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# Five-year outcomes following PCI with DES versus CABG for unprotected LM coronary lesions: meta-analysis and meta-regression of 2914 patients

*Desfechos de 5 anos do tratamento de lesões de TCE por stents farmacológicos versus CRM: meta-análise e meta-regressão de 2914 pacientes*

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*Abstract*

*Objective:* To compare the safety and efficacy at long-term follow-up of coronary artery bypass grafting (CABG) with percutaneous coronary intervention (PCI) using drug-eluting stents (DES) in patients with unprotected left main coronary artery (ULMCA) disease.

*Methods:* MEDLINE, EMBASE, CENTRAL/CCTR, SciELO, LILACS, Google Scholar and reference lists of relevant articles were searched for clinical studies that reported outcomes at 5-year follow-up after PCI with DES and CABG for the treatment of ULMCA stenosis. Five studies (1 randomized controlled trial and 4 observational studies) were identified and included a total of 2914 patients (1300 for CABG and 1614 for PCI with DES).

*Results:* At 5-year follow-up, there was no significant difference between the CABG and PCI-DES groups in the risk for death (odds ratio [OR] 1.159, *P*=0.168 for random effect) or the composite endpoint of death, myocardial infarction, or stroke (OR 1.214, *P*=0.083). The risk for target vessel revascularization (TVR) was significantly lower in the CABG group compared to the PCI-DES group (OR 0.212, *P*<0.001). The risk of major adverse cardiac and cerebrovascular events (MACCE) was significantly lower in the CABG group compared to the PCI-DES group (OR 0.526, *P*<0.001). It was observed no publication bias about outcomes and considerably heterogeneity effect about MACCE.

*Conclusion:* CABG surgery remains the best option of treatment for patients with ULMCA disease, with less need of TVR and MACCE rates at long-term follow-up.

*Descriptors:* Meta-analysis. Myocardial revascularization. Drug-eluting stents.

*Resumo*

*Objetivo:* Comparar segurança e eficácia do seguimento a longo prazo da cirurgia de revascularização miocárdica (CRM) com intervenção coronária percutânea (ICP), utilizando stents farmacológicos (SF) em pacientes com lesão de tronco de coronária esquerda não-protegida (TCE).

*Métodos:* MEDLINE, EMBASE, CENTRAL/CCTR, SciELO, LILACS, Google Scholar e listas de referências de

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| Abbreviations, Acronyms & Symbols | |
|---|---|
| CABG | Coronary artery bypass graft |
| CENTRAL/CCTR | Cochrane Central Register of Controlled Trials |
| CI | Confidence interval |
| DES | Drug-eluting stents |
| EuroSCORE | European System for Cardiac Operative Risk Evaluation |
| LILACS | Literatura Latino-Americana e do Caribe em Ciências da Saúde |
| MACCE | Major adverse cardiac and cerebrovascular events |
| MeSH | Medical subject heading |
| OR | Odds ratio |
| PCI | Percutaneous coronary intervention |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| SciELO | Scientific Electronic Library Online |
| TVR | Target vessel revascularization |
| ULMCA | Unprotected left main coronary artery |

artigos relevantes foram escaneados para estudos clínicos que relataram resultados em 5 anos de seguimento após ICP-SF e CRM para o tratamento de lesão de TCE. Cinco estudos (um ensaio clínico randomizado e quatro estudos observacionais) foram identificados e incluíram um total de 2914 pacientes (1300 para CRM e 1614 para ICP-SF).

*Resultados:* Aos 5 anos de seguimento, não houve diferença significativa entre os grupos CRM e ICP-SF no risco de morte (odds ratio [OR] 1,159, *P*=0,168) ou desfecho composto de morte, infarto do miocárdio , ou AVC (OR 1,214, *P*=0,083). O risco de necessidade de nova revascularização foi significativamente menor no grupo CRM em comparação com o grupo de ICP-SF (OR 0,212, *P*<0,001). O risco de eventos adversos cardíacos maiores e cerebrovasculares (EACMC) foi significativamente menor no grupo CRM em comparação com o grupo de ICP-SF (OR 0,526, *P*<0,001). Não foi observado viés de publicação sobre os resultados e considerável heterogeneidade dos efeitos sobre EACMC.

*Conclusão:* CRM continua sendo a melhor opção de tratamento para pacientes com lesão de TCE, com menos necessidade de novas revascularizações e EACMC no seguimento a longo prazo.

*Descritores:* Metanálise. Revascularização miocárdica. Stents farmacológicos.

## INTRODUCTION

### Rationale

Current guidelines recommend percutaneous coronary intervention (PCI) of unprotected left main coronary artery (ULMCA) with stents as a Class IIa or IIb alternative to coronary artery bypass graft (CABG) in patients with conditions that are associated with a low risk of PCI procedural complications and/or increased risk of adverse surgical outcomes [1]. Capodanno et al. [2] recently published a meta-analysis of 4 randomized controlled trials and suggested, boldly, that "based on that study, revision of the guidelines regarding left main PCI is warranted, raising the level of evidence of current recommendations from B to A". Although recent randomized controlled trials have suggested that PCI with drug-eluting stents (DES) could be a non-inferior strategy that might be used safely [3,4], sample sizes are small (and some conclusions may be affected by this aspect) and observational studies ("real-world" studies) should not be ignored in meta-analyses.

Recently, Sá et al. [5] published a new meta-analysis with 16 studies (three randomized and 13 observational) with 1-year follow up results. This one argued against the "non-inferiority" of PCI with DES in comparison to CABG surgery and against the idea that PCI could be considered a reasonable choice in elective cases (not mentioning prohibitive risk patients, acute patients and those who reject surgery), given that, although the rates of death between both strategies were not statistically different, the need of new procedures and major adverse cardiac and cerebrovascular events rates were clearly lower in patients treated with CABG surgery. Sá et al. [5] emphasized that the length of follow-up considered for their study may have been too short (1-year) to truly detect differences between the treatment groups, and so was the study of published by Capodanno et al. [2].

Performing a quick search on medical literature, we found no meta-analyses that evaluated the long-term results regarding this topic (PCI with DES versus CABG in ULMCA disease). Taking into considerations all these aspects, it is necessary to evaluate the long-term results of CABG surgery versus PCI with DES in scenario of ULMCA disease, using the highest level of existing evidence.

### Objective

We performed a meta-analysis of randomized controlled trials and observational studies to compare

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CABG to PCI with DES for the treatment of patients with ULMCA disease, according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [6].

METHODS

**Eligibility Criteria**

Using PICOS studies were considered if: (1) population comprised patients with ULMCA disease; (2) compared efficacy or effectiveness between CABG and PCI with DES; (3) outcomes studied included myocardial infarction, cerebrovascular events, death, target vessel revascularization (TVR) or combined outcomes (MACCE – major adverse cardiac and cerebrovascular events); (4) presented follow-up of at least 5 years.

**Information Sources**

The following databases were used (until July 2012): MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL/CCTR), ClinicalTrials.gov, SciELO (Scientific Electronic Library Online), LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde – The Latin American and Caribbean Health Sciences), Google Schoolar and reference lists of relevant articles.

**Search**

We conducted the search using Medical Subject Heading (MeSH) terms "coronary artery bypass graft" OR "coronary artery bypass grafting" OR "coronary artery bypass surgery" OR "coronary bypass surgery" OR "coronary artery bypass graft surgery" OR "coronary artery bypass" OR "coronary bypass" AND "drug-eluting stent" OR "sirolimus-eluting stent" OR "paclitaxel-eluting stent" AND "unprotected left main" OR "left main stenting" OR "left main coronary artery disease" OR "left main PCI" OR "unprotected left main coronary artery" OR "left main stenosis" OR "left main coronary artery stenting" OR "unprotected left main stenting".

**Study Selection**

The following steps were done: (1) identification of titles of records through databases searching; (2) removal of duplicates; (3) screening and selection of abstracts; (4) assessment for eligibility through full-text articles; (5) final inclusion in study.

One reviewer followed the steps 1 to 3. Two independent reviewers followed step 4 and selected studies. Inclusion

or exclusion of studies was decided unanimously. When there was disagreement, a third reviewer took the final decision.

**Data Items**

The primary endpoint was the Odds Ratio (OR) for mortality after PCI or CABG, up to 5 years. Secondary end points were the OR for composite endpoint of death, myocardial infarction or stroke; TVR (target vessel revascularization – repeat revascularization of the treated vessel) after the procedure; and MACCE (major adverse cardiac and cerebrovascular events – composite endpoint of death, myocardial infarction, stroke or TVR).

**Data Collection Process**

Two independent reviewers extracted the data. When there was disagreement about data, a third reviewer (the first author) checked the data and took the final decision about it. From each study, we extracted patient characteristics, study design, and outcomes at 5-year after treatment of ULMCA stenosis. When possible, actual probabilities of mortality and death after 5-year following PCI or CABG were used to calculate odds ratios. Alternatively, probabilities of mortality or MACCE were estimated from published Kaplan-Meier survival curves. We also extracted TVR from the total MACCE events and reported this outcome as a separate measure. When MACCE was not reported, we calculated it using the events of death, myocardial infarction, stroke and TVR and reported this outcome as a separate measure.

**Risk of Bias in Individual Studies**

Included studies were assessed for the following characteristics: design (prospective or retrospective), randomization (yes or no), multicenter enrollment (yes or no), characteristics of participants and personnel (performance bias), outcome assessment (detection bias), incomplete outcome data addressed (attrition bias) and adequacy of multivariate adjustment for possible confounders.

Two independent reviewers assessed risk of bias. Agreement between the two reviewers was assessed using kappa statistics for full text screening, and rating of relevance and risk of bias. When there was disagreement about risk of bias, a third reviewer (the first author) checked the data and took the final decision about it.

**Summary Measures**

The principal summary measures were OR's with

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95% Confidence Interval (CI) and *P* values (that will be considered statistically significant when <0.05). The meta-analysis was completed using the software Comprehensive Meta-Analysis version 2 (Biostat Inc., Englewood, New Jersey, USA).

### Synthesis of Results

Forest plots were generated for graphical presentations for clinical outcomes and we performed the $I^2$ test and $Chi^2$ statistics for assessment of heterogeneity across the studies [7]. Each study was summarized by the OR for PCI compared to CABG. The OR's were combined across studies using DerSimonian-Laird random effects model [8] and with the fixed effects model using the Mantel-Haenszel model [9]. Both models were weighted by number of events in each study.

### Risk of Bias Across Studies

To assess publication bias, a funnel plot was generated (for each outcome), being statistically assessed by Begg and Mazumdar's test [10] and Egger's test [11].

### Meta-regression Analysis

Meta-regression analyses were performed to determine whether the effects of CABG were modulated by pre-specified factors. Meta-regression graphs describe the effect of CABG on the outcome (plotted as a log OR on the y-axis) as a function of a given factor (plotted as a mean or proportion of that factor on the x-axis). Meta-regression coefficients show the estimated increase in log OR per unit increase in the covariate. Since log OR >0 corresponds to OR >1 and log OR <0 corresponds to OR<1, a negative coefficient would indicate that as a given factor increases, the OR decreases.

The pre-determined modulating factors for all outcomes to be examined were: sex, age, diabetes and prior PCI. Sex was represented as the proportion of females in the studies. Age was represented as the mean age of the patients participating in the studies. Diabetes was represented as the proportion of diabetics in the studies. Prior PCI was represented as the proportion of patients who underwent PCI before any interventions in the studies.

### RESULTS

### Study Selection

A total of 14.705 citations were identified, of which 31 studies were potentially relevant and retrieved as full-text. Five publications fulfilled our eligibility criteria [12-16]. Interobserver reliability of study relevance was excellent (Kappa=0.84). Agreement for decisions related to study validity was very good (Kappa=0.81). The search strategy can be seen in Figure 1.

### Study Characteristics

Characteristics of each study are shown in Table 1. A total of 2914 patients were studied with 1300 receiving CABG and 1614 receiving PCI with DES. Of the 5 studies, one was randomized controlled trial [14], one matched the treatment cohorts using European System for Cardiac Operative Risk Evaluation (EuroSCORE) [16], two used other propensity scores to guarantee like-to-like comparisons [12,15], Four studies mostly used Cypher stent (sirolimus) or Taxus stent (paclitaxel) and one study did not report which DES was used. The overall internal validity was moderate risk of bias and is illustrated in Table 2.

### Synthesis of Results

The OR of the risk of death in the CABG group compared with the PCI-DES group in each study, at the 5-year time point, is reported in Figure 2. There was no evidence for heterogeneity of treatment effect among the studies for death. The overall OR (95% confidence interval) of mortality showed no difference between CABG and PCI-DES at 5-year (fixed effect model: OR 1.159, *P*=0.168; random effect model: OR 1.159, *P*=0.168).
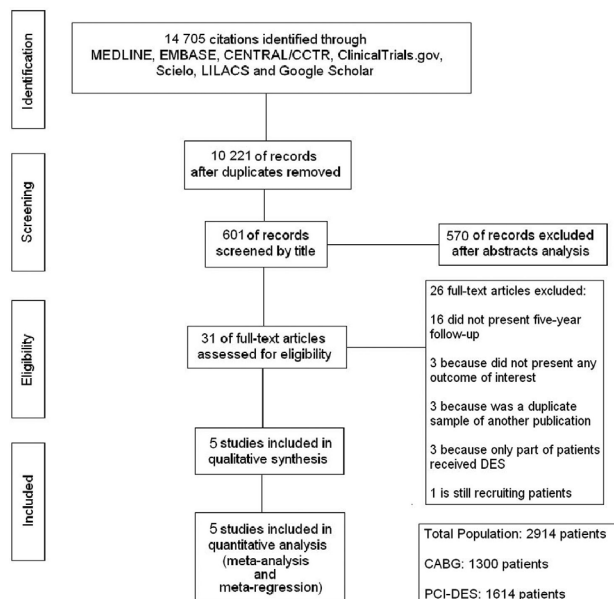


*Fig. 1 – Flow diagram of studies included in data search*

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Table 1.    Study characteristics.

| Study | PCI (n) | DES | Complete revascularization with PCI (%) | CABG (n) | LIMA to LAD (%) | Off-pump (%) | Complete revascularization with CABG (%) | Unadjusted risk | Method of Adjustment |
|---|---|---|---|---|---|---|---|---|---|
| Chang et al. 2012 [12] | 556 | NR | NR | 309 | NR | NR | NR | CABG higher risk clinical profile; EuroSCORE higher risk profile; SYNTAX score higher risk profile | Propensity matched |
| Terazawa et al. 2012 [13] | 68 | Cypher (88%) Taxus (12%) | NR | 57 | 93 | 51 | NR | CABG higher risk clinical profile; EuroSCORE higher risk profile | Multivariate logistic regression and multivariable Cox regression |
| Boudriot et al. 2011 [14] | 100 | Cypher (98%) Taxus (2%) | 98 | 101 | 99 | 46 | 97 | Randomized, same risk | Unneeded |
| MAIN-COMPARE registry 2010 [15] | 396 | Cypher (79%) Taxus (21%) | NR | 396 | 98 | 42 | NR | Propensity score matched | Unneeded |
| Chieffo et al. 2010 [16] | 107 | Cypher (51.4%) Taxus (48.2%) | NR | 142 | NR | NR | NR | CABG higher risk clinical profile | Propensity score adjusted (EuroSCORE) |

*CABG: coronary artery bypass grafting; DES: drug-eluting stent; LAD: left anterior descending; LIMA: left internal mammary artery; PCI: percutaneous coronary intervention; NR: non-reported*

Table 2.    Analysis of risk of bias – internal validity.

| Study | Study design | Selection bias | Performance bias | Attrition bias | Detection bias | Multivariate adjustment for possible confounders |
|---|---|---|---|---|---|---|
| Chang et al. 2012 [12] | NP, NR, M | B | B | C | B | Probably adequate |
| Terazawa et al. 2012 [13] | NP, NR, NM | B | B | B | B | Probably adequate |
| Boudriot et al. 2011 [14] | P, R, M | A | B | A | B | Probably adequate |
| MAIN-COMPARE registry 2010 [15] | P, NR, M | B | B | B | B | Probably adequate |
| Chieffo et al. 2010 [16] | NP, NR, NM | B | B | C | B | Probably adequate |

*This was performed by 2 independent reviewers. The overall bias of the combined studies was considered moderate. A: risk of bias is low; B: risk of bias is moderate; C: risk of bias is high; D: incomplete reporting*



| Model | Study name | Odds ratio | P-Value | Relative weight (%) Weight (Fixed) | Relative weight (%) Weight (Random) |
|---|---|---|---|---|---|
| | Chang 2012 | 1,155 | 0,467 | 29,25 | 29,25 |
| | Terazawa 2012 | 1,195 | 0,626 | 8,61 | 8,61 |
| | Boudriot 2011 | 0,989 | 0,980 | 5,61 | 5,61 |
| | MAIN-COMPARE registry 2011 | 0,172 | 0,311 | 46,74 | 46,74 |
| | Chieffo 2010 | 1,187 | 0,617 | 9,79 | 9,79 |
| Fixed | | 1,159 | 0,168 | | |
| Random | | 1,159 | 0,168 | | |

Total (95% CI): 1300 (CABG); 1614 (PCI-DES)
Total events: 205 (CABG); 225 (PCI-DES)
Test for heterogeneity: Chi$^2$ = 0.14; df = 4 (P = 0.998); I$^2$ = 0.0%
Test for overall fixed effect: Z = 1.38 (P = 0.168)
Test for overall random effect: Z = 1.38 (P = 0.168)

*Fig. 2 – Odds ratio and conclusions plot of mortality associated with CABG versus DES*

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Fig. 3 – Odds ratio and conclusions plot of composite endpoint (death, myocardial infarction or stroke) associated with CABG versus DES
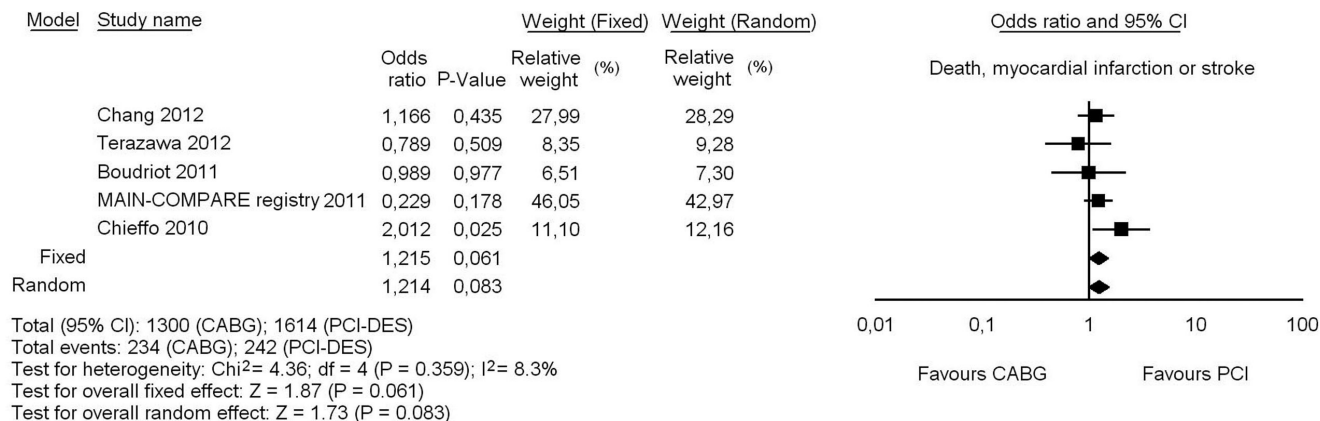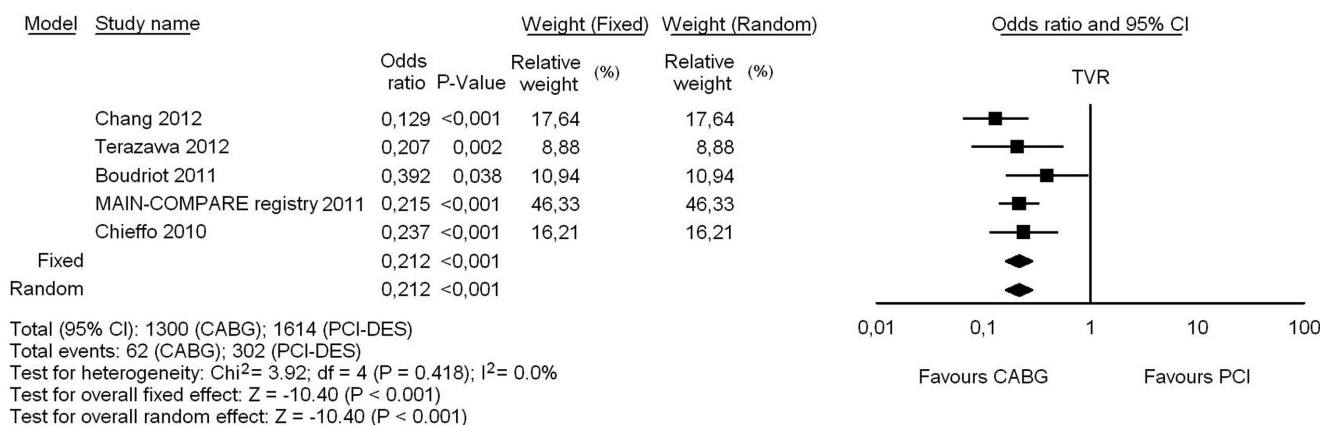


Fig. 4 – Odds ratio and conclusions plot of target vessel revascularization (TVR) associated with CABG versus DES

The OR of the risk of composite endpoint of death, myocardial infarction or stroke in the CABG group compared with the PCI-DES group in each study, at the 5-year time point, is reported in Figure 3. There was evidence of low heterogeneity of treatment effect among the studies for this composite endpoint. The overall OR (95% confidence interval) of composite end point showed no difference between PCI-DES and CABG at 5-year (fixed effect model: OR 1.215, *P*=0.061; random effect model: OR 1.214, *P*=0.083).

The OR of the risk of TVR in the CABG group compared with the PCI-DES group in each study, at the 5-year time point, is reported in Figure 4. There was no evidence for heterogeneity of treatment effect among the studies for TVR. The overall OR (95% confidence interval) of TVR showed an important difference between CABG and PCI-DES at 5-year (fixed effect model: OR 0.212, *P*<0.001;

random effect model: OR 0.212, *P*<0.001), which favors the CABG strategy.

The OR of the risk of MACCE in the CABG group compared with the PCI-DES group in each study, at the 5-year time point, is reported in Figure 5. There was a considerably evidence for heterogeneity of treatment effect among the studies for MACCE. The overall OR (95% confidence interval) of MACCE showed an important difference between CABG and PCI-DES at 5-year (fixed effect model: OR 0.543, *P*<0.001; random effect model: OR 0.526, *P*<0.001), which favors the CABG strategy.

**Risk of Bias Across Studies**

Funnel plot analysis (Figure 6) disclosed symmetry around the axis for the treatment effect in all outcomes, which means we probably do not have publication bias related to these end points.

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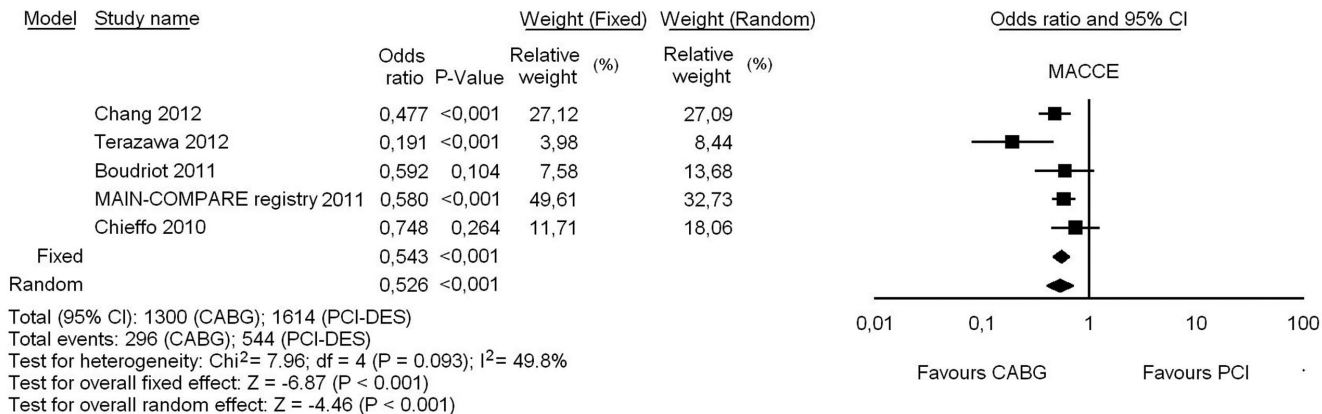*Rev Bras Cir Cardiovasc 2013;28(1):83-92*

Fig. 5 – Odds ratio and conclusions plot of major adverse cardiac and cerebrovascular events (MACCE) associated with CABG versus DES
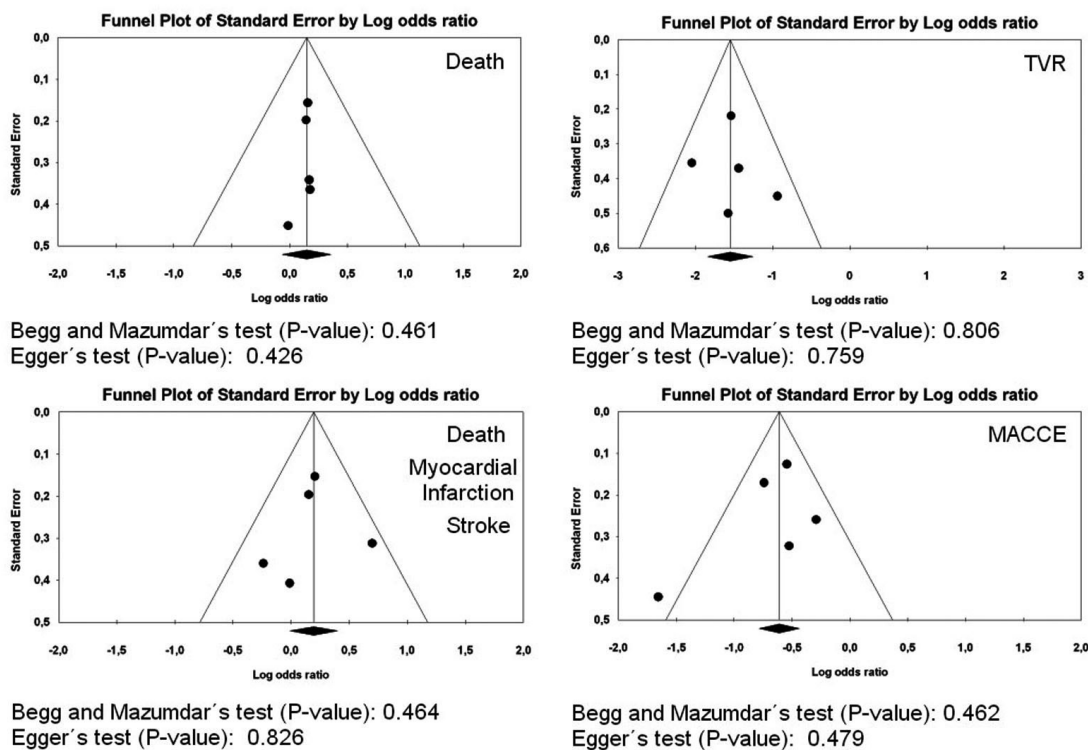


Fig. 6 – Publication bias analysis by funnel plot graphic

### Meta-regression Analysis

We observed a statistically significant coefficient for 2 situations: (1) MACCE and proportion of diabetic patients (coefficient -0.04, 95% CI -0.07 to -0.01, $P$=0.016); (2) MACCE and proportion of prior PCI (coefficient -0.03, 95% CI -0.05 to -0.01, $P$=0.010). It means that the greater the proportion of diabetic patients and prior PCI in a population undergoing CABG, the lower the OR for MACCE in CABG group, i.e., the greater the protective effect of CABG for diabetic patients and/or submitted to prior PCI in relation to the incidence of MACCE (Figure 7).

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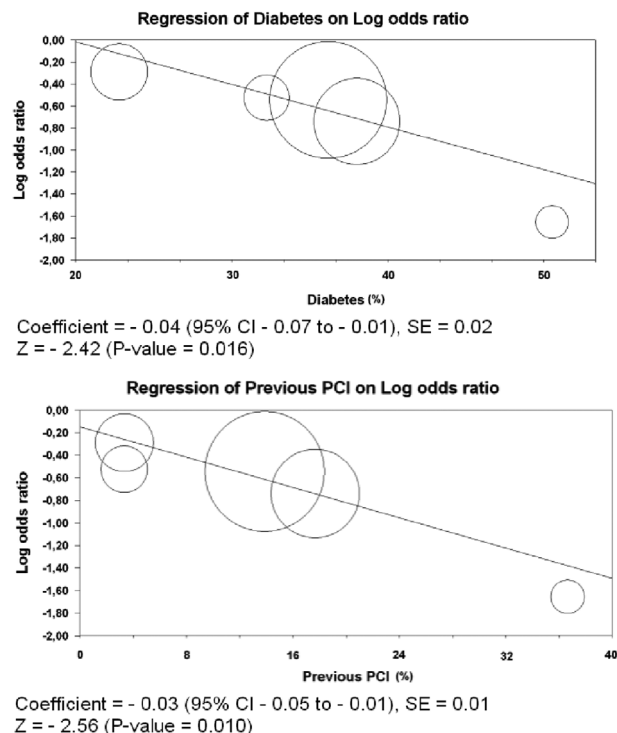
### Regression of Diabetes on Log odds ratio

Coefficient = - 0.04 (95% CI - 0.07 to - 0.01), SE = 0.02
Z = - 2.42 (P-value = 0.016)

### Regression of Previous PCI on Log odds ratio

Coefficient = - 0.03 (95% CI - 0.05 to - 0.01), SE = 0.01
Z = - 2.56 (P-value = 0.010)

*Fig. 7 – Meta-regression analysis by representative plots*

## DISCUSSION

### Summary of Evidence

The results of this meta-analysis demonstrate that
CABG remains the best option for ULMCA disease. At
5-year follow-up, although there was no difference in the
risk for death and composite endpoint of death, myocardial
infarction and stroke, there was a significantly higher risk
for TVR and MACCE (this last one under the influence
of heterogeneity of the effects) associated with PCI with
DES, with no publication bias of the summary measures
of all outcomes.

### Considerations About this Meta-Analysis

To our knowledge, this is the first meta-analysis of
studies with 5-years follow-up performed to date about
PCI-DES versus CABG in ULMCA disease, providing
incremental value by demonstrating that CABG reduces
the incidence of TVR and MACCE compared with PCI-
DES. Furthermore, this analysis suggests that PCI-DES
does not significantly reduce the incidence of long-term
all-cause mortality and composite endpoint of death,
myocardial infarction and stroke in comparison with

CABG. The potential benefits of CABG on these outcomes
appear to be influenced by diabetes and previous PCI.

Diabetes mellitus is a powerful independent predictor
of cardiovascular events. It is associated with extensive
coronary artery disease, increased mortality regardless
of revascularization mode and unfavorable prognosis if
treated medically [17]. The SYNTAX trial [18] has shown
in the diabetic subset of patients at 1 year, similar death/
infarction/stroke rates between the two revascularization
groups, increased risk across all SYNTAX terciles and
higher mortality and MACCE in diabetic patients with
SYNTAX score ≥33 with PCI over surgery. As we can see
by meta-analysis and meta-regression, the total population
of patients with ULMCA disease benefit from surgery (in
comparison with PCI-DES) and the population of diabetics
benefit more, since the presence of diabetes modulate the
effect toward the protective effect (lesser odds ratio).

In case of prior PCI, the severity of the progression of
coronary atherosclerotic disease may justify the greater
MACCE in PCI-DES group previously submitted to PCI,
making CABG appears to be more protective. Currently,
patients undergoing initial PCI with a stent have severe
atherosclerotic disease, but not as severe as those undergoing
initial surgical treatment; when treatment with stents fails,
these patients are referred for surgical revascularization,
however the atherosclerotic disease is then more severe and
diffuse [19]. At present, the totality of evidence suggests
that CABG appears better for the "sicker" patients, i.e.,
those with multivessel disease or ULMCA disease and
characteristics indicative of extensive atheroma burden with
or without depressed left ventricle ejection fraction [20]. We
should not forget that SYNTAX trial showed the undoubted
benefits of surgery (in comparison with PCI-DES) in the
group with higher SYNTAX score, i.e., more extensive and
complex lesions [4].

### Risk of Bias and Limitations

Another limitation is the heterogeneity of the strategies
across the studies. Among PCI strategies, studies used
many combinations of sirolimus-stent and paclitaxel-
stents (one did not report). Among CABG strategies, there
is variability in rates of use of internal thoracic artery (two
did not report), use of cardiopulmonary bypass (on-pump
versus off-pump CABG; two did not report), etc. And
among both studies, an important aspect to consider is the
rate of complete revascularization (not reported in four
studies), which reflects in outcomes.

There are inherent limitations with meta-analyses,
including the use of cumulative data from summary

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estimates. Patient data were gathered from published data, not from individual patient follow-up. Access to individual patient data would have enabled us to conduct further subgroup analysis and propensity analysis to account for differences between the treatment groups. This meta-analysis included data from nonrandomized observational studies, which reflects the "real world" but are limited by treatment bias, confounders, and a tendency to overestimate treatment effects. Patient selection alters outcome and thus makes nonrandomized studies less robust.

We tried to analyze the influence of surgical risk profile and profile of lesion complexity; however, it was not possible because studies did not report these issues more systematically and broadly; it would be interesting, for example, that studies always evaluate SYNTAX score of groups, as this would allow further analysis of outcomes with respect to this variable, including meta-analyzes on this topic.

A final limitation is the absence of adequate published comparative data for the third therapeutic option, medical therapy. PCI with DES has not been compared with medical therapy alone when we consider ULMCA disease, but CABG has been shown to be superior to medical therapy in this set.

### Perspectives

Ongoing and planned trials (Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease - PRECOMBAT 1 and 2; Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization - EXCEL) will further facilitate evidence-based clinical decisions for ULMCA disease. Furthermore, the 5-year SYNTAX results (not published yet) will provide us a valuable extension of the 3-year information and possibly elucidate whether PCI should be further performed even in high-risk, very complex coronary disease by experienced teams in large volume centers. Others important registries (as CUSTOMIZE registry [11]) did not report their 5-year results yet. We hope that with the publication of all these studies, we will have more evidence about the long-term results, which will enable new meta-analyses with larger samples and other meta-regression analyses, in search of other factors that modulate the results.

### CONCLUSIONS

We found evidence that argues against the "non-inferiority" of PCI with DES in comparison to CABG surgery and against the idea that PCI can be considered a reasonable choice in elective cases (not mentioning prohibitive risk patients, acute patients and those who reject surgery), given that, although the rates of death and composite endpoint (death, myocardial infarction or stroke) between both strategies were not statistically different, the need of new procedures and MACCE rates were clearly lower in patients treated with CABG surgery. However, careful analysis of the data shows that no definite conclusion can be drawn from the evidence available due to the heterogeneity of studies with respect to some outcomes, heterogeneity of strategies (different drug-eluting stents, different ways to perform surgery, etc) and heterogeneity of coronary lesions complexity. Rigorous studies are necessary to define the best way to treat each subset of ULMCA disease.

Based on our findings, we conclude that there is not clear evidence that left main PCI presents non-inferiority to CABG surgery and revision of the guidelines regarding left main PCI must be viewed with caution, and we still do not have enough evidences that make the level of evidence of current recommendations raises from B to A".

### REFERENCES

1. Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association Association for Cardio-Thoracic Surgery (EACTS), Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization. Eur Heart J. 2010;31(20):2501-55.

2. Capodanno D, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: a meta-analysis of randomized clinical data. J Am Coll Cardiol. 2011;58(14):1426-32.

3. Park SJ, Kim YH, Park DW, Yun SC, Ahn JM, Song HG, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med. 2011;364(18):1718-27.

4. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al; SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360(10):961-72.

5. Sá MP, Soares AM, Lustosa PC, Martins WN, Browne F, Ferraz PE, et al. Meta-analysis of 5674 patients treated with percutaneous coronary intervention and drug-eluting stents for coronary artery bypass graft surgery for unprotected

Sá MPBO, et al. - Five-year outcomes following PCI with DES versus CABG for unprotected LM coronary lesions: meta-analysis and meta-regression of 2914 patients

*Rev Bras Cir Cardiovasc 2013;28(1):83-92*

left main coronary artery stenosis. Eur J Cardiothorac Surg. 2013;43(1):73-80.

6. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151(4):264-9.

7. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-60.

8. DerSimonian R, Kacker R. Random-effects model for meta-analysis of clinical trials: an update. Contemp Clin Trials. 2007;28(2):105-14.

9. Lau J, Ioannidis JP, Schmid CH. Quantitative synthesis in systematic reviews. Ann Intern Med. 1997;127(9):820-6.

10. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994;50(4):1088-101.

11. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-34.

12. Chang K, Koh YS, Jeong SH, Lee JM, Her SH, Park HJ, et al. Long-term outcomes of percutaneous coronary intervention versus coronary artery bypass grafting for unprotected left main coronary bifurcation disease in the drug-eluting stent era. Heart. 2012;98(10):799-805.

13. Terazawa S, Tajima K, Takami Y, Tanaka K, Okada N, Usui A, et al. Early and late outcomes of coronary artery bypass surgery versus percutaneous coronary intervention with drug-eluting stents for dialysis patients. J Card Surg. 2012;27(3):281-7.

14. Boudriot E, Thiele H, Walther T, Liebetrau C, Boeckstegers P, Pohl T, et al. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. J Am Coll Cardiol. 2011;57(5):538-45.

15. Park DW, Seung KB, Kim YH, Lee JY, Kim WJ, Kang SJ, et al. Long-term safety and efficacy of stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: 5-year results from the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) registry. J Am Coll Cardiol. 2010;56(2):117-24.

16. Chieffo A, Magni V, Latib A, Maisano F, Ielasi A, Montorfano M, et al. 5-year outcomes following percutaneous coronary intervention with drug-eluting stent implantation versus coronary artery bypass graft for unprotected left main coronary artery lesions the Milan experience. JACC Cardiovasc Interv. 2010;3(6):595-601.

17. Flaherty JD, Davidson CJ. Diabetes and coronary revascularization. JAMA. 2005;293(12):1501-8.

18. Banning AP, Westaby S, Morice MC, Kappetein AP, Mohr FW, Berti S, et al. Diabetic and nondiabetic patients with left main and/or 3-vessel coronary artery disease: comparison of outcomes with cardiac surgery and paclitaxel-eluting stents. J Am Coll Cardiol. 2010;55(11):1067-75.

19. Borges JC, Lopes N, Soares PR, Góis AF, Stolf NA, Oliveira SA, et al. Five-year follow-up of angiographic disease progression after medicine, angioplasty, or surgery. J Cardiothorac Surg. 2010;5:91.

20. Smith PK, Califf RM, Tuttle RH, Shaw LK, Lee KL, Delong ER, et al. Selection of surgical or percutaneous coronary intervention provides differential longevity benefit. Ann Thorac Surg. 2006;82(4):1420-8.

21. Caggegi A, Capodanno D, Capranzano P, Chisari A, Ministeri M, Mangiameli A, et al. Comparison of one-year outcomes of percutaneous coronary intervention versus coronary artery bypass grafting in patients with unprotected left main coronary artery disease and acute coronary syndromes (from the CUSTOMIZE Registry). Am J Cardiol. 2011;108(3):355-9.