Intracoronary Ultrasound-guided Stenting Improves Outcomes: a Meta-analysis of Randomized Trials

Graciele Sbruzzi[1], Alexandre Schaan de Quadros[1], Rodrigo Antonini Ribeiro[1], Aníbal Pereira Abelin[1], Otávio Berwanger[4], Rodrigo Della Méa Plentz[1,2], Beatriz D'Agord Schaan[1,3]

Instituto de Cardiologia do Rio Grande do Sul/Fundação Universitária de Cardiologia[1]; Universidade Federal de Ciências da Saúde de Porto Alegre[2]; Hospital de Clínicas de Porto Alegre/Universidade Federal do Rio Grande do Sul[3], Porto Alegre, RS; Instituto de Ensino e Pesquisa do HCor (Hospital do Coração)[4], São Paulo, SP, Brazil

Abstract

Background: Intracoronary ultrasound (IVUS) has been used as an adjunctive method in order to optimize implantation of stents. However, the impact of this method in some outcomes is controversial.

Objective: To systematically review the impact of routine IVUS-guided coronary stent as compared to angiographic-guided, on clinical and angiographic outcomes.

Methods: A search of databases (MEDLINE, Cochrane CENTRAL, EMBASE) and references of published studies, from 1982 to 2010, was conducted. Randomized clinical trials (RCTs) that compared angiography plus IVUS-guided (IVUS) vs. angiography alone guided (ANGIO) coronary stent implantation were included. Minimum follow-up was 6 months and the outcomes assessed were major adverse cardiac events (MACE), target lesion revascularization (TLR) and angiographic restenosis. Two reviewers independently extracted the data. Summary risk ratio and 95% confidence intervals (CI) were calculated with random-effects models. The GRADE approach was used to determine the overall quality of evidence for each outcome.

Results: Out of 3,631 articles identified, 8 RCTs evaluating a total of 2,341 patients were included. There was a 27% reduction in angiographic restenosis (95%CI: 3%-46%) and a 38% reduction in TLR (95%CI: 17%-53%) in favor of IVUS vs. ANGIO. However, MACE were not reduced by IVUS (RR: 0.79; 95%CI: 0.61-1.03). The MACE data represent only 47% of the optimal information size required to reliably detect a plausible treatment effect.

Conclusions: We observed that IVUS-guided coronary stenting provides significant reductions in TLR and angiographic restenosis compared to angiographically-guided stenting, but it does not reduce MACE. (Arq Bras Cardiol 2012;98(1):35-44)

Keywords: Ultrasound, interventional, coronary disease, review.

Introduction

Coronary stent implantation represents the main percutaneous revascularization method in the current practice because it reduces restenosis and major adverse cardiac events (MACE)[1] when compared to balloon angioplasty. To assess the appropriateness of stent deployment during the procedure, quantitative coronary angiography and intravascular ultrasound (IVUS) can be used. As compared to the IVUS-guided procedure, the first method is cheaper, easier to perform and available in all centers. On the other hand, IVUS can provide important additional diagnostic information not assessed by angiography.

After percutaneous coronary interventions, restenosis rates are strongly influenced by a small luminal diameter and a reduced cross sectional area of the vessel treated. The conceptual framework for the hypothesis that IVUS-guided percutaneous coronary intervention would result in better long-term angiographic and clinical outcomes when compared to the standard strategy (angiographic-guided only) is based on the observation that IVUS examination after stenting allows a safe and controlled aggressive post-dilatation, with large final diameters[2,3]. Colombo et al[4] were among the first to show that IVUS guided coronary stenting is safe, feasible and provides a better apposition of the prosthesis to the vascular wall than that obtained in the procedure without IVUS. In their seminal work, IVUS use to guide coronary stenting was associated with larger final luminal diameter and lower residual stenosis than not using IVUS during the procedure, with a significant lowering of thrombosis rates. Subsequent studies presented similar results[5,6] and also indicated beneficial effects of IVUS on MACE[6,7]. However, other authors did not show major clinical benefits of IVUS-guided stenting[8,9].

Correspondência: Beatriz D´Agord Schaan•
Av Princesa Isabel, 370, 3º andar, Bairro Santana - CEP: 99620-000 - Porto Alegre, RS, Brazil.
E-mail: beatrizschaan@gmail.com
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In the last decade, a number of observational and randomized studies have investigated the benefit of routine IVUS-guided stenting on long-term outcomes, but these studies have small sample sizes and conflicting results. In this study, we assessed the impact of routine IVUS-guided coronary stent implantation on long-term clinical and angiographic outcomes by means of a systematic review with meta-analysis of randomized clinical trials.

Methods

Eligibility criteria

We included randomized clinical trials (RCTs) that compared angiography plus IVUS-guided (hereinafter referred to as IVUS) vs. angiography alone guided (hereafter referred to as ANGIO) coronary stent implantation in patients with symptomatic coronary lesion or silent ischemia, which evaluated any of the following outcomes: MACE, revascularization and/or angiographic restenosis. Trials with follow-up shorter than 6 months were excluded. If a trial had multiple publications (or substudies), the study was included only once.

Search strategy and study selection

We searched independently, in duplicate, from 1982 to March 2010, the following electronic databases: MEDLINE (accessed by PubMed), Cochrane Central Register of Controlled Trials (Cochrane CENTRAL) and EMBASE. In addition, we searched the references of published studies. The search was performed in March 2010 and comprised the following terms: "intravascular ultrasound", "intracoronary ultrasound", "IVUS", "coronary artery disease", associated with a high sensitivity strategy for the search of randomized clinical trials[10]. The searches were limited to English, Spanish and Portuguese language articles. The detailed strategies used are available on request.

Data extraction

Titles and abstracts of all articles identified by the search strategy were independently evaluated by two investigators (G.S. and A.P.A.), in duplicate. None of the abstracts provided sufficient information regarding the inclusion and exclusion criteria selected for full-text evaluation. In the second phase, the same reviewers independently evaluated these full-text articles and made their selection in accordance with the eligibility criteria. Disagreements between reviewers were solved by consensus, and, if the disagreement persisted, it was evaluated by a third reviewer (A.S.Q). To avoid potential double counting of patients included in more than one report of the same authors/working groups, patient recruitment periods and recruitment areas were evaluated, and authors were contacted for clarification. If the required data could not be found in the published report, the corresponding author was contacted to provide the missing data of interest.

Two reviewers (G.S. and R.A.R.) independently conducted data extraction with regard to the methodological characteristics of the studies, interventions and outcomes using standardized forms; disagreements were solved by consensus or by a third reviewer (A.S.Q). The primary endpoint extracted was MACE, which was defined as death, myocardial infarction or revascularization procedure [as established by the authors, including new percutaneous coronary intervention (re-PCI), coronary artery bypass grafting surgery (CABG), target vessel revascularization (TVR) or target lesion revascularization (TLR)]. (Table 1). In addition, angiography restenosis (defined as >50% diameter stenosis at 6 months), as well as all the aforementioned components of MACE, were also analyzed individually as secondary endpoints.

Assessment of risk of bias

Study quality assessment included adequate sequence generation, allocation concealment, blinding of assessors of outcomes, use of intention-to-treat analysis and description of losses and exclusions. Studies without a clear description of an adequate sequence generation were considered not to have fulfilled these criteria. A lack of description of how the allocation list was concealed (which could include terms like "central", "web-based" or "telephone randomization", or a clear statement that the allocation list was concealed) was judged to characterize absence of allocation concealment. Use of intention-to-treat analysis was considered as: confirmation on study assessment that the number of participants randomized and the number analyzed were identical, except for patients lost to follow-up or who withdrew consent for study participation. Studies without this characteristic were considered not to have fulfilled this criterion. Quality assessment was independently performed by two reviewers (G.S. and R.A.R.).

Data analysis

Summary risk ratios (RR) and 95% confidence intervals (CI) were calculated with random-effect models (Mantel-Haenszel) according to the number of events reported in the original studies or substudies intention-to-treat analysis. For the angiographic restenosis

outcome, we used the case analysis available[11]. For this outcome, sensitivity analysis was carried out considering intention-to-treat analysis. Statistical heterogeneity of the treatment effects among studies was assessed using the Cochran's Q test and the inconsistency I^2 test, in which values above 25% and 50% were considered to indicate moderate and high heterogeneity, respectively[12]. All analyses were conducted using Review Manager version 5.0 (Cochrane Collaboration)[13].

Sensitivity analyses were carried out considering the methodological characteristics of the studies (intention-to-treat analysis, adequate sequence generation, allocation concealment and blinding of assessors of outcomes).

The authors had full access to the data and take full responsibility for its integrity. All authors gave their approval for submission of the final manuscript.

Summary of findings

We presented the overall quality of evidence using the GRADE approach as recommended by the Cochrane Handbook for Systematic Reviews of Interventions.[11] For each specific outcome, the quality of evidence was based on 5 factors: (1) limitations of the study design; (2) consistency of results; (3) directness; (4) precision and (5) potential for publication bias. The quality was reduced by one level for each of the factors not met. The GRADE approach resulted in 4 levels of quality of evidence: high, moderate, low and very low[14]. GRADE profiler software (version 3.2) was used[15].

Reliability and conclusiveness of data

The optimal information sizing of evidence available on IVUS *vs.* ANGIO stenting was based on the composite outcome of MACE[16,17]. The sample size needed for a reliable and conclusive meta-analysis is at least as large as that for a single optimally powered RCT, so we calculated the sample size requirement for our meta-analysis. We used this optimal information size as a way of determining whether evidence in our meta-analysis was reliable and conclusive.

Results

Description of studies

Out of 3,631 potentially relevant citations retrieved from electronic databases and searches of reference lists, 8 RCTs[5-9,18-20] met the inclusion criteria. Figure 1 shows the flow diagram of studies in this review. The studies included had a total of 2,397 patients (1,182 in the IVUS-guided stenting group). Table 1 summarizes the characteristics of these studies.

Risk of bias

Out of the studies included, 37% presented adequate sequence generation, 62% reported allocation concealment, 62% had blinded assessment of outcomes, 87% described losses to follow-up and exclusions and 100% used the intention-to-treat principle for statistical analyses (Table 2).

Effects of interventions

Primary endpoint: Major adverse cardiac events

Seven articles[5-9,18,19] (n = 2.186) evaluated MACE (Figure 2). IVUS stenting was associated with a nonsignificant reduction of 21% in MACE compared to ANGIO stenting (RR: 0.79; 95% CI: 0.61-1.03; I^2: 44%). Based on the GRADE approach, the quality of the evidence for this outcome was considered low, mainly because of imprecision and the inconsistency of the results (Table 3).

Analyzing individual outcomes, we observed that IVUS stenting was associated with a non-significant increase of 35% in all-cause mortality[5-9,18-20] (RR: 1.35; 95% CI: 0.73-2.48; I^2: 0%) and a non-significant reduction of 39% in myocardial infarction[5-9,18,19] (RR: 0.61; 95% CI: 0.29-1.26; I^2: 37%) as compared to ANGIO stenting (Figure 2). Based on the GRADE approach, the overall quality of evidence was moderate for all-cause mortality (on basis of the imprecision of the results) and low for myocardial infarction (based on imprecision and the inconsistency of the results) (Table 3).

Secondary endpoints

Angiographic restenosis

Figure 3 shows the comparison between IVUS vs. ANGIO stenting in relation to angiographic restenosis[5-8,18,20]. The IVUS-guided strategy determined a 27% reduction in angiographic restenosis (RR: 0.73; 95% CI: 0.54-0.97; I^2: 51%). The number of patients needed to treat (NNT) in order to prevent one angiographic restenosis was 11. According to the GRADE approach, the quality of the evidence for this outcome was moderate based on the inconsistency of the results in this analysis (Table 3).

Target lesion revascularization and target vessel revascularization

Five RCTs[5,6,9,18,19] evaluated TLR and 2 articles[5,7] evaluated TVR (Figure 4). There was a 38% reduction in TLR (RR: 0.62; 95% CI: 0.47-0.83; I^2: 0%) in patients submitted to IVUS stenting vs. ANGIO stenting. The NNT to prevent one TLR was 20. Based on the GRADE

approach, the evidence for TLR was of high quality (Table 3). Furthermore, there was a non-significant reduction of 42% in TVR (RR: 0.58; 95% CI: 0.30-1.12; I^2: 0%) in favor of IVUS. According to GRADE, there was moderate quality evidence for this outcome on the basis of the imprecision of the results (Table 3).

New percutaneous coronary intervention and coronary artery bypass grafting surgery

Two articles[7,8] evaluated re-PCI and three[7,9] evaluated CABG surgery. IVUS stenting determined a non-significant reduction of 43% in re-PCI (RR: 0.57; 95% CI: 0.16-2.01; I^2: 84%) and a non-significant reduction of 4% in CABG surgery (RR: 0.96; 95% CI: 0.52-1.77; I^2: 0%) as compared to ANGIO stenting. Based on the GRADE approach, re-PCI and CABG surgery presented very low and moderate quality evidence, respectively (Table 3).

Reliability and conclusiveness of data

To determine the optimal information size, we assumed a 20% control event rate (the control event rate in our meta-analysis for MACE) and a

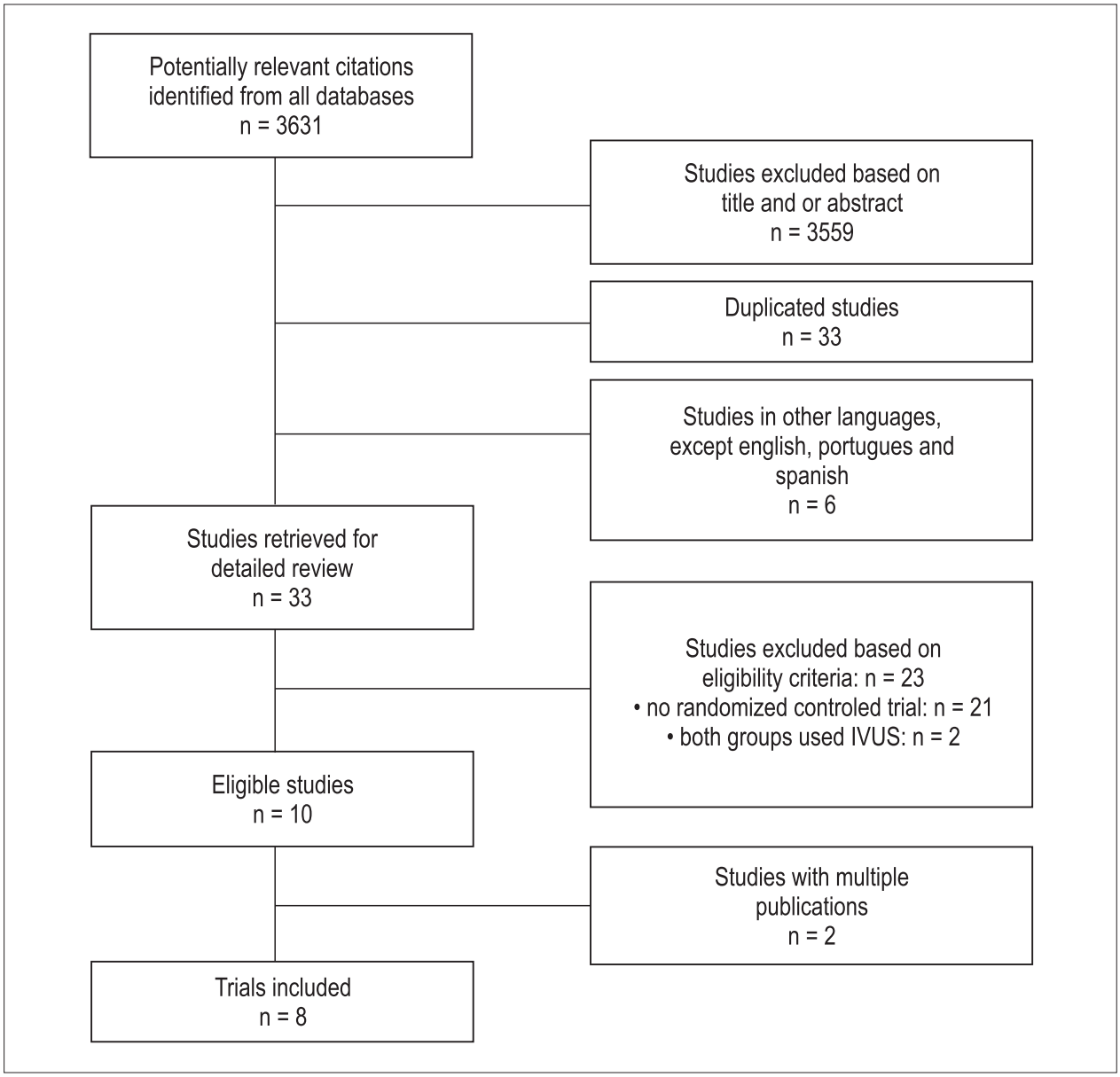

Figure 1 - *Flow diagram of included studies*

20% relative risk reduction with 90% power and a 0.01 two-sided α. This calculation indicated that the optimal information size needed to reliably detect a plausible treatment effect for this outcome is at least 4,655 patients.

Sensitivity analyses

Sensitivity analyses were performed for the outcomes, MACE and angiographic restenosis.

For MACE, no sensitivity analysis was performed considering the intention-to-treat analysis, because all studies included in this meta-analysis included this methodological characteristic. Regarding allocation concealment, the studies from Frey et al[18] and Oemrawsingh et al[6] were removed from the meta-analysis because they did not fulfill the criterion, though the result of the analysis remained unchanged (RR: 0.85, 95% CI: 0.64 -1.13; I^2: 35%). We also observed the same pattern in relation to the proper description of the sequence of randomization, when, following the removal of studies[5,6,8,19] that failed to fulfill this characteristic, there was no change to the outcome of the analysis (RR: 0.83, 95% CI: 0.63-1.09 , I^2: 36%). Furthermore, considering the blinding of assessors of outcomes, two articles[7,19] were removed from the meta-analysis and no difference was observed in the outcome (RR: 0.81, 95% CI: 0.59-1.11; I^2: 52%). In addition, with the withdrawal of

Table 1 - Characteristics of the included studies

Study, year	Patients (n) IVUS/Angio	Population	Stent	Length of follow-up	MACE definition	Reported clinical outcomes
Schiele et al., 1998[20]	79/76	CAD, single-vessel or native multivessel disease, PTCA followed by stenting.	Palmaz-Schatz, AVE, NIR, Freedom.	6-month	Not evaluated	AR, death.
Frey et al., 2000[18]	121/148	Elective or urgent PTCA or primary stenting in vessels of 2.2- 4.6 mm.	Palmaz-Schatz.	6-month angiographic, 24-month clinical.	Death, MI, re-PTCA, CABG.	MACE, death, MI, TLR, AR.
Mudra et al., 2001[8]	273/275	Angina or ischemia: lesion length ≤25 mm, diameter ≥2.5 mm.	JJIS, Power Grip, Crown or NIR.	6-month	Death, MI, CABG, re-PTCA.	MACE, death, MI, CABG surgery, re-PTCA, AR.
Gaster et al., 2003[7]	54/54	Stable angina pectoris with de novo lesions for PTCA.	Not reported	6-month angio, 30-month clinical	Death, MI, or revascularization procedures.	MACE, death, MI, CABG surgery, re-PTCA, TLR, AR.
Oemrawsingh et al., 2003[6]	73/71	Elective PTCA, lesion >20 mm, vessel ≥3 mm.	AVE GFX-XL	6-month	Death, MI, TLR.	MACE, death, MI, TLR, AR.
Gil et al., 2007[5]	83/80	Stable angina pectoris, 1 or 2 vessels disease, diameter > 2.75 mm, lesion < 25 mm.	Not reported	6-month	Death, MI and any repeated coronary artery revascularization.	MACE, death, MI, TLR, TVR, AR.
Russo et al., 2009[9]	369/375	Elective coronary stent placement, diameter ≥2.5 mm.	Palmaz-Schatz, NIR, Crown, AVE, MultiLink.	12-month	Death, MI, TLR.	MACE, death, MI, TLR, CABG surgery.
Jakabcin et al., 2010[19]	105/105	Unrestrictive, Vessel <2.5 mm, length >20 mm.	Drug-eluting stents	18-month	Death, MI, TLR	MACE, death, MI, TLR.

IVUS - intracoronary ultrasound; Angio - angiographic-guided stenting; PTCA - percutaneous transluminal coronary angioplasty; MACE - major adverse cardiac events; MI - myocardial infarction; AR - angiographic restenosis; TLR - target lesion revascularization; TVR - target vessel revascularization; CABG - coronary artery bypass graft.

the study that used drug eluting stents (DES)[19] from the analysis, no change was observed in the results (RR: 0.76, 95% CI: 0.57-1.03; I^2: 53%).

The angiographic restenosis outcome was presented using the case analysis available. Therefore, sensitivity analysis was performed using intention-to-treat analysis through data imputation[11]. For this outcome, non-use of intention-to-treat analysis by the authors did not influence the meta-analysis result (RR: 0.80, 95% CI: 0.64-0.98; I^2: 45%).

Discussion

In this article, we performed a systematic review and meta-analysis evaluating the impact of routine IVUS-guided coronary stent implantation on long-term outcomes. Our results demonstrated a significant reduction of 38% in TLR and 27% in angiographic restenosis with this strategy, but no statistically significant differences on total MACE, death or myocardial infarction.

In the current interventional cardiology practice, IVUS penetration has been highly heterogeneous, according to the experience and preference of each center and operator. The last updated Guidelines for Percutaneous Coronary Intervention assign a class IIa recommendation, level of evidence B, for IVUS guided coronary stent implantation[21]. Our results may serve to strengthen this recommendation, since angiographic and clinical restenoses were significantly lowered with IVUS guidance.

Table 2 - Risk of bias of included studies

Study, year	Adequate Sequence Generation	Allocation Concealment	Blinding of Outcome Assessors	Description of Losses and Exclusions	Intention-to-treat Analysis
Schiele et al., 1998[20]	No	No	Unclear	Yes	Yes
Frey et al., 2000[18]	Yes	No	Yes	Yes	Yes
Mudra et al., 2001[8]	No	Yes	Yes	Yes	Yes
Gaster et al., 2003[7]	Yes	Yes	No	Yes	Yes
Oemrawsingh et al., 2003[6]	No	No	Yes	Yes	Yes
Gil et al., 2007[5]	No	Yes	Yes	Yes	Yes
Russo et al., 2009[9]	Yes	Yes	Yes	Yes	Yes
Jakabcin et al., 2010[19]	No	Yes	No	No	Yes

Table 3 - Quality of evidence using the GRADE approach

Outcome Measure	N of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Risk Ratio	Quality of Evidence
MACE	7	no serious limitations	Serious*	no serious indirectness	serious†	0.79 (0.61 to 1.03)	Low
Death	8	no serious limitations	no serious inconsistency	no serious indirectness	serious†	1.35 (0.73 to 2.48)	Moderate
Myocardial Infarction	7	no serious limitations	Serious*	no serious indirectness	serious†	0.61 (0.29 to 1.26)	Low
Angiographic Restenosis	6	no serious limitations	serious‡	no serious indirectness	no serious imprecision	0.73 (0.54 to 0.97)	Moderate
Target Lesion Revascularization	5	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	0.62 (0.47 to 0.83)	High
Target Vessel Revascularization	2	no serious limitations	no serious inconsistency	no serious indirectness	serious†	0.58 (0.3 to 1.12)	Moderate
Re-PCI	2	no serious limitations	very serious‡	no serious indirectness	serious†	0.57 (0.16 to 2.01)	Very Low
CABG surgery	3	no serious limitations	no serious inconsistency	no serious indirectness	serious†	0.96 (0.52 to 1.77)	Moderate

** moderate statistical heterogeneity; † large confidence interval; ‡ high statistical heterogeneity; Re-PCI - new percutaneous coronary intervention; MACE - major adverse cardiac events; CABG - coronary artery bypass graft.*

However, the cost of this technology should also be taken into account. Considering the NNT to prevent one TLR (20) and the usual additional cost to include IVUS in a PCI procedure (circa R$ 2,000), a total expenditure of R$ 40,000 would be needed to prevent one TLR.

It is also important to consider if IVUS should be performed in all patients, or only in those at high risk of restenosis. Our analysis does not provide insights regarding the existence of subgroups with greater benefits, but it is reasonable to suggest that more complex patients could benefit more. The cost-benefit ratio of interventions aimed at reducing repeated revascularizations is also more favorable in those at high baseline restenosis risks[22].

Drug eluting stents are currently recommended for reduction of restenosis/re-occlusion, as long as no contraindication to extended dual antiplatelet therapy exists[23-26]. Our study did not address the question of whether routine IVUS-guided stenting is better than angiography alone when a DES is implanted[19]. Although some of the predictors of restenosis after DES or bare metal

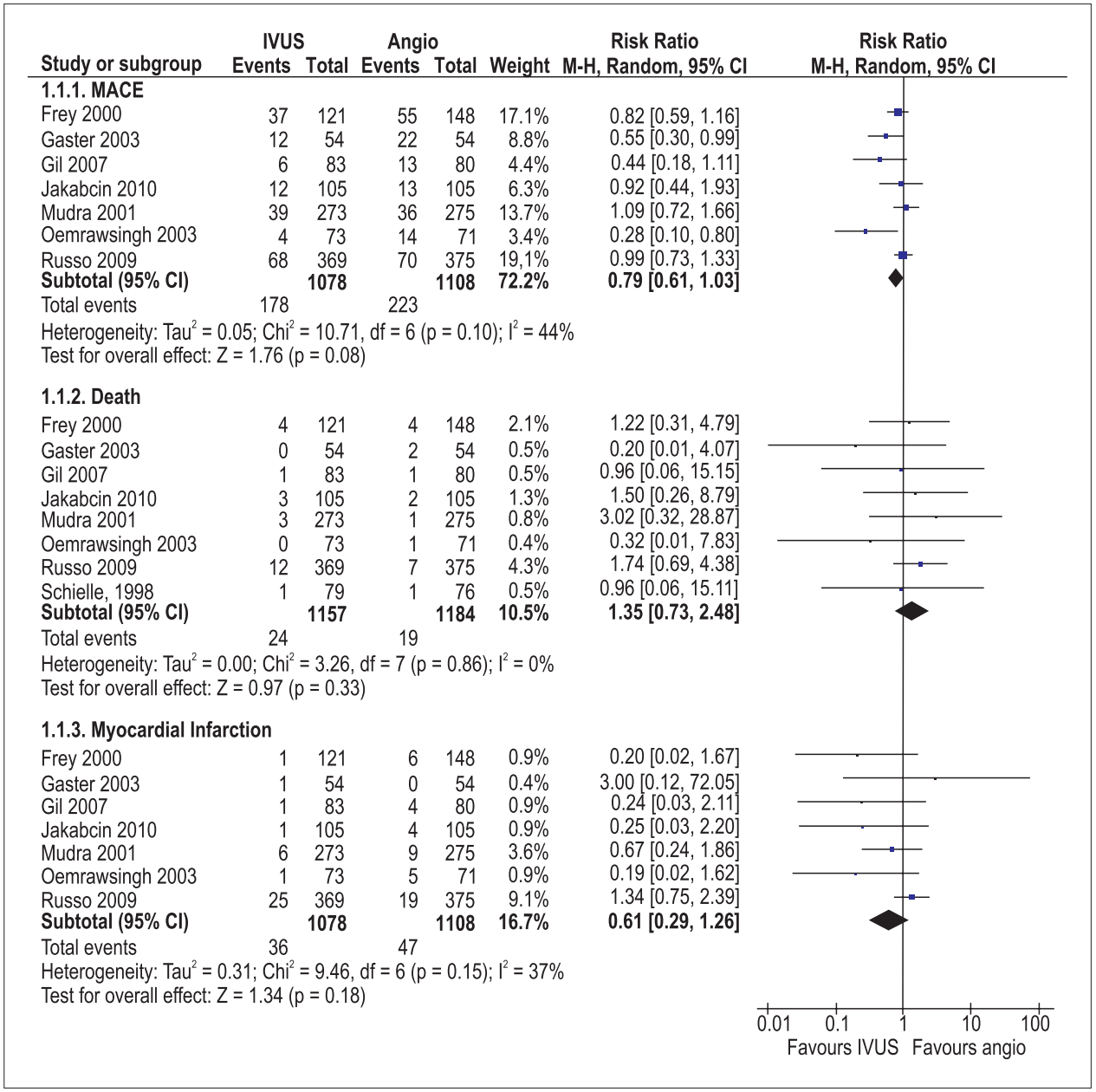

Figure 2 - *Major adverse cardiac events (MACE) for IVUS-guided stenting vs. angiographically-guided stenting; IVUS - intracoronary ultrasound; Angio - angiographically-guided stenting; CI - confidence interval.*

stent are similar[27,28], extrapolation of the data from one population to the other may not be appropriate. However, our results should also be put into the perspective that not all patients in daily practice will be good candidates to receive a DES. Patients with contraindications or known poor adherence to long term dual antiplatelet therapy, planned noncardiac surgery and comorbidities associated with increased risk of bleeding represent some of these situations[24,29-32].

The sensitivity analyses performed did not change the global results of the meta-analysis. Frey et al[18] performed a randomized clinical with IVUS-guided provisional stenting vs. conventional treating, but a stent was not actually implanted in all patients. We decided to include this trial in this meta-analysis, and sensitivity analysis removing this study did not alter the results for MACE, mortality, myocardial infarction, angiographic restenosis and TLR. The study performed by Jakabcin et al[19] adopted routine DES implantation by protocol, and we have also decided to include data from this trial. In the sensitivity analysis performed where this study was removed, the results were not modified.

Our study has several methodological strengths, which are: 1. Focused review questions, 2. A

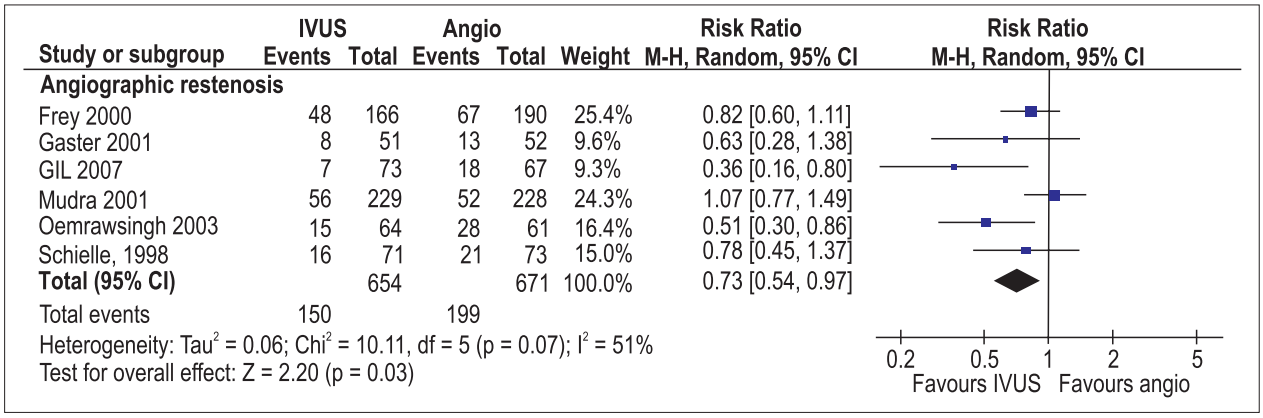

Figure 3 - *Angiographic restenosis for IVUS-guided stenting vs. angiographically-guided stenting; IVUS - intracoronary ultrasound; Angio - angiographically-guided stenting; CI -confidence interval.*

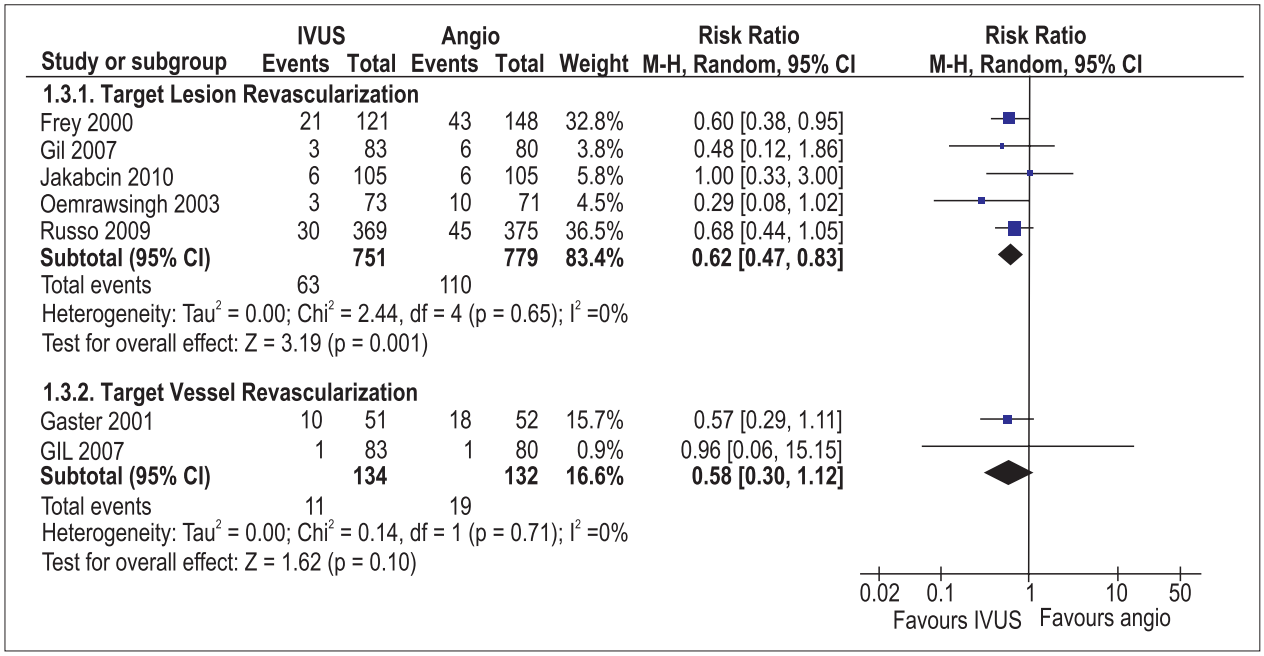

Figure 4 - *Target lesion revascularization and target vessel revascularization for IVUS-guided stenting vs. angiographically-guided stenting; IVUS - intracoronary ultrasound; Angio - angiographically-guided stenting; CI - confidence interval.*

comprehensive and systematic literature search and 3. The collaboration of a multidisciplinary team of interventional cardiologists, healthcare researchers and methodologists, that used explicit and reproducible eligibility criteria and duplicate highly independent and reproducible eligibility decisions and data abstractions. We employed meta-analysis to quantitatively express the results obtained and evaluated the quality of evidence for each outcome analyzed. Another important strength of this report is that we calculated the sample size (optimal information size) requirement for our meta-analysis as a way of determining whether evidence in our meta-analysis was reliable and conclusive.

Casella et al[33] have also conducted a meta-analysis in this field, which was published several years ago. This work included only 5 RCTs (n=1.883), while this review included 3 new RCTs, totaling 8 clinical trials (n=2.341). Considering only the analysis of RCTs of the first review[33], IVUS-guided stenting did not reduce MACE (OR: 0.82, 95% CI: 0.64-1.04), death (OR: 1.27, 95% CI: 0.47-3.42) or myocardial infarction (OR: 0.96, 95% CI: 0.59-1.56), similar to the findings of this study. However, we did observe lower restenosis rates with IVUS-guided stenting in comparison with angiographically-guided stenting, which was not seen by Casella et al[33] (OR: 0.81, 95% CI: 0.62-1.06). It should be emphasized that our systematic review only included RCTs and had a larger number of studies as compared to that of Casella et al[33], which may have contributed towards a better estimation of the data found by our group.

Parise et al[34] have also performed a systematic review on this topic recently. In their paper, the results regarding restenosis were similar, but they have also found a benefit of IVUS in the reduction of MACE (OR 0.72, 95% CI 0.52 – 0.99), which was not shown in our analysis. The major difference between the two meta-analyses is the omission of the RESIST trial MACE data in our calculations[20], which, in its publication, did not present the definition of MACE. In fact, a secondary publication of that trial suggests that the numbers used in the Parise et al[34] paper included only revascularization and death, what falls out of our definition (and the one from all other trials) of MACE, which included myocardial infarction[35]. Moreover, our analysis based on the GRADE approach suggests low-quality evidence for this outcome, and our calculation of the optimal information size shows that the question about the benefit of IVUS regarding MACE is far from being adequately responded.

Some limitations of our study should be pointed out. Firstly, most studies included in our systematic review may not represent the current PCI practice, since the stents used in the trials are not the ones employed today. PCI techniques have considerably changed, interventional cardiologists have more experience today than before, antiplatelet therapy is more aggressive and the complexity of the cases has increased[25]. Furthermore, the sample size was not ideal, since the total data available on MACE represent only 47% of the optimal information size required to reliably detect a plausible treatment effect. However, with more studies and with a larger number of patients, IVUS-guided stenting could significantly reduce MACE, since the p value for this analysis was 0.08.

Conclusions

This systematic review and meta-analysis demonstrates that IVUS-guided stenting reduces angiographic restenosis and TLR compared to angiographic-guided stenting, but do not reduce MACE. This data should provide further support for IVUS use, but the conduction of large scale and high-quality RCTs is needed to clarify the potential benefit of IVUS guidance regarding hard endpoints.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

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