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INTRAVASCULAR ULTRASOUND-GUIDED VERSUS ANGIOGRAPHY-GUIDED PERCUTANEOUS CORONARY INTERVENTION IN COMPLEX LEFT MAIN CORONARY ARTERY DISEASE: A NARRATIVE REVIEW

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Abstract

Background: *Left main (LM) coronary artery disease threatens a large myocardial territory, and angiography alone assesses the LM imprecisely. Guidelines now endorse intravascular ultrasound (IVUS) guidance in complex PCI, but recent randomised data have questioned its benefit in LM disease.*

Objective: *To appraise evidence comparing IVUS-guided with angiography-guided percutaneous coronary intervention (PCI) in LM disease.*

Methods: *Narrative review of observational studies, randomised trials, meta-analyses and guidelines identified from PubMed and society sources up to 30 October 2026. Published values were tabulated; figures were produced in R without re-pooling.*

Results: *Fourteen key sources were tabulated (five randomised, four observational, five meta-analyses). Observational data consistently favoured IVUS; in MAIN-COMPARE, 3-year mortality in matched drug-eluting stent pairs was 4.7% versus 16.0%, and a meta-analysis of 11 studies (24,103 patients) reported a pooled hazard ratio of 0.59 for all-cause mortality. Randomised evidence was discordant: the RENOVATE-COMPLEX-PCI LM substudy (n=192) reported target vessel failure of 6.8% versus 25.1% (HR 0.31), whereas OPTIMAL (n=806) found no difference in its composite endpoint (33.7% versus 30.9%; HR 1.11, 95% CI 0.87–1.42) and numerically more stroke with IVUS. Meta-analyses restricted to randomised trials showed non-significant trends.*

Conclusion: *IVUS is a guideline-supported adjunct in LM PCI, but a clinical-outcome advantage over expert angiographic guidance has not been*

firmly established. Adequately powered, long-term trials with standardised optimisation criteria are needed.

1. Introduction

The left main coronary artery (LMCA) supplies a large share of the left ventricular myocardium, so a significant LM stenosis, or a suboptimal LM stent result, carries a disproportionate prognostic penalty. Over the past two decades, percutaneous coronary intervention (PCI) with drug-eluting stents (DES) has become an accepted alternative to coronary artery bypass grafting (CABG) in selected patients with LM disease of low-to-intermediate anatomical complexity [1,2]. Long-term randomised data nevertheless show that the quality of the LM procedure matters: in the NOBLE trial, five-year major adverse cardiac and cerebrovascular events were 28% after PCI versus 19% after CABG (hazard ratio [HR] 1.58), although all-cause mortality was similar (about 9% in both arms) [2].

Angiography is a lumenogram: it projects a three-dimensional vessel onto a two-dimensional silhouette. In the LM, which is short, often foreshortened and overlapped by the catheter and adjacent branches, this limitation is particularly important, and IVUS studies have long shown that LM disease may be unrecognised or underestimated at angiography [3]. IVUS provides cross-sectional images of the lumen, plaque, calcium and stent, allowing measurement of reference vessel size, minimal lumen and stent areas, stent expansion, apposition and edge dissection. These data can also inform the choice of stenting strategy in distal LM bifurcations, which accounted for 81% of lesions in NOBLE [2].

Guideline support for intracoronary imaging in LM PCI has strengthened progressively, from Class IIa (Level B) in earlier US and European documents to Class I (Level A) in the 2024 European Society of Cardiology (ESC) chronic coronary syndrome guideline and the 2025 ACC/AHA acute coronary syndrome guideline [4–6]. In March 2026, however, OPTIMAL, the largest randomised trial dedicated to unprotected LM PCI, reported that IVUS guidance did not reduce a patient-oriented composite endpoint compared with angiographic guidance [7]. Together with a neutral result in IVUS-guided complex high-risk PCI (IVUS-CHIP) [8], this has reopened the question of whether routine imaging is necessary in every LM procedure.

The aim of this narrative review was to summarise and critically appraise the available observational, randomised and meta-analytic evidence comparing IVUS-guided with angiography-guided PCI in LM disease, to place it in the context of current guideline recommendations, and to identify the gaps that future trials should address.

2. Methods

2.1 Review design

This was a narrative review structured according to the principles of the SANRA (Scale for the Assessment of Narrative Review Articles) quality criteria. Because the objective was to describe and interpret published evidence rather than to generate a new pooled estimate, no new meta-analysis was performed and no formal risk-of-bias scoring was undertaken.

2.2 Literature search

PubMed/MEDLINE and PubMed Central were searched, supplemented by the websites of the American College of Cardiology, the European Society of Cardiology, and conference and trial-registry summaries, using combinations of the terms “left main”, “unprotected left main”, “intravascular ultrasound”, “IVUS”, “intravascular imaging”, “angiography-guided” and “percutaneous coronary intervention”. The last search was performed on 30 October 2026. Reference lists of recent meta-analyses and reviews were screened manually for additional sources.

2.3 Eligibility and data extraction

Eligible sources were (i) observational studies or randomised trials comparing IVUS-guided with angiography-guided PCI in patients with LM disease, or reporting an LM-specific subgroup; (ii) meta-analyses addressing this comparison, or large imaging-versus-angiography meta-analyses relevant to LM PCI; and (iii) clinical practice guidelines. Case reports, studies using IVUS

only for diagnostic assessment without a comparator, and sources without extractable outcome data were excluded. For each included source we recorded design, setting, sample size, comparison, follow-up, primary endpoint definition and the reported effect estimates with 95% confidence intervals (CI). Screening and extraction were performed by a single reviewer; values were transcribed exactly as reported in the source.

2.4 Tables and figures

Tabulated values were exported to comma-separated files and visualised in R (version 4.3.3) using the ggplot2, ggrepel and ragg packages. Figures comprise a pie chart of the evidence base by study design (Figure 1), a graph of the evolution of the evidence by year and sample size (Figure 2), a bar chart of reported event rates (Figure 3) and a forest-style plot of published effect estimates (Figure 4). The forest-style plot displays estimates as published by the original authors; it is not a new meta-analysis, and endpoints differ between sources and should not be compared directly.

3. Results

3.1 Characteristics of the evidence base

Fourteen key sources were tabulated: five randomised or randomised-derived studies, four observational registries or cohorts, and five meta-analyses (Figure 1; Tables 1 and 2). The evidence has evolved from observational registries of about 1,000 patients in 2009–2014, through meta-analyses dominated by observational data, to small randomised substudies and, most recently, the 806-patient OPTIMAL trial in 2026 (Figure 2). Guideline documents were reviewed separately (Section 3.5).

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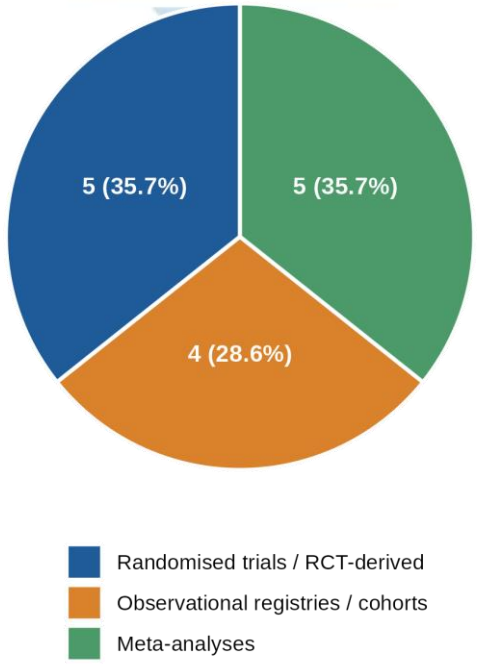


Figure 1. Distribution of the 14 key evidence sources tabulated in this review by study design (randomised or randomised-derived, n=5; observational, n=4; meta-analyses, n=5). Created in R (ggplot2).

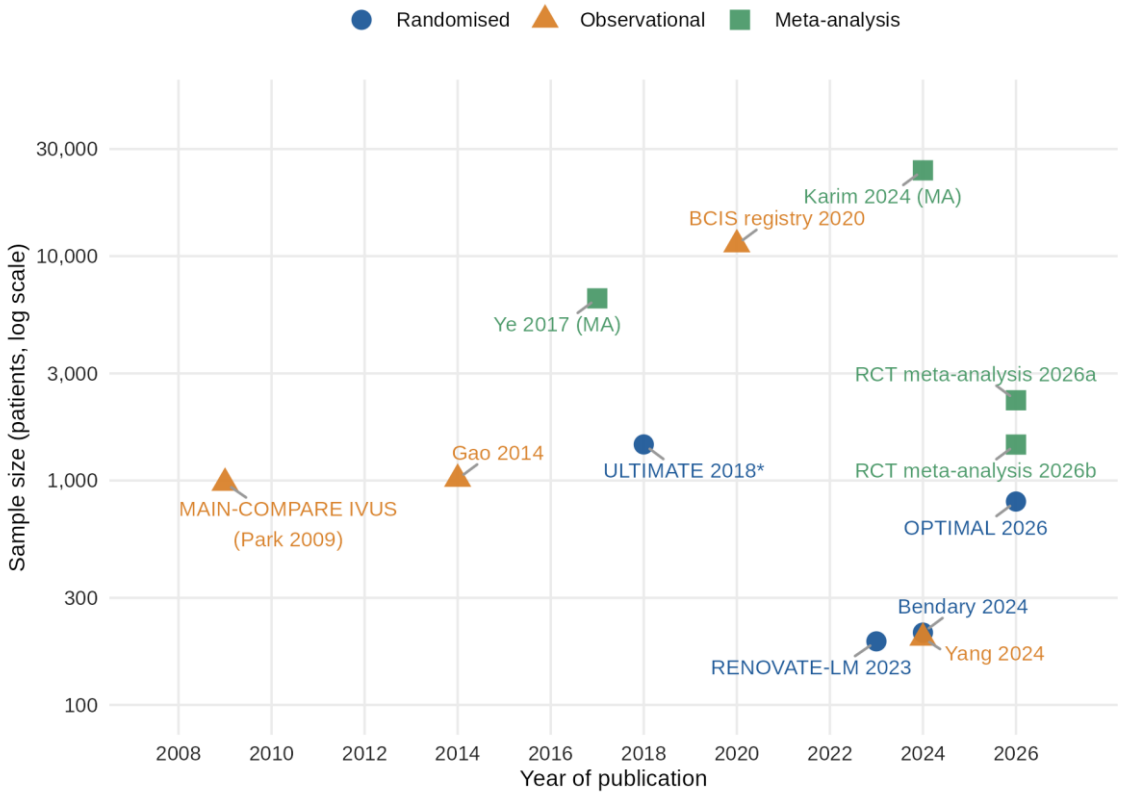


Figure 2. Evolution of the evidence base on imaging-guided versus angiography-guided PCI in left main (LM) disease by year of publication and sample size (log scale). *ULTIMATE enrolled all-comers (LM lesions in 9.9%). The single-centre randomised trial by Liu et al. and the network meta-analysis by Stone et al. are not plotted because the randomised sample size or total sample size was not extracted. MA, meta-analysis. Created in R (ggplot2, ggrepel).

Table 1. Key primary studies comparing IVUS-guided with angiography-guided PCI in left main disease (or with an LM-specific analysis).

Study	Design / setting	Population (n)	Follow-up	Main findings (IVUS or imaging vs angiography)
MAIN-COMPARE IVUS substudy (Park 2009) [9]	Registry; elective stenting of unprotected LM	975 (IVUS 756; angiography 219); 145 matched DES pairs	3 years	3-year mortality 4.7% vs 16.0% in DES pairs (HR 0.39; log-rank P=0.048); no difference in 47 bare-metal stent pairs (8.6% vs 10.8%)
Gao 2014 [10]	Single-centre registry, China	1,016 (IVUS 337; angiography 679); 291 matched pairs	1 year	1-year MACE 14.8% vs 27.7% (P<0.001); after matching 16.2% vs 24.4% (P=0.014)

Study	Design / setting	Population (n)	Follow-up	Main findings (IVUS or imaging vs angiography)
BCIS database (Kinnaird 2020) [11]	National registry, UK	11,264 (imaging 5,056; angiography 6,208)	12 months	Mortality 8.9% vs 12.9% (OR 0.66; 95% CI 0.57–0.77)
Yang 2024 [12]	Retrospective single-centre cohort, China	199 (IVUS 81; angiography 118)	Up to 3 years	Lower 1-year MACE (P=0.002) and 3-year cardiac mortality (P=0.018) with IVUS
Liu 2019 [13]	Single-centre open-label RCT, China	Unprotected LM ≥50% stenosis; 348 consecutive patients (Dec 2010–Dec 2015)	1 year	Composite MACE (cardiac death, MI, TVR) significantly lower with IVUS guidance
Bendary 2024 [14]	RCT	210 (mean age 62 y; 71.3% men)	1 year	Adjusted 84.4% lower MACE risk with IVUS
RENOVATE-COMPLEX-PCI LM substudy (Kwon 2023) [15,16]	Prespecified substudy of multicentre RCT, Korea	192 (imaging 138; angiography 54); IVUS used in 93%	Median 2.1 years	TVF 6.8% vs 25.1% (HR 0.31; 95% CI 0.13–0.76); cardiac death or spontaneous TV-MI 1.6% vs 12.7% (HR 0.16)
ULTIMATE (all-comers; LM lesions 9.9%) [17,18]	Multicentre RCT, 8 Chinese centres	1,448 (724 vs 724)	12 months; 3 years	TVF 2.9% vs 5.4% (HR 0.53; 95% CI 0.31–0.90) at 12 months; 6.6% vs 10.7% (P=0.01) at 3 years
OPTIMAL (Testa 2026) [7,8]	International multicentre RCT; 28 centres (Italy, Spain, UK)	806 (IVUS 401; angiography 405); mean age 71.4 y; diabetes 34.7%; mean SYNTAX 29.7	Median 2.9 years	Composite of stroke, MI, revascularisation or death 33.7% vs 30.9% (HR 1.11; 95% CI 0.87–1.42; P=0.40); stroke 3% vs 1% (HR 3.11); procedure time 88.6 vs 63.9 min

DES, drug-eluting stent; HR, hazard ratio; LM, left main; MACE, major adverse cardiac events; MI, myocardial infarction; OR, odds ratio; RCT, randomised controlled trial; TV-MI, target vessel myocardial infarction; TVF, target vessel failure; TVR, target vessel revascularisation.

3.2 Observational evidence

The earliest and most influential LM-specific signal came from the MAIN-COMPARE registry, in which 756 patients with unprotected LM stenosis underwent elective stenting under IVUS guidance and 219 under angiographic guidance [9]. In 145 propensity-matched pairs treated with DES, 3-year mortality was 4.7% with IVUS versus 16.0% with angiography (HR 0.39); no such difference was seen in 47 matched pairs treated with bare-metal stents (8.6% versus 10.8%) [9]. A Chinese single-centre registry of 1,016 patients reported an unadjusted 1-year MACE rate of 14.8% with IVUS versus 27.7% with angiography, and 16.2% versus

24.4% after propensity matching (P=0.014), the difference being driven mainly by cardiac death and target vessel revascularisation [10].

Larger real-world data are consistent. In the British Cardiovascular Intervention Society (BCIS) database, 12-month mortality after unprotected LM PCI was 8.9% with intravascular imaging (n=5,056) versus 12.9% with angiography alone (n=6,208), an odds ratio of 0.66 (95% CI 0.57–0.77) [11]. A smaller retrospective cohort of 199 patients likewise reported lower 1-year MACE and 3-year cardiac mortality with IVUS [12]. These studies are, however, vulnerable to selection bias, operator and centre effects, and residual confounding even after matching, since imaging may preferentially be used in lower-risk patients or by more experienced operators.

3.3 Randomised evidence

Randomised LM-specific data were initially limited to small single-centre trials. In a Chinese single-centre trial, IVUS-guided DES implantation (with a procedural success definition including a minimal stent lumen area above 6.9 mm², full apposition and expansion, and no dissection) was associated with fewer composite MACE at one year [13]. Another randomised study of 210 patients reported a markedly lower adjusted MACE risk with IVUS (84.4% reduction) at one year [14].

The prespecified LM substudy of RENOVATE-COMPLEX-PCI randomised 192 patients (138 to imaging guidance, 54 to angiography; consistent with the 2:1 allocation of the parent trial), with IVUS used in 93% of the imaging arm and about half of patients presenting with an acute coronary syndrome [15]. At a median follow-up of 2.1 years, target vessel failure occurred in 6.8% versus 25.1% (HR 0.31; 95% CI 0.13–0.76), driven by cardiac death or spontaneous target vessel myocardial infarction (1.6% versus 12.7%; HR 0.16; 95% CI 0.03–0.82) [15]. In the full parent trial of 1,639 patients with complex lesions, imaging guidance likewise reduced target vessel failure, and cardiac death was 1.7% versus 3.8% [16]. In the all-comers ULTIMATE trial, in which LM lesions accounted for 9.9% of lesions, 12-month target vessel failure was 2.9% with IVUS versus 5.4% with angiography (HR 0.53), and the benefit persisted at 3 years (6.6% versus 10.7%) [17,18]. Importantly, within the IVUS arm, patients who met all prespecified optimisation criteria had a 12-month failure rate of 1.6% versus 4.4% in those who did not [17].

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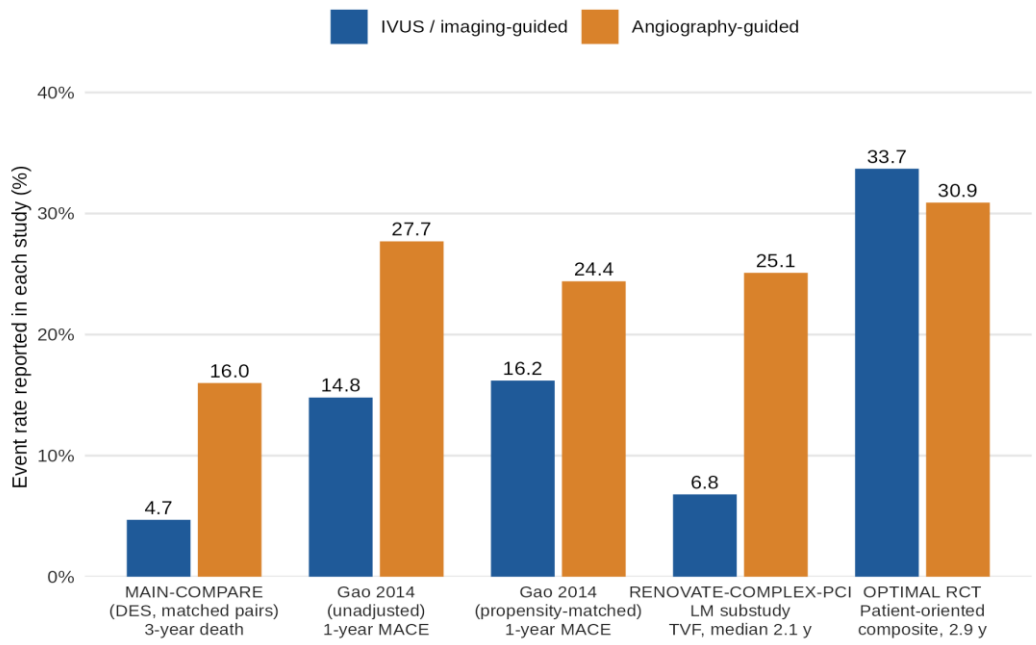


Figure 3. Primary event rates reported for IVUS/imaging-guided versus angiography-guided PCI in left main disease. Endpoints and follow-up differ between studies (3-year death in MAIN-COMPARE matched DES pairs; 1-year MACE in Gao 2014; target vessel failure [TVF] in the RENOVATE-COMPLEX-PCI LM substudy; patient-oriented composite of stroke, MI, any revascularisation or death in OPTIMAL) and the bars should not be compared across studies. Data from references [7,9,10,15]. Created in R (ggplot2).

The pivotal contrary result came from OPTIMAL, an international, open-label trial in 28 European centres that randomised 806 patients with unprotected LM disease (mean age 71.4 years, 34.7% diabetic, mean SYNTAX score 29.7) to IVUS-guided or angiography-guided PCI [7,8]. At a median follow-up of 2.9 years, the primary composite of stroke, myocardial infarction, any revascularisation or death from any cause occurred in 33.7% of the IVUS group and 30.9% of the angiography group (HR 1.11; 95% CI 0.87–1.42; P=0.40) [7]. Stroke was numerically more frequent with IVUS (3% versus 1%; HR 3.11; 95% CI 1.00–9.65), and procedures were longer (88.6 versus 63.9 minutes), while other safety events were similar [8]. The investigators concluded that IVUS showed no additional benefit and suggested that angiography-only guidance may be appropriate when procedures are performed by IVUS-experienced operators in high-volume centres [7,8]. A second 2026 trial in complex high-risk PCI (IVUS-CHIP; n=2,020) also found no reduction in target vessel failure with routine IVUS (13.9% versus 11.1%; HR 1.25; 95% CI 0.97–1.60) and longer procedures [8].

Evidence for the alternative modality, optical coherence tomography (OCT), is accumulating in related populations: in the OCTOBER trial of complex bifurcation lesions, in which LM PCI constituted roughly 19% of each arm, OCT guidance reduced the primary endpoint at 2 years (10.1% versus 14.1%; P=0.035) [19,20].

3.4 Meta-analyses

Meta-analyses that pooled predominantly observational LM data consistently favoured IVUS (Table 2; Figure 4). In ten studies (nine non-randomised, one randomised; 6,480 patients), IVUS guidance was associated with lower all-cause death (RR 0.60; 95% CI 0.47–0.75; I^2 = 19%) and cardiac death (RR 0.47; 95% CI 0.33–0.66) [21]. A later analysis of 11 studies (two randomised, nine observational; 24,103 patients) of DES-treated LM disease reported pooled HRs of 0.59 for all-cause mortality, 0.39 for cardiovascular mortality, 0.66 for myocardial infarction, 0.45 for target lesion revascularisation and 0.38 for stent thrombosis,

although heterogeneity for cardiovascular mortality was high (I^2 = 75%) [22]. An earlier DES-specific meta-analysis of 4,592 patients addressed the same question [23]. In the broader population of randomised trials of imaging-guided DES implantation (all lesion types), the network meta-analysis by Stone et al. found reductions in target lesion failure (RR 0.71), cardiac death (RR 0.55), stent thrombosis (RR 0.52) and all-cause death (RR 0.75), with similar outcomes for IVUS and OCT [24].

Table 2. Meta-analyses relevant to IVUS- versus angiography-guided PCI in left main disease.

Meta-analysis	Studies included	Patients	Main pooled results (IVUS/imaging vs angiography)
Ye 2017 [21]	10 (9 non-randomised, 1 RCT)	6,480	All-cause death RR 0.60 (0.47–0.75; I^2 = 19%); cardiac death RR 0.47 (0.33–0.66); lower TLR and stent thrombosis also reported
Karim 2024 [22]	11 (2 RCTs, 9 observational)	24,103	All-cause mortality HR 0.59 (0.53–0.66); CV mortality HR 0.39 (0.26–0.58); MI HR 0.66 (0.48–0.90); TLR HR 0.45 (0.38–0.54); stent thrombosis HR 0.38 (0.26–0.57)
Stone 2024 network meta-analysis [24]	Randomised trials of imaging-guided DES PCI (all lesion types; not LM-specific)	Not extracted	TLF RR 0.71 (0.63–0.80); cardiac death RR 0.55 (0.41–0.75); all-cause death RR 0.75 (0.60–0.93); stent thrombosis RR 0.52 (0.34–0.81)
RCT meta-analysis with GRADE, 2026 [25]	4 RCTs (unprotected LM)	2,278	All-cause death RR 0.64 (not statistically significant); numerically lower cardiac death, TLR and TVR; MI and stent thrombosis similar
Updated RCT meta-analysis, 2026 [26]	4 RCTs (unprotected LM)	1,446	MACE RR 0.57 (0.30–1.09; P=0.09); cardiac death RR 0.68 (0.27–1.73); MI RR 0.93 (0.68–1.28); MACE significantly lower after leave-one-out exclusion of OPTIMAL

CV, cardiovascular; HR, hazard ratio; MACE, major adverse cardiac events; MI, myocardial infarction; RR, risk ratio; TLF, target lesion failure; TLR, target lesion revascularisation; TVR, target vessel revascularisation. Confidence intervals in parentheses.

Meta-analyses confined to randomised LM trials are less conclusive. One analysis of four randomised trials (2,278 patients) found numerically lower all-cause death (RR 0.64), cardiac death, target lesion revascularisation and target vessel revascularisation with IVUS, but none reached statistical significance, and myocardial infarction and stent thrombosis were similar between strategies [25]. A separate updated analysis of four randomised trials (1,446 patients) reported MACE RR 0.57 (95% CI 0.30–1.09; P=0.09), cardiac mortality RR 0.68 (95% CI 0.27–1.73) and myocardial infarction RR 0.93 (95% CI 0.68–1.28); the MACE reduction became statistically significant only when OPTIMAL was excluded in a leave-one-out analysis, highlighting how strongly this single trial influences the pooled result [26]. The two 2026 analyses pooled different sets of trials and should therefore not be regarded as independent confirmation of each other. The effect estimates are collated in Table 3 and Figure 4.

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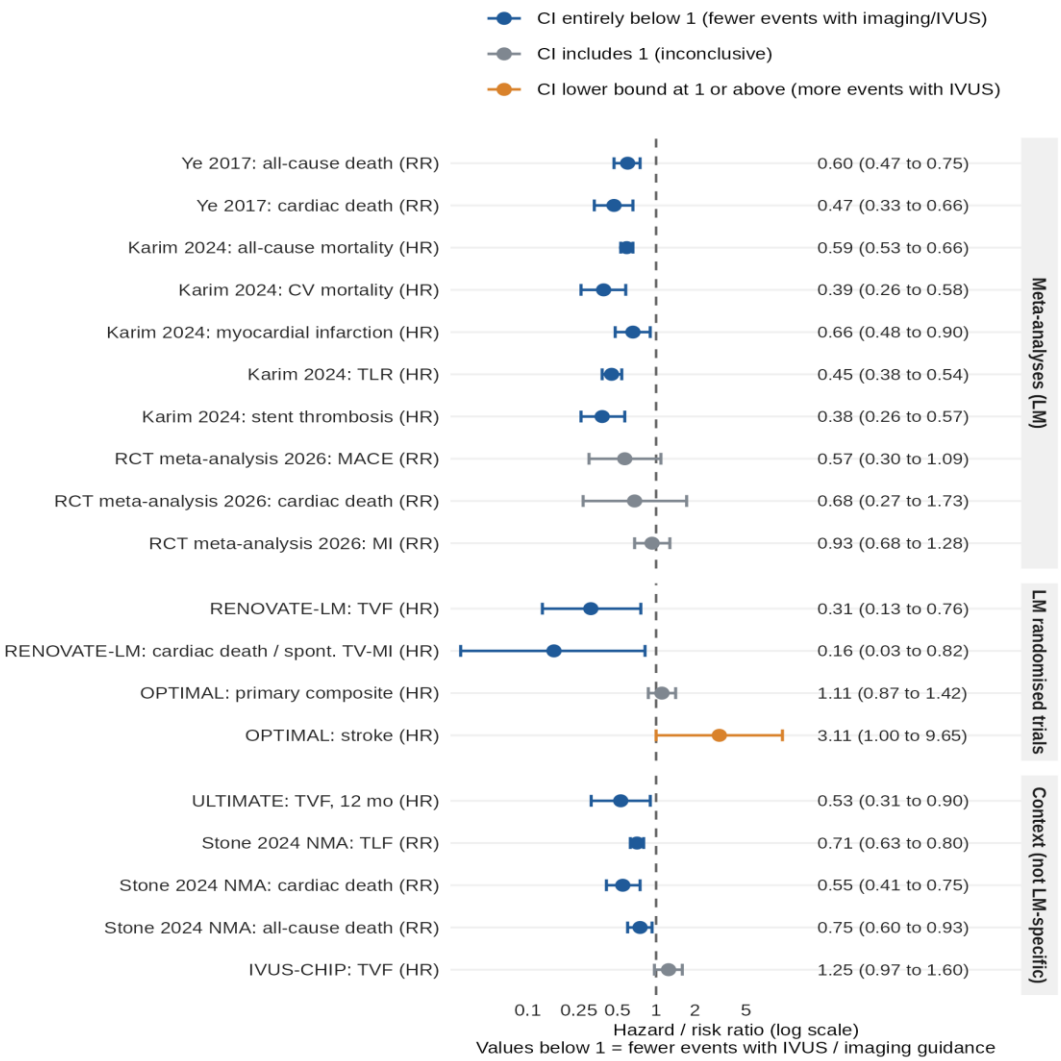


Figure 4. Forest-style summary of effect estimates published for imaging-guided versus angiography-guided PCI. Points show reported hazard or risk ratios with 95% confidence intervals on a log scale; values below 1 indicate fewer events with IVUS/imaging guidance. Colours indicate whether the published interval lies entirely below 1, includes 1, or has a lower bound at or above 1. These are estimates as published; they are not re-pooled and endpoints differ between sources. MI, myocardial infarction; NMA, network meta-analysis; RR, risk ratio; TLF, target lesion failure; TLR, target lesion revascularisation; TVF, target vessel failure; TV-MI, target vessel myocardial infarction. Created in R (ggplot2).

Table 3. Published effect estimates displayed in Figure 4.

Evidence group	Source and outcome	Estimate	95% CI
Meta-analyses (LM)	Ye 2017: all-cause death (RR)	0.60	0.47 to 0.75
Meta-analyses (LM)	Ye 2017: cardiac death (RR)	0.47	0.33 to 0.66
Meta-analyses (LM)	Karim 2024: all-cause mortality (HR)	0.59	0.53 to 0.66
Meta-analyses (LM)	Karim 2024: CV mortality (HR)	0.39	0.26 to 0.58
Meta-analyses (LM)	Karim 2024: myocardial infarction (HR)	0.66	0.48 to 0.90
Meta-analyses (LM)	Karim 2024: TLR (HR)	0.45	0.38 to 0.54

Evidence group	Source and outcome	Estimate	95% CI
Meta-analyses (LM)	Karim 2024: stent thrombosis (HR)	0.38	0.26 to 0.57
Meta-analyses (LM)	RCT meta-analysis 2026: MACE (RR)	0.57	0.30 to 1.09
Meta-analyses (LM)	RCT meta-analysis 2026: cardiac death (RR)	0.68	0.27 to 1.73
Meta-analyses (LM)	RCT meta-analysis 2026: MI (RR)	0.93	0.68 to 1.28
LM randomised trials	RENOVATE-LM: TVF (HR)	0.31	0.13 to 0.76
LM randomised trials	RENOVATE-LM: cardiac death / spont. TV-MI (HR)	0.16	0.03 to 0.82
LM randomised trials	OPTIMAL: primary composite (HR)	1.11	0.87 to 1.42
LM randomised trials	OPTIMAL: stroke (HR)	3.11	1.00 to 9.65
Context (not LM-specific)	ULTIMATE: TVF, 12 mo (HR)	0.53	0.31 to 0.90
Context (not LM-specific)	Stone 2024 NMA: TLF (RR)	0.71	0.63 to 0.80
Context (not LM-specific)	Stone 2024 NMA: cardiac death (RR)	0.55	0.41 to 0.75
Context (not LM-specific)	Stone 2024 NMA: all-cause death (RR)	0.75	0.60 to 0.93
Context (not LM-specific)	IVUS-CHIP: TVF (HR)	1.25	0.97 to 1.60

Sources: Ye 2017 [21]; Karim 2024 [22]; 2026 RCT meta-analysis [26]; RENOVATE-COMPLEX-PCI LM substudy [15]; OPTIMAL [7,8]; ULTIMATE [17]; Stone 2024 [24]; IVUS-CHIP [8]. HR, hazard ratio; RR, risk ratio. RR/HR type is shown in parentheses in the outcome label.

3.5 Guideline recommendations

Recommendations for intracoronary imaging in LM PCI have been upgraded over time (Table 4). Earlier documents gave IVUS a Class IIa (Level B) recommendation for assessing angiographically indeterminate LM disease or optimising LM stenting [27–29]. The 2024 ESC guideline for chronic coronary syndromes recommends IVUS or OCT guidance for PCI of anatomically complex lesions, in particular LM stem, true bifurcations and long lesions (Class I, Level A), supported by RENOVATE-COMPLEX-PCI, IVUS-XPL and OCTOBER [4,16,19,30]; it additionally gives a Class IIa (Level B) recommendation to consider IVUS to evaluate the severity of intermediate LM stenoses [4]. The 2025 ACC/AHA acute coronary syndrome guideline gives a Class I (Level A) recommendation for IVUS or OCT in patients with ACS undergoing stenting of the LM or complex lesions [5,6]. US guidance regards OCT as a reasonable alternative to IVUS except in ostial LM disease [29]. OPTIMAL was published after these documents; its authors note that the findings may challenge a requirement for imaging in every LM procedure [7,8].

Table 4. Guideline recommendations for intracoronary imaging in left main PCI.

Guideline	Recommendation (imaging in LM / complex PCI)	Class	Level
2011 ACCF/AHA/SCAI PCI [27]	IVUS reasonable for assessment of angiographically indeterminate LM disease	IIa	B
2014 ESC/EACTS revascularisation [28]	IVUS to assess severity and optimise treatment of unprotected LM lesions	IIa	B
2021 ACC/AHA/SCAI revascularisation [29]	IVUS useful for procedural guidance, particularly in LM or complex stenting; OCT a reasonable alternative except ostial LM	IIa	B
2024 ESC chronic coronary syndromes [4]	IVUS or OCT guidance recommended for PCI of anatomically complex lesions, in particular LM stem, true bifurcations and long lesions	I	A
2024 ESC chronic coronary syndromes [4]	IVUS should be considered to evaluate severity of intermediate LM stenoses when invasive angiography is indicated	IIa	B
2025 ACC/AHA/ACEP/NAEMSP/SCAI acute coronary syndromes [5,6]	IVUS or OCT recommended for procedural guidance when stenting LM or complex lesions in ACS	I	A

ACS, acute coronary syndrome; LM, left main; OCT, optical coherence tomography.

4. Discussion

4.1 Why do observational and randomised data disagree?

The principal finding of this review is a gradient in apparent benefit by study design. Observational registries and the meta-analyses built on them report relative reductions of roughly 35–60% in mortality, whereas the largest LM-specific randomised trial, OPTIMAL, found no difference in a broad patient-oriented composite [7,9,11,21,22]. Several explanations are plausible and are not mutually exclusive.

First, confounding and selection: in non-randomised comparisons, imaging is more likely to be used in selected patients, by more experienced operators and in better-resourced centres, and propensity matching can address only measured variables. Second, the control arm in contemporary trials is no longer "naïve" angiography; in NOBLE, 74% of PCI patients already received post-PCI IVUS, and in OPTIMAL the participating centres were high-volume and experienced in imaging, which can narrow the difference between arms [2,7,8]. Third, endpoint definitions differ: the RENOVATE-LM substudy used target vessel failure (cardiac death, target vessel MI, clinically driven TVR), whereas OPTIMAL used a broader patient-oriented composite counting any stroke, any MI, any revascularisation and all-cause death, which dilutes procedure-specific effects [7,15]. Fourth, the randomised LM substudies were small: the RENOVATE-LM comparison included only 54 angiography-arm patients, with wide confidence intervals around the hazard ratios [15]. Finally, benefit may depend on how imaging is used rather than whether it is used. In ULTIMATE, patients meeting predefined IVUS optimisation criteria had markedly fewer events than those who did not [17]; if optimisation targets are not applied, imaging may add time and cost without changing the result, which is consistent with the neutral IVUS-CHIP findings [8].

4.2 Mechanistic rationale for imaging in the LM

The rationale for IVUS in the LM remains physiologically and technically sound (Table 5). Angiography can under-recognise LM disease, cannot assess stent expansion or apposition, and is limited in the ostium and the shaft where

foreshortening and catheter overlap are common [3]. IVUS allows quantitative assessment of lesions of uncertain severity, detection of calcium that requires modification, selection of appropriately sized stents with proximal optimisation, identification of side-branch ostial disease in distal bifurcations, and detection of edge dissection or under-expansion that could precipitate early stent thrombosis or restenosis [4,17]. The meta-analytic reductions in stent thrombosis and target lesion revascularisation are biologically consistent with this mechanism, even though hard-outcome benefit is not confirmed in the randomised LM trials [22,24].

Table 5. Conceptual comparison of angiography-guided and IVUS-guided PCI in left main disease (authors' synthesis of the cited sources; not a quantitative comparison).

Domain	Angiography-guided	IVUS-guided
Assessment of intermediate LM stenosis [3,4]	Visual estimate of diameter stenosis; LM disease may be unrecognised or underestimated	Direct measurement of lumen area and plaque burden
Ostial and shaft lesions	Foreshortening and catheter overlap limit visualisation	Cross-sectional imaging independent of projection angle
Plaque and calcium	Calcium seen only when severe; plaque composition not assessed	Quantifies calcium arc and plaque burden; informs lesion preparation
Stent sizing	Based on visual reference diameter; risk of under-sizing and proximal–distal mismatch	Vessel and lumen dimensions at reference segments guide stent and post-dilation balloon size
Post-implantation optimisation [17]	Cannot assess expansion, apposition or edge dissection	Detects under-expansion, malapposition, edge dissection and residual inflow or outflow disease against predefined criteria
Bifurcation strategy	Medina classification by eye	Identifies side-branch ostial disease; supports choice between provisional and two-stent strategies
Procedure time and cost [7,8]	Shorter (OPTIMAL: 63.9 min)	Longer (OPTIMAL: 88.6 min); additional catheter cost

IVUS, intravascular ultrasound; LM, left main; PCI, percutaneous coronary intervention.

4.3 Safety and procedural considerations

The numerically higher stroke rate with IVUS in OPTIMAL (3% versus 1%; 95% CI of the hazard ratio 1.00–9.65) is based on few events and a borderline interval, and its mechanism is uncertain; it may represent a chance finding, but it deserves systematic attention in future LM imaging studies and in pooled individual-patient analyses [8]. Longer procedures with IVUS were consistently observed in both OPTIMAL and IVUS-CHIP, and procedural complexity and cost are important practical trade-offs [8].

4.4 Choice of imaging modality

Current European and US guidance accepts either IVUS or OCT for complex PCI, with OCT considered a reasonable alternative except in ostial LM disease, where complete blood clearance and visualisation of the ostium can be difficult [4,20,29]. Network meta-analytic data show similar outcomes for IVUS and OCT across lesion types [24], while LM-specific randomised comparisons between the two modalities are still lacking.

4.5 Implications for practice

Taken together, the evidence supports IVUS as a reasonable, guideline-recommended adjunct for LM PCI, particularly where angiographic uncertainty is greatest: angiographically intermediate LM stenosis, distal bifurcations requiring a stenting strategy decision, heavily

calcified or long lesions, and ostial or shaft disease where angiographic assessment is least reliable [3,4,29]. At the same time, OPTIMAL suggests that, in high-volume centres with experienced operators using high-quality angiographic technique, routine imaging may not add measurable benefit in unselected patients [7,8]. In centres where cost or availability limits imaging, a pragmatic approach is therefore to prioritise IVUS for the lesion subsets listed above rather than to use it universally; this is the authors' interpretation and has not been tested prospectively.

4.6 Strengths and limitations of this review

Strengths include the inclusion of the most recent randomised and meta-analytic data (2026), the transparent tabulation of published effect estimates, and the reproducible R-based figures. Limitations should be acknowledged. This was a narrative rather than a systematic review: the search was not registered, was not exhaustive across all databases, and screening and extraction were performed by a single reviewer, so relevant studies may have been missed. Effect estimates were taken from the original publications, endpoints and follow-up differ across sources and were not harmonised, and the forest-style plot juxtaposes ratio measures (RR and HR) that are not strictly interchangeable. Several sources, including two 2026 meta-analyses, were available only as abstracts or summaries at the time of writing, and some full-text details (such as author lists) require verification against the original articles. The overlap of trials between meta-analyses means that they are not independent. No formal risk-of-bias or GRADE assessment was performed by the authors of this review.

4.7 Future directions

Priorities for future research include extended follow-up of OPTIMAL and RENOVATE-COMPLEX-PCI; individual-patient-data meta-analysis of the randomised LM trials, with attention to stroke, bifurcation anatomy, calcification, acute coronary syndrome presentation and operator experience; trials that mandate standardised IVUS-based optimisation targets and report adherence to them; head-to-head comparison of IVUS and OCT in LM disease; and economic evaluations in settings where imaging catheters are costly or scarce.

5. Conclusion

Observational data and meta-analyses dominated by non-randomised studies show consistently better outcomes with IVUS-guided than with angiography-guided PCI in left main disease, and guidelines now recommend intracoronary imaging for complex PCI including the LM. However, the largest randomised LM trial to date, OPTIMAL, and meta-analyses restricted to randomised trials do not demonstrate a statistically significant clinical benefit over expert angiographic guidance, and small randomised substudies that did show benefit are limited by sample size. IVUS should therefore be regarded as a valuable but not yet definitively outcome-improving adjunct, best targeted at lesions in which angiographic assessment is least reliable, and used with explicit optimisation criteria. Adequately powered, long-term randomised trials and individual-patient-data analyses are needed to define which patients benefit most.

Declarations

Ethical approval: Not applicable. This narrative review is based exclusively on previously published literature.

Conflict of interest: The authors declare no conflict of interest.

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Data availability: All data were extracted from the cited publications. The extracted values (CSV files) and the R script used to produce the figures are available from the corresponding author on reasonable request.

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CI, confidence interval; DES, drug-eluting stent; HR, hazard ratio; IVUS, intravascular ultrasound; LM, left main; MACE, major adverse cardiac events; MI, myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; RCT,

randomised controlled trial; RR, risk ratio; TLR, target lesion revascularisation; TVF, target vessel failure; TVR, target vessel revascularisation.

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