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Use of IVUS guided coronary stenting with drug eluting stent☆ A systematic review and meta-analysis of randomized controlled clinical trials and high quality observational studies

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ABSTRACT

Background/objectives: Long term safety of DES, particularly regarding thrombosis is of concern. The hypothesized underlying mechanisms (stent underexpansion, malapposition) could be prevented by IVUS guidance.
Aim of this meta-analysis of randomized controlled clinical trials (RCT) and high quality observational cohort studies (HQ-OBS) is to quantify the potential clinical benefit of intravascular ultrasound (IVUS) guidance in drug-eluting stents (DES) implantation.
Methods: We performed an extensive literature search for full-text articles published in 2003–2013. The primary outcome was the rate of major adverse cardiac events (MACE) in RCT and HQ-OBS; secondary outcomes were death, myocardial infarction (MI), revascularization, thrombosis and post-procedural minimum lumen diameter (MLD). Fixed/random effect relative risks (RRs) or standardized mean difference (SMD) and 95% confidence interval (95% CI) were computed for the meta-analysis.
Results: Thirty-four articles were retrieved from 268 found; of these 3 were RCT and 9 were HQ-OBS; 18,707 patients were enrolled, 1037 in RCT and 17,670 in OBS. Median follow-up was 20 months. IVUS guidance was associated with a significantly lower rate of MACE (RR = 0.80, 95% CI 0.71–0.89, $p < 0.001$), death (RR = 0.60, 95% CI 0.48–0.74, $p < 0.001$), MI (RR = 0.59, 95% CI 0.44–0.80, $p = 0.001$) and thrombosis (RR = 0.50, 95% CI 0.32–0.80, $p = 0.007$) and larger MLD (SMD = 0.15, 95% CI 0.03 to 0.27, $p = 0.014$), but not of revascularization (RR = 0.95, 95% CI 0.82–1.09, $p = 0.75$).
Conclusions: In this meta-analysis, IVUS guidance in DES implantation appears to reduce MACE, mortality and MI, possibly by reducing thrombosis rather than restenosis rate. Patients at high risk for thrombosis might be identified as the best candidate for IVUS guidance.

1. Introduction

Drug eluting stents (DES) reduce the need for repeat revascularization, with no influence on death and myocardial infarction, when compared to bare metal stents (BMS) [1]. However some doubts about their long term safety, particularly with regard to thrombosis,

Table 1
Eligibility criteria[a].

Criterium	Inclusion	Exclusion
Type of design	RCT or cohort study (prospective, retrospective)	Case–control
Type of intervention	Guided vs. IVUS not guided stent positioning	Single uncontrolled IVUS arm
Type of stent	First generation drug eluting stent (DES)	Bare metal stent
Type of patients	Ischemic patients undergoing DES implantation	Primary angioplasty[a]
Type of publication	Articles in peer-reviewed journals	–
Year of publication	2003–2013	Abstract, gray literature
Language of pubblication	English, German, French, Italian, Spanish	–

[a] Note: articles including specific case series undergoing primary angioplasty were collected but used in sensitivity analyses only.

Abbreviations: BMS, bare metal stent; DES, drug eluting stent; IVUS, intravascular ultrasound; MACE, major adverse cardiac events; MI, myocardial infarction; MLD, minimum lumen diameter; RCT, randomized controlled clinical trials; RD, risk difference; RR, relative risk; SMD, standardized mean difference; 95% CI, 95% confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

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[1] These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 2
Bibliographic search strategy.

Database	Search strategy	Limits	Articles retrieved
Web of Science	'Intravascular ultrasound guided' AND ('DES OR drug eluting stent*')	Timespan = 2003–2013. Databases = SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH.	34
PubMed	(IVUS OR intravascular ultrasound) AND guid* AND (DES OR drug eluting stent*)	Limits: English, French, German, Italian, Spanish, Publication Date from 2003/01/01 to 2013/27/03	98
Cinahl	(IVUS OR intravascular ultrasound guid*) AND (DES OR drug eluting stent)	Limiters — Published Date from: 20030101–20132703; Language: English, French, German, Italian, Spanish	31
Cochrane	(IVUS guid* OR intravascular ultrasound guid*) AND (DES or drug eluting stent)	From 2003 to 2013 in all products from 2003 to 2013 in Cochrane central register of controlled trials	9
Embase	(IVUS OR 'intravascular ultrasound') AND guid* AND (DES OR 'drug eluting stent')	[embase]/lim AND [medline]/lim AND ([english]/lim OR [french]/lim OR [german]/lim OR [italian]/lim OR [spanish]/lim) AND [2003–2013]/py	87

have been raised [2,3]. Stent underexpansion and malapposition are considered as potential mechanisms favoring thrombosis; intravascular ultrasound (IVUS), by providing precise visualization of the intracoronary anatomy, may optimize DES implantation, potentially reducing the rate of thrombosis [4]. However, the real clinical benefit of IVUS is still controversial [5]; most available studies are non-randomized, and some include a small number of patients. A recent meta-analysis of randomized clinical trials by Parise et al. [6] showed that IVUS guidance for BMS implantation improved acute procedural results (angiographic minimum lumen diameter), reduced angiographic restenosis, and repeat revascularization and major adverse cardiac events, with a neutral effect on death and myocardial infarction over a follow-up of

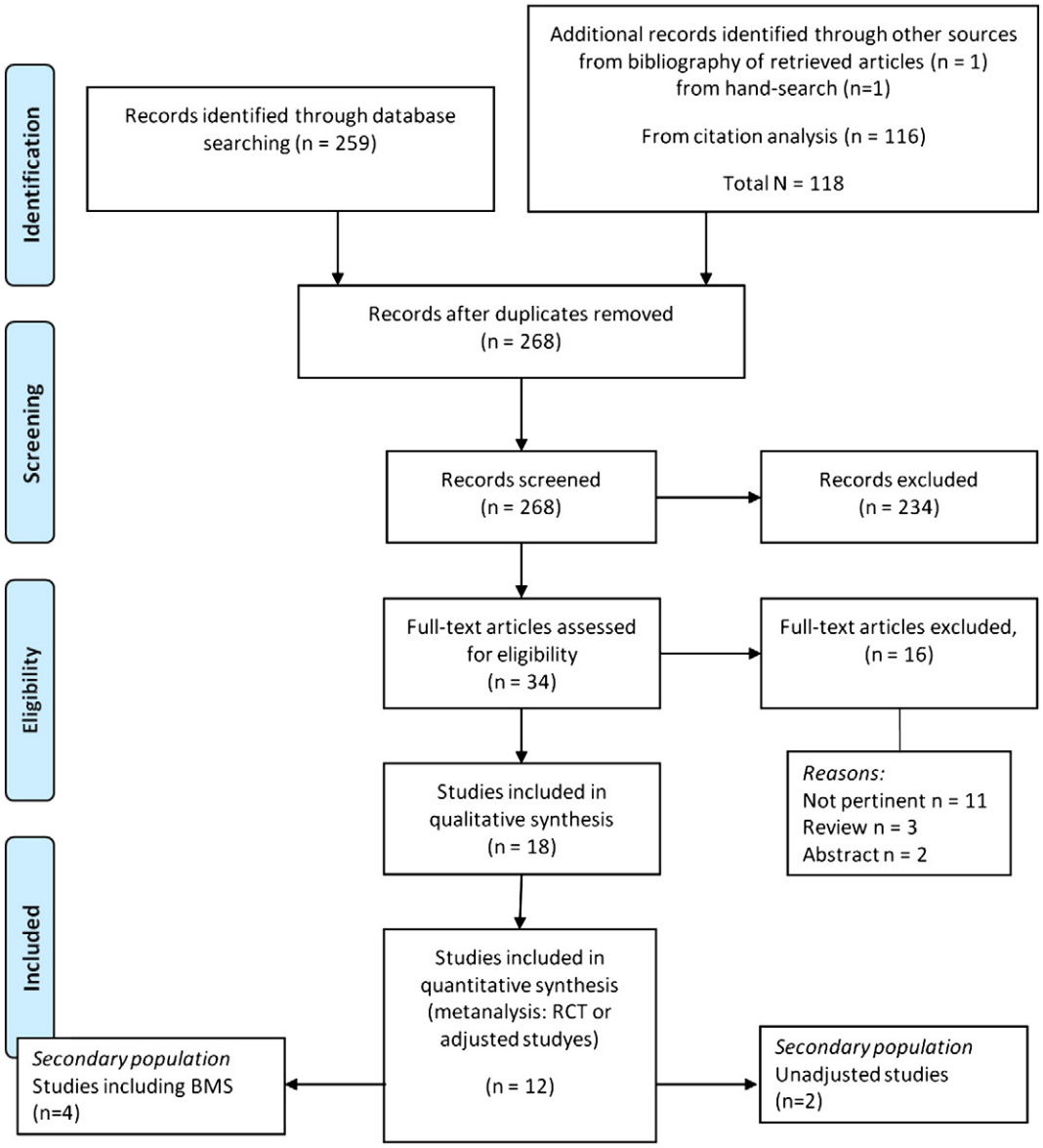

Fig. 1. PRISMA 2009 Flow diagram — IVUS guided vs. not guided coronary stent placement. Articles disposition is described. Reasons for exclusion are listed.