Simple Versus Complex Bifurcation Stenting Strategies A Meta Analysis of Randomized Controlled Trials in the Drug Eluting Stent Era

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Background --- The ideal approach to coronary bifurcation lesions in the drug eluting stent era is a matter of debate between simple (main branch plus provisional side branch stenting) and complex (main branch plus routine side branch stenting) strategies. The purpose of this study was to perform a systematic review of randomized controlled trials in the drug eluting stent era comparing a strategy of simple versus complex coronary bifurcation lesion stenting.

Methods --- PubMed, Cardiosource, MyAHA, and other databases were searched from 2003 for randomized controlled trials comparing simple versus complex bifurcation lesion stenting strategies. Published randomized trials comparing simple and complex bifurcation lesion stenting strategies using drug eluting stents were included. Patients were adults with stable or unstable angina pectoris. Studies were excluded if they enrolled acute ST elevation myocardial infarction, restenotic lesions, heavily calcified or thrombus laden disease. Outcomes of interest included 1) the composite of major cardiac events (MACE-cardiac death, non-fatal myocardial infarction, target lesion revascularization, and stent thrombosis), 2) the individual MACE components, and 3) restenosis rates. Quality assessment was performed. Meta-analyses are presented as odds ratio (OR) using fixed effect model. Heterogeneity between trials was assessed.

Results --- Four randomized trials were included in the analysis. A total of 791 patients were randomized to simple versus complex coronary bifurcation lesion stenting using the Sirolimus stent platform. Clinical and angiographic outcomes data were available up to 1 year of follow-up. There was no difference in MACE between the simple and complex bifurcation lesion stenting strategy. There were 9.2 % and 6.9% adverse events in the complex and simple stenting strategy, respectively (OR for MACE 1.11 [95% CI 0.64-1.92], p=0.71). Likewise, there was no difference between strategies with regards to the individual MACE components and restenosis rates.

Conclusion --- A strategy of complex bifurcation lesion stenting, even with the use of Sirolimus drug eluting stent, is not associated with a reduction in MACE and restenosis rates.

Plain Language Summary --- In the drug eluting stent era, patients who undergo stenting for coronary bifurcation lesions do not derive any benefit from more aggressive revascularization of both main and side branches. Therefore, side branch stenting should not be routinely performed unless there is a specific indication to intervene on the side branch. ***Phil Heart Center J 2012;16:12-21.***

Key Words: Bifurcation Stenting ■ Drug Eluting Stent ■ Meta-analysis

Bifurcation lesions of the coronary arteries are frequently encountered in 15-25% of all interventions. The optimal approach to bifurcation lesions continues to be a matter of debate. In the era of bare metal stents, the restenosis rates of bifurcation lesion stenting ranged from 30-40%. The introduction of drug eluting stents has significantly reduced the restenosis rates of simple coronary lesions to 3-7%. However, the the restenosis rate of more complex lesions (total occlusions, long lesions, bifurcation lesions) continues to be higher. Non-randomized studies of bifurcation lesion stenting with the use of drug eluting stents have reported restenosis rates ranging from 7-25%.[1]

Currently, there are two competing schools of thought regarding the approach to bifurcation lesions. The simple approach advocates stenting

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of the main branch only with the option of stenting the side branch when there is hemodynamic compromise resulting from dissection or persistent severe residual stenosis. This strategy results in less implanted metal and should lessen the risk of stent thrombosis. The alternative strategy is more complex and advocates routine stenting of both main and side branches. This approach has the advantage of more complete revascularization of the coronary arteries The aim of this study was to perform a systematic review and meta-analysis of all published randomized controlled trials comparing a simple versus complex strategy of bifurcation lesion stenting with the use of drug eluting stents.

The objective of this study is to assess the outcome of drug eluting stenting of the coronary bifurcation lesions using a simple versus complex stenting strategy. Types of studies published that were included in the analysis were randomized controlled trials in the drug eluting stent era comparing a strategy of simple stenting versus complex stenting for coronary bifurcation lesions Participants of the study were adult patients with stable angina or acute coronary syndromes (unstable angina and non-Q MI).

Types of intervention

Simple strategy - Drug eluting stenting of the main branch only with option to stent the side branch in the presence of severe residual stenosis or dissection of the side branch

Complex strategy - Drug eluting stenting of both the main and side branches.

Types of outcome measures

(1) Composite of Major Adverse Cardiovascular Events (MACE).

(2) Individual components of MACE:
- a. cardiac death
- b. non-fatal myocardial infarction
- c. stent thrombosis
- d. target lesion revascularization

(3) main coronary branch restenosis rate

(4) side coronary branch restenosis rate.

Search methods for identification of studies

The search incorporated a number of methods to identify published randomized controlled trials: (1) searching of electronic databases; (2) hand searching of recent journals and conferences in relevant fields; (3) scanning web pages relevant to topic of review.

The "advanced search strategy" in PubMed began by specifying -bifurcation lesion AND stenting AND sirolimus OR paclitaxel. Further limiters included: English publication, only publications with abstracts, the period from July 2003-November 2008 (drug eluting stents were introduced in the latter half of 2003), humans, randomized controlled trials, age between 20-65+ years old. The limited search yielded 6 citations whose abstracts were then screened.

Hand-searching of references cited in the selected articles as well as recent issues of cardiology journals and proceedings included the Journal of the American College of Cardiology, American Heart Journal, American Journal of Cardiology, Catheterization and Cardiovascular Interventions, New England Journal of Medicine, Lancet, British Medical Journal, Journal of the American Medical Association, Heart, European Society of Cardiology and International Journal of Cardiology. An additional 5 citations were obtained and further screened. Internet based searches included: http://www.tctmd.com; http://theheart.org; http://crtonline.org; http://cardiosource.org; http://myaha.org; http://europcronline.org.

METHODOLOGY

Study selection and quality assessment The citations identified in the search process were retrieved as title and/or abstract and preliminarily screened. Relevant reports were obtained as complete manuscripts and assessed for compliance to inclusion/exclusion criteria and methodological quality.

Inclusion Criteria. (1) randomized comparison of simple versus complex bifurcation lesion stenting with the use of drug eluting stents; (2) de-novo lesion with >50% stenosis of the main branch or the side branch; (3) main branch > 2.5 mm in diameter; (4) side branch > 2.25 mm in diameter; (5) clinical follow-up rate >85%; (6) angiographic follow-up rate >75%; (7) angiographic and clinical follow-up available >6 months after the procedure.

Exclusion criteria. (1) STEMI within the past 24 hours; (2) large thrombus burden; (3) significant calcification of the bifurcation; (4) left main stenosis.

Details of the randomization method, concealment of allocations, whether the trial was masked (blinded), whether intention to treat analyses were possible from the available data and whether the number of patients lost to follow-up or subsequently excluded from the study was recorded. The number of cross-over from between strategies was also recorded.

It was also anticipated that trials on percutaneous coronary intervention would have difficulty masking (blinding) outcome assessors to the treatment applied. Measures taken to minimize bias were recorded.

Quality was assessed using the method of the Heart Collaborative Review Group:

1. Adequacy of randomization
a - Adequate randomization refers to sequence generation either by computer or randomization tables. Inadequate randomization includes use of alternation, case record numbers, birth dates or days of week.
b - Did not specify one of the adequate reported methods in (A) but mentioned randomization.
c - Other methods of allocation that appear unbiased.

2. Adequacy of the allocation concealment process
a - Adequate measures to conceal allocations-Concealment was adequate when randomization was centralized or pharmacy-controlled, or where the following are used: on-site computer-based systems where assignment is unreadable until after allocation, other methods that prevent knowledge of the allocation sequence to clinicians and patients; b - Unclearly concealed trials- the authors either did not report an allocation concealment approach at all, or reported an approach that did not fall into one of the categories in (a); c - Inadequately concealed trials- method of allocation is not concealed. Inadequate approaches will include: the use of alternation, case record numbers, days of the week, open random number lists and serially numbered envelopes even if opaque.

3. Potential for selection bias after allocation
a - Studies where an intention to treat analysis is possible and few exclusions (with adequate reporting of these exclusions); b - Studies which reported exclusions as reported in (A), but exclusions were less than 10 percent; c - No reporting of exclusions; exclusions of 10 percent or more or wide differences in exclusion between groups.

4. Adequacy of masking
a - Double (or triple) blind; b - Single blind; c - Non-blind; d - Unclear.

Data extraction. Data extraction included the outcome measures detailed above, as well as information on study design and participants (including baseline characteristics and co-morbidity eg. diabetes and previous heart disease). For binary outcome measures, data on the number of patients with each outcome event by allocated treated group, irrespective of compliance and whether or not the patient was later thought to be ineligible or otherwise excluded from treatment or follow-up was performed to allow an intention-to-treat analysis. No continuous outcome data was obtained in this study.

Data synthesis. For binary outcomes, a pooled estimate of the treatment effect for each outcome across studies was calculated, (the odds of an outcome among treatment allocated patients to the corresponding odds among controls).

Heterogeneity between trials results were tested using a multi-step process:

- Forest Plots were examined and the presence of overlap in the confidence intervals was noted. Lack of overlap of confidence intervals indicated heterogeneity;
- The chi-squared test for heterogeneity was performed;
- The I^2 statistic was obtained to describe the proportion of the variability due to heterogeneity.

Data was analyzed using a fixed effect model with odds ratio and 95% confidence intervals. Review Manager v. 5 software application (Plone Foundation, Houston Texas) was used for data analysis.

RESULTS

Description of Studies

Selection of Included Studies - the structured search initially retrieved 11 citations. Review of titles and/or abstracts further limited the selection to 7 eligible citations. These were further assessed for compliance to inclusion and exclusion criteria and methodology. Three studies were excluded: 1 study enrolled STEMI patients and was not yet published, one study was not yet published, and the last study was not randomized.

Included studies - all studies reported relevant baseline clinical variables, parent and branch vessel dimensions and percent stenosis, type of stent used, and technique of bifurcation stenting. All studies reported on clinical outcomes at a minimum follow-up of 6 months and angiographic follow up at 9 months. All relevant clinical outcomes data and angiographic variables including restenosis rates were available in all 4 studies.

One study pre-specified the technique of bifurcation stenting (T stenting, Bad Krozingen trial), 2 while in the other trials, the stenting technique was left to the discretion of the operator.

One study (Nordic)[3] specifically requested operators not to perform any intervention in a vessel that was not to be stented. Only the SIRIUS[4] trial was analyzed according to the actual treatment received, while the rest of the 3 trials were analyzed on an intention to treat basis. Only the Nordic[3] trial had a clinical primary endpoint (MACE). The 3 other trials were mechanistic trials whose primary endpoint was angiographic restenosis or late loss. The 4 trials included in this meta-analysis randomized a total of 791 patients to either a strategy of main branch stenting with provisional stenting of the side branch only when there was angiographic or clinical compromise (>50% residual stenosis, dissection) or routine stenting of both the main and side branches. All stu-dies utilized the sirolimus eluting stent platform. Differing nomenclature/classification schemes of bifurcations lesions were used.

There were 75% males, and 55% underwent the procedure because of unstable angina. The average vessel diameter of the main branch and side branch was 2.97 $\pm$ 0.2 mm. and 2.36 $\pm$ 0.1 mm. respectively. The smallest vessel dimensions were encountered in the SIRIUS trial[4] where the average vessel size was 2.5 mm and 2.1 mm for the main and side branch respectively.

All studies reported a high degree of procedural success (>90%) although the SIRIUS trial[4] was notable for a high percentage (52%) of cross-over from simple to complex stenting of the side branch because of the greater rate of hemodynamic and angiographic compromise of the side branch with the simple strategy. Follow up duration ranged from 6 months to 2 years.

Clinical follow-up was obtained in >95% of all subjects and angiographic follow up was performed in >75% of all subjects. All repeat target lesion revascularization procedures were driven by clinical indications rather than angiographic stenosis.

METHODOLOGIC QUALITY

The randomization process was described and appeared adequate for the four trials. These studies also appeared to use adequate allocation concealment. There was little evidence of selection bias after allocation in the trials. An intention-to-treat analysis was used in all trials except the SIRIUS study.[4] This study also had the highest rate of cross over between arms. Potential for masking was limited in these intervention trials, however, outcome assessors were blinded to the treatment allocation. In addition, in all the trials, the need for target lesion revascularization was based on clinical parameters, and not solely on the basis of angiographic restenosis. The results of the quality assessment are presented in Table 3.

OUTCOMES

All studies reported the clinical outcomes of total death, cardiac death, non-fatal myocardial infarction, stent thrombosis, target lesion revascularization. All trials likewise reported main and side branch restenosis rates.

A. Major adverse cardiac event rate

With regards to the clinical endpoint MACE (the composite of cardiac death, non-fatal myocardial infarction, target lesion revascularization

Table 1. Characteristics of Included Studies comparing simple to complex bifurcation lesion stenting using drug eluting stents

Study (Author)	Bad Krozingen (Ferenc 2008)[2]	NORDIC (Steigen 2006)[3]	SIRIUS (Colombo 2004)[4]	Pan 2004[5]
(N)	202	413	85	91
Study Period	2005-6	2004-5	2003	2002-3
Design	Prospective randomized single center, non-blinded	Prospective randomized multi-center, non-blinded	Prospective randomized multi-center, non-blinded	Prospective randomized single-center, non-blinded
Inclusion Criteria	Stable/unstable	Stable/unstable	Stable/unstable/silent ischemia	Symptomatic CAD
Exclusion Criteria	MI w/in 72hr Left main	MI w/in 24hr, restenosis, crea. > 3	MI w/in 24hr, restenosis, unprotected left main EF <35, crea >3	Diffuse side branch disease
Vessel Size (mm)	MB 2.5-4 SB $\geq$ 2.25	MB $\geq$ 2.5 SB $\geq$ 2	MB 2.5-3.5 SB $\geq$ 2.5	MB 2.5 $\geq$ 3.5 SB $\geq$ 2.25
Medications	ASA 100mg Clopidogrel 600mg, then 75mg for 6 mo.	ASA 75mg Clopidogrel 300 load, then 75mg for 6-12 mo.	ASA 325mg Clopidogrel 300 load, then 75mg for 3 mo. only	ASA 150mg Clopidogrel 75mg for 12mo.
Intervention	Sirolimus stenting, only T stenting bifurcation technique allowed, simple strategy n=101 complex strategy n = 101	Operator dertermines what stenting technique to use, operator avoids pre-treatment of unstented segment. Only Sirolimus stents used. simple strategy n=207 complex strategy n= 206	Sirolimus stent used, operator determined what stenting technique to use, however, no Cullotte stenting allowed	Operator determines stenting technique to use; side branch was dilated even if it was not stented. Sirolimus stent used simple strategy n= 47 complex strategy n= 44
StentingTechnique	T-stenting	Operator determined	Operator determined, no cullotte stenting allowed	Operator determined
DES	SES	SES	SES	SES
Primary Endpoint	In-segment diameter stenosis of side brach at 9mo.	MACE	In-segment restenosis analyzed according to treatment actually received	MACE, restenosis
Follow-up	MACE 1, 12, 24m, QCA 9mo.	MACE 1 and 6m, QCA 8mo.	MACE 1 and 6m, QCA 6mo.	MACE 11 months QCA 6 months and 6m, QCA 6mo.
Comments	Higher risk patients, higher (90%) rate of FKB.	Low cross-over rate, 32% undergo final kissing balloon. Stress testing was not performed at follow-up.	3.5% overall stent thrombosis, but increases to 6.3% in the complex stenting group, 50% cross-over rate, smaller vessel treated with a mean MB 2.6mm/ SB 2.1mm	FKB in 68% of cases SB was dilated whether it was stented or not

DES = Drug Eluting Stent(s); MACE = Major Adverse Cardiac Events; MI = Myocardial Infarction; SES = Sirolimus-Eluting Stent(s)
FKB = Final Kissing Balloon; MB Main Branch; SB = Side Branch; QCA = Quantitative Coronary Angiogram; DS = Diameter

tion, and stent thrombosis), there were 38 events (9.2%) in the complex stenting arm and 26 events (6.9%) in the simple stenting arm. Routine complex stenting of both the main and side branch was not associated with a significantly better outcome (OR for MACE 1.11 [95% CI 0.64-1.92], p=0.71, I2=0%).

Table 3. Methodologic Quality Assessment of Included Studies

Quality Assessment	Pan[5] (2004)	SIRIUS (Colombo[4] 2004)	NORDIC (Steigen[3] 2006)	Bad Krozingen (Ferenc[2] 2008)
Adequate Randomization	A	A	A	A
Adequate Concealment	B	B	A	A
Selection Bias	A	B	A	A
AdequateMasking	C	C	C*	C*

* Outcome assessors blinded to allocation

B. Individual MACE components

The individual components of MACE (cardiac death, non-fatal myocardial infarction, target lesion revascularization, and stent thrombosis) were analyzed independently. Each individual component did not show a significantly better outcome with complex stenting. There were 5 cardiac deaths reported (1.2%) in the complex stenting group versus 4 (1.1%) in the simple stenting category (OR for cardiac death 1.03 [95% CI 0.3-3.46], p=0.97, I^2=0%). There were 10 non-fatal MI's in the complex stenting group (2.4%) versus 5 (1.3%) in the simple stenting category (OR for non-fatal MI 1.12 [95% CI (OR for stent thrombosis 1.21 [95% CI 0.39-3.74], p=0.73, I^2=0%). 0.39-3.23], p=0.61, I^2=0%). There were 19 target lesion revascularization events (4.6%) in the complex stenting category and 17 events (4.5%) in the simple stenting group (OR for target lesion revascularization 0.92 [95% CI 0.46-1.86], p=0.64, I^2=0%). There were 7 stent thrombosis events (1.7%) in the complex stenting group and 4 events (1.1%) in the simple stenting category.

C. Main Branch and side branch restonis rates

Comparing the angiographic endpoint of main branch restenosis, there was no significant advantage of complex stenting to simple stenting of bifurcation lesions using drug eluting stents (OR for main branch restenosis 0.91 [95% CI 0.44-1.87], p=0.55, I2=0%). There were 16 events in the complex stenting arm (4.6%) and 16 events in the simple stenting category (5%). Similarly, there was no advantage of complex stenting strategy using drug eluting stents with regards to side branch restenosis (OR 0.92 [95% CI 0.58-1.45], p=0.51, I^2=0%). There were 45 events in the complex stenting arm (13.1%) versus 43 events in the simple stenting group (13.4%).

Table 2. Characteristics of Excluded Studies

Author	Notes
Colombo[6] (CACTUS Trial) 2007	Not published
Hildick-Smith[7] (BBC-1) 2008	Enrolled STEMI cases, not published
Grube[8] 2007	Not randomized

OUTCOMES

Key findings

This meta-analysis was based on the statistical pooling of 4 randomized controlled trials that enrolled a total of 791 patients comparing a strategy of simple to complex bifurcation lesion stenting using drug eluting stents. This meta-analysis shows no advantage of a complex stenting strategy with regards to the composite endpoint of MACE, its individual components (cardiac death, non-fatal myocardial infarction, target lesions revascularization, and stent thrombosis), and restenosis rates of both the main and side branches.

Clinical Interpretation/implication

The finding of this meta-analysis suggests that a simple stenting strategy is the procedure of choice in bifurcation lesions. Stenting of the side branch should only be considered when there is hemodynamic compromise of the side branch resulting from severe residual stenosis or dissection. In the SIRIUS study[4], the strategy of complex stenting resulted in a greater rate of documented stent thrombosis (4% versus 2%). The SIRIUS study, compared to the three other trials, enrolled smaller vessels. This suggests that a simple stenting strategy is even more important in smaller

Analysis 1 Comparison of MACE at 12 months

Study or Subgroup	Complex Stenting Events	Complex Stenting Total	Simple Stenting Events	Simple Stenting Total	Weight	Odds Ratio M-H, Fixed, 95% CI
BBK 2008	12	101	13	101	47.4%	0.91 [0.39, 2.11]
Nordic 2006	5	206	7	207	28.2%	0.71 [0.22, 2.28]
PAN 2004	4	44	3	47	10.9%	1.47 [0.13, 6.96]
Siruis 2004	17	63	3	22	13.4%	2.34 [0.61, 8.93]
Total (95% CI)		**414**		377	**100.0%**	**1.11 [0.64, 1.92]**
Total Events	38		26			

Heterogeneity $Chi^2 = 2.09$, df = 3 (P = 0.55); I^2=0%

Test for overall effect: Z = 0.37 (P = 0.71)

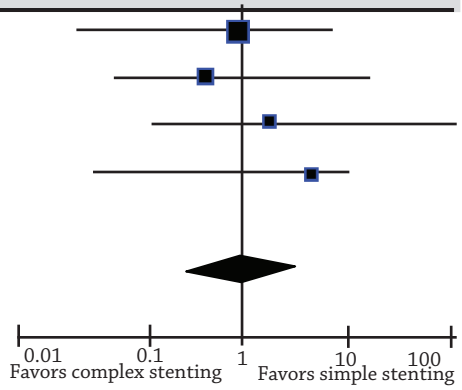

Figure 1. Analysis of MACE at 12 months among studies comparing Simple and Complex Stenting in bifurcation esions

Analysis 2.1 Comparison of Cardiac Death at 12 months

Study or Subgroup	Complex Stenting Events	Complex Stenting Total	Simple Stenting Events	Simple Stenting Total	Weight	Odds Ratio M-H, Fixed, 95% CI
BBK 2008	1	101	2	101	38.5%	0.49 [0.04, 5.55]
Nordic 2006	2	206	2	207	38.4%	1.00 [0.14, 7.20]
PAN 2004	1	44	0	47	9.1%	3.28 [0.13, 82.56]
Siruis 2004	1	63	0	22	14.0%	1.08 [0.04, 27.48]
Total (95% CI)		414		377	100.0%	1.03 [0.30,3.46]
Total Events	5		4			

Heterogeneity $Chi^2 = 0.85$, df = 3 (P = 0.84); I^2=0%

Test for overall effect: Z = 0.04 (P = 0.97)

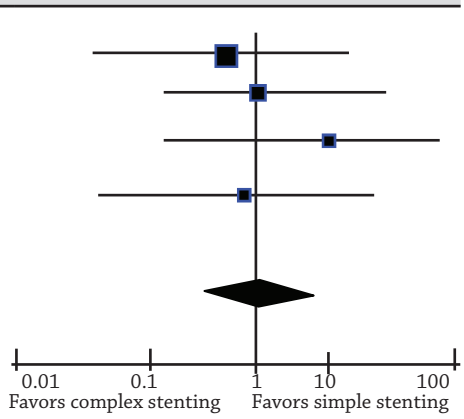

Figure 2. Analysis of Cardiac Death at 12 months among studies comparing Simple and Complex Stenting in bifurcation lesions

caliber vessels. The combination of small vessel size and more metal theoretically could increase the stent thrombosis rate. Why is routine stenting of the side branch with a drug eluting stent not associated with a favor able outcome? Intravascular ultrasound (IVUS) has shown that the higher restenosis rates associated with stenting of the side branch is due to geographic miss of the ostium (the stent is not able to cover the side branch ostium sufficiently). Different side branch stenting techniques (T stenting, crush technique, cullote, V-stenting) are associated with varying degrees of geographic miss.[9-11] In addition to geographic miss, there is considerable side branch stent under-expansion and deformation at the tostium. This problem of stent strut deformation is intrinsic to bifurcation stenting because currently available stents were not designed to address branching lesions. Stent deformation, polymer disruption, and loss of stent to endothelial surface apposition have all been demonstrated in IVUS studies of bifurcation stenting[11] Theoretically, these problems can contribute to the increased restenosis rates associated with side branch stenting even if complete ostium coverage is achieved. This underlies the importance of developing dedicated stent systems for branch lesions. These bifurcation stent systems should be designed for complete coverage of the side branch ostium and complete stent

Analysis 2.2 Comparison of Nonfatal MI at 12 months

Study or Subgroup	Complex Stenting Events	Complex Stenting Total	Simple Stenting Events	Simple Stenting Total	Weight	Odds Ratio M-H, Fixed, 95% CI
BBK 2008	2	101	1	101	15.1%	2.02 [0.18, 2.64]
Nordic 2006	1	206	0	207	7.6%	3.03 [0.12, 74.79]
PAN 2004	0	44	2	47	36.8%	0.20 [0.01, 4.38]
Siruis 2004	7	63	2	22	40.5%	1.25 [0.24, 6.52]
Total (95% CI)		414		377	100.0%	1.12 [0.39, 3.23]
Total Events	10		5			

Heterogeneity Chi² = 1.80, df = 3 (P = 0.61); I²=0%

Test for overall effect: Z = 0.20 (P = 0.84)

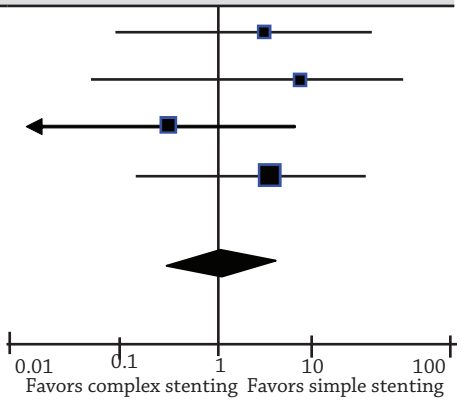

Figure 3. Analysis of Non-fatal MI at 12 months among studies comparing Simple and Complex Stenting in bifurcation lesions

Analysis 2.3 Comparison of Target Lesion Revascularization at 12 months

Study or Subgroup	Complex Stenting Events	Complex Stenting Total	Simple Stenting Events	Simple Stenting Total	Weight	Odds Ratio M-H, Fixed, 95% CI
BBK 2008	9	101	11	101	61.7%	0.80 [0.32, 2.02]
Nordic 2006	2	206	4	207	24.3%	0.50 [0.09, 2.75]
PAN 2004	2	44	1	47	5.7%	2.19 [0.19, 25.05]
Siruis 2004	6	63	1	22	8.3%	2.21 [0.25, 19.46]
Total (95% CI)		414		377	100.0%	0.92 [0.46, 1.86]
Total Events	19		17			

Heterogeneity Chi² = 1.70, df = 3 (P = 0.64); I²=0%

Test for overall effect: Z = 0.23 (P = 0.82)

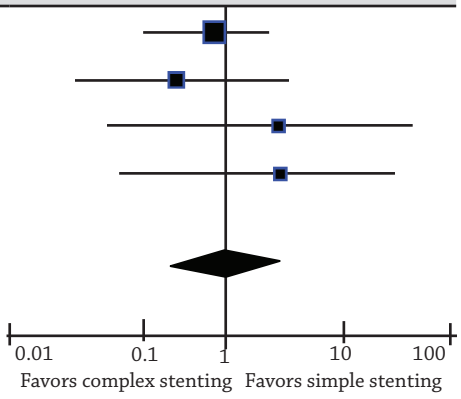

Figure 4. Analysis of Target Lesion Revascularization at 12 months among studies comparing Simple and Complex Stenting in bifurcation lesions

expansion with a minimum of stent deformation.

Limitations

As with any meta-analysis there will be inherent difficulties in using data from multiple studies with different baseline characteristics.

1. The reported trials used various anatomic definitions of bifurcation lesions. Only recently has there been a consensus to adopt a uniform system of reporting. Subsequent trials will adopt the Medina Classification[12]

2. In addition, there is no single universally accepted technique of bifurcation lesion stenting. Three trials included in this meta analysis left the stenting technique to the operator's discretion. Only the BBK trial specified the use of T-stenting for the side branch.

3. The reported trials used the sirolimus eluting stent platform. Outcome with the use of paclitaxel eluting stent platform is unknown.

Analysis 2.4 Comparison of Stent Thrombosis at 12 months

Study or Subgroup	Complex Stenting Events	Complex Stenting Total	Simple Stenting Events	Simple Stenting Total	Weight	Odds Ratio M-H, Fixed, 95% CI
BBK 2008	3	101	3	101	52.3%	1.00 [0.20, 5.08]
Nordic 2006	0	206	1	207	26.8%	0.33 [0.01, 8.23]
PAN 2004	1	44	0	47	8.4%	3.28 [0.13, 82.56]
Siruis 2004	3	63	0	22	12.5%	2.60 [0.13, 52.42]
Total (95% CI)		414		377	100.0%	1.21 [0.39, 3.74]
Total Events	7		4			

Heterogeneity Chi² = 1.29, df = 3 (P = 0.73); I²=0%

Test for overall effect: Z = 0.34 (P = 0.74)

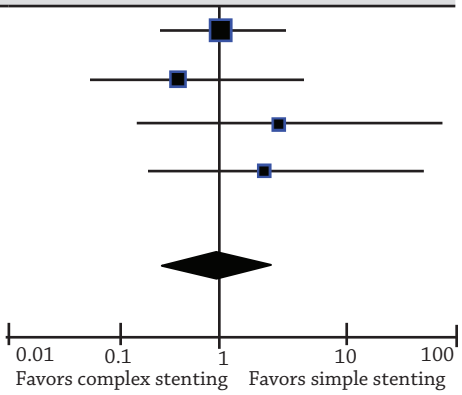

Figure 5. Analysis of Stent thrombosis at 12 months among studies comparing Simple and Complex Stenting in bifurcation lesions

Analysis 2.5 Comparison of Side Branch Restenosis Rates at 9 months

Study or Subgroup	Complex Stenting Events	Complex Stenting Total	Simple Stenting Events	Simple Stenting Total	Weight	Odds Ratio M-H, Fixed, 95% CI
BBK 2008	12	96	9	96	20.6%	1.38 [0.55, 3.45]
Nordic 2006	18	151	29	156	65.8%	0.59 [0.31, 1.12]
PAN 2004	4	44	2	47	4.6%	2.25 [0.39, 12.95]
Siruis 2004	11	53	3	21	8.9%	1.57 [0.39, 6.31]
Total (95% CI)		344		320	100.0%	0.92 [0.58, 1.45]
Total Events	45		43			

Heterogeneity Chi² = 4.16, df = 3 (P = 0.24); I²=28%

Test for overall effect: Z = 0.36 (P = 0.72)

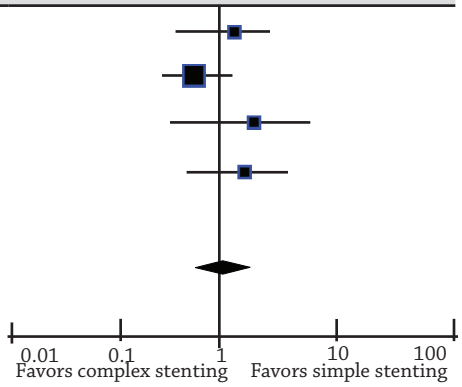

Figure 6. Analysis of side branch restenosis at 9 months among studies comparing Simple and Complex Stenting in bifurcation lesions

AUTHOR'S CONCLUSION

Implications for practice

With the current generation of drug eluting stents and bifurcation stenting techniques, coronary bifurcation lesions should be treated with a simple strategy of stenting only the main branch. Routine side-branch stenting is a more complex strategy that does not result in a reduction in death, non-fatal myocardial infarction, stent thrombosis, target lesion revascularization and restenosis. Stenting of the side branch should only be performed if there is hemodynamic compromise that will result in significant ischemia of the side branch.

Implications for research

There is already a uniform nomenclature for classifying bifurcation lesions. No doubt, this will allow accurate comparison of future trials. The current generation of stents has several design flaws that make them unfavorable for bifurcation stenting. Future trials will have to wait for dedicated stent designs that will address side

Analysis 2.6 Comparison of Main Branch Restenosis Rates at 9 months

Study or Subgroup	Complex Stenting Events	Complex Stenting Total	Simple Stenting Events	Simple Stenting Total	Weight	Odds Ratio M-H, Fixed, 95% CI
BBK 2008	3	96	7	96	43.5%	0.41 [0.10, 1.64]
Nordic 2006	8	151	7	156	41.9%	1.19 [0.42, .37]
PAN 2004	2	44	1	47	5.9%	2.19 [0.19, 25.05]
Siruis 2004	3	53	1	21	8.7%	1.10 [0.12, 12.23]
Total (95% CI)		344		320	100.0%	0.91 [0.44, 1.87]
Total Events	16		16			

Heterogeneity $Chi^2 = 2.09$, df = 3 (P = 0.56); I^2=0%

Test for overall effect: Z = 0.25 (P = 0.80)

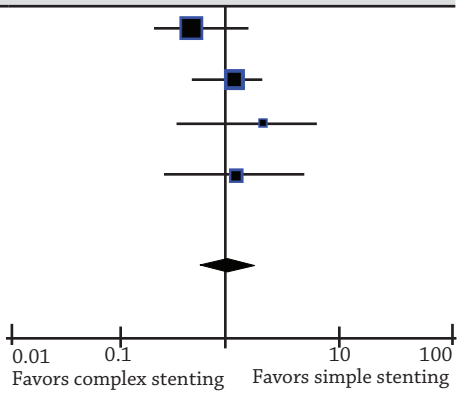

Figure 7. Analysis of main branch restenosis at 9 months among studies comparing Simple and Complex Stenting in bifurcation lesions

branch access, side branch ostial coverage, and adequate stent expansion without deformation.

CONCLUSION

This review presents the meta-analysis of data derived from 4 RCT's enrolling 791 patients comparing a strategy of simple versus complex bifurcation lesion stenting. The analysis shows no reduction in MACE and restenosis with routine side branch stenting using current drug eluting stent platforms and stenting techniques.

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