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ABSTRACT

Background In the last decade, direct stenting has been proposed as an alternative strategy to conventional stenting with balloon predilation. The aim of this study was to perform a meta-analysis of randomised trials comparing a direct stenting strategy versus a conventional one.

Methods A literature search was performed using Medline, EMBASE, the Cochrane Central Register of Controlled Trials, scientific session abstracts and relevant websites, from inception of each database to June 2009. Included studies comprised randomised controlled trials evaluating direct versus conventional stenting in patients undergoing percutaneous coronary intervention. Primary endpoint was the composite of death or myocardial infarction and secondary endpoints were myocardial infarction and target-vessel revascularisation occurrence.

Results 24 trials met inclusion criteria, with 6803 patients enrolled (3412 or 50.15% randomised to direct stenting and 3391 or 49.85% randomised to conventional stenting). Up to 6-month follow-up, the composite of death or myocardial infarction was significantly reduced with direct stenting compared with conventional stenting (3.95% versus 5.10% respectively, OR=0.76 (95% CI 0.60 to 0.96), p=0.02). This reduction was primarily driven by a lower myocardial infarction occurrence (3.16% versus 4.04%, respectively, OR=0.77 (0.59 to 0.99), p=0.04). Furthermore, direct stenting was not associated with a reduction in target-vessel revascularisation (6.50% versus 6.96%, respectively, OR=0.92 (0.76 to 1.12), p=0.42).

Conclusion This meta-analysis demonstrates that, in selected coronary lesions, direct stenting improves outcome in patients undergoing percutaneous coronary intervention, primarily reducing myocardial infarction incidence.

INTRODUCTION

In everyday clinical practice, stent implantation occurs in about 95% of patients with coronary artery disease undergoing percutaneous coronary intervention (PCI).[1] In the last decade, direct stenting (DS), usually referred to stent deployment without predilation of the target lesion, has become a feasible and safe technique, thanks to dramatic improvements in stent and deliver system design (eg, lower crossing profiles, greater flexibility, trackability and pushability).[2] Initially, experimental data supported the concept of a reduced vessel wall damage with DS compared to conventional (with predilation) stenting (CS).[3] Afterwards, several clinical studies evaluated DS and CS in patients treated with PCI, reporting conflicting results. Thus, the issue of whether DS can improve clinical outcomes still remains unsolved. Therefore, we performed a meta-analysis of randomised trials to assess the clinical impact of a DS strategy compared with CS in patients undergoing PCI.

METHODS

Search strategy and selection criteria

We searched Medline, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), scientific session abstracts in *Circulation*, *Journal of the American College of Cardiology*, *European Heart Journal* and the *American Journal of Cardiology*, and relevant websites (www.acc.org, www.americanheart.org, www.europcr.com, www.escardio.org, www.cardiosource.com/clinicaltrials, www.clinicaltrialresults.org, www.tctmd.com and www.theheart.org) for studies in any language (from inception of each database until June 2009). The reference list of relevant studies was additionally scanned. The key words used were: 'randomised trial', 'direct stenting', 'predilation', 'percutaneous coronary intervention', 'angioplasty', 'stent', 'coronary artery disease'. To be included, the citation had to meet the following criteria: (1) random treatment allocation; (2) availability of complete clinical features. Exclusion criteria were: (1) ongoing studies or irretrievable data, and (2) >10% of patients lost to follow-up.

Data collection and quality assessment

Two investigators (SC and RP) independently assessed reports for eligibility at title and/or at abstract level, with divergences resolved with a third reviewer (FP), and studies that met the inclusion criteria were selected for further analysis. Two investigators (SC and RP) took care of data extraction. Studies were evaluated with respect to the following methodological items: randomisation, adequacy of allocation concealment, performance of the analysis according to the intention-to-treat principle, sample size calculation and specification of loss of patients.

Outcome variables

The primary endpoint was the composite of death or myocardial infarction. Patients with both events

were considered in the same way as those with a single event. Secondary endpoints were myocardial infarction (MI) and target-vessel revascularisation (TVR). If TVR was not available, target-lesion revascularisation was considered instead. All clinical endpoints were evaluated according to per protocol definitions, up to 6-month follow-up.

Statistical analysis

The κ statistic was used to assess agreement between reviewers for study selection, as previously reported.[4] We used the Peto fixed effects model to calculate the pooled ORs and 95% CIs, since this is the most appropriate model when relatively few events occur in individual trials and when there are roughly equal numbers per treatment group.[5 6] However, to test the robustness of significant results, we performed a secondary analysis by using a fixed-effect model with the Mantel-Hænzel method[7] or DerSimonian and Laird random-effect model in case of significant heterogeneity across studies.[8] The Breslow-Day χ^2 test was calculated to test the statistical evidence of heterogeneity across the studies.[9] In addition, we used the I^2 statistic, which describes the percentage variation across studies that is due to heterogeneity rather than chance. As a guide, I^2 values <25% indicated low heterogeneity, 25–50% indicated moderate heterogeneity and >50% indicated high heterogeneity.[10 11] A funnel plot and the adjusted rank correlation test, according to the method of Begg and Mazumdar,[12] were used to assess publication bias with respect to each endpoint. Moreover, we performed a sensitivity analysis, in which the meta-analysis estimates are computed omitting one study at time. Finally, we performed a meta-regression in order to evaluate the influence of crossover rates of each trial on the primary endpoint. In all the studies, crossover was decided whenever the lesion could not be crossed by DS, the device was withdrawn and predilation was performed before re-attempting stent deployment. Briefly, we undertook a weighted least-square regression, using a linear regression model, with weighting provided by the number of patients included in each trial; R^2 and β-coefficients with 95% CI were reported. Crossover rates were considered as an independent variable and the natural logarithm of the primary endpoint as a dependent variable.[13] Statistical analyses were performed with Review Manager 5.0.16 (RevMan, The Nordic Cochrane Centre, The Cochrane Collaboration, 2008), Stata 10.0 statistical software and SPSS 16.0 statistical package.

The study was performed in compliance with the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines.[14]

RESULTS

Eligible studies

As showed in figure 1, we screened the title or the abstract of 627 potentially eligible publications and identified initially 27 randomised trials.[15–41] Two trials were excluded because of prospective single-arm study design.[39 40] One trial was excluded since investigators randomised to DS or CS coronary lesions and not to patients.[41] Finally, a total of 24 trials were included in the meta-analysis, enrolling 6803 patients (3412 or 50.15% randomised to DS and 3391 or 49.85% randomised to CS). The inter-observer agreement for study selection was very good, with

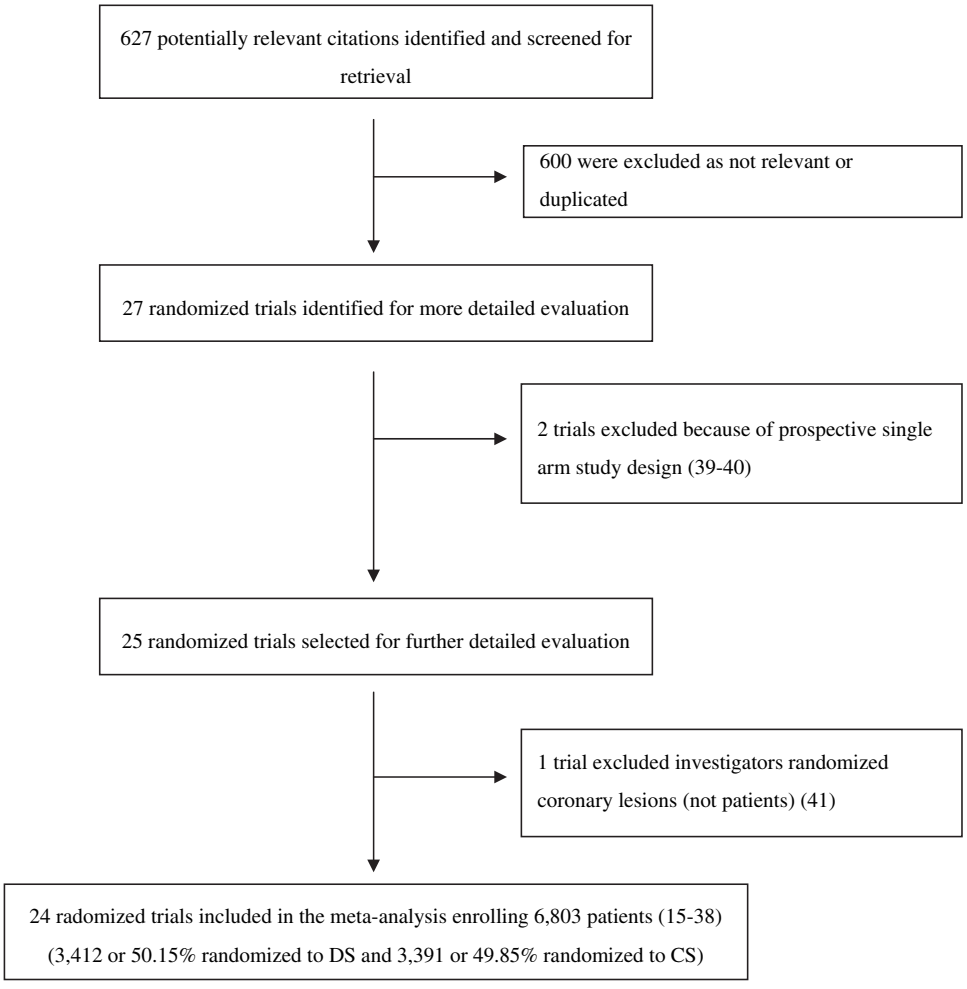

Figure 1 Flow diagram of trial selection.

κ=0.97. Table 1 summarises the main characteristics of included studies. All implanted stents were bare-metal stents, with the exception of those in 34 patients in the study by Cuisset *et al*.[20] Crossover rates ranged from 0% to 29.7%, probably owing to different inclusion criteria and patient selection. As reported in table 1, routine angiographic follow-up was planned in 11 trials.

Table 1 Main characteristics of included trials

Trial name	Study design	Multicentre	Primary endpoint	Age (years)	Angiographic follow-up	Exclusion criteria	Stent type	Crossover (%)
Airoldi *et al*[15]	DS (n=140) vs CS (n=131)	Yes	Procedural outcome	59	No	Left main disease, calcified, tortuous, bifurcation lesions, CTO, IRS	Crossflex (Cordis)	13.2
BET[16]	DS (n=173) vs CS (n=165)	Yes	Death, MI, UA, CABG, re-PCI	64	No	Ostial lesion, calcified, tortuous lesions, thrombus	Tenax (Biotronik)	13.9
Brueck *et al*[17]	DS (n=171) vs CS (n=164)	No	Procedural success	63	Yes	Left main disease, calcified, tortuous, bifurcation lesions, CTO, IRS, LVEF <30%	Bx Velocity (Cordis)	5
CK TEST[18]	DS (n=59) vs CS (n=44)	Yes	Procedural outcome, death, MI, TVR	64	No	Left main disease, CTO, bifurcation, calcified, tortuous, restenotic lesions	Several	0
CONVERTIBLE[19]	DS (n=101) vs CS (n=101)	Yes	Mean lumen diameter by QCA after stent placement	63	Yes	Calcified, tortuous, bifurcation lesions, CTO, IRS, LVEF <30%	BeStent2 (Medtronic)	6
Cuisset *et al*[20]	DS (n=25) vs CS (n=25)	No	Index of microcirculatory resistance	66	No	LVEF <30%, previous MI, CTO, ISR, calcified, bifurcation, ostial lesions.	Not reported	0
Danzi *et al*[21]	DS (n=61) vs CS (n=61)	No	Procedural success	58	Yes	Calcified lesions, CTO	NIR (Medinol), Paragon (Progressive Angioplasty System)	3
DECIDE[22]	DS (n=64) vs CS (n=64)	Yes	Angiographic restenosis	56	Yes	Ostial, tortuous, calcified lesions, CTO	NirElite (Boston Scientific)	29.7
DIRAMI[23]	DS (n=110) vs CS (n=107)	No	Procedural success	56	Yes	Cardiogenic shock, pulmonary oedema	Bx Velocity (Cordis), Multilink (Guidant), other	12
DIRECT[24]	DS (n=210) vs CS (n=201)	Yes	Death, MI, TVR	60	No	Left main disease, calcified, tortuous, bifurcation lesions, CTO, AMI	Not reported	2.8
DIRECTO[25]	DS (n=65) vs CS (n=72)	Yes	Difference in mean length of stent	59	No	Calcified, tortuous, bifurcation, CTO, long lesions	NIR (Medinol)	11
DISCO[26]	DS (n=210) vs CS (n=206)	Yes	Feasibility and safety	59	Yes	Left main disease, calcified, tortuous, bifurcation, AMI, CTO, IRS	Several	3
Hoffman *et al*[27]	DS (n=125) vs CS (n=124)	No	Endothelin levels after stent implantation	63	Yes	Ostial, calfied, bifurcation, tortuous lesions, CTO, thrombus	Bx Velocity (Cordis)	9
Ijsselmuiden *et al*[28]	DS (n=200) vs CS (n=200)	No	Death, MI, TVR and stent thrombosis	61	Yes	Ostial, bifurcation, calcified lesions and CTO	AVE S670 (Medtronic)	11.7
ISAR-DIRECT[29]	DS (n=456) vs CS (n=454)	No	Angiographic restenosis	65	Yes	AMI, left main disease, total vessel occlusion	Several	21.7
Kovar *et al*[30]	DS (n=37) vs CS (n=40)	Yes	Mean number of utilised device	62	No	CTO, vein graft, AMI	Several	5.4
Loubeyre *et al*[31]	DS (n=102) vs CS (n=104)	No	Angiographic and clinical outcomes	59	No	Calcified lesions, left main disease, vein graft	Bx Velocity (Cordis), Multilink (Guidant), AVE (Medtronic), other	7.8
NIR future[32]	DS (n=39) vs CS (n=42)	Yes	Equipment cost, fluoroscopy time, contrast use	61	No	Ostial, bifurcation, calcified lesions, ISR, thrombus, CTO, LVEF <35%, TIMI grade 0-1	NIR Primo (Boston Scientific)	7.7
Ozedmir *et al*[33]	DS (n=25) vs CS (n=25)	No	Angiographic results	57	No	Cardiogenic shock, left main disease	divYsio (Biocompatibles Ltd)	0
PREDICT[34]	DS (n=198) vs CS (n=201)	Yes	Death, MI, TLR and stent thrombosis	62	Yes	Calcified, tortuous, thrombotic lesions, recent AMI, LVEF<30%	AVE S670 (Medtronic)	8
Sabatier *et al*[35]	DS (n=65) CS (n=65)	No	No reflow	61	No	Left main disease, calcified, tortuous lesions, ISR, vein graft	NIR PRIMO (Boston Scimed)	6
SWIBAP[36]	DS (n=197) vs CS (n=199)	Yes	Angiographic success	60	No	Left main disease, AMI, UA, bifurcation, restenotic, calcified lesions	NIR (Medinol)	2.5
TRENDS[37]	DS (n=379) vs CS (n=395)	Yes	Death, MI, TLR	60	Yes	Left main disease, calcified, ostial lesions, recent AMI	Multilink (Guidant)	5.7
VELVET[38]	DS (n=200) vs CS (n=201)	Yes	Death, MI, CABG, TLR stroke	61	No	Left main disease, recent AMI, LVEF <30%, bifurcation, ISR, TIMI 0, SVG	Bx Velocity (Cordis)	9.2

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; CS, conventional stenting; CTO, chronic total occlusion; DS, direct stenting; ISR, in-stent restenosis; LEVF, left ventricular ejection fraction; MI, myocardial infarction; SVG, saphenous vein graft; TIMI, Thrombolysis in Myocardial Infarction; TLR, target-lesion revascularisation; TVR, target-vessel revascularisation; UA, unstable angina.

All studies included were randomised and 14 out of 24 provided detailed descriptions of appropriate randomisation methods, mainly based on computer-generated randomisation lists.[15 16 18 20 23–27 29 30 32 36 38] All trials reported the number of patients, if any, lost to follow-up and 15 trials reported sample-size calculations.[18–21 24–30 32 36–38] The analysis according to the intention-to-treat principle was performed in all trials.

Primary endpoint

The composite endpoint of death or myocardial infarction occurred in a total of 308 patients (4.53%). As reported in figure 2, DS was associated with a significant death/myocardial infarction reduction (3.95% versus 5.10%, DS vs CS, respectively, OR=0.76 (95% CI 0.60 to 0.96), p=0.02). No significant heterogeneity was observed across trials (I^2=12%, p_{het}=0.30). This reduction was primarily driven by a lower MI incidence, since no significant difference in the occurrence of death was found between groups (0.72% vs 1.00%, DS vs CS, respectively, OR=0.73 (0.42 to 1.26), p=0.26).

Secondary endpoints

Myocardial infarction was experienced by a total of 245 patients (3.60%). As depicted in figure 3, patients treated with DS experienced less MI than CS patients (3.16% versus 4.04%, respectively, OR=0.77 (95% CI 0.59 to 0.99), p=0.04). A modest heterogeneity was observed across trials (I^2=16%, p_{het}=0.24), probably owing to different MI definition across the included trials (see supplementary data). However, even if we excluded trials that did not report MI definition or did not clearly adopt creatine kinase MB isoenzyme (CK-MB) evaluation, MI was still significantly reduced in patients allocated to DS (OR=0.69 (95% CI 0.49 to 0.98), p=0.04).

Target-vessel revascularisation was needed in a total of 458 patients (6.73%) (figure 4). We found similar rates among DS and CS groups, without a significant difference between two groups (6.51% versus 6.96%, respectively, OR=0.92 (95% CI 0.76 to 1.12), p=0.42). No heterogeneity was observed across trials (I^2=0%, p_{het}=0.86).

Bias and sensitivity analysis

None of the funnel plots showed skewed distributions, suggesting that no publication bias was present. Furthermore, the adjusted rank correlation test did not point out any publication bias. Sensitivity analysis demonstrated that no single study significantly altered the summary ORs. Also with the Mantel-Haenzel method, the primary endpoint remained in favour of DS (OR=0.76 (95% CI 0.60 to 0.96), p =0.02) and myocardial infarction (OR=0.77 (95% CI 0.60 to 1.00), p=0.05).

Meta-regression

Using a weighted least-square regression, no significant relation was found between crossover rates and the natural logarithm of OR for death/MI (R^2=0.007, β-coefficient=0.08 (95% CI −0.04 to 0.06), p =0.70) (see supplementary data).

DISCUSSION

The main finding of this meta-analysis is that a DS strategy is associated with a reduction in the occurrence of death or MI, driven primarily by lower rates of MI, up to the 6-month follow-up.

Most of the included trials were originally designed to evaluate a possible role in reducing restenosis associated with DS technique, as suggested from initial experimental data.

Study or Subgroup	Direct stenting Events	Total	Conventional stenting Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Airoldi et al.	3	140	3	131	2.0%	0.93 [0.19, 4.70]
BET	3	173	10	165	4.3%	0.31 [0.10, 0.94]
Brueck et al.	9	171	9	164	5.9%	0.96 [0.37, 2.47]
CK TEST	4	59	9	44	3.9%	0.29 [0.09, 0.94]
CONVERTIBLE	2	101	5	101	2.3%	0.41 [0.09, 1.86]
Cuisset et al.	3	25	7	25	2.8%	0.38 [0.10, 1.48]
Danzi et al.	0	61	0	61		Not estimable
DECIDE	1	64	3	64	1.3%	0.36 [0.05, 2.61]
DIRAMI	5	110	3	107	2.7%	1.63 [0.40, 6.67]
DIRECT	14	210	15	201	9.3%	0.89 [0.42, 1.88]
DIRECTO	3	65	4	72	2.3%	0.82 [0.18, 3.76]
DISCO	3	210	7	206	3.4%	0.43 [0.12, 1.52]
Hoffman et al.	6	125	7	124	4.3%	0.84 [0.28, 2.57]
Ijsselmuiden et al.	11	200	8	200	6.2%	1.39 [0.55, 3.49]
ISAR-DIRECT	27	456	19	454	15.1%	1.44 [0.79, 2.60]
Kovar et al.	1	37	5	40	1.9%	0.26 [0.05, 1.36]
Loubeyre et al.	2	102	6	104	2.7%	0.36 [0.09, 1.48]
NIR future trial	1	39	1	42	0.7%	1.08 [0.07, 17.57]
Ozedmir et al.	0	25	3	25	1.0%	0.12 [0.01, 1.25]
PREDICT	14	198	20	201	10.7%	0.69 [0.34, 1.40]
Sabatier et al.	0	65	2	65	0.7%	0.13 [0.01, 2.15]
SWIBAP	2	197	0	199	0.7%	7.50 [0.47, 120.38]
TRENDS	16	379	21	395	12.1%	0.79 [0.41, 1.52]
VELVET	5	200	6	201	3.7%	0.83 [0.25, 2.76]
Total (95% CI)		**3412**		**3391**	**100.0%**	**0.76 [0.60, 0.96]**
Total events	135		173			

Heterogeneity: Chi² = 25.02, df = 22 (P = 0.30); I² = 12%
Test for overall effect: Z = 2.35 (P = 0.02)

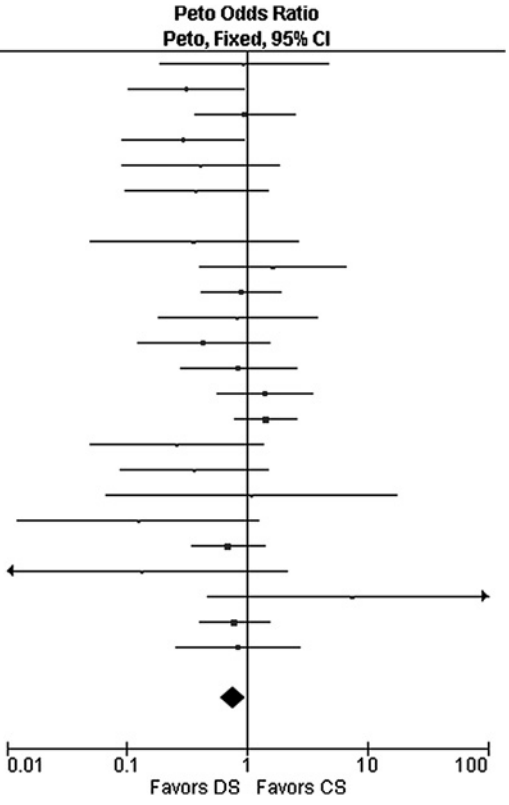

Figure 2 OR of the composite endpoint of death or myocardial infarction associated with direct stenting versus conventional stenting. The squares and the horizontal lines indicate the OR and the 95% CIs for each included trial; the size of each square is proportional to the statistical weight of a trial in the meta-analysis; diamond indicates the effect estimate derived from meta-analysis, with the centre indicating the point estimate and the left and the right ends the 95% CIs.

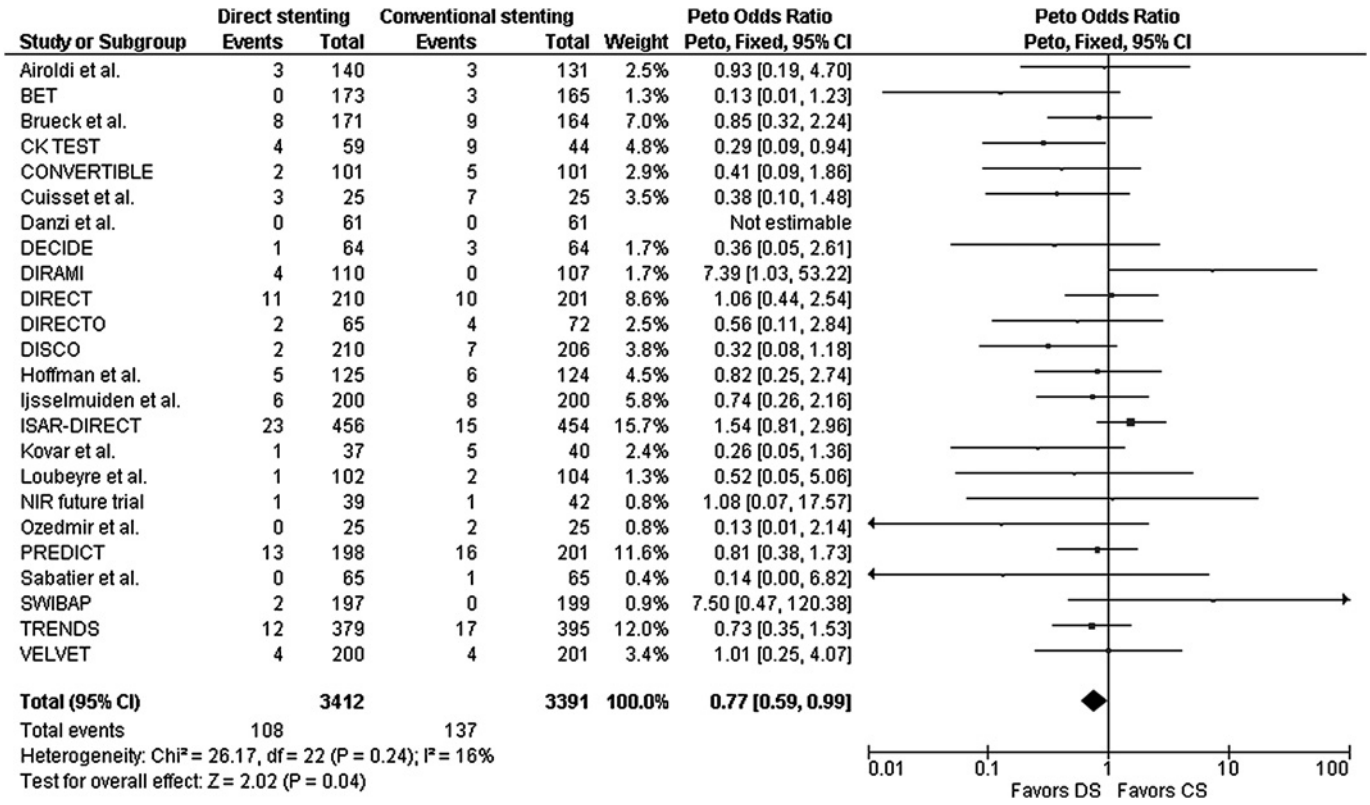

Figure 3 OR of myocardial infarction associated with direct stenting versus conventional stenting.

According to those data, there would be much more endothelial preservation and less vascular inflammatory response associated with DS compared with CS, leading to lower restenosis rates.[3] However, none of included trials demonstrated a significant benefit in patients treated with DS in terms of TVR incidence, with the exception of Brueck *et al*.[17] As reported above, the present meta-analysis showed no differences between DS and CS in terms of TVR, consistently with an earlier meta-analysis

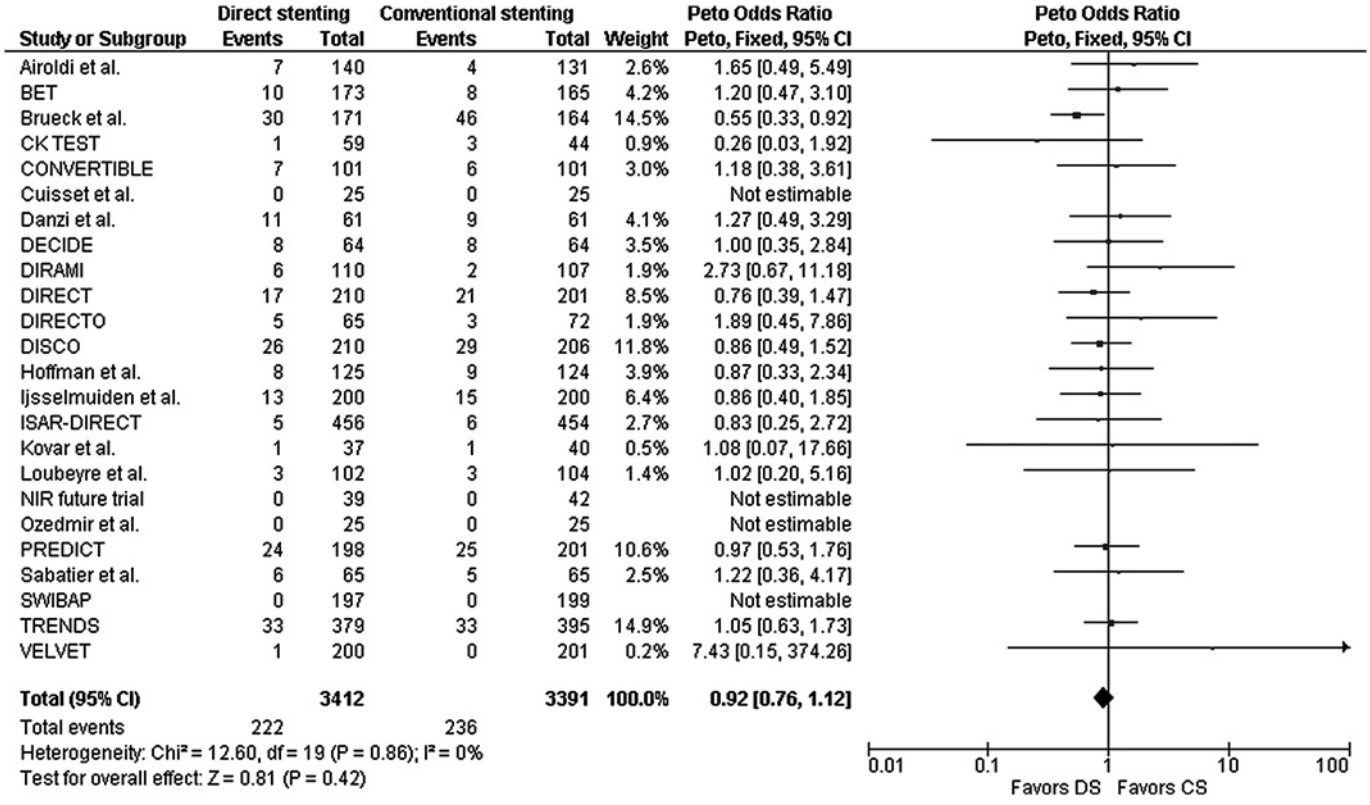

Figure 4 OR of target-vessel revascularisation associated with direct stenting versus conventional stenting.

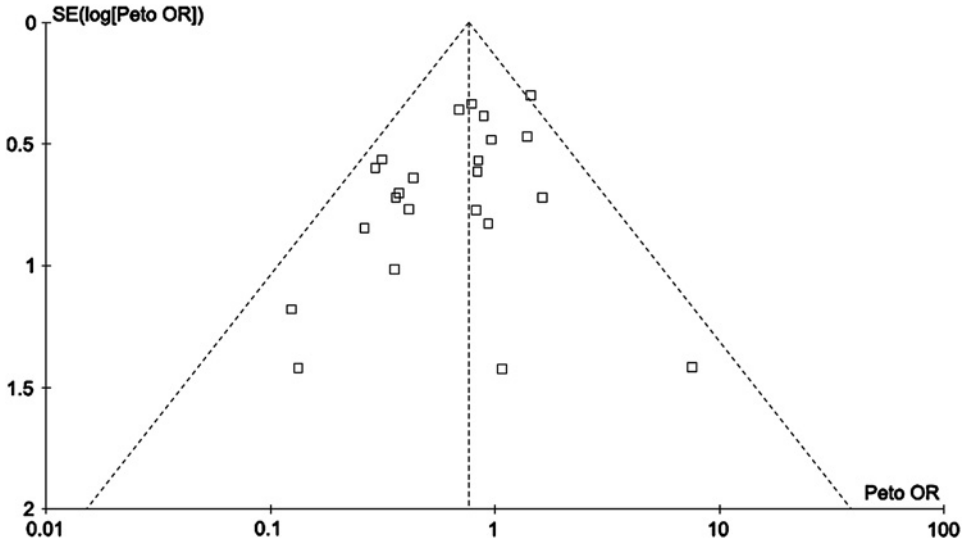

Figure 5 Funnel plot of all studies included in the meta-analysis. The SE of the ln OR was plotted against the OR for the composite of death or myocardial infarction.

including only less than half of patients.[42] Unfortunately, initial encouraging experimental data did not translate in a significant clinical benefit in terms of reduced restenosis. Of note, the aforementioned data were performed in healthy animal vessels, using low pressure balloon inflation, which might have positively influenced endothelial response to mechanical injury.[2] In addition, the function of endothelial cells after DS in humans still remains unclear. Furthermore, although no data exist to suggest that MI after revascularisation reduces the likelihood of restenosis, it would be expected that patients who experience myocyte necrosis in the territory of a restenotic vessel would be less likely, according to the presence of non-viable myocardium, to experience angina as a result of recurrent narrowing. In turn, these patients would be less likely to undergo referral for ischaemia-driven TVR. This aspect might deserve additional research to explain how the TVR incidence was not affected by the DS strategy.

Besides reinforcing the safety and the feasibility of DS approach, we also observed a 23% reduction in the odds of MI associated with DS. In this respect, a randomised study showed a benefit of DS compared with CS in patients going elective PCI in terms of lower levels of post-PCI microvascular resistance and lower myocardial injury as mirrored from higher post-PCI troponin T values.[20] Similarly, a prospective study found higher post-PCI troponin I levels in patients treated with a conventional stenting approach,[43] which are associated with a worse prognosis.[44 45] A further theoretical advantage is that DS could avoid clot and plaque material distal microembolisation, with a possible improvement in coronary and myocardial perfusion, thus minimising myocardial cell injury.[2] Of note, microembolisation of plaque debris and side-branch occlusion has been proposed as the most likely mechanism of troponin release after PCI.[46 47] Furthermore, we previously demonstrated an improvement in post-procedural TIMI 3 grade flow and corrected TIMI frame count in patients undergoing PCI with DS.[48]

As specified above, the vast majority of included trials in this meta-analysis performed PCI with bare-metal stent implantation. For this reason, these results cannot be extended to drug-eluting stents and must be taken only as generating a hypothesis, since some concerns have been raised about the potential damage of polymer coating or a non-uniform drug elution associated with the DS technique. This aspect was confirmed from the exclusion of the DS approach in the preliminary trials evaluating both sirolimus-eluting and paclitaxel-eluting stents.[49–52] However, recent studies have shown the feasibility and the effectiveness of DS with both drug-eluting stents, possibly reducing angiographic restenosis and TVR.[39 40]

Despite these considerations, DS has some intrinsic potential disadvantages that need to be pointed out: a higher risk of failure to cross the lesion, stent dislodgment, loss or embolisation, inadequate choice of stent diameter and length. In addition, specific coronary lesion subsets, like chronic total occlusions, calcified, tortuous or angulated lesions, are not really suitable for a direct stenting approach.[2] In fact, these lesions have been excluded in most of the included trials (table 1). Notably, meta-regression did not report a significant relation between crossover rates and the occurrence of the primary endpoint. On the other hand, DS is advocated when PCI is performed in saphenous vein graft lesions since it has been associated with decreased major cardiac events when compared to CS.[53]

This meta-analysis presents several important limitations. First, this is a meta-analysis at study level, and we could not properly assess the role of confounding factors. However, a clear limitation of patient level data analysis is that patient-level data are not always available from all investigators, introducing several biases. Second, some RCTs were underpowered to detect significant differences between interventions in the main outcomes; however, this reinforces the necessity of the present study. Third, different MI definitions, adopted among the included trials, possibly could have influenced the final results, despite a low and not significant heterogeneity being reported. Fourth, although the observed reduction in MI seems to be related to lower peri-procedural MIs, we were unable to evaluate this issue in detail, since post-PCI incidence was available for only a few studies. However, in-hospital MI data, available for 20 studies (4619 patients), showed a significant reduction in patients allocated to the DS arm (1.42% versus 2.52%, p=0.007, OR=0.56 (95% CI 0.37 to 0.85)).

In conclusion, this meta-analysis demonstrates that, in selected coronary lesions, direct stenting is not only a feasible technique, but also reduces the occurrence of myocardial infarction.

Competing interests None.

Contributors FP had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: FP, RP, MC. Acquisition of data: SC, RDR, CD'A. Analysis and interpretation of data: FP, RP, SC. Drafting of the manuscript: RP, SC, GG, CD'A. Critical revision of the

manuscript for important intellectual content: FP, MC, GG. Statistical analysis: FP, GG, RDR. Study supervision: FP, MC.

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REFERENCES

1. **Serruys PW,** Kutryk MJ, Ong AT. Coronary-artery stents. *N Engl J Med* 2006;**354**:483—95.
2. **Barbato E,** Marco J, Wijns W. Direct stenting. *Eur Heart J* 2003;**24**:394—403.
3. **Rogers C,** Parikh S, Seifert P, *et al*. Endogenous cell seeding. Remnant endothelium after stenting enhances vascular repair. *Circulation* 1996;**94**:2909—14.
4. **Maclure M,** Willett WC. Misinterpretation and misuse of the kappa statistic. *Am J Epidemiol* 1987;**126**:161—9.
5. **Bradburn MJ,** Deeks JJ, Berlin JA, *et al*. Much ado about nothing: a comparison of the performance of meta-analytical methods with rare events. *Stat Med* 2007;**26**:53—77.
6. **Sweeting MJ,** Sutton AJ, Lambert PC. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. *Stat Med* 2004;**23**:1351—75.
7. **Mantel N,** Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959;**22**:719—48.
8. **DerSimonian R,** Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;**7**:177—88.
9. **Dickersin K,** Berlin JA. Meta-analysis: state-of-the-science. *Epidemiol Rev* 1992;**14**:154—76.
10. **Higgins JP,** Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;**21**:1539—58.
11. **Higgins JP,** Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557—60.
12. **Begg CB,** Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;**50**:1088—101.
13. **Biondi-Zoccai GG,** Abbate A, Agostoni P, *et al*. Long-term benefits of an early invasive management in acute coronary syndromes depend on intracoronary stenting and aggressive antiplatelet treatment: a metaregression. *Am Heart J* 2005;**149**:504—11.
14. **Liberati A,** Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;**339**:b2700.
15. **Airoldi F,** Di Mario C, Gimelli G, *et al*. A randomized comparison of direct stenting versus stenting with predilatation in native coronary artery disease: results from the multicentric Crosscut study. *J Invasive Cardiol* 2003;**15**:1—5.
16. **Elbaz M,** El Mokhtar E, Khalife K, *et al*. Is direct coronary stenting the best strategy for long-term outcome? Results of the multicentric randomized benefit evaluation of direct coronary stenting (BET) study. *Am Heart J* 2002;**144**:E7.
17. **Brueck M,** Scheinert D, Wortmann A, *et al*. Direct coronary stenting versus predilatation followed by stent placement. *Am J Cardiol* 2002;**90**:1187—92.
18. **Balducelli M,** Varani E, Vecchi G, *et al*. CK TEST Investigators. Direct coronary stenting versus stenting with balloon pre-dilation: incidence of enzyme release and follow-up results of a multicentre, prospective, randomized study. The CK and Troponin I Estimation in direct STenting (CK TEST) trial. *Minerva cardioangiol* 2007;**55**:281—9.
19. **Wijns W,** Verheye S, Manoharan G, *et al*. CONVERTIBLE investigators. Angiographic, intravascular ultrasound, and fractional flow reserve evaluation of direct stenting vs. conventional stenting using BeStent2 in a multicentre randomized trial. *Eur Heart J* 2005;**26**:1852—9.
20. **Cuisset T,** Hamilos M, Melikian N, *et al*. Direct stenting for stable angina pectoris is associated with reduced periprocedural microcirculatory injury compared with stenting after pre-dilation. *J Am Coll Cardiol* 2008;**51**:1060—5.
21. **Danzi GB,** Capuano C, Fiocca L, *et al*. Stent implantation without predilation in patients with a single, noncalcified coronary artery lesion. *Am J Cardiol* 1999;**84**:1250—3, A8.
22. **Tan HC,** Lim YT, Rosli TL, *et al*. Direct stenting compared to conventional stenting in Diabetic Patients Undergoing Elective Angioplasty for Coronary Artery Disease (DECIDE): a multicenter, open label, randomized, controlled efficacy study. *Am Heart J* 2004;**148**:1007—11.
23. **Gasior M,** Gierlotka M, Lekston A, *et al*. Comparison of outcomes of direct stenting versus stenting after balloon predilation in patients with acute myocardial infarction (DIRAMI). *Am J Cardiol* 2007;**100**:798—805.
24. **Brito FS Jr,** Caixeta AM, Perin MA, *et al*. DIRECT Study Investigators. Comparison of direct stenting versus stenting with predilation for the treatment of selected coronary narrowings. *Am J Cardiol* 2002;**89**:115—20.
25. **Ballarino MA,** Moreyra E Jr, Damonte A, *et al*. Multicenter randomized comparison of direct vs. conventional stenting: the DIRECTO trial. *Catheter Cardiovasc Interv* 2003;**58**:434—40.
26. **Martinez-Elbal L,** Ruiz-Nodar JM, Zueco J, *et al*. Direct coronary stenting versus stenting with balloon pre-dilation: immediate and follow-up results of a multicentre, prospective, randomized study. The DISCO trial. DIrect Stenting of COronary Arteries. *Eur Heart J* 2002;**23**:633—40.
27. **Hoffmann R,** Takimoglu-Boerekci M, Langenberg R, *et al*. Randomized comparison of direct stenting with predilatation followed by stenting on vessel trauma and restenosis. *Am Heart J* 2004;**147**:E13.
28. **IJsselmuiden AJ,** Serruys PW, Scholte A, *et al*. Direct coronary stent implantation does not reduce the incidence of in-stent restenosis or major adverse cardiac events: six month results of a randomized trial. *Eur Heart J* 2003;**24**:421—9.
29. **Mehilli J,** Kastrati A, Dirschinger J, *et al*. Intracoronary stenting and angiographic results: restenosis after direct stenting versus stenting with predilation in patients with symptomatic coronary artery disease (ISAR-DIRECT trial). *Catheter Cardiovasc Interv* 2004;**61**:190—5.
30. **Kovar LI,** Monrad ES, Sherman W, *et al*. A randomized trial of stenting with or without balloon predilation for the treatment of coronary artery disease. *Am Heart J* 2001;**142**:E9.
31. **Loubeyre C,** Morice MC, Lefevre T, *et al*. A randomized comparison of direct stenting with conventional stent implantation in selected patients with acute myocardial infarction. *J Am Coll Cardiol* 2002;**39**:15—21.
32. **Ormiston JA,** Webster MW, Ruygrok PN, *et al*. A randomized study of direct coronary stent delivery compared with stenting after predilatation: the NIR future trial. On behalf of the NIR Future Trial Investigators. *Catheter Cardiovasc Interv* 2000;**50**:377—81;discussion 82—3.
33. **Ozdemir R,** Sezgin AT, Barutcu I, *et al*. Comparison of direct stenting versus conventional stent implantation on blood flow in patients with ST-segment elevation myocardial infarction. *Angiology* 2006;**57**:453—8.
34. **Baim DS,** Flatley M, Caputo R, *et al*. Comparison of PRE-dilatation vs direct stenting in coronary treatment using the Medtronic AVE S670 Coronary Stent System (the PREDICT trial). *Am J Cardiol* 2001;**88**:1364—9.
35. **Sabatier R,** Hamon M, Zhao QM, *et al*. Could direct stenting reduce no-reflow in acute coronary syndromes? A randomized pilot study. *Am Heart J* 2002;**143**:1027—32.
36. **Le Breton H,** Boschat J, Commeau P, *et al*. Stent Without Balloon Predilation (SWIBAP) Study Group. Randomised comparison of coronary stenting with and without balloon predilatation in selected patients. *Heart* 2001;**86**:302—8.
37. **Dawkins KD,** Chevalier B, Suttorp MJ, *et al*. Effectiveness of "direct" stenting without balloon predilatation (from the Multilink Tetra Randomised European Direct Stent Study [TRENDS]). *Am J Cardiol* 2006;**97**:316—21.
38. **Serruys PW,** IJsselmuiden S, Hout B, *et al*. Direct stenting with the Bx VELOCITY balloon-expandable stent mounted on the Raptor rapid exchange delivery system versus predilatation in a European randomized Trial: the VELVET trial. *Int J Cardiovasc Intervent* 2003;**5**:17—26.
39. **Ormiston JA,** Mahmud E, Turco MA, *et al*. Direct stenting with the TAXUS Liberté Drug-Eluting Stent. *JACC Cardiovasc Interv* 2008;**1**:150—60.
40. **Moses JW,** Weisz G, Mishkel G, *et al*. The SIRIUS-DIRECT trial: a multi-center study of direct stenting using the sirolimus-eluting stent in patients with de novo native coronary artery lesions. *Catheter Cardiovasc Interv* 2007;**70**:505—12.
41. **Katritsis DG,** Korovesis S, Karvouni E, *et al*. Direct versus predilatation drug-eluting stenting: a randomized clinical trial. *J Invasive Cardiol* 2006;**18**:475—9.
42. **Burzotta F,** Trani C, Prati F, *et al*. Comparison of outcomes (early and six- month) of direct stenting with conventional stenting (a meta-analysis of ten randomized trials). *Am J Cardiol* 2003;**91**:790—6.
43. **Nageh T,** Thomas MR, Sherwood RA, *et al*. Direct stenting may limit myocardial injury during percutaneous coronary intervention. *J Invasive Cardiol* 2003;**15**:115—18.
44. **Cantor WJ,** Newby LK, Christenson RH, *et al*. Prognostic significance of elevated troponin I after percutaneous coronary intervention. *J Am Coll Cardiol* 2002;**39**:1738—44.
45. **Nienhuis MB,** Ottervanger JP, Bilo HJ, *et al*. Prognostic value of troponin after elective percutaneous coronary intervention: a meta-analysis. *Catheter Cardiovasc Interv* 2008;**71**:318—24.
46. **Bahrmann P,** Figulla HR, Wagner M, *et al*. Detection of coronary microembolisation by Doppler ultrasound during percutaneous coronary interventions. *Heart* 2005;**91**:1186—92.
47. **Kralev S,** Poerner TC, Basorth D, *et al*. Side branch occlusion after coronary stent implantation in patients presenting with ST-elevation myocardial infarction: clinical impact and angiographic predictors. *Am Heart J* 2006;**151**:153—7.
48. **Capozzolo C,** Piscione F, De Luca G, *et al*. Direct coronary stenting: effect on coronary blood flow, immediate and late clinical results. *Catheter Cardiovasc Interv* 2001;**53**:464—73.
49. **Morice MC,** Serruys PW, Sousa JE, *et al*. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002;**346**:1773—80.
50. **Grube E,** Silber S, Hauptmann KE, *et al*. TAXUS I: six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel-eluting stent for de novo coronary lesions. *Circulation* 2003;**107**:38—42.
51. **Moses JW,** Leon MB, Popma JJ, *et al*. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;**349**:1315—23.
52. **Stone GW,** Ellis SG, Cox DA, *et al*. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;**350**:221—31.
53. **Leborgne L,** Cheneau E, Pichard A, *et al*. Effect of direct stenting on clinical outcome in patients treated with percutaneous coronary intervention on saphenous vein graft. *Am Heart J* 2003;**146**:501—6.