ORIGINAL ARTICLE

Analysis of 14 Trials Comparing Sirolimus-Eluting Stents with Bare-Metal Stents

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ABSTRACT

BACKGROUND

The long-term effects of treatment with sirolimus-eluting stents, as compared with bare-metal stents, have not been established.

METHODS

We performed an analysis of individual data on 4958 patients enrolled in 14 randomized trials comparing sirolimus-eluting stents with bare-metal stents (mean follow-up interval, 12.1 to 58.9 months). The primary end point was death from any cause. Other outcomes were stent thrombosis, the composite end point of death or myocardial infarction, and the composite of death, myocardial infarction, or reintervention.

RESULTS

The overall risk of death (hazard ratio, 1.03; 95% confidence interval [CI], 0.80 to 1.30) and the combined risk of death or myocardial infarction (hazard ratio, 0.97; 95% CI, 0.81 to 1.16) were not significantly different for patients receiving sirolimus-eluting stents versus bare-metal stents. There was a significant reduction in the combined risk of death, myocardial infarction, or reintervention (hazard ratio, 0.43; 95% CI, 0.34 to 0.54) associated with the use of sirolimus-eluting stents. There was no significant difference in the overall risk of stent thrombosis with sirolimus-eluting stents versus bare-metal stents (hazard ratio, 1.09; 95% CI, 0.64 to 1.86). However, there was evidence of a slight increase in the risk of stent thrombosis associated with sirolimus-eluting stents after the first year.

CONCLUSIONS

The use of sirolimus-eluting stents does not have a significant effect on overall long-term survival and survival free of myocardial infarction, as compared with bare-metal stents. There is a sustained reduction in the need for reintervention after the use of sirolimus-eluting stents. The risk of stent thrombosis is at least as great as that seen with bare-metal stents.

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Restenosis after percutaneous coronary intervention (PCI) reduces the quality of life and increases the morbidity of patients with this complication[1]; it may even increase the risk of death.[2] Drug-eluting stents are highly effective in preventing restenosis after PCI.[3] It has been anticipated that by reducing the rate of restenosis, drug-eluting stents may have the potential to improve the long-term prognosis of patients treated with these devices. However, initial randomized studies focused on restenosis itself and had insufficient power and duration to assess the incidence of less frequent adverse events, such as death.

Recent reports have identified pathologic responses of the vessel wall to drug-eluting stents that may serve as precursors to adverse clinical events.[4] Such studies have raised concern that drug-eluting stents might actually worsen, rather than improve, long-term prognosis. However, efforts to examine this issue by combining data from previous randomized trials have been limited to published trial-level data and have not included all the relevant studies.[5-7] The aim of this study was to assess the long-term outcome after implantation of sirolimus-eluting stents on the basis of data from individual patients from randomized clinical trials comparing this device with bare-metal stents.

METHODS

INCLUSION CRITERIA

We included in our analysis the results of randomized clinical trials that compared sirolimus-eluting stents (Cypher or Cypher Select, Cordis) with bare-metal stents for management of coronary artery disease if results for a mean follow-up period of at least 1 year were reported or made available by the trials' investigators or sponsors.

DATA SOURCES

We searched the National Library of Medicine (PubMed, at www.pubmed.gov), the National Institutes of Health clinical trials registry (www.clinicaltrials.gov), and the Cochrane Central Register of Controlled Trials (www.mrw.interscience.wiley.com/cochrane/cochrane_clcentral_articles_fs.html) for randomized trials comparing sirolimus-eluting stents with bare-metal stents in patients with coronary artery disease. We also searched Internet-based sources of information on the results of clinical trials in cardiology (www.cardiosource.com/clinicaltrials, www.theheart.org, www.clinicaltrialresults.com, and www.tctmd.com), as well as conference proceedings from meetings of the American College of Cardiology, the American Heart Association, and the European Society of Cardiology. Relevant reviews and editorials published within the past year in major medical journals were identified and assessed for possible information on trials of interest. Searches were restricted to the period from January 2002 through September 2006.

We found and screened 16 randomized trials,[8-23] the main characteristics of which are shown in Table 1. Two randomized trials, Reduction of Restenosis in Saphenous Vein Grafts with Cypher Sirolimus-Eluting Stent (RRISC)[16] and Sirolimus-Eluting Stent in the Prevention of Restenosis in Small Coronary Arteries (SES-SMART),[19] were not included in this analysis because each had a mean follow-up of less than 1 year; the findings of these trials are displayed in Table 1 of the Supplementary Appendix (available with the full text of this article at www.nejm.org).

DATA COLLECTION AND QUALITY ASSESSMENT

An electronic form containing the data fields to be completed for individual patients was sent to all principal investigators or sponsors of the trials. Data from nine randomized trials[8,11,13,14,17,18,20,22,23] were provided by the principal investigators; data from the remaining five trials[9,10,12,15,21] were provided by the sponsor, who had no role in the study design or analysis or in the writing of or decision to publish the manuscript.

The data requested for each patient included the date of randomization, treatment allocation, diabetes status, event status (including death, myocardial infarction, coronary reintervention [percutaneous or surgical], and stent thrombosis and the respective dates of occurrence), and the date of the last follow-up visit. All data were thoroughly checked for consistency (logical checking and checking against the original publications). Any queries were resolved and the final database entries verified by the responsible trial investigator.

We also evaluated each trial for the adequacy of allocation concealment, performance of the analysis according to the intention-to-treat principle, and blind assessment of the outcomes of interest. We used the criteria recommended by Altman and Schulz[24] and by Jüni et al.[25] to de-

Table 1. Main Characteristics of the Trials.*

Study	No. of Patients	No. of Patients with Diabetes	Mean Age	Double Blinding	Patient Profile	Primary End Point	Protocol-Mandated Follow-up Angiography	Length of Thienopyridine Therapy	Mean Length of Follow-up
			yr					*mo*	
BASKET[8]	545	101	64.0	No	Unselected patients	Cost-effectiveness based on the composite of death, myocardial infarction, and reintervention	No	6	18.3
C-SIRIUS[9]	100	24	60.5	Yes	Small vessels, long lesions	Minimal luminal diameter on follow-up angiography	Yes	2	48.5
DECODE[10]	83	83	60.0	No	Patients with diabetes	Late luminal loss on angiography	Yes	3	12.7
DIABETES[11]	160	160	66.6	No	Patients with diabetes	Late luminal loss on angiography	Yes	12	25.3
E-SIRIUS[12]	352	81	62.3	Yes	Long lesions	Minimal luminal diameter on follow-up angiography	Yes	2	49.4
Pache et al.[13]	500	154	66.6	No	Unselected patients	Binary restenosis on angiography	Yes	6	46.1
PRISON II[14]	200	27	59.5	No	Total occlusions	Binary restenosis on angiography	Yes	6	24.6
RAVEL[15]	238	44	60.8	Yes	Selected patients	Late luminal loss on angiography	Yes	2	58.1
RRISC[16]	75	11	72.5	No	Venous bypass grafts	Late luminal loss on angiography	Yes	2	6.0
SCANDSTENT[17]	322	58	62.7	No	Complex lesions	Minimal luminal diameter on follow-up angiography	Yes	12	12.2
SCORPIUS[18]	193	193	64.9	No	Patients with diabetes	Late luminal loss on angiography	Yes	3	12.7
SES-SMART[19]	257	64	63.4	No	Small vessels	Binary restenosis on angiography	Yes	2	8.0
SESAMI[20]	320	65	61.6	No	Patients with acute myocardial infarction	Binary restenosis on angiography	Yes	12	12.3
SIRIUS[21]	1058	279	62.2	Yes	Relatively selected patients	Death, myocardial infarction, or reintervention	Yes	3	58.9
STRATEGY[22]	175	26	62.6	No	Patients with acute myocardial infarction	Death, myocardial infarction, stroke, or binary restenosis on angiography	Yes	3	24.2
TYPHOON[23]	712	116	59.3	No	Patients with acute myocardial infarction	Death from cardiac causes, myocardial infarction, or reintervention	Yes	6	12.1

* Two randomized trials that are listed in the table — RRISC[16] and SES-SMART[19] — were not included in the analysis because they each had a mean follow-up of less than 1 year. BASKET denotes Basel Stent Kosten Effektivitäts Trial (ISRCTN.org number, ISRCTN75663024), C-SIRIUS Canadian Study of the Sirolimus-Eluting Stent in the Treatment of Patients with Long De Novo Lesions in Small Native Coronary Arteries (ClinicalTrials.gov number, NCT00381420), DECODE Randomized Trial of Cypher versus Bare Metal Stents in Diabetics, DIABETES Diabetes and Sirolimus-Eluting Stent Trial, E-SIRIUS European Multicenter, Randomized, Double-Blind Study of the Sirolimus-Coated Bx Velocity Balloon-Expandable Stent in the Treatment of Patients with De Novo Coronary Artery Lesions (NCT00235144), PRISON II Primary Stenting of Totally Occluded Native Coronary Arteries II (NCT00258596), RAVEL Randomized Study of the Sirolimus-Coated Bx Velocity Balloon-Expandable Stent in the Treatment of Patients with De Novo Native Coronary Artery Lesions (NCT00233805), RRISC Reduction of Restenosis in Saphenous Vein Grafts with Cypher Sirolimus-Eluting Stent (NCT00263263), SCANDSTENT Stenting Coronary Arteries in Non-Stress/Benestent Disease Trial (NCT00151658), SCORPIUS German Multicenter, Randomized, Controlled, Open-Label Study of the Cypher Sirolimus-Eluting Stent in the Treatment of Diabetic Patients with De Novo Native Coronary Artery Lesions, SES-SMART Sirolimus-Eluting Stent in the Prevention of Restenosis in Small Coronary Arteries, SESAMI Randomized Trial of Sirolimus Stent vs. Bare Stent in Acute Myocardial Infarction (NCT00288210), SIRIUS Sirolimus-Eluting Balloon Expandable Stents in the Treatment of Patients with De Novo Coronary Artery Lesions (NCT00232765), STRATEGY Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent vs. Abciximab and Bare-Metal Stent in Myocardial Infarction (NCT00229515), and TYPHOON Trial to Assess the Use of the Cypher Stent in Acute Myocardial Infarction Treated with Balloon Angioplasty (NCT00232830).

cide whether the treatment allocation was adequately concealed. Some trials used a modified intention-to-treat principle (i.e., excluding patients who did not receive the study stent) (see Table 2 of the Supplementary Appendix).

STUDY OUTCOMES

The primary end point of this analysis was death from any cause. Secondary end points were the composite of death or myocardial infarction and the composite of death, myocardial infarction, or reintervention (major adverse cardiac events). We also assessed the occurrence of stent thrombosis (see Table 2 of the Supplementary Appendix for the end-point definitions used in individual trials). It is important to note that in eight trials, data for patients who underwent target-lesion revascularization were censored with respect to the subsequent assessment of stent thrombosis. The adjudication of events in each trial was performed by the same event committee over the entire follow-up period.

STATISTICAL ANALYSIS

We performed survival analyses with the use of the Mantel–Cox test stratified according to trial. Survival was defined as the interval from randomization until the event of interest. Data for patients who did not have the event of interest were censored at the date of the last follow-up visit. The log-rank test was used to calculate hazard ratios and their 95% confidence intervals (CIs).

Trials in which the event of interest was not observed in either study group were omitted from the analysis of that event. For trials in which only one of the groups had no event of interest, the estimate of treatment effect and its standard error were calculated after adding 0.5 to each cell of the 2×2 table for the trial.[26]

We assessed the heterogeneity across trials by the Cochran test and by calculating the I^2 statistic (describing the percentage of total variation across trials that was due to heterogeneity rather than chance), as proposed by Higgins et al.[27] We pooled hazard ratios from individual trials according to the method of DerSimonian and Laird for random effects.[28]

Sensitivity analyses were performed by comparing the treatment effects obtained with each trial removed consecutively from the analysis with the overall treatment effects. In addition, we used a random-effects meta-regression analysis to estimate the extent to which including four covariates — the nature of the study with respect to blinding (double blinding or no double blinding), the length of follow-up, the protocol-mandated duration of dual antiplatelet therapy, and the presence of acute myocardial infarction — as

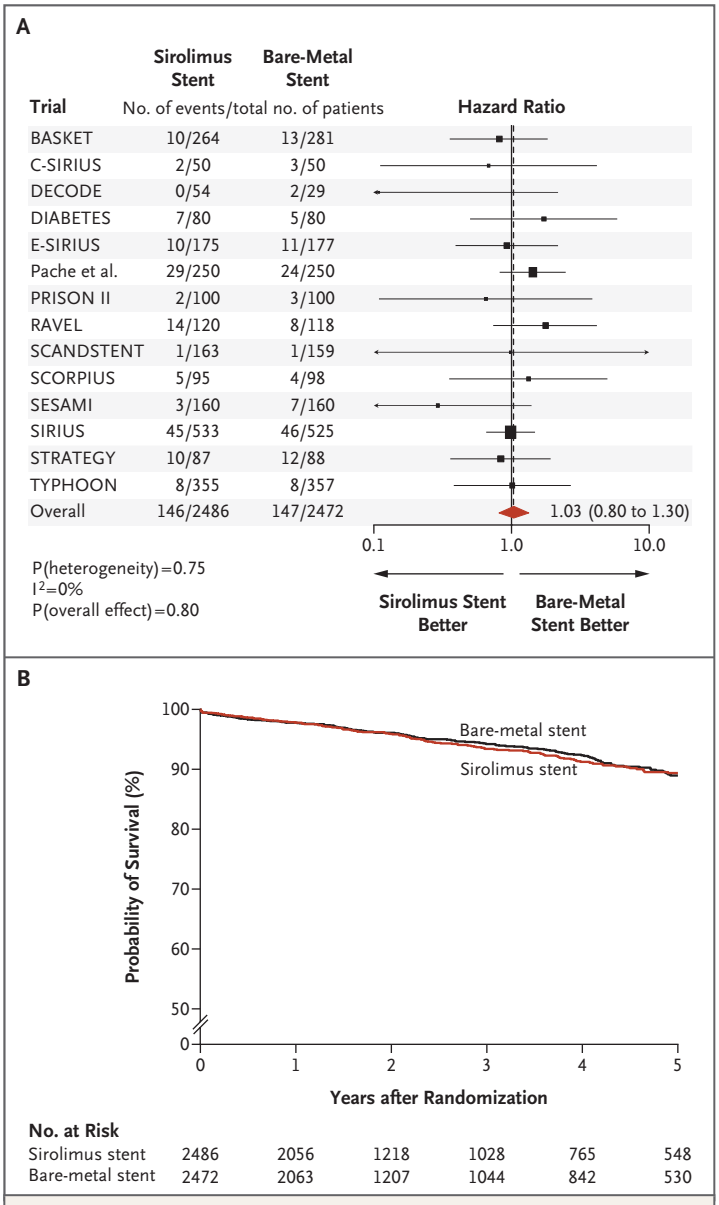

Figure 1. Hazard Ratios for Individual Trials and for the Pooled Population and Kaplan–Meier Estimates for 5-Year Survival.

In Panel A, hazard ratios are shown on a logarithmic scale. The size of each square is proportional to the weight of the individual study, measured as the inverse of the estimated variance of the log hazard ratio. In Panel B, Kaplan–Meier curves are shown for survival for the pooled population during a 5-year period in each of the stent groups.

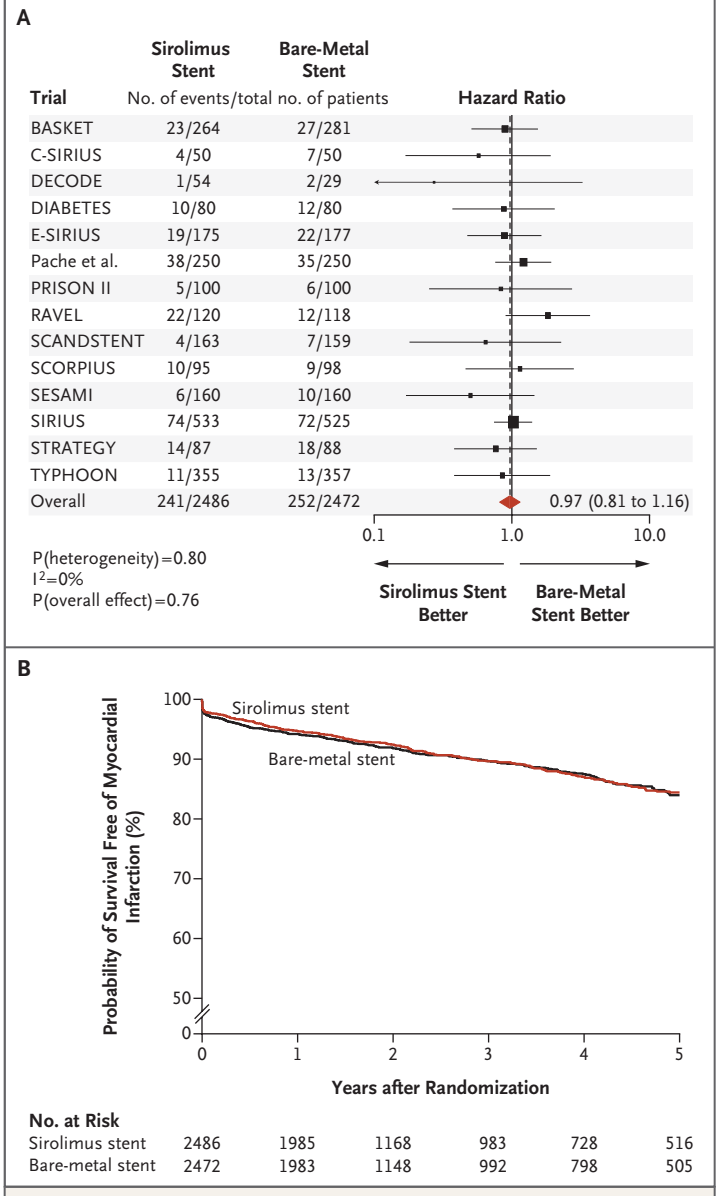

Figure 2. Hazard Ratios for Death or Myocardial Infarction and Kaplan–Meier Estimates for Survival Free of Myocardial Infarction.

In Panel A, hazard ratios are shown on a logarithmic scale. The size of each square is proportional to the weight of the individual study, measured as the inverse of the estimated variance of the log hazard ratio. In Panel B, Kaplan–Meier curves are shown for survival free of myocardial infarction for the pooled population during a 5-year period in each of the stent groups.

inclusion criteria for the trial might have influenced the treatment effect. Using the Mantel–Cox model, we checked for statistically significant interaction between the treatment effect (sirolimus-eluting stent vs. bare-metal stent) and the presence of diabetes mellitus (the only prespecified subgroup that was analyzed).

All P values are two-sided. Results were considered to be statistically significant at a P value of less than 0.05. Statistical analysis was performed with the use of Stata software, version 9.2 (Stata). Survival curves are presented as simple, nonstratified Kaplan–Meier curves across all trials and constructed with the use of S-Plus software, version 4.5 (Insightful).

RESULTS

Our analysis included 14 trials and 4958 patients, 1411 of whom had diabetes mellitus.[8-15,17,18,20-23] Table 1 displays the main characteristics of these trials. The age of the patients in the trials ranged from 59.3 to 66.6 years, and the length of follow-up ranged from 12.1 to 58.9 months.

Figure 1A shows the absolute numbers of deaths in each trial according to treatment group, with the hazard ratio for each trial. There was no statistical evidence of heterogeneity across the 14 trials. In total, there were 146 deaths (83 from cardiac causes) in patients with sirolimus-eluting stents and 147 deaths (79 from cardiac causes) in patients with bare-metal stents. Overall, the use of sirolimus-eluting stents was associated with a hazard ratio for death of 1.03 (95% CI, 0.80 to 1.30; P=0.80), as compared with that of bare-metal stents.

Sequential exclusion of each individual trial from the analysis of death yielded hazard ratios that ranged from 0.96 (95% CI, 0.74 to 1.25) to 1.06 (95% CI, 0.84 to 1.34) and were not significantly different from the overall hazard ratio (P≥0.71). No significant influence of prespecified covariates on the treatment effect was observed, including the length of follow-up (P=0.44), the protocol-mandated duration of dual antiplatelet therapy (P=0.69), the presence of patients with acute myocardial infarction in the trial (P=0.56), or the presence of double blinding in the trial design (P=0.70). Figure 1B shows the overall 5-year survival curves for the two treatment groups.

Figure 2A shows the absolute numbers of patients who died or had a myocardial infarction in each trial according to treatment group, with the hazard ratio for each trial. There was no statistical evidence of heterogeneity across the 14 trials. In total, 241 patients with sirolimus-eluting stents

either died or had a myocardial infarction, as compared with 252 patients with bare-metal stents. Overall, use of sirolimus-eluting stents was associated with a hazard ratio for death or myocardial infarction of 0.97 (95% CI, 0.81 to 1.16; P=0.76), as compared with use of bare-metal stents. Figure 2B shows the overall 5-year curves for survival free of myocardial infarction in the two study groups.

Figure 3A shows the absolute numbers of patients who died, had a myocardial infarction, or required reintervention in each trial according to treatment group, with the hazard ratio for each trial. In total, 331 patients with sirolimus-eluting stents died, had a myocardial infarction, or required reintervention, as compared with 649 patients with bare-metal stents. Overall, the use of sirolimus-eluting stents was associated with a hazard ratio for death, myocardial infarction, or reintervention of 0.43 (95% CI, 0.34 to 0.54; P<0.001), as compared with the use of bare-metal stents. Although the point estimates for individual trials all favored sirolimus-eluting stents, there was a significant heterogeneity across trials with a high I^2 value. Figure 3B shows the overall 5-year curves for survival free of myocardial infarction and reintervention in the two study groups.

No significant interaction between treatment groups and the diagnosis of diabetes was observed for any of the three end points of the study, including death (P=0.19), death or myocardial infarction (P=0.39), and death, myocardial infarction, or reintervention (P=0.49). We nonetheless performed a separate analysis of the rate of death in the subgroup of patients with diabetes. Figure 4A shows the absolute numbers of deaths in each trial by treatment group, with the hazard ratio for the subgroup of patients with diabetes in each trial. There was no significant heterogeneity across trials. In total, 59 patients with diabetes and sirolimus-eluting stents died, as compared with 56 patients with diabetes and bare-metal stents. The overall hazard ratio associated with sirolimus-eluting stents was 1.27 (95% CI, 0.83 to 1.95; P=0.26). Figure 4B shows the overall 5-year survival curves in the subgroup of patients with diabetes.

Stent thrombosis (as defined by the individual

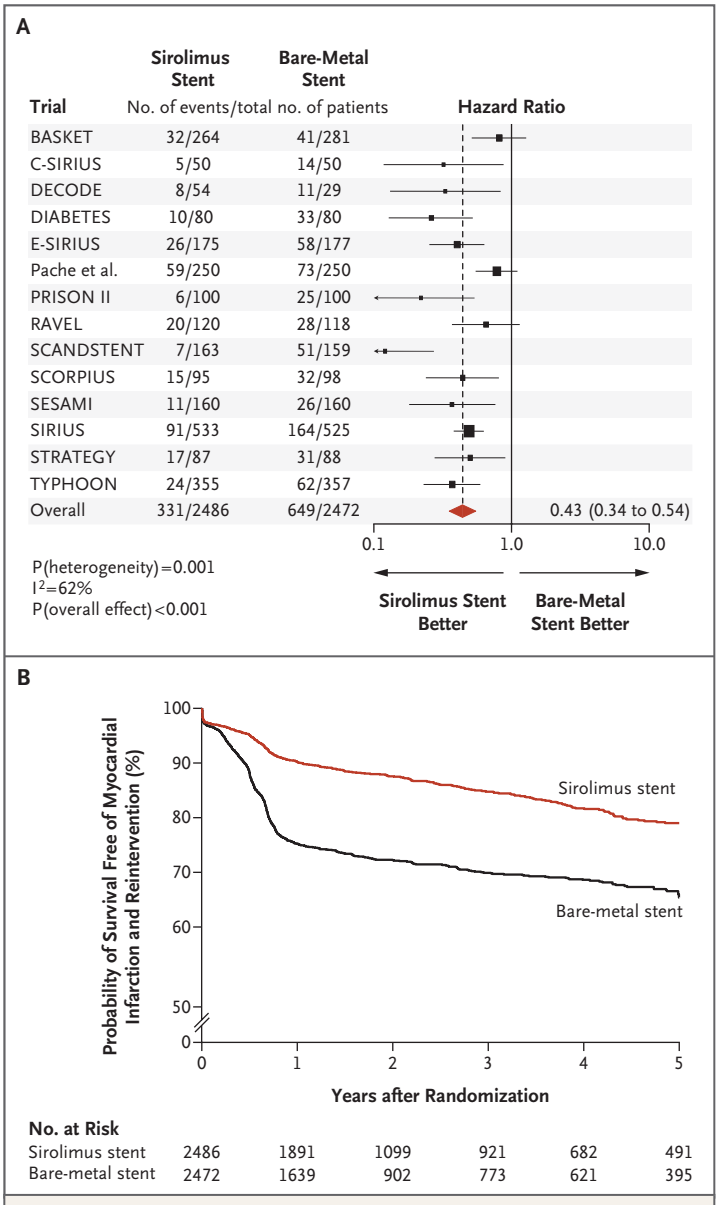

Figure 3. Hazard Ratios for Death, Myocardial Infarction, or Reintervention and Kaplan–Meier Curves for Survival Free of Myocardial Infarction and Reintervention.

Panel A shows significant heterogeneity in the effect of treatment resulting from the differing magnitude of risk reduction observed in patients with sirolimus-eluting stents among the 14 trials. Hazard ratios are shown on a logarithmic scale. The size of each square is proportional to the weight of the individual study, measured as the inverse of the estimated variance of the log hazard ratio. In Panel B, Kaplan–Meier curves are shown for survival free of myocardial infarction and reintervention for the pooled population during a 5-year period in each of the stent groups.

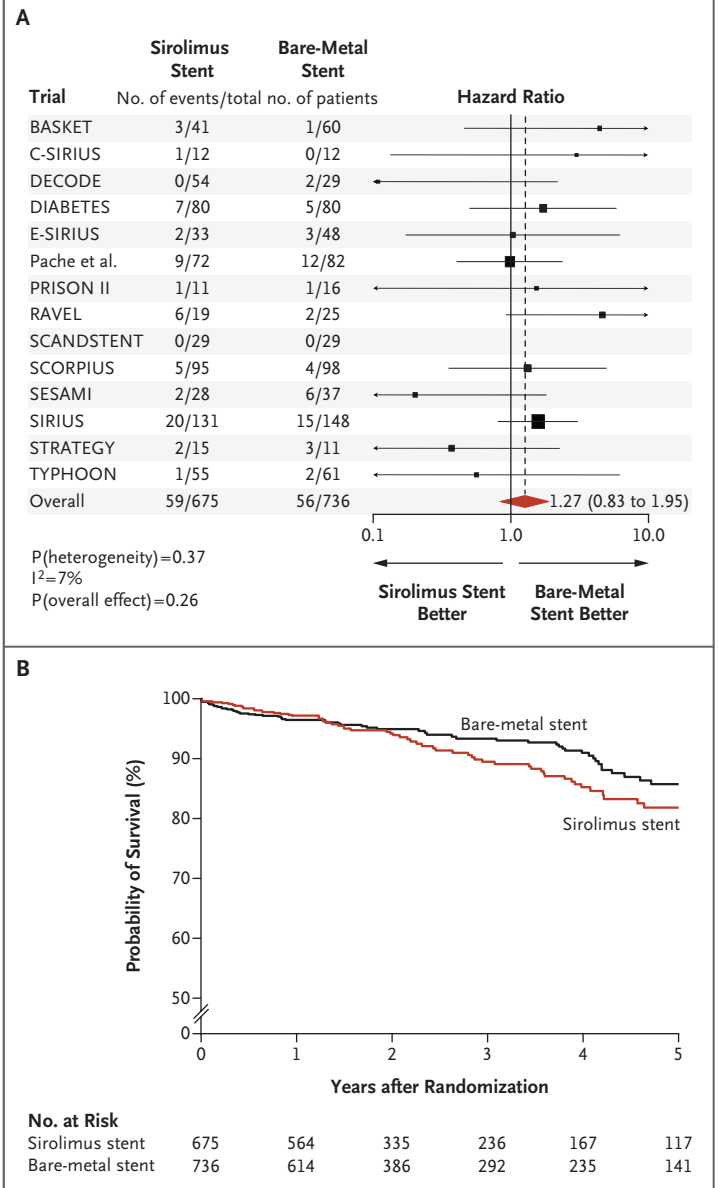

Figure 4. Hazard Ratios for Death in a Subgroup of Patients with Diabetes and Kaplan–Meier Curves for Overall Survival.

In Panel A, hazard ratios are shown on a logarithmic scale. The size of each square is proportional to the weight of the individual study, measured as the inverse of the estimated variance of the log hazard ratio. In Panel B, Kaplan–Meier curves are shown for survival for the pooled subgroup of patients with diabetes during a 5-year period in each of the stent groups.

trials) was observed in 65 patients (34 with sirolimus-eluting stents and 31 with bare-metal stents). The hazard ratio for stent thrombosis was 1.09 (95% CI, 0.64 to 1.86; P=0.75). After the first year, stent thrombosis occurred in nine patients, eight of whom had sirolimus-eluting stents (Fig. 5A). Over the 4-year period after the first year following the procedure, the overall risk of stent thrombosis was 0.6% (95% CI, 0.3 to 1.2) in the sirolimus-stent group and 0.05% (95% CI, 0.01 to 0.4) in the bare-metal–stent group (P=0.02). Figure 5B shows the curves of probability of stent thrombosis in the two study groups after the trial-defined minimum duration of recommended use of dual antiplatelet therapy (Table 1). The overall risk of stent thrombosis during 4 years after this time was 0.8% (95% CI, 0.5 to 1.5) in the sirolimus-stent group and 0.3% (95% CI, 0.1 to 0.6) in the bare-metal–stent group (P=0.16).

In 8 of the 14 trials, data for patients undergoing target-lesion revascularization were censored with respect to the subsequent assessment of stent thrombosis. This censoring resulted in the exclusion of five additional cases of stent thrombosis, all in the bare-metal–stent group. In contrast, in the other six trials, such censoring did not occur, which resulted in the inclusion of one case of stent thrombosis that occurred after target-lesion revascularization in the sirolimus-stent group.

DISCUSSION

In our study, we analyzed individual data for patients with coronary heart disease from 14 randomized trials comparing sirolimus-eluting stents with bare-metal stents. We found that the use of sirolimus-eluting stents was associated with rates of death alone or combined with myocardial infarction that were similar to those observed with the use of bare-metal stents. Sirolimus-eluting stents were also associated with a sustained reduction in the need for reintervention but with an overall risk of stent thrombosis that was at least as high as that seen with bare-metal stents.

Several previous analyses of trials comparing drug-eluting stents and bare-metal stents in patients with coronary artery disease have been reported.[5-7,29-34] In these previous studies, aggregate data from published reports, rather than data from individual patients, were examined. The superiority of analysis of data from individual patients over meta-analysis of lumped study outcomes has been emphasized.[35-38] In particular for survival data, the lack of adjustment for censoring leads to an imprecise estimate of the overall treatment effect and interstudy heterogeneity.[39] Access to data for individual patients also makes

it possible to analyze the timing of events. We made an extensive effort to identify and incorporate all trials comparing sirolimus-eluting stents with bare-metal stents. As a result, we believe that we have reduced the likelihood of study-selection bias, the major risk of any meta-analysis, which may have been present in previous reports.

The effect of the use of sirolimus-eluting stents on long-term mortality has not previously been established. Contrary to the expectation that prevention of restenosis by sirolimus-eluting stents might lead to improved survival, recent reports suggested that sirolimus-eluting stents were associated with an increased rate of death as early as 2 years after the procedure.[5,6] Although this finding was not statistically significant, it generated much concern among the medical community.[40] Our study shows no difference in mortality between patients with sirolimus-eluting stents and those with bare-metal stents during a 5-year period. The same finding was true for the combined end point of death or myocardial infarction.

No significant increase in the overall rate of stent thrombosis was seen with sirolimus-eluting stents. However, this complication was significantly more frequent in patients with sirolimus-eluting stents after the first year following the procedure, a finding that was consistent with another recent report.[41] This difference is chronologically associated with the end of the protocol-specified interval of dual antiplatelet therapy with thienopyridines and aspirin. Although an accurate assessment of this issue cannot be made without knowledge of the actual timing of discontinuation of thienopyridine therapy in individual patients, our findings, as well as other recently published observations,[42] may suggest the need for a longer duration of dual antiplatelet therapy in patients receiving sirolimus-eluting stents.

As noted, there were another five cases of stent thrombosis that were censored from the analysis of the original trials because they occurred after target-lesion revascularization. One case of stent thrombosis that was included in our count would have been excluded if such censoring had been applied to all the trials. Whether such cases of stent thrombosis should be included in comparisons of this kind is open to question. Proponents of inclusion would argue that post-revascularization episodes of stent thrombosis are an inseparable part of the experience of receiving a stent and that such episodes are more common with bare-metal stents because target-lesion revascularization is required more often in patients with such stents. The argument for excluding such episodes is that they may have occurred not as a result of the original stent choice, but as a result of the subsequent revascularization procedure, and thus that they do not reflect the biologic effects of the specific stent type.

Our observation that there is no late difference in hard end points (death or myocardial infarction) despite an increase in late stent thrombosis

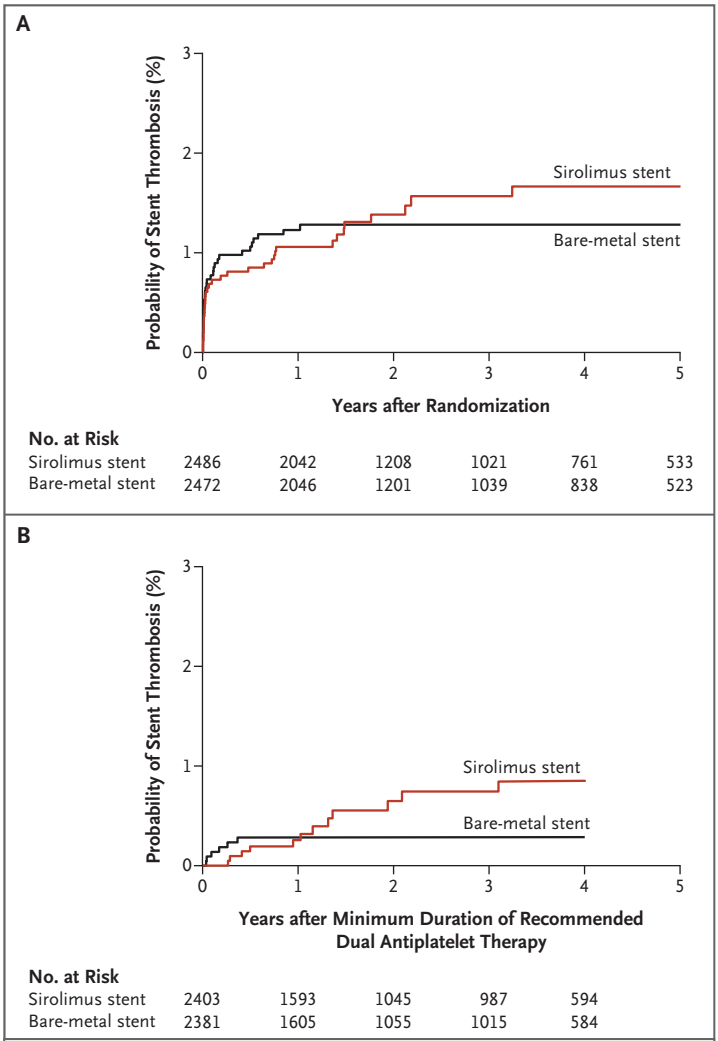

Figure 5. Kaplan–Meier Curves for Stent Thrombosis in the Pooled Population According to Stent Type and the Duration of Dual Antiplatelet Therapy.

Panel A shows that after the first year following the index procedure, stent thrombosis occurred in eight patients in the sirolimus-stent group and in only one patient in the bare-metal–stent group. Panel B shows the probability of stent thrombosis after the use of a trial-defined minimum duration of recommended dual antiplatelet therapy, according to stent type.

associated with sirolimus-eluting stents may be explained by the small proportion of patients with this complication in the trials. Also, the negative effect of late stent thrombosis on clinical outcome might have been offset by the reduction in the need for reintervention with the sirolimus-eluting stent and, consequently, by the exposure of a lower number of patients to postprocedural complications, as suggested by recent analyses.[43]

We paid special attention to patients with diabetes through a prespecified subgroup analysis. Patients with diabetes are at increased risk for adverse events after PCI,[44,45] and aortocoronary bypass surgery is often considered to be a better treatment option for them. The effect of drug-eluting stents on the long-term outcome of patients with diabetes is not known. In the Sirolimus-Coated Bx Velocity Balloon-Expandable Stent in the Treatment of De Novo Native Coronary Artery Lesions (SIRIUS) trial, the largest trial in our analysis, patients with diabetes continued to have a relatively high rate of restenosis even after receiving drug-eluting stents.[21] In our study, there was no statistical interaction between the presence of diabetes and the effect of sirolimus-eluting stents on the outcome of patients, including the rate of death. However, when we analyzed mortality in the subgroup of patients with diabetes, there was a trend toward a higher hazard ratio in patients with sirolimus-eluting stents. This observation suggests that patients with diabetes should be observed and followed especially carefully after treatment with sirolimus-eluting stents. It also justifies further collection of data on the long-term outcome of patients with diabetes who are treated with such stents. In addition, it will be important to evaluate whether other available or new drug-eluting stents may offer better results to patients with diabetes.

In conclusion, the use of sirolimus-eluting stents did not have a significant effect on overall long-term survival or on survival free of myocardial infarction, as compared with bare-metal stents. There was a sustained reduction in the need for reintervention after the placement of sirolimus-eluting stents. The risk of stent thrombosis was at least as great as that seen with bare-metal stents.

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