Letter to the Editor

Intravascular ultrasound-guided versus angiography-guided percutaneous coronary intervention in patients with unprotected left main coronary artery disease: a systematic review and meta-analysis of randomized controlled trials and propensity score-matched studies

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The unprotected left main coronary artery (ULMCA) disease is regarded as the highest-risk lesion subset of coronary artery disease (CAD). It is linked to significantly higher risks of cardiovascular morbidity and mortality when compared to other obstructive CAD. It has a mortality rate of up to 50% on a 3-year follow-up if left untreated [1]. For individuals with unprotected LMCA disease, the conventional revascularization method has been coronary artery bypass surgery (CABG).

With the development of percutaneous management of the LMCA lesions, percutaneous coronary intervention (PCI) using drug-eluting stents (DES) is now recognized as an alternative for CABG in some individuals and midterm clinical follow-up has shown it to be safe and practical [2]. In the landmark EXCEL trial, PCI was non-inferior to CABG at 3-year follow-up in patients with significant coronary artery stenosis in terms of death, stroke, or myocardial infarction [3]. However, the clinical outcomes of patients undergoing angiography-guided PCI for complex lesions are significantly worse than those of patients with noncomplex lesions. Moreover, it is restricted to a two-dimensional representation of the anatomy of the coronary.

Intravascular ultrasound (IVUS) is a high-resolution intracoronary imaging modality that can help overcome this limitation as it provides a detailed 3-dimensional tomographic view of coronary plaque, blood vessels, and stent morphological characteristics, which can guide optimal stent implantation [4]. This meta-analysis aims to investigate the clinical impact of IVUS guidance versus angiography guidance in ULMCA PCI by pooling all the randomized controlled trials (RCTs) and propensity score-matched (PSM) studies published to date.

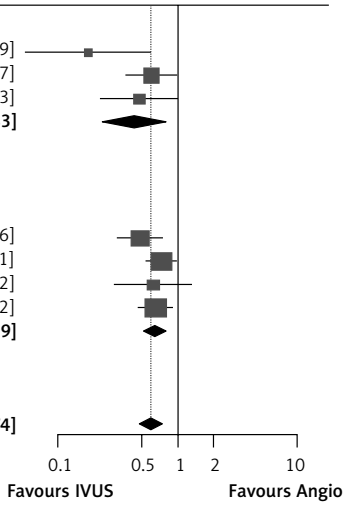
This study followed the guidelines established by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).

A comprehensive literature search was performed using PubMed, Embase, the Cochrane Library, and ClinicalTrials.gov from inception to March 15, 2024. The search strategy was based on keywords related to "IVUS", "angiography", "PCI" and "ULMCA". We included all RCTs and observational studies that performed PSM analysis. The quality assessment of the included RCTs was performed using version 2 of the Cochrane Risk of Bias (RoB 2.0) tool and PSM studies were assessed using the Cochrane Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) tool. The primary outcome included major adverse cardiovascular events (MACE). The secondary outcomes included all-cause death, cardiac death, myocardial infarction (MI), target lesion revascularization (TLR), target vessel revascularization (TVR), and stent thrombosis (ST). We conducted a subgroup analysis based on the study design (RCTs vs. PSM studies). R version 4.3.2 was used for conducting meta-analysis. The pooled risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using the random effects model.

We included 12 studies (3 RCTs and 9 PSM studies) in our meta-analysis. The study screening and selection process is shown in the PRISMA flowchart Supplementary Figure S1. We observed a low risk of bias for the included studies (Supplementa-

A MACE

Study or subgroup	IVUS Events	IVUS Total	Angio Events	Angio Total	Weight (%)	Risk ratio, MH, random, 95% CI
RCT						
Bendary A *et al.*	3	90	17	91	2.9	0.18 [0.05; 0.59]
Liu *et al.*	22	167	37	169	14.5	0.60 [0.37; 0.97]
Tan Q *et al.*	8	61	17	62	6.7	0.48 [0.22; 1.03]
Total (95% CI)		**318**		**322**	**24.1**	**0.44 [0.23; 0.83]**
Heterogeneity: $\tau^2 = 0.1607$; $\chi^2 = 3.45$, $df = 2$ ($p = 0.18$); $I^2 = 42\%$						
Test for overall effect: $Z = -2.55$ ($p = 0.1$)						
PSM-S						
Kim YH *et al.*	26	122	32	74	17.3	0.49 [0.32; 0.76]
DeLa Torre *et al.* (1)	60	505	81	505	26.9	0.74 [0.54; 1.01]
DeLa Torre *et al.* (2)	10	124	16	124	6.9	0.62 [0.30; 1.32]
Gao *et al.*	47	291	71	291	24.8	0.66 [0.48; 0.92]
Total (95% CI)		**1042**		**994**	**75.9**	**0.65 [0.53; 0.79]**
Heterogeneity: $\tau^2 = 0$; $\chi^2 = 2.3$, $df = 3$ ($p = 0.31$); $I^2 = 0\%$						
Test for overall effect: $Z = -4.38$ ($p < 0.01$)						
Total (95% CI)		**1360**		**1316**	**100.0**	**0.60 [0.49; 0.74]**
Heterogeneity: $\tau^2 = 0.0166$; $\chi^2 = 7.16$, $df = 6$ ($p = 0.31$); $I^2 = 16\%$						
Test for overall effect: $Z = -4.83$ ($p < 0.01$)						
Test for subgroup differences: $\chi^2 = 1.34$, $df = 1$ ($p = 0.25$)						



B All-cause death

Study or subgroup	IVUS Events	IVUS Total	Angio Events	Angio Total	Weight (%)	Risk ratio, MH, random, 95% CI
RCT						
Bendary A *et al.*	0	90	2	91	0.1	0.20 [0.01; 4.15]
PSM-S						
Andell *et al.*	37	340	63	340	6.6	0.59 [0.40; 0.86]
DeLa Torre *et al.* (1)	37	505	66	505	6.4	0.56 [0.38; 0.82]
DeLa Torre *et al.* (2)	4	124	7	124	0.7	0.57 [0.17; 1.90]
Kang *et al.*	38	208	58	208	7.2	0.66 [0.46; 0.94]
Kinnaird *et al.*	450	5056	652	5056	73.2	0.69 [0.62; 0.77]
Park *et al.*	12	201	27	201	2.2	0.44 [0.23; 0.85]
Tian *et al.*	12	542	21	542	1.9	0.57 [0.28; 1.15]
Kim YH *et al.*	9	122	16	74	1.6	0.34 [0.16; 0.73]
Total (95% CI)		**7098**		**7050**	**99.9**	**0.65 [0.59; 0.72]**
Heterogeneity: $\tau^2 = 0$; $\chi^2 = 6.13$, $df = 7$ ($p = 0.53$); $I^2 = 0\%$						
Test for overall effect: $Z = -8.56$ ($p < 0.01$)						
Total (95% CI)		**7188**		**7141**	**100.0**	**0.65 [0.59; 0.72]**
Heterogeneity: $\tau^2 = 0$; $\chi^2 = 6.71$, $df = 8$ ($p = 0.57$); $I^2 = 0\%$						
Test for overall effect: $Z = -8.59$ ($p < 0.01$)						
Test for subgroup differences: $\chi^2 = 0.58$, $df = 1$ ($p = 0.45$)						

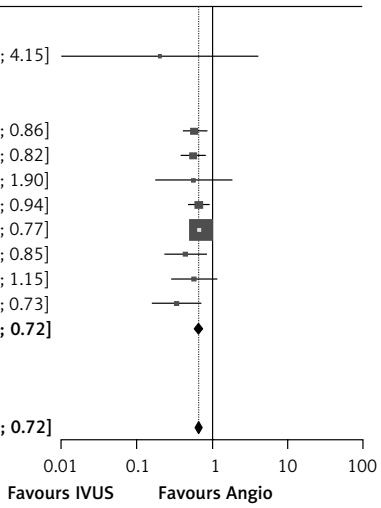


Figure 1. Forest plots for MACE (**A**), all-cause death (**B**)

MACE – major adverse cardiovascular events, PSM-S – propensity score-matched studies.

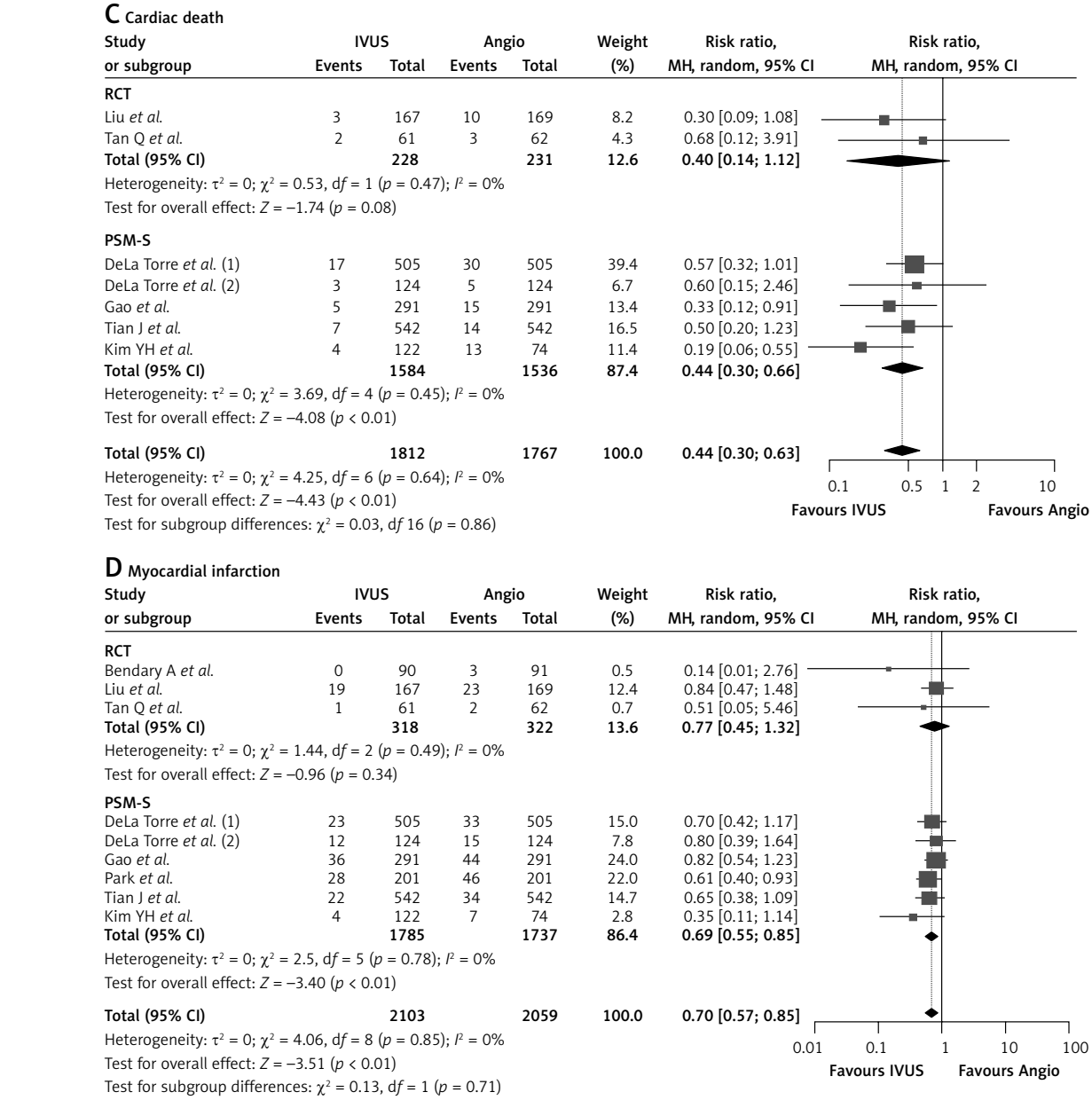


Figure 1. Cont. Forest plots for cardiac death (**C**), and myocardial infarction (**D**)

MACE – major adverse cardiovascular events, PSM-S – propensity score-matched studies.

ry Figures S2, S3). The study details and baseline characteristics of included patients are provided in Supplementary Table SI. There was a statistically significant reduced risk of MACE with IVUS-guided PCI compared to angiography-guided PCI (RR = 0.60 [95% CI: 0.49–0.74]; $p < 0.01$, Figure 1 A), with the results consistent across the subgroups of RCTs and PSM studies. The pooled estimates favored IVUS-guided PCI for a statistically significant reduction in the risk of all-cause death (RR = 0.65 [95% CI: 0.59–0.72]; $p < 0.01$, Figure 1 B). We observed a significantly reduced risk of cardiac death with IVUS-guided PCI (RR = 0.44 [95% CI: 0.30–0.63]; $p < 0.01$, Figure 1 C). IVUS guidance led to a significantly reduced risk of MI (RR = 0.70 [95% CI: 0.57–0.85]; $p < 0.01$, Figure 1 D) and stent thrombosis (RR = 0.38 [95% CI: 0.21–0.70]; $p < 0.01$, Supplementary Figure S4 A) compared to angiography-guided PCI. IVUS-guided PCI significantly reduced the risk of TLR (RR = 0.55 [95% CI: 0.33–0.91]; $p = 0.02$, Supplementary Figure S4 B) and TVR (RR = 0.64 [95% CI: 0.46–0.91]; $p = 0.01$, Supplementary Figure S4 C). We observed < 50% heterogeneity for all pooled outcomes except TLR ($I^2 = 67\%$).

Our pooled analysis of 15,370 patients with ULMCA demonstrated that IVUS guidance significantly reduced the risk of MACE, all-cause death,

cardiac death, MI, stent thrombosis, TLR, and TVR. IVUS guidance results in an accurate assessment of lesion size, vessel diameter, and stenosis of the affected area. This helps clinicians regarding the usage of calcium modification techniques and optimal stent sizing. The use of post-procedural IVUS leads to stent optimization by allowing the quantification of plaque burden and assessing the edge dissections involving the vessel media.

Although there are earlier meta-analyses on this subject, their results are limited by small sample sizes, limited number of RCTs, and pooling of crude data from observational studies. We pooled recent RCTs by Bendary *et al.* which was not included in prior reviews. Moreover, we included those observational studies that performed PSM analysis which allows the removal of confounding bias in observational cohorts by matching intervention and control groups when randomization is not possible in contrast to previous meta-analysis [5]. This allows our review to present accurate pooled effect sizes and limit the risk of confounding bias.

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Ethics approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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