment strategies. However, OCT demonstrated a statistically significantly higher detection rate of both stent malapposition (48% vs. 16%, p = 0.015) and neoatherosclerosis (52% vs. 20%, p = 0.018) compared to IVUS.

Discussion

In terms of demographic characteristics, there was no statistically significant difference in age between the two groups, with a mean age of 63.8 ± 10.01 years in the OCT group and 64.4 ± 12.8 years in the IVUS group. These findings are consistent with Chaudhary et al.[9], who studied 34 patients with ISR and found that most were between 51 and 65 years of age. Regarding gender, both groups showed a male predominance, with males representing 56% in the OCT group and 52% in the IVUS group. This observation aligns with the results of Chaudhary et al.[9], Sung Yun et al.[10], and Abdelmonaem et al.[11], all of whom reported a higher prevalence among males.

In our study, the LAD was the most frequently affected vessel in both groups, accounting for 60% in the OCT group and 68% in the IVUS group. In the OCT group, the LAD was followed by the LCX, whereas in the IVUS group, the RCA and LM were the next most common. These findings are consistent with Saad et al.[12], who also reported the LAD as the most commonly involved culprit vessel in both the staged-PCI and complete revascularization groups.

Earlier studies suggested that the key determinant of long-term clinical outcomes after re-intervention for ISR was the final minimum lumen area (MLA) achieved, regardless of the technique used.[13] In our study, there was no significant difference in MLA between the two modalities, measuring 2.35 ± 0.85 in the OCT group and 2.38 ± 0.77 in the IVUS group. Using OCT, the main mechanisms of in-stent restenosis identified were neoatherosclerosis (52%), malapposition (48%), underexpansion (24%), edge dissection (24%), and neointimal hyperplasia (16%).

In the present study, IVUS revealed stent underexpansion as the most common finding (48%), followed by malapposition (16%), neoatherosclerosis (20%), neointimal hyperplasia (20%), and edge dissection (12%). Similarly, Sung Yun et al. (2018) evaluated 58 patients with ISR using pre-intervention IVUS before treatment with PEB angioplasty. They reported that, in the PEB failure group, both neointimal area (4.0 ± 0.7 vs. 2.9 ± 0.8 mm², p = 0.05) and neointimal hyperplasia (%) (59.4 ± 12.0 vs. 46.0 ± 24.9%, p = 0.05) were significantly higher compared to the non-failure group. Interestingly, stent underexpansion was identified in 24 ISR lesions (48.0%) within the non-failure group, but was absent in the PEB failure group.

When comparing the two imaging modalities in our study, OCT demonstrated a significantly greater ability to detect malapposition, identifying it in 12 patients (48%) compared to only 4 patients (16%) in the IVUS group. These findings are supported by previous research; for example, in the OPUS-CLASS study (Optical Coherence Tomography Compared with Intravascular Ultrasound in a Coronary Lesion Assessment Study), OCT detected post-PCI incomplete stent apposition more than twice as often as IVUS (39% vs. 14%).[14]

Large cross-sectional studies using IVUS and OCT have shown notable differences in the detection of acute stent malapposition. IVUS identified a prevalence of 12.6% per lesion after successful DES implantation,[15] whereas OCT detected it in 62% of lesions.[16] Similarly, Soeda et al.[17] and Prati et al.[18] reported malapposition rates of 39.1% and 49.3%, respectively, using OCT. The superior resolution of OCT contributes to better detection, resulting in fewer untreated major malappositions with OCT guidance compared to IVUS, and fewer overall malappositions than with angiographic guidance.[19]

In our study, OCT also demonstrated a significantly higher ability to detect neoatherosclerosis (13 patients, 52%) compared with IVUS (5 patients, 20%). This aligns with Adriaenssens et al.[20], who reported neoatherosclerosis as a major risk factor in 31.3% of patients with very late stent thrombosis (VLST), and with Taniwaki et al.[21], who found it in 27.6% of cases using OCT. Ali et al.[22] further emphasized that both OCT and IVUS are valuable for monitoring PCI outcomes and predicting major adverse cardiovascular events, but OCT remains the preferred modality for visualizing neoatherosclerosis, restenosis, and stent thrombosis due to its higher resolution.

Regarding stent underexpansion, our study found no significant difference between the two groups: 6 patients (24%) in the OCT group versus 12 patients (48%) in the IVUS group. Similarly, the ILUMIEN II study[23], which analyzed 286 propensity-matched pairs, showed comparable stent expansion between IVUS- and OCT-guided PCI.

For edge dissection, our study found no statistically significant difference between OCT and IVUS. Nevertheless, owing to its higher resolution, OCT is able to detect smaller edge dissections that are often overlooked by IVUS and angiography. In the ILUMIEN-3 trial, OCT identified twice as many dissections as IVUS, with an overall incidence of 37.8%; notably, 84% of these were not visible on angiography.[24]

In terms of treatment, there was no significant difference between the two groups. In the OCT group, DCB was used in 52% of cases, DES in 36%, and NC balloons in 20%. In the IVUS group, DES was used in 56%, DCB in 36%, and NC balloons in 8%. According to the recommendations of Neumann et al.[25], management of ISR with either DES implantation or DCB therapy is superior to plain balloon angioplasty alone. This was further supported by Siontis et al.[26,27] in a meta-analysis, which showed that PCI with an everolimus-eluting stent was more effective than DCB angioplasty for reducing percentage diameter stenosis.

Limitations

1. The main limitation of this study is the relatively small sample size.
2. Plaque composition analysis of neointimal atherosclerosis was not performed.

Recommendations

Future studies should include larger patient cohorts in a multicenter setting to validate these findings**.**

Conclusion

Intracoronary imaging plays a crucial role in identifying the mechanisms underlying stent failure, thereby guiding appropriate management and improving clinical outcomes. OCT, in particular, demonstrates superior ability in detecting malapposition and neoatherosclerosis compared with IVUS.

Conflict of interest

The author declares no conflicts of interest.

Author Contributions

All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement

Written informed consent for the procedure and to publish this paper has been obtained from the patients.

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