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Long-term impact of intravascular ultrasound-guidance for percutaneous coronary intervention on unprotected left main. The IMPACTUS-LM, an observational, multicentric study

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ABSTRACT

Introduction: The potential benefit on long term outcomes of Percutaneous Coronary Intervention (PCI) on Unprotected Left Main (ULM) driven by IntraVascular UltraSound (IVUS) remains to be defined.
Methods: IMPACTUS LM-PCI is an observational, multicenter study that enrolled consecutive patients with ULM disease undergoing coronary angioplasty in 13 European high-volume centers from January 2002 to December 2015. Major Adverse Cardiovascular Events (MACEs) a composite of cardiovascular (CV) death, target vessel revascularization (TVR) and myocardial infarction (MI) were the primary endpoints, while its single components along with all cause death the secondary ones.
Results: 627 patients with ULM disease were enrolled, 213 patients (34%) underwent IVUS-guided PCI while 414 (66%) angioguided PCI. Patients in the two cohorts had similar prevalence of risk factors except for active smoking and clinical presentation. During a median follow-up of 7.5 years, 47 (22%) patients in the IVUS group and 211 (51%) in the angio-guided group underwent the primary endpoint (HR 0.42; 95% CI [0.31–0.58] $p < 0.001$). After multivariate adjustment, IVUS was significantly associated with a reduced incidence of the primary endpoint (adj HR 0.39; 95% CI [0.23–0.64], $p < 0.001$), mainly driven by a reduction of TVR (ad HR 0.30, 95%

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CI [0.15–0.62], $p = 0.001$) and of all-cause death (adj HR 0.47, 95% CI [0.28–0.82], $p = 0.008$). IVUS use, age, diabetes, side branch stenosis, DES and creatinine at admission were independent predictors of MACE.
Conclusions: In patients undergoing ULM PCI, the use of IVUS was associated with a reduced risk at long-term follow-up of MACE, all-cause death and subsequent revascularization.

1. Introduction

The management of critical stenosis of the Left Main Coronary Artery (LMCA) has deeply changed during the last years, due to the improvement of both surgical and percutaneous revascularization techniques [1,2].

These improvements allowed Percutaneous Coronary Revascularization (PCI) to be comparable in terms of death and myocardial infarction with Coronary Artery Bypass Graft (CABG), especially in patients with low and intermediate anatomical complexity [3,4]. However, left-main coronary interventions remain a high-risk and highly complex procedure, in which intra-vascular imaging gained a relevant role over the years [5].

Actually, the angiographic evaluation does not always allow the identification of the correct sizing of the vessel, calcium burden, involvement of the side branch, and the correct expansion/apposition of the stents.

From a technical point of view, IVUS has a key role in the pre-procedural phase (providing information for choice of strategy), in the intraprocedural phase (evaluation of effective plaque preparation, correct wires positioning), and in the post-procedural phase (correct expansion/apposition of the stent, evidence of edge dissection, correct carina distribution).

Over the years, an IVUS-based approach was demonstrated to be superior to angio-guided PCI in terms of Major Cardiac Adverse Events (MACE) and subsequent revascularization, both consistently for bare metal stents (BMS) and drug-eluted stents (DES) [6–9].

However, while the short and intermediate-term advantages of IVUS-guided PCI are well-established, there exists a critical knowledge gap regarding the enduring impact of such guidance. It may be argued that the aging process and comorbidities, along with the natural progression of atherosclerosis could mitigate the periprocedural and mid-term benefits of ancillary PCI techniques, potentially resulting in non-significant differences in hard outcomes over a long-term follow-up [10].

Since IVUS utilization in real-life cath lab workflow is still limited both by reimbursement issues and by the confidence of physicians with the clinical impact of evidence, it appears paramonunt to establish the durability of procedural benefits [11].

Therefore, the aim of the IMPACTUS LM study is to evaluate the long-term impact on major clinical endpoints of left main IVUS-guided PCI compared with left main PCI guided by angiography alone.

2. Methods

2.1. Study design

IMPACTUS LM-PCI (long term IMPACT of ivUS guided LM-PCI) is an observational, retrospective, multicenter, international study that enrolled consecutive patients with unprotected left main disease undergoing coronary angioplasty in 13 European high-volume centers from 1st January 2002 to 31st December 2015 with a long-term follow-up available.

2.2. Inclusion criteria and definitions

Patients >18 years/old and with unprotected left main disease with an indication for percutaneous myocardial revascularization were included, according to the study protocol.

The left main PCI indication, except for patients with hemodynamic instability, has always been performed after collegial evaluation by the local Heart Team of the participating centers where the patients were hospitalized; in case of hemodynamic instability, the choice of intervention was left to the operator. Patients underwent CABG, with life expectancy<12 months due to comorbidities, with cardiogenic shock at presentation and with intra-hospital death were excluded. Only patients with at least 2-year follow-up available were included in the registry. Data collected included: pre-procedural demographic and clinical characteristics, anatomical complexity characteristics of lesions, technical procedural characteristics, and pharmacological therapy at discharge.

Anatomic complexity features were gathered from a review of angiographic images by two study investigators and included number of diseased vessels, the presence of severe calcification (requiring debulking), the SYNTAX score, the percentage of left main stenosis, the severity of side branch involvement, the Medina-class and the angle of bifurcation between the anterior descending artery and the circumflex artery. The choice of angiographic-only or IVUS-guided strategy was driven by the operator's preferences and experience.

From the combined review of the procedural reports and the angiographic images, related data were collected: including the number and type of stent implanted, their diameter and length, the bifurcation technique used, discriminating single stent (provisional) from 2-stent strategy (T-stent, Culotte and Crush technique) and the techniques used to optimize stent implantation (POT and/or Kissing Balloon).

Procedures were performed by experienced operators (> 250 PCIs/year and > 25 LM PCIs/year) and IVUS assessments were performed with manual or automatic pullback with commercially available systems (Boston Scientific Corporation, San Jose, CA; or Volcano Corporation, Rancho Cordova, CA).

The post-procedure antiplatelet therapy administered to the patients was chosen according to the European guidelines at the time of the coronary angioplasty [12].

The follow-up of the clinical events was carried out by clinical visits, patient telephone contact, and, when available, by reviewing the informatic system of the referral hospital.

Individual patient data was inserted into a pre-specified database and the correctness and appropriateness of individual variables were substantiated and verified by 4 study investigators. Written informed consent was obtained from all patients before the procedure and the study was approved by the local Ethics Committees.

2.3. Study endpoint

The primary endpoint of the study was major cardiovascular events (MACE), a composite of cardiovascular (CV) death, target vessel revascularization (TVR) and myocardial infarction (MI). Secondary endpoints were all-cause death and the single components of the primary endpoint. The follow-up of the events was collected at the time of the insertion into the database by the study investigators.

2.4. Statistical analysis

Continuous data are reported as mean and standard deviation or median and interquartile range (IQR) if skewed and categorical variables as frequencies and percentages, as appropriate. Differences in clinical and procedural characteristics according to IVUS use were examined using the 2-tailed Kruskal-Wallis test for continuous data and by applying the Chi-squared test for categorical data, with *p*-values below 0.05 (two-tailed) considered significant. Survival curves and the related cumulative incidence curves were obtained using the Kaplan-Meier method. Crude and multivariable-adjusted survival analyses were performed using a proportional hazard regression model of Cox, with a calculation of their respective hazard ratio (HR) and their confidence interval (CI) at 95%. All the baseline and procedural characteristics associated with the primary endpoint in univariable analysis (at $p \leq 0.10$) were entered into a Cox regression model in a step-wise fashion. Moreover, a propensity score (PS) was generated for each patient from a multivariable logistic regression model based on pre-treatment covariates as independent variables with IVUS use as dependent outcome. Pairs of patients were derived using greedy 1:1 matching with a caliper of width of 0.2 standard deviation of the logit of the PS. A Cox regression model, stratified by propensity was used to analyze outcomes. All the variables used for PS analysis as well as the *p* values of their standardized differences in the PS population are reported in **Supplemental Table 1**. All analyses were performed on complete cases with STATA v17 (StataCorp, College Station, Texas) and SPSS software.

3. Results

3.1. Baseline characteristics

Between 1st January 2002 and 31st December 2015, a total of 627 patients with unprotected left main disease were enrolled in the IMPACTUS LM-PCI study: 213 patients (34%) underwent IVUS-guided PCI while 414 (66%) angio-guided PCI; the study-flow chart is summarized in Fig. 1.

Baseline clinical, angiographic, and procedural characteristics of the whole population are presented in Table 1.

Patients in the IVUS-guided group compared to the angio-guided group had similar age (69 vs 68, $p = 0.68$) and prevalence of risk factors (hypertension 87% vs 83%, $p = 0.19$; hyperlipidemia 71% vs 65%, $p = 0.12$; diabetes 26% vs 23%, $p = 0.22$) except for active smoking (48% vs 34%, $p = 0.001$) and clinical presentation (STEMI 21% vs 14%, NSTEMI 25% vs 20%, unstable angina 20% vs 32%, p for trend = 0.02). The patients in the IVUS-guided group showed an increased anatomical complexity (assessed by the SYNTAX score and distal left main involvement), compared with patients who received angio-guided revascularization, Table 1.

Table 1
Baseline Characteristics.

	Angio-guided PCI ($n = 414$)	IVUS guided PCI ($n = 213$)	P value
Age	69 (60–76)	68 (59–75)	0.68
Female	115 (28)	60 (28)	0.92
Hypertension	345 (83)	186 (87)	0.19
Hyperlipidemia	270 (65)	152 (71)	0.12
Diabetes	94 (23)	56 (26)	0.22
Active Smoker	140 (34)	103 (48)	**0.001**
Previous PCI	126 (30)	67 (31)	0.79
Clinical presentation			**0.02**
STEMI	59 (14)	44 (21)	
NSTEMI	84 (20)	54 (25)	
Unstable angina	131 (32)	43 (20)	
Stable Angina	139 (34)	72 (34)	
Creatinine	1.1 (0.9–1.3)	1.2 (0.9–1.5)	0.12
LVEF	50 (45–56)	55 (48–60)	**0.008**
Site of left main			**<0.001**
Ostial	99 (24)	17 (8)	
Mid	66 (16)	18 (9)	
Distal	249 (60)	176 (83)	
Medina 111	95 (23)	35 (16)	0.12
Number of diseased vessels	2 (1–3)	2 (2–3)	0.54
Severe calcifications	53 (13)	23 (11)	0.15
SB stenosis >70%	227 (55)	53 (25)	**<0.001**
Syntax Score	24 (22–27)	21.8 (20–27)	**<0.001**
BMS	99 (24)	5 (2)	**<0.001**
DES	315 (76)	208 (98)	**<0.001**
Stent strategy			0.60
1-stent	351 (84)	174 (82)	
2-stents	63 (15)	39 (18)	
POT	150 (36)	204 (96)	**<0.001**
Final Kissing Balloon	144 (35)	189 (89)	**<0.001**
Diameter max	3.5 (3.5–3.6)	4 (3.5–4)	**<0.001**
Length of stent	16 (12–20)	23 (16–28)	**<0.001**

Legend: PCI percutaneous coronary intervention, CABG coronary artery bypass graft, STEMI ST-elevation myocardial infarction, NSTEMI non-ST elevation myocardial infarction, LVEF Left ventricle ejection fraction, SB Side Branch, BMS bare metal stent, DES Drug-eluting stent, POT Proximal Optimization, IVUS Intravascular ultrasound.

Regarding procedural data, patients treated with IVUS-guided PCI were more often revascularized with drug-eluted stent implantation (98% vs 76%, $p = 0.001$) and more often received optimization of PCI with POT (Proximal Optimization Technique; 96% vs 36%, p = 0.001)

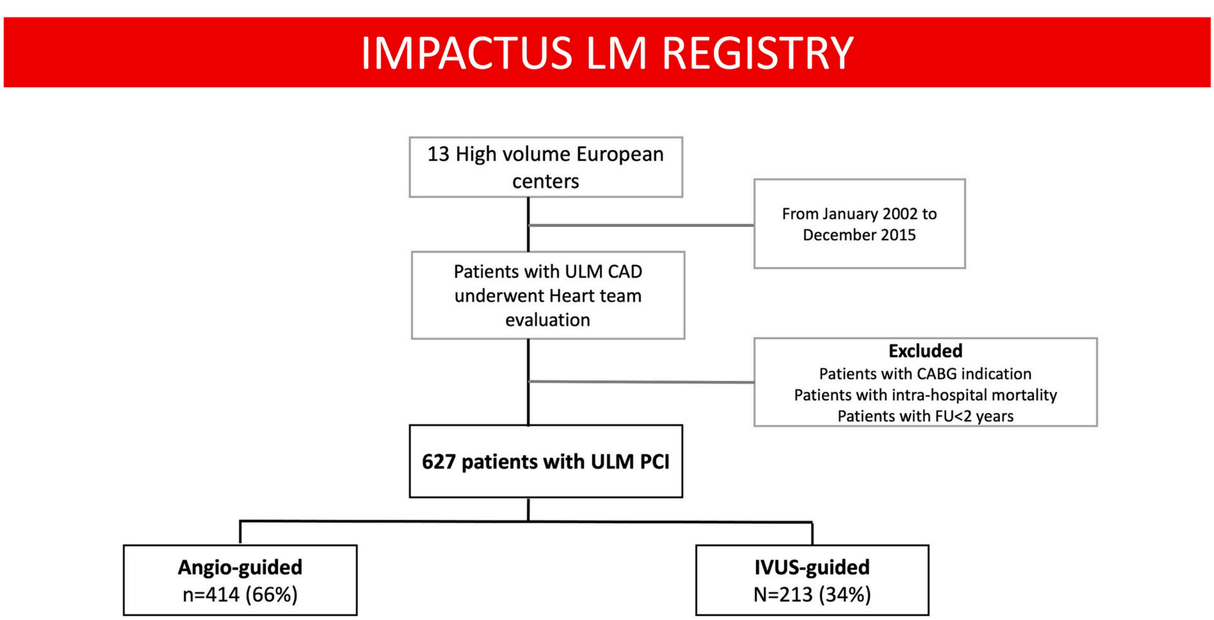

Fig. 1. The study-flow chart.

and FKB (Final Kissing Balloon; 89% vs 35%, p = 0.001).

3.2. Primary outcome

The median follow-up time was 7.5 years (IQR 2.3–12.3). During follow-up, 47 (22%) patients in the IVUS group and 211 (51%) in the angio-guided group underwent the primary endpoint ($p < 0.001$). In the unadjusted Kaplan–Meier time-to-event curves, patients in the IVUS group had a lower cumulative incidence of the primary endpoint compared to the angio-guided group (p at log rank <0.001, unadjusted HR 0.42; 95% CI [0.31–0.58]), Fig. 2. The benefit of an IVUS-guided PCI was consistent across all the time periods, as confirmed by the landmark analysis at 1 and 5 years, **Supplementary Fig. 1**.

After multivariate adjustment, IVUS was significantly associated with a reduced incidence of the primary endpoint (adjusted HR 0.39; 95% CI [0.23–0.64]), Table 2.

The improved outcome in the IVUS-guided LM PCI was confirmed also after propensity-score matching (25% vs. 54%, $p < 0.01$), Table 3.

3.3. Secondary outcomes

During follow-up, all-cause death occurred in 39 (18%) patients in the IVUS group and 182 (44%) in angio-guided group (HR 0.34 [0.22–0.60], $p < 0.001$), CV death in 19 (9%) patients in IVUS group and 67 (19%) in angio-guided (HR 0.55 [0.33–0.92], $p = 0.002$), TVR in 22 (10%) patients in IVUS group and 105 (25%) in angio-guided (HR 0.44 [0.28–0.69], p < 0.001), while MI in 6 (3%) patients in IVUS group and 39 (9%) in angio-guided group, $p = 0.005$. Unadjusted cumulative incidence of all-cause death, CV death, TVR and MI are reported in Fig. 3. After multivariate adjustment, IVUS use was associated with a reduced incidence of all-cause death (adjusted HR 0.47 [0.28–0.82], $p = 0.008$) and TVR (adjusted HR 0.30 [0.15–0.62, $p = 0.001$), but not CV death (adjusted HR 0.51 [0.23–1.18], $p = 0.117$) and MI (adjusted HR 0.87 [0.25–3,00], $p = 0.83$). The results were consistent also in the propensity-score matching population, Table 3.

3.4. Subgroup analysis

Subgroup analysis regarding the impact of IVUS on the primary endpoint is reported in Fig. 4. No evidence of interaction between IVUS and other baseline characteristics both clinical and procedural was identified after adjusting for multiple comparisons (Bonferroni test) except for acute coronary syndrome at presentation (p for interaction = 0.01).

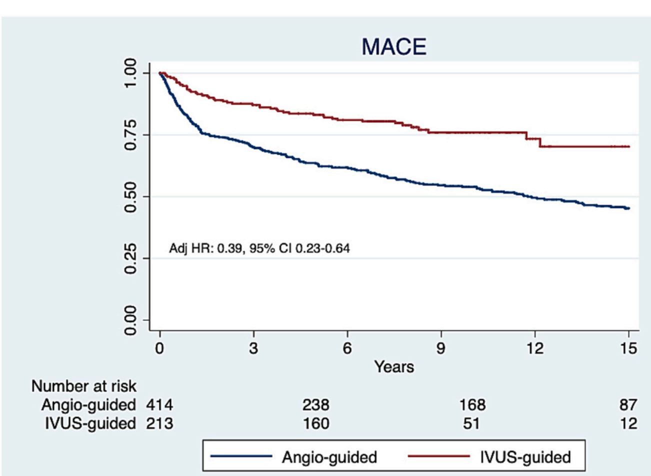

Fig. 2. KM curves in IVUS guided vs Angioguided cohorts.

Table 2
Predictors of primary endpoint at follow-up included in the multivariate model.

	Univariate HR 95% CI	P value	Multivariate HR 95% CI	P value
IVUS use	*0.42 (0.31–0.58)*	*<0.001*	***0.39 (0.23–0.65)***	***<0.001***
Age > 70 years	1.58 (1.23–2.02)	<0.001	**1.47 (1.12–1.93)**	**0.006**
Diabetes	1.17 (0.99–1.38)	0.06	**1.24 (1.03–1.50)**	**0.03**
Active smoker	0.72 (0.56–0.93)	0.01	0.93 (0.70–1.23)	0.59
Medina 111	1.14 (0.98–1.34)	0.09	1.10 (0.86–1.35)	0.52
SB stenosis >70%	1.82 (1.43–2.32)	<0.001	**1.57 (1.17–2.11)**	**0.003**
DES	0.59 (0.46–0.77)	<0.001	**0.64 (0.49–0.85)**	**0.002**
Diameter max	0.71 (0.54–0.95)	0.02	0.89 (0.66–1.19)	0.42
POT	0.74 (0.58–0.95)	0.02	1.26 (0.88–1.79)	0.20
Final Kissing Balloon	0.71 (0.55–0.91)	0.007	0.97 (0.70–1.36)	0.87
Syntax score	1.03 (1.01–1.05)	0.003	0.99 (0.97–1.02)	0.75
Creatinine at admission	1.29 (1.14–1.46)	<0.001	**1.24 (1.07–1.43)**	**0.004**
LVEF<40%	1.47 (1.06–2.03)	0.02	1.25 (0.89–1.77)	0.20
Year of procedure	0.57 (0.42–0.77)	<0.001	1.29 (0.76–2.18)	0.34

Legend: LVEF Left ventricle ejection fraction, SB Side Branch, BMS bare metal stent, DES Drug-eluting stent, POT Proximal Optimization, IVUS Intravascular ultrasound.

Table 3
Incidence of primary and secondary endpoints in the overall and PS matched population.

	All population			PS matched population		
	Angio-guided PCI (n = 414)	IVUS guided PCI (n = 213)	P value	Angio-guided PCI ($n = 91$)	IVUS guided PCI (n = 91)	P value
MACE	211 (51%)	47 (22%)	<0.001	49 (54%)	23 (25%)	<0.001
All cause death	182 (44%)	39 (18%)	<0.001	33 (36%)	17 (19%)	0.008
CV death	67 (19%)	19 (9%)	0.002	13 (15%)	7 (8%)	0.12
TVR	105 (25%)	22 (10%)	<0.001	36 (40%)	11 (12%)	<0.001
MI	39 (9%)	6 (3%)	0.005	8 (9%)	7 (8%)	0.79

4. Discussion

IMPACTUS LM-PCI is an observational, retrospective, multicenter, and international study comparing the long-term follow-up of angiographic vs IVUS-guided angioplasty in patients undergoing unprotected left main PCI.

The most important findings of the data reported can be summarized as: 1) use of IVUS for left main PCI was associated with a lower MACE rate at a 15-year follow-up in the overall and in the PS matched population, 2) mortality for all causes and TVR were significantly lower in patients undergoing LM-PCI IVUS-guided, 3) the benefit of IVUS use was consistent across all the subgroups and in the landmark analysis after 1 year and after 5 years, 4) IVUS use, age, diabetes, side branch stenosis, DES and creatinine at admission were independent predictors of MACE

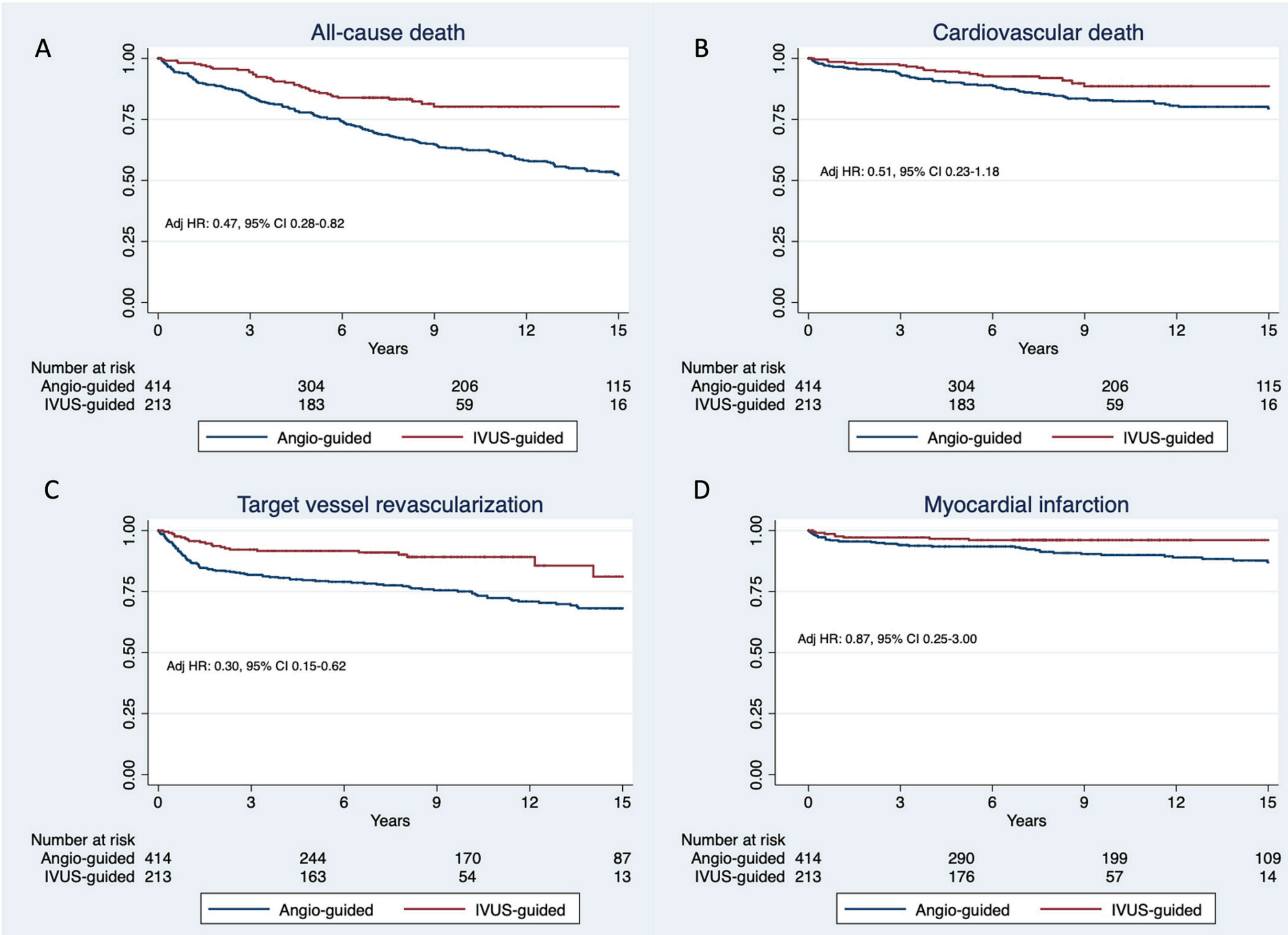

Fig. 3. Unadjusted cumulative incidence of all-cause death, CV death and MI.

in LM PCI.

The use of intracoronary imaging allows an accurate assessment of the coronary lesion providing the operators highly relevant data that cannot be evaluated correctly by angiography alone, including the real size of the vessel and plaque composition [13].

These informations not only allow a correct plaque debulking for the correct implantation of the stent, but also make the procedure safer from a technical point of view, especially in the context of left main disease [14,15]. Intravascular imaging could contribute to a bigger stent size which is associated with decreased rate of stent restenosis [16]. Recently the ILUMIEN IV trial reported a bigger minimal stent area in the OCT guided group compared to the angiography guided group, although a difference in MACE was not observed in the study [17]. Consistently, in our study, patients in the IVUS guided group showed significantly higher stent diameter and stent length and a higher number of POT and final kissing balloon performed [18]. Moreover, post-PCI IVUS examination can ensure optimal stent strut apposition and expansion with subsequent post-dilatation and achieve larger stent diameters [15]. Thus, the beneficial effect of intravascular imaging on clinical outcomes may be remarkable in patients undergoing PCI for complex coronary lesions, such as bifurcation PCI, especially in LMCA disease. The recent OCTOBER trial reported a reduction of MACE in OCT guided PCI compared to angiography guided PCI in patients with true bifurcation PCI. However, only 20% of patients enrolled had a LMCA PCI, while the majority of patients had a LAD-Dg bifurcation treatment [19].

To date the currently ESC and AHA guidelines recommend the use of IVUS in LM PCI with a class IIA recommendation [20,21]. Data in the literature from randomized trials are still limited, however, the latest meta-analysis and observational studies suggest a superiority, in terms of mortality from all causes, MI, TVR and stent thrombosis of left main angioplasty guided by intra-vascular imaging versus angiography alone at short and mid-term follow-up [22–25]. Our results confirmed that the use of IVUS for left main PCI is associated with a lower MACE rate at long-term follow-up and also a lower incidence of mortality for all causes and TVR. The results were consistent regardless of the type of bifurcation lesion (Medina class and side branch stenosis percentage), the presence of severe calcifications, the extent of the disease and bifurcation technique with 1 or 2 stents. Interestingly, we observed a possible significant interaction of IVUS use in patients with ACS where IVUS use could a have a less marked benefit.

In routine clinical practice, the use of IVUS for LMCA PCI has increased and IVUS-guided PCI was performed in >70% of patients enrolled in the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) and NOBLE (Nordic–Baltic–British Left Main Revascularization) clinical trials [26–27]. However, data on long term impact of IVUS guided PCI in LM are scant in literature.

Recently, the 10-year follow-up of the MAIN Compare registry showed that the use of IVUS in left main PCI is associated with a lower risk of all-cause mortality and a composite of death, myocardial infarction, and stroke, while the reduction in TVR and MI was not significant [27]. In this context, our results consistently reported a lower incidence of MACE, all-cause death and also TVR in the IVUS guided PCI group at long-term follow-up with a very similar incidence of all the

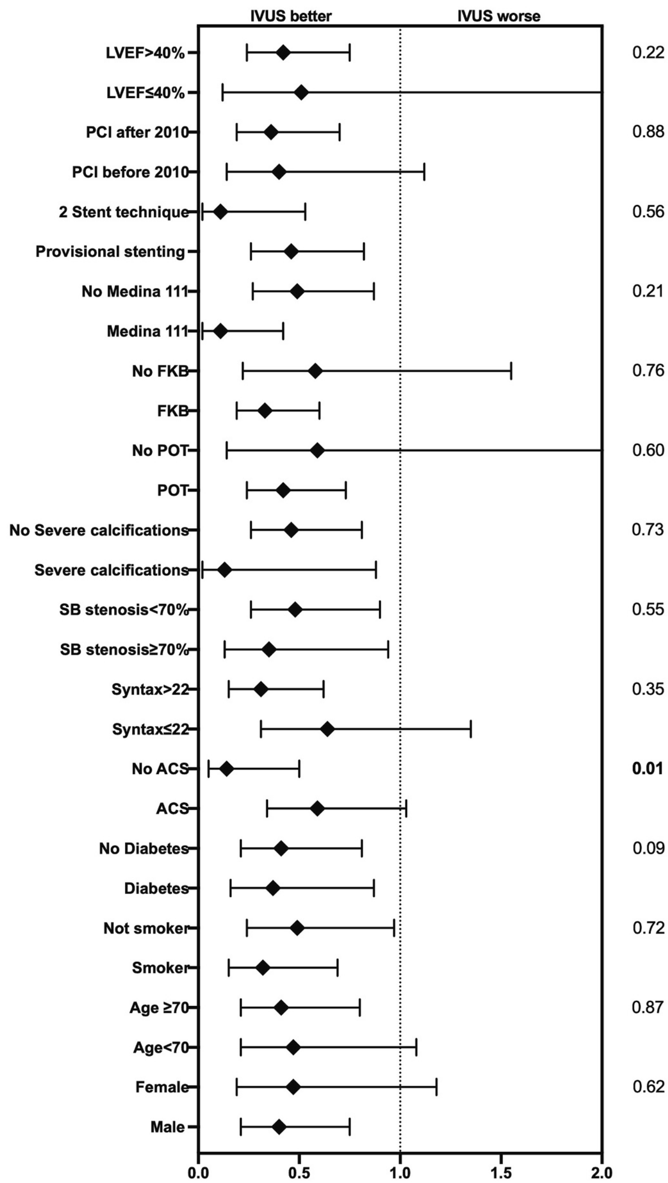

Fig. 4. Subgroup analysis regarding the impact of IVUS on the primary endpoint.
Legend: LVEF Left ventricle ejection fraction, SB Side Branch, BMS bare metal stent, DES Drug-eluting stent, POT Proximal Optimization, IVUS Intravascular ultrasound.

endpoints compared to the MAIN compare registry [28].

Of note, the advantage of using IVUS starts as early as the first year after the procedure, a period in which there is known to be an increased risk of stent thrombosis and TVR, but it consistently maintained also after 1 year and after 5 years, as reported in the landmark KM curves. Beyond the stent implantation optimization, IVUS could led to a more efficient lesion evaluation and burden of coronary disease also outside the culprit artery, as reported by an increased total length of stent implanted in our study, which can contribute to a reduction of MACE also after many years from the procedure.

4.1. Which role for IVUS in left main PCI and complex and high-risk procedures?

Despite accumulating evidence consistently pointing towards a significant improvement in both procedural and long-term outcomes with IVUS-guided PCI for left main lesions, this ancillary technique remains underutilized in clinical practice, arguably less than its potential warrants [29]. Clinical guidelines struggle to position IVUS within more stringent recommendation classes that would probably endorse its broader implementation. The existing body of literature, including the compelling findings from the recent RENOVATE trial, underscores the need for a paradigm shift in the adoption of IVUS in left main PCI, particularly in the intricate landscape of complex and high-risk procedures (CHIP) [30]. In these scenarios, where intricate lesion morphology and composition pose unique challenges, IVUS emerges as an invaluable tool for comprehensive intravascular imaging. The trial's findings emphasize the pivotal role of IVUS, positioning it as a cornerstone in the management of CHIP cases, in conjunction with plaque modification techniques, mechanical support strategies and the establishment of a safe vascular access [31,32]. This study, in alignment with previous research, underscores the role of IVUS in optimizing also long-term outcomes for patients being treated for such challenging scenarios. However, the current utilization patterns and guideline recommendations fail to reflect the robust evidence supporting IVUS's efficacy in enhancing procedural precision and long-term success. Looking forward, ongoing randomized controlled trials, such as the OPTIMAL (Optimization of Left Main Percutaneous Coronary Intervention With Intravascular Ultrasound; NCT04111770) and INFINITE (Intravascular Ultrasound-Versus Angiography-Guided Percutaneous Coronary Intervention for Patients With Left Main Bifurcation Lesion; NCT04072003) trials, hold the promise of reshaping the narrative around IVUS in left main PCI. These trials are expected to provide compelling data that could bridge the existing gap between the proven benefits of IVUS and its underutilization in real-world clinical scenarios.

5. Limitations

Our study has several limitations. First, this was not a randomized controlled study and although we used multivariate analysis and propensity score matching, baseline characteristics of the two populations were different, in particular regarding stent kind and technical procedural aspects, and a potential bias due to the effect of unmeasured and unknown variables cannot be excluded [33,34]. Second, the choice of IVUS- or angiography-guided PCI was left to the physician's discretion; thus, our findings might be venerable to selection bias. Moreover, the data relating to the method of use of the IVUS is not available, therefore it is not possible to establish exactly whether the advantage is related to a pre-procedural evaluation, only post-procedural or both. Moreover, IVUS features and images of both stented and non-stented lesions were not recorded and analyzed in the current study consequently limiting the inferential aim in prediction of adverse events. Participating centers were all located in Europe; therefore, our results may not be generalizable to not-European countries. Further, the time gap in which the procedures were performed is >10 years so, although we corrected for the time of PCI and stent type, it appears evident that the outcomes of the procedures performed before 2010 can be affected by the use of old generation stents and by the less expertise of the operators. POT and FKB were less often performed in the non IVUS group. This could have been mainly driven by the poor stepwise approach during LM bifurcation PCI in this group which inevitably was missed and not corrected by IVUS and it could be affected the results, although POT and FKB were not independent predictors of MACE when corrected in the multivariable model. The cause of death was not assessed for all the patients and the events were not centrally adjudicated; thus the possibility of an adjudication bias could not be excluded especially for CV death. Finally, quantitative IVUS or angiographic analyses were not performed in this registry. Therefore, the relationship of quantitative imaging parameters and clinical outcomes could not be assessed.

6. Conclusion

In a real-world, multicentric cohort of patients undergoing LM PCI, the use of IVUS was associated with a reduced risk at long-term follow-up of MACE, all-cause death and TVR, consistently across all the subgroups. Randomized controlled trials are needed to address this topic and to guide future guidelines indications.

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CRediT authorship contribution statement

Ovidio de Filippo: Conceptualization, Writing – original draft, Writing – review & editing. **Andrea Sardone:** Conceptualization, Writing – original draft, Writing – review & editing. **Piera Capranzano:** Supervision, Validation, Visualization, Writing – review & editing. **Federico Conrotto:** Supervision, Validation, Visualization, Writing – review & editing. **Imad Sheiban:** Supervision, Validation, Visualization, Writing – review & editing. **Federico Giacobbe:** Validation, Visualization, Writing – review & editing. **Claudio Laudani:** Investigation, Writing – review & editing. **Javier Escaned:** Writing – review & editing. **Sergio Raposeiras Roubin:** Writing – review & editing. **Massimo Mancone:** Writing – review & editing. **Christian Templin:** Writing – review & editing. **Alessandro Candreva:** Writing – review & editing. **Daniela Trabattoni:** Writing – review & editing. **Giulio Stefanini:** Writing – review & editing. **Alaide Chieffo:** Writing – review & editing. **Bernardo Cortese:** Writing – review & editing. **Gianni Casella:** Writing – review & editing. **Wojciech Wojakowski:** Writing – review & editing. **Francesco Colombo:** Supervision, Validation, Visualization, Writing – review & editing. **Gaetano Maria De Ferrari:** Validation, Visualization, Writing – review & editing. **Giacomo Boccuzzi:** Validation, Visualization, Writing – review & editing. **Fabrizio D'Ascenzo:** Formal analysis, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing. **Mario Iannaccone:** Conceptualization, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

None.

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