Clinical Outcomes and Prevalence of Intravascular Ultrasound Use at a Tertiary Care Hospital in a South Asian Country

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INTRODUCTION

Intravascular ultrasound (IVUS) is an invasive imaging modality used to visualize coronary cross-sectional anatomy.¹ IVUS technology has been proven to be superior to coronary angiography in terms of the assessment of vessel size, plaque composition, vessel dissection, calcium content, and lesion severity. However, despite these benefits, routine IVUS use is limited by cost and additional time that is needed to perform the procedure.²

Percutaneous coronary intervention (PCI) of the left main (LM) vessel and complex lesions remains challenging with a higher risk of procedural complications and poor early and late outcomes. The role of IVUS guidance has been previously explored, however, limited
information is available on how the pre-procedural use of IVUS might impact the intervention strategy and clinical outcome, particularly when approaching complex coronary lesions. We believe that additional information provided by IVUS beyond angiography leads to more optimal results and improving the outcome after PCI, particularly in the LM intervention. Given the continuous expansion of PCI for treating sicker patients and more complex coronary lesions, we believe that IVUS plays a pivotal role in the current practice era of complex PCI.

In this study, we described the prevalence and clinical outcomes in current practice at a tertiary care hospital in a low- to middle-income South Asian country, Pakistan.

MATERIAL AND METHODS

This is a single-center, retrospective observational study.

Objectives

The objective of the study was to determine the clinical outcomes associated with using IVUS for percutaneous treatment of coronary arteries lesions and prevalence of IVUS use in a tertiary care hospital of low- to middle-income country.

Study population

This was a single-center retrospective observational study conducted after the approval of the ethical review committee in the Department of Medicine section of Cardiology at the Aga Khan University Hospital, Pakistan. We retrospectively studied 134 consecutive patients who had IVUS done from January 2013 to March 2020. Data were collected on a pre-designed pro forma from the patient medical record using Health Information Management Service. Total data of 71 variables were collected, including, age, gender, comorbidities at presentation, mode of hospital presentation, procedural details, IVUS details, PCI details including, dissection, stent size/length/type, discharge medications, and follow-up. Final follow-up and informed consent were taken by reviewing medical records and telephonic interviews.

Exclusion criteria

The following criteria were excluded from the study:
1. Patients who were <18 years of age and
2. Those who lost follow-up and we were unable to contact them through phone calls/e-mails.

PCI procedure

All patients were pre-medicated with aspirin and clopidogrel. Therapeutic activated clotting time was achieved during PCI using unfractionated heparin. IVUS imaging was done using 20 MHz, 2.9 French Eagle Eye® Platinum RX digital IVUS catheter (Eagle Eye, Philips Volcano San Diego, CA, USA) and data recorded. PCI was performed as per standard protocol.

Gray scale IVUS analysis

IVUS images were interpreted by interventional cardiologist and radiographer during the procedure and IVUS details were recorded on DVD-ROM for offline interpretation, which was done both after the procedure and during our study by an expert team including an interventional cardiologist, interventional cardiology fellows, and a radiographer. All IVUS data were analyzed using standard validated software. External elastic membrane (EEM) and minimal luminal area (MLA) were measured proximal to the lesion, at the lesion, and distal to the lesion. Plaque and media cross-sectional area (CSA) was calculated as EEM minus lumen CSA. A cross-sectional analysis was carried out at the MLA.

Follow-up

Follow-up of clinical events was performed by reviewing hospital medical charts, clinic visits, hospital admission, and telephonic interview with the patient or immediate family member in case if the patient was deceased or unapproachable. The clinical events recorded were cardiovascular death, all-cause mortality, non-fatal myocardial infarction (MI), arrhythmias, target vessel revascularization (TVR), admission with heart failure, and stroke. MI was defined as having typical cardiac symptoms, elevated cardiac enzymes, and/or ischemic ECG changes. Life-threatening arrhythmias were defined as ventricular tachycardia or ventricular fibrillation recorded by ECG or device interrogation. TVR was defined as PCI or application of bypass grafts for restenosis of the previously done IVUS-guided PCI.

Statistical analysis

All the data analyses were conducted using STATA software (version 14.2; StataCorp). Mean and standard deviation were computed for quantitative variables and frequencies/percentages were reported for qualitative variables. Chi-square test or Fisher’s exact test was used to compare qualitative data whereas quantitative data were compared using independent t-test or Mann–Whitney U-test, as appropriate, considering two-sided P < 0.05 statistically significant.

RESULTS

A total of 134 patients who underwent IVUS imaging between January 2013 and March 2020 and fulfilled the inclusion
criteria were included in our study. Baseline characteristics are shown in Table 1. The majority of the patients included in our study were male (72.3%) and the mean age at presentation was 63.1 ± 12.9 years. The prevalence of utilization of IVUS at our center was 3% and the majority of IVUS was done in 2020 [Figure 1]. The most common comorbidity noted was dyslipidemia (n = 111 [82.8%]) followed by hypertension (n = 104 [77.6%]). Notably, non-ST-elevation MI (n = 50 [37.3%]) was observed to be the main reason for presentation. The most common medication prescribed at discharge was statins (n = 128 [99.2%]) followed by dual antiplatelet (n = 125 [97.9%]).

The procedural characteristics are shown in Table 2. The most common route of access adopted for the procedure in our study population was femoral access (n = 69 [51.5%]). Although the LM disease was found (n = 46 [34.3%]), single-vessel disease was most commonly noted (n = 51 [38.1%]). Drug-eluting stents (n = 92 [68.6%]) were deployed in the majority of patients.

The IVUS details are shown in Table 3. The IVUS was done mostly in the left anterior descending artery (n = 94 [70.1%]) followed by the LM (n = 46 [34.3%]). The LM mean MLA was 6.0 ± 2.6 mm² and the mean MLD was 4.53 ± 0.6 mm. Coronary artery dissection was noted in 11.2% of patients (n = 15).

In our study, we were able to collect follow-up of all patients [Table 4]. The mean duration of follow-up in our study was 40.3 ± 30.1 months. MACE occurred in n = 13 (9.7%), which was largely driven by heart failure n = 4 (3%). Cardiovascular death and TVR occurred in n = 3 (2.2%).

DISCUSSION

The results of the present study help us to acknowledge the prevalence and outcomes of IVUS guided PCI in our

| Table 1: Baseline characteristics of patients. |
|-----------------------------------------------|
| Mean age (years)                              | 63.1±12.9 |
| Male (%)                                      | 97 (72.4%)|
| Hypertension                                  | 104 (77.6%)|
| Diabetes                                      | 73 (54.3%) |
| Dyslipidemia                                  | 111 (82.8%)|
| Current smoker                                | 13 (9.7%)  |
| Former smoker                                 | 40 (29.8%) |
| CKD                                           | 13 (9.7%)  |
| Prior PCI                                     | 58 (43.2%) |
| Prior CABG                                    | 8 (6%)     |
| Mean ejection fraction at presentation (%)    | 44.9±11.9  |
| Mean hospital stay (days)                     | 4.11±4.2 days |
| Diagnosis at presentation                     |            |
| Stable angina                                 | 39 (29.1%) |
| Unstable angina                               | 13 (9.7%)  |
| NSTEMI                                        | 50 (37.3%) |
| STEMI                                         | 32 (23.9%) |
| Discharge medications                         |            |
| Aspirin                                       | 125 (97.9%)|
| Clopidogrel                                   | 113 (87.6%)|
| Ticagrelor                                    | 12 (9.3%)  |
| Statins                                       | 128 (99.2%)|
| Beta-blockers                                 | 115 (89.1%)|
| ACEi/ARBs                                     | 62 (48%)   |
| Anticoagulants                                | 16 (12.4%) |

CKD: Chronic kidney disease, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass grafting, NSTEMI: Non-ST-elevation myocardial infarction, STEMI: ST-elevation myocardial infarction, ACEi/ARBs: Angiotensin-converting enzyme inhibitors/angiotensin receptors blockers

Figure 1: A 56-year-old lady came to emergency with chest pain and recurrent polymorphic ventricular tachycardia. Intravascular imaging of the left anterior descending artery done showing mean luminal area and mean luminal diameter.
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This is the first study from Pakistan on IVUS with such an extended period of follow-up. Our analysis demonstrated that the use of this ancillary modality improves clinical outcomes of PCI in terms of MACE. Similar improvement in MACE has been noted in the previous studies from upper and upper-middle-income countries.5-12

The utilization rate of IVUS in our hospital is 3.0% which in comparison to upper and upper-middle-income countries is significantly low [Figure 4]. The use of IVUS varies in different parts of the world. Data from the USA demonstrated IVUS use in 5.6–20% of cases,13-15 Japanese multicenter PCI registry data show IVUS use in 84% of cases,16 in Italy, IVUS was used in 5.2% of cases in bifurcations lesions,17 and a large center Korean registry showed IVUS use in 27.9% of cases of complex PCI.18 The previously published data from Japan demonstrated frequent use of IVUS in the last decade and that's might be the reason for reduced mortality, stent thrombosis, and in-stent restenosis (ISR) as compared to many European countries.15 The major reason behind low utilization of IVUS was increased cost of the procedure, additional time needed for the procedure, and lack of confidence in intravascular imaging (IVI). However, we observed an upgoing trend of utilization of IVUS in the last several years at our center. But still, the use of IVUS

**Table 2: Procedural details.**

| Vascular access site for procedure |  |
|-----------------------------------|--|
| Femoral                           | 69 (51.5%) |
| Radial                            | 65 (48.5%) |

| Angiographic details             |
|----------------------------------|
| LM disease                       | 46 (34.3%) |
| Single-vessel disease            | 51 (38.1%) |
| Two-vessel disease               | 21 (17.2%) |
| Three-vessel disease             | 23 (17%)   |

| PCI details                      |
|----------------------------------|
| DES                              | 92 (68.6%) |
| BMS                              | 7 (5.2%)   |
| POBA                             | 18 (13.4%) |

| LM main stent diameter (mean)    | 3.5±0.4 mm |
| LM main stent length (mean)      | 25.9±8.1 mm|
| Other vessel's stent diameter    | 3.12±0.5 mm|
| Other vessel's stent length      | 23.6±9.2 mm|
| CABG                             | 8 (6%)     |

LM: Left main. PCI: Percutaneous coronary intervention, DES: Drug-eluting stent, BMS: Bare-metal stent, CABG: Coronary artery bypass grafting

**Table 3: IVUS details.**

**IVUS details (n=134)**

| Pre-stent deployment IVUS done in | 99 (73.9%) |
|-----------------------------------|
| Post-stent deployment IVUS done in | 102 (76.1%) |
| Both pre- and post-stent deployment | 67 (50%) |
| In-stent restenosis               | 36 (26.9%) |
| Calcifications                    | 77 (57.5%) |
| Coronary dissection               | 15 (11.2%) |
| Stent underexpansion              | 46 (34.3%) |
| IVUS of LM                        | 46 (34.3%) |
| IVUS of LAD                       | 94 (70.1%) |
| IVUS of LCX                       | 8 (6%)     |
| IVUS of RCA                       | 12 (9%)    |
| IVUS of ramus intermedius         | 1 (0.8%)   |
| IVUS of diagonal                  | 1 (0.8%)   |
| IVUS of graft                      | 2 (1.5%)   |
| LM MLA (mean)                     | 6.0±2.6 mm |
| LM minimal luminal diameter (mean) | 4.5±0.6 mm |
| Other vessels MLA (mean)          | 4.2±4.2 mm |
| Other vessels diameter (mean)     | 3.98±0.6 mm|

LM: Left main, LAD: Left anterior descending, LCX: Left circumflex, RCA: Right coronary artery, MLA: Minimal luminal area

Figure 2: A 66-year-old gentleman came with complaint of unstable angina. Intravascular imaging of the left anterior descending artery done showing significant calcification (arrow).

Figure 3: A 68-year-old gentleman came with complaint of stable angina. The patient had previous stenting in LAD 6 months back. Intravascular imaging of the left anterior descending artery done showing significant underexpansion of stent (Stent: Solid arrow, vessel wall: Hollow arrow).
technology needs a significant increase to improve both short- and long-term outcomes by decreasing incidences of iatrogenic coronary dissection, stent thrombosis, and ISR. In our study, iatrogenic coronary dissection with IVUS use was zero. Iatrogenic coronary dissection rates of 4.26% were reported by Khalid et al. in the IVUS arm while[7] the SIPS trial reported 3% rate of iatrogenic coronary dissection due to IVUS, with exclusion of chronic total occlusion (CTO) lesions and emergent procedures.[19] A possible explanation for this difference could be relatively smaller sample size in our study.

In our study, post-PCI IVUS evaluating stent expansion revealed suboptimal expansion in \( n = 46 \) (34%) of cases thus requiring further post-dilation. It was also observed in our study that IVUS was more frequently used post PCI for the assessment of adequate stent expansion and ruling out edge dissections in suspected cases. The higher incidence of stent underexpansion can also be explained by selection bias, with IVUS being primarily done in cases where non-optimal post-PCI results such as under expansion were suspected. Our follow-up period in comparison to other studies was longer.[8,19] In the present data, total events rates on follow-up were 13% which is comparable to what Schroeder et al.,[18] observed, 14%, and were 12% in SIP trial.[19] In our study, target vessel/lesion failure was only 2.24% (\( n = 3 \)), which is incredibly very low in comparison to Intracoronary Stenting and Antithrombotic Regimen trial,[20] 14.6%, SIPS trial TLR was 17%, Jeremias et al. have also used IVUS guidance for stent placement and found 33.3% restenosis rate at 6 months.[21] However, we need a multicenter randomized trials and further large sample size studies in this regard. The findings of our study will help to increase the confidence in utilization of IVUS and would improve clinical outcomes.

Two predominant IVI modalities are IVUS and optical coherence tomography (OCT). The basic principle of IVUS imaging is the oscillatory movement of a piezoelectric transducer (crystal), resulting in generation of sound waves when electrically excited.[1] The sound waves generated by transducers propagate through and reflect off different tissues, varying according to acoustic properties of the tissues. OCT generates images by measuring the echo time delay and intensity of light that are reflected/backscattered from the tissues. OCT has high resolution and low penetration while IVUS has lower resolution but high penetrance as compared in Table 5.[22-26] Due to scattering of light from erythrocytes, OCT requires temporary clearance of the vessel lumen using contrast injection to improve image quality.[24]

Our study has several limitations; it’s a retrospective, single-center study, coronary angiography and revascularization were clinically driven, so were performed only in those patients who were symptomatic after the index procedure. IVUS use during PCI was dependent on the operator’s decision either for pre-PCI assessment of lesion or post-PCI, for evaluation of stent expansion or suspicion of dissection. Detailed IVUS parameters such as plaque burden, plaque contents quantification, calcium quantification, or post-PCI measurements were not recorded.

**CONCLUSION**

IVUS technology is an adjunctive tool to coronary angiography in lesions requiring detailed assessment, stent

| Table 4: Follow-up details. | Follow-up (\( n=134 \)) |
|----------------------------|--------------------------|
| MACE (%)                   | 14 (10.4%)               |
| Cardiovascular death (%)   | 3 (2.2%)                 |
| Non-fatal MI (%)           | 3 (2.2%)                 |
| Stroke (%)                 | 1 (0.8%)                 |
| Heart failure (%)          | 4 (3%)                   |
| Life-threatening arrhythmias (%) | 3 (2.2%)           |
| TVR (%)                    | 3 (2.2%)                 |

MACE: Major adverse cardiac event, MI: Myocardial infarction, TVR: Target vessel revascularization.

![Figure 4: Prevalence of IVUS use over years 2013–2020. IVUS: Intravascular ultrasound.](image)

**Table 5: Comparison of IVUS and OCT.**[1,22-26]

|                       | IVUS                          | OCT               |
|-----------------------|-------------------------------|-------------------|
| Source of image       | Ultrasound waves              | Light waves       |
|                       | (near infrared)               |                   |
| Wavelength            | 20–60 µm                      | 1.3 µm            |
| Axial resolution      | 20–170 µm                     | 10–20 µm          |
| Lateral resolution    | 50–260 µm                     | 20–40 µm          |
| Tissue penetration    | 4–8 mm                        | 2–3.5 mm          |
| Pullback type         | Mechanical/ manual            | Mechanical        |
| Pullback length       | 150 mm                        | Up to 150 mm      |
| Pullback speed        | 0.5–1.0 mm/s                  | Up to 40mm/sec    |
| Need for blood        | No                            | Yes               |
| clearance             |                               |                   |

IVUS: Intravascular ultrasound, OCT: Optical coherence tomography. Wavelength, resolution, and penetrance vary by vendor and device used.
deployment, evaluating stent expansion, and dissection which results in a significant decrease in MACE, both in hospital and on follow-up and hence cost effective. Our data might support the broader use of IVUS in both developed and in our part of the world.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Garcia-Garcia HM, Gogas BD, Serruys PW, Bruining N. IVUS-based imaging modalities for tissue characterization: Similarities and differences. Int J Cardiac Imaging 2011;27:215-24.
2. Mintz GS, Popma JJ, Pichard AD, Kent KM, Satler LF, Chuang YC, et al. Limitations of angiography in the assessment of plaque distribution in coronary artery disease: A systematic study of target lesion eccentricity in 1446 lesions. Circulation 1996;93:924-31.
3. Baptista J, di Mario C, Escaned J, Arnese M, Ozaki Y, de Feyter P, et al. Intracoronary two-dimensional ultrasound imaging in the assessment of plaque morphologic features and the planning of coronary interventions. Am Heart J 1995;129:177-87.
4. Sipahi I, Nicholls SJ, Tuzcu EM. Intravascular ultrasound in the current percutaneous coronary intervention era. Cardiol Clin 2006;24:163-73.
5. Li L, Wang L, Zhai CJ, Mou YR, Wang JH, Cui LQ. Clinical utility of intravascular ultrasonography-guided therapy in a small-vessel coronary lesion associated with Type 2 diabetes mellitus. Anatol J Cardiol 2019;22:68-76.
6. Zhang Y, Farooq V, Garcia-Garcia HM, Bourantas CV, Tian N, Dong S, et al. Comparison of intravascular ultrasound versus angiography-guided drug-eluting stent implantation: A meta-analysis of one randomised trial and ten observational studies involving 19,619 patients. Eurointervention 2012;8:855-65.
7. Khalid M, Patel NK, Amgai B, Bakhit A, Khalid M, Kafle P, et al. In-hospital outcomes of angiography versus intravascular ultrasound-guided percutaneous coronary intervention in STElevation myocardial infarction patients. J Community Hosp Intern Med Perspect 2020;10:436-42.
8. Zhang J, Gao X, Kan J, Ge Z, Han L, Lu S, et al. Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: The ULTIMATE trial. J Am Coll Cardiol 2018;72:3126-37.
9. Tian NL, Gami SK, Ye F, Zhang JJ, Liu ZZ, Lin S, et al. Angiographic and clinical comparisons of intravascular ultrasound-versus angiography-guided drug-eluting stent implantation for patients with chronic total occlusion lesions: Two-year results from a randomised AIR-CTO study. Eurointervention 2015;10:1409-17.
10. Kim BK, Shin DH, Hong MK, Park HS, Rha SW, Mintz GS, et al. Clinical impact of intravascular ultrasound-guided chronic total occlusion intervention with zotarolimus-eluting versus biolimus-eluting stent implantation: Randomized study. Circ Cardiovasc Interv 2015;8:e002592.
11. Hong SJ, Kim BK, Shin DH, Nam CM, Kim JS, Ko YG, et al. Effect of intravascular ultrasound-guided vs angiography-guided everolimus-eluting stent implantation: The IVUS-XPL randomized clinical trial. JAMA 2015;314:2155-63.
12. Kim JS, Kang TS, Mintz GS, Park BE, Shin DH, Kim BK, et al. Randomized comparison of clinical outcomes between intravascular ultrasound and angiography-guided drug-eluting stent implantation for long coronary artery stenoses. JACC Cardiovasc Interv 2013;6:369-76.
13. Dattilo PB, Prasad A, Honeycutt E, Wang TY, Messenger JC. Contemporary patterns of fractional flow reserve and intravascular ultrasound use among patients undergoing percutaneous coronary intervention in the United States: Insights from the national cardiovascular data registry. J Am Coll Cardiol 2012;60:2337-9.
14. Mentias A, Sarrazin MV, Saad M, Panaich S, Kapadia S, Horwitz PA, et al. Long term outcomes of coronary stenting with and without use of intravascular ultrasound. JACC Cardiovasc Interv 2020;13:1880-90.
15. Lemor A, Patel N, Jain T, Baber U, Hernandez G, Villablanca P, et al. Trends and outcomes of intravascular imaging-guided percutaneous coronary intervention in the United States. Crit Pathw Cardiol 2020;19:69-74.
16. Kuno T, Numasawa Y, Sawano M, Abe T, Ueda I, Kodaira M, et al. Real-world use of intravascular ultrasound in Japan: A report from contemporary multicenter PCI registry. Heart Vessels 2019;34:1728-39.
17. Biondi-Zoccai G, Sheiban I, Romagnoli E, de Servi S, Tamburino C, Colombo A, et al. Similarities and differences. Int J Cardiovasc Imaging 2011;27:215-24.
18. Hur SH, Kang SJ, Kim YH, Ahn JM, Park DW, Lee SW, et al. Impact of intravascular ultrasound-guided percutaneous coronary intervention on long-term clinical outcomes in a real world population. Catheter Cardiovasc Interv 2013;81:407-16.
19. Frey AW, Hodgson JM, Müller C, Bestehorn HP, Roskamm H. Ultrasound-guided strategy for provisional stenting with focal balloon combination catheter: Results from the randomized strategy for intracoronary ultrasound-guided PTCA and stenting (SIPS) trial. Circulation 2000;102:2497-502.
20. Kastrati A, Schühlen H, Hausleiter J, Walter H, Zitzmann-Roth E, Hadamitzky M, et al. Restenosis after coronary stent placement and randomization to a 4-week combined antiplatelet or anticoagulant therapy: Six-month angiographic follow-up of the intracoronary stenting and antithrombotic regimen (ISAR) trial. Circulation 1997;96:462-7.
21. Jeremias A, Görge G, Konorza T, Haude M, von Birgelen C, Ge J, et al. Stepwise intravascular ultrasound (IVUS)
guidance of high-pressure coronary stenting does not result in an improved acute or long-term outcome: A randomized comparison to “final-look” IVUS assessment. Catheter Cardiovasc Interv 1999;46:135-41.

22. Rahim HM, Shlofmitz E, Gore A, Hakemi E, Mintz GS, Maehara A, et al. Ivus-versus OCT-guided coronary stent implantation: A comparison of intravascular imaging for stent optimization. Curr Cardiovasc Imaging Rep 2018;11:1-5.

23. Prati F, Regar E, Mintz GS, Arbustini E, di Mario C, Jang IK, et al. Expert review document on methodology, terminology, and clinical applications of optical coherence tomography: Physical principles, methodology of image acquisition, and clinical application for assessment of coronary arteries and atherosclerosis. Eur Heart J 2010;31:401-15.

24. Maehara A, Mintz GS, Stone GW. OCT versus IVUS: Accuracy versus clinical utility. JACC Cardiovasc Imaging 2013;6:1105-7.

25. Kubo T, Akasaka T, Shite J, Suzuki T, Uemura S, Yu B, et al. OCT compared with IVUS in a coronary lesion assessment: The OPUS-CLASS study. JACC Cardiovasc Imaging 2013;6:1095-104.

26. Kawase Y, Suzuki Y, Ikeno F, Yoneyama R, Hoshino K, Ly HQ, et al. Comparison of nonuniform rotational distortion between mechanical IVUS and OCT using a phantom model. Ultrasound Med Biol 2007;33:67-73.

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