Am J Cardiol (2004);94:1297-300
Comparison of clinical and angiographic outcome of sirolimus-eluting stent implantation versus cutting balloon angioplasty for coronary in-stent restenosis
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Sixty in-stent restenotic lesions were treated with sirolimus-eluting stent implantation and retrospectively compared with a group of matched lesions treated with cutting balloon angioplasty. The results indicate a good safety profile of the procedure and a 57% reduction in the incidence of recurrent restenosis in comparison with cutting balloon angioplasty.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15541251

J Am Coll Cardiol (2004);43:943-9
Cutting balloon versus conventional balloon angioplasty for the treatment of in-stent restenosis: results of the restenosis cutting balloon evaluation trial (RESCUT)
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OBJECTIVES: The aim of this trial was to compare cutting balloon angioplasty (CBA) with conventional balloon angioplasty (i.e., percutaneous transluminal coronary angioplasty [PTCA]) for the treatment of patients with coronary in-stent restenosis (ISR). BACKGROUND: Retrospective studies suggest CBA might be superior to conventional PTCA in the treatment of ISR. METHODS: The Restenosis Cutting Balloon Evaluation Trial (RESCUT) is a multicenter, randomized, prospective European trial including 428 patients with all types of ISR (e.g., focal, multifocal, diffuse, proliferative). RESULTS: In both groups, the majority of ISR lesions were shorter than 20 mm. The length of restenotic stents was similar (CBA: 18.6 +/- 9.7 mm; PTCA: 18.3 +/- 8.7 mm). The number of balloons used to treat ISR was lower in the CBA group: only one balloon was used in 82.3% of CBA cases, compared with 75% of PTCA procedures ($p = 0.03$). Balloon slippage was less frequent in the CBA group (CBA 6.5%, PTCA 25%; $p < 0.01$). There was a trend toward a lower need for additional stenting in the CBA group (CBA 3.9%, PTCA 8.0%; $p = 0.07$). At seven-month angiographic follow-up, the binary restenosis rate was not different between the groups (CBA 29.8%, PTCA 31.4%; $p = 0.82$), with a similar pattern of recurrent restenosis. Clinical events at seven months were also similar. CONCLUSIONS: Cutting balloon angioplasty did not reduce recurrent ISR and major adverse cardiac events, as compared with conventional PTCA. However, CBA was associated with some procedural advantages, such as use of fewer balloons, less requirement for additional stenting, and a lower incidence of balloon slippage.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15028348

Eur Heart J (2004);25:1829-35
Therapeutic implications of in-stent restenosis located at the stent edge. Insights from the restenosis intra-stent balloon angioplasty versus elective stenting (RIBS) randomized trial
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AIMS: In patients with in-stent restenosis (ISR) several anatomic subgroups have been identified. ISR affecting the stent edge (EDG) is a poorly characterised subgroup with undefined therapeutic implications. We sought to determine the implications of ISR affecting the stent EDG. METHODS AND RESULTS: 450 patients included in the "Restenosis Intra-stent: Balloon angioplasty vs elective Stenting" (RIBS) randomized study, were analysed. EDG ISR was predefined in the protocol and the pattern of ISR analysed in a centralized core-lab. Fifty-two patients (12%) had EDG ISR (29 stent group, 23 balloon arm). Patients with EDG ISR had less severe [minimal lumen diameter (MLD) (0.78+/-0.3 vs 0.66+/-0.3 mm, p=0.05)] and shorter lesions (lesion length 10.2+/-6 vs 13.2+/-7 mm, p=0.003). Patients with EDG ISR more frequently required crossover (12% vs 3%, p=0.006) but eventually the immediate angiographic result and the long-term clinical and angiographic outcome was similar to that found in patients without EDG ISR. Patients with EDG ISR treated in the balloon and stent arms had similar baseline characteristics. However, after intervention, the immediate angiographic result was better in the stent arm (MLD 2.79+/-0.4 vs 2.35+/-0.3 mm, p=0.001). This difference persisted at late follow-up: MLD (1.93+/-0.7 vs 1.39+/-0.7 mm, p=0.01), recurrent restenosis (20% vs 50%, p=0.03). In addition, the 1-year event-free survival was significantly better (83% vs 52%, log rank p=0.01; Cox HR 0.28, 95%CI 0.09-0.79) in the stent arm. Moreover, stent implantation was an independent predictor of freedom from target vessel revascularization (HR 0.15, 95%CI 0.03-0.67, p=0.003). CONCLUSIONS: EDG ISR constitutes a specific subgroup with relevant therapeutic implications. In patients with EDG ISR, repeat stent implantation provides better clinical and angiographic outcome than conventional balloon angioplasty.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15474698

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Sirolimus-eluting vs uncoated stents for prevention of restenosis in small coronary arteries: a randomized trial
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CONTEXT: Percutaneous coronary revascularization of small vessels is associated with a high restenosis rate. Sirolimus-eluting stents reduce restenosis in simple and previously untreated lesions of large coronary arteries, but their outcomes in small vessels have not been adequately investigated. OBJECTIVE: To determine whether sirolimus-eluting stents are associated with a reduced 8-month rate of angiographic restenosis in comparison with an uncoated stent. DESIGN, SETTING, AND PATIENTS: This was a randomized, multicenter, single-blind, prospective trial performed with 257 patients undergoing percutaneous coronary revascularization for ischemic heart disease, and who had a previously untreated atherosclerotic lesion located in a small segment with a diameter of 2.75 mm or less, in 20 Italian centers between August 2002 and December 2003. INTERVENTION: Patients were randomly assigned to receive a sirolimus-eluting stent (129 patients) or an uncoated stent having an identical architecture and radiographic appearance (128 patients). MAIN OUTCOME MEASURES: The primary end point was the 8-month binary in-segment restenosis rate;

secondary end points included procedural success and the 8-month rate of major adverse cardiac and cerebrovascular events. RESULTS: The mean (SD) reference diameter of the treated segment was 2.2 (0.28) mm; the lesion length, 11.84 (6.15) mm. After 8 months, the binary in-segment restenosis rate was 53.1% (60/113) in the patients receiving an uncoated stent and 9.8% (12/123) in those receiving a sirolimus-eluting stent (relative risk [RR], 0.18; 95% confidence interval [CI], 0.10-0.32; P<.001). Fewer patients randomized to sirolimus-eluting stents experienced major adverse cardiac events (12/129 [9.3%] vs 40/128 [31.3%]; RR, 0.30; 95% CI, 0.15-0.55; P<.001) mainly because of a reduction in target lesion revascularization (9/129 [7%] vs 27/128 [21.1%]; RR, 0.33; 95% CI, 0.14-0.70; P =.002) and myocardial infarction (2/129 [1.6%] vs 10/129 [7.8%]; RR, 0.20; 95% CI, 0.01-0.93; P =.04). CONCLUSION: The use of sirolimus-eluting stents to treat atherosclerotic lesions in small coronary arteries reduces restenosis and may also reduce major adverse cardiac events.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15585732

J Am Coll Cardiol (2004);44:1786-91
Impact of mild or moderate chronic kidney disease on the frequency of restenosis: results from the PRESTO trial
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OBJECTIVES: The goal of this study was to determine if restenosis is increased in mild and moderate chronic kidney disease (CKD) patients after percutaneous coronary intervention (PCI). BACKGROUND: Mortality is increased in CKD after PCI. Restenosis may contribute to increased late mortality. METHODS: We analyzed 11,187 patients with a creatinine <1.8 mg/dl from the Prevention of REStenosis with Tranilast and its Outcomes (PRESTO) trial, grouped by estimated creatinine clearance (CrCl) (<60, 60 to 89, >89 ml/min). The Cox proportional hazards models investigated the association between CrCl group and death, myocardial infarction, and target vessel revascularization (TVR). Generalized estimating equation regression models determined the association between CrCl group and lesion-specific restenosis. RESULTS: At 30 days, there was no difference in myocardial infarction, death, or TVR between the CrCl groups. At nine months, mortality was higher in the lowest CrCl group (2.2%, 1.2%, 0.8%; p < 0.001), which was no longer significant after adjusting for

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OBJECTIVES: We investigated the effect of oral verapamil on clinical outcome and angiographic restenosis after percutaneous coronary intervention (PCI).
BACKGROUND: Thus far, there is no established systemic pharmacologic approach for the prevention of restenosis after PCIs. Five small studies reported encouraging results for calcium channel blockers. METHODS: Our randomized double-blind trial included 700 consecutive patients with successful PCI of a native coronary artery. Patients received the calcium channel blocker verapamil, 240 mg twice daily for six months, or placebo. Primary clinical end point was the composite rate of death, myocardial infarction, and target vessel revascularization (TVR) during one-year follow-up; the angiographic end point was late lumen loss at the six-month follow-up angiography.
RESULTS: We obtained complete clinical follow-up in 95% of the patients, and scheduled angiography was performed in 94%. The proportion of patients treated with stents was 83%. The primary clinical end point was reached in 67 (19.3%) patients on verapamil and in 103 (29.3%) patients on placebo (relative risk [RR] 0.66 [95% confidence interval (CI) 0.48 to 0.89]; p = 0.002). This difference between the groups was driven by TVR (17.5% with verapamil vs. 26.2% with placebo; RR 0.67 [95% CI 0.49 to 0.93]; p = 0.006). Late lumen loss was 0.74 +/- 0.70 mm with verapamil and 0.81 +/- 0.75 mm with placebo (p = 0.11). Compared with placebo, verapamil reduced the rate of restenosis > or =75% (7.8% vs. 13.7%; RR 0.57 [95% CI 0.35 to 0.92]; p = 0.014). CONCLUSIONS: Verapamil compared with placebo improves long-term clinical outcome after PCI of native coronary arteries by reducing the need for TVR. This was caused by a reduction in the rate of high-grade restenosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15193674

Circulation (2004);109:861-6
Volumetric analysis of in-stent intimal hyperplasia in diabetic patients treated with or without abciximab: results of the Diabetes Abciximab steNT Evaluation (DANTE) randomized trial
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BACKGROUND: In diabetic patients in the Evaluation of Platelet IIb/IIIa Inhibitor for Stenting (EPISTENT) trial, abciximab reduced target vessel revascularization by approximately 50% compared with placebo. Whether this is a result of a lower restenosis rate caused by inhibition of intimal hyperplasia remains to be defined.
METHODS AND RESULTS: The purpose of this study was to determine whether abciximab at the time of stent implantation would reduce in-stent intimal hyperplasia measured by intravascular ultrasound at 6-month follow-up in type 2 diabetics. Ninety-six diabetic patients (96 lesions) who underwent elective stent implantation for a de novo lesion in a native coronary artery were randomly assigned to receive abciximab or no abciximab. In-stent intimal hyperplasia volume, expressed as percentage of stent volume, did not differ between groups: 41.3+/-21.0% for those treated with abciximab versus 40.5+/-18.3% for those treated without abciximab (P=0.9). There were also no significant differences in angiographic minimal luminal diameter at follow-up

(1.74+/-0.69 versus 1.66+/-0.63 mm; P=0.5), late loss (1.03+/-0.63 versus 1.07+/-0.58 mm; P=0.7), restenosis rate (17.8% versus 22.9%; P=0.5), or cumulative incidence of major adverse cardiac events at 12 months (19.1% versus 20.4%; P=0.9). CONCLUSIONS: Six-month intravascular ultrasound volumetric analysis showed that abciximab, at the time of coronary stent implantation, was not associated with a reduction of in-stent intimal hyperplasia in diabetic patients.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14757690

Circulation (2004);110:1226-30
Beyond restenosis: five-year clinical outcomes from second-generation coronary stent trials
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BACKGROUND: In the first year after coronary stent implantation, clinical failures are driven mainly by procedural complications and restenosis, but the subsequent relative contributions of restenosis and disease progression to late failures are less clear. METHODS AND RESULTS: We observed 1228 patients for 5 years after the implantation of stents as part of pivotal second-generation coronary stent trials. Clinical events of death, myocardial infarction, repeat revascularization, and repeat hospitalization for acute coronary syndrome or congestive heart failure were attributed to the index stented (target) lesion or other distinct sites (either in the target or other coronary vessels) and further classified as procedural, restenosis, or nonrestenosis. During the first year the hazard rate was 18.3% for target-lesion events and 12.4% for events unrelated to the target lesion. After the first year the average annual hazard rate was 1.7% for target-lesion events and 6.3% for nontarget-lesion events. By the fifth year, restenosis events occurred in 20.3% of patients, whereas 30-day procedural complications or later nonrestenosis events occurred in 37.9%, including 11.4% who

RESULTS: The study population consisted of 86 patients with in-stent restenosis (ISR) (n=41) or de novo lesions (n=45) treated with SES and evaluated by IVUS post-procedure and at follow-up. One 18-mm SES was used for de novo lesions while 16 patients with ISR received >1SES (total stented length 17.9 mm vs 22.0 mm respectively; P=0.004). At follow-up, no differences were observed between the ISR and de novo groups with respect to changes in the mean external elastic membrane (1.7% vs 1.3%; P=0.53), plaque behind the stent (1.2% vs 3.4%; P=0.49), and lumen areas (0.7% vs 1.9%; P=0.58). No positive remodelling or edge effect was observed. A gap between stents was observed in two patients with ISR, where more prominent, though non-obstructive, neointimal proliferation was noted. CONCLUSION: Sirolimus-eluting stenting is equally effective at inhibiting neointimal proliferation in de novo and ISR lesions without inducing edge restenosis or positive vascular remodelling.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14683740

Am J Cardiol (2004);93:1038-40
Analysis of nonintervention strategy for in-stent restenosis in Pauci- or asymptomatic patients
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Between January 1996 and May 2000, we retrospectively identified 66 patients (61 +/- 11 years) with in-stent restenosis who did not undergo percutaneous coronary intervention and/or bypass surgery and were maintained on medical treatment alone. In-stent restenosis was diffuse or proliferative in 86% of these patients. At 33 +/- 11 months, 2 patients died, none developed myocardial infarction, and 6 (9%) had target lesion revascularization only (repeat percutaneous transluminal coronary angioplasty). Medical treatment alone was associated with a good long-term clinical follow-up in selected patients with significant documented in-stent restenosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15081452

Catheter Cardiovasc Interv (2004);63:52-6
Contribution of early lumen loss after balloon angioplasty for in-stent restenosis to lumen loss at follow-up
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The treatment of in-stent restenosis using balloon angioplasty alone often produces excellent early results, but is associated with high rate of recurrence. Previous studies have demonstrated significant tissue reintrusion shortly after the treatment of in-stent restenosis with balloon angioplasty. The study was designed to elucidate the contribution of early lumen loss 6 hr after balloon angioplasty to lumen loss at follow-up. We prospectively performed quantitative coronary angiography and intravascular ultrasound in 12 patients with in-stent restenosis before intervention, after the final procedure, 6 hr later (5.6 +/- 1.4 hr), and at follow-up (7.7 +/- 2.3 months). Compared with immediately after balloon angioplasty, by 6 hr postintervention, the minimum lumen

diameter (MLD) and lumen cross-sectional area had decreased significantly (2.48 +/- 0.44 to 2.01 +/- 0.57 mm, P = 0.01, and 7.0 +/- 1.2 to 5.5 +/- 1.4 mm2, P = 0.004, respectively). Furthermore, the MLD decreased further between 6 hr postintervention and long-term follow-up (2.01 +/- 0.57 to 1.55 +/- 0.64 mm; P = 0.001). Patients who showed recurrence of restenosis at follow-up had greater early lumen loss than patients without recurrence of restenosis (0.71 +/- 0.31 vs. 0.23 +/- 0.13 mm; P = 0.006). Diffuse lesions had greater early lumen loss compared to focal lesions (0.75 +/- 0.35 vs. 0.28 +/- 0.13 mm; P = 0.008). Early lumen loss is common after the treatment of in-stent restenosis by balloon angioplasty. Within the first 6 hr postintervention, 32% +/- 29% of acute lumen gain is lost, and early lumen loss contributed to 42% +/- 18% of total lumen loss at follow-up.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15343567

Circulation (2004);109:1085-8
Contribution of stent underexpansion to recurrence after sirolimus-eluting stent implantation for in-stent restenosis
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BACKGROUND: We used intravascular ultrasound (IVUS) to evaluate recurrence after sirolimus-eluting stent (SES) implantation treatment of in-stent restenosis (ISR).
METHODS AND RESULTS: Forty-eight ISR lesions (41 patients with objective evidence of ischemia) were treated with SES. Recurrent ISR was identified in 11 lesions (all focal); repeat revascularization was performed in 10. These were compared with 16 patients (19 lesions) without recurrence as documented by angiography. Nine of 11 recurrent lesions had a minimum stent area (MSA) <5.0 mm2 versus 5 of 19 nonrecurrent lesions (P=0.003); 7 of 11 recurrent lesions had an MSA <4.0 mm2 versus 4 of 19 nonrecurrent lesions (P=0.02); and 4 of 11 recurrent lesions had an MSA <3.0 mm2 versus 1 of 19 nonrecurrent lesions (P=0.03). A gap betwts g- diameter (MLD) and lu

angiography and every day for seven days after the intervention, and each WBC fraction count was analyzed. At scheduled six-month follow-up, all patients received angiographic and volumetric intravascular ultrasound analysis. RESULTS: The circulating monocyte count increased and reached its peak two days after stent implantation (from 350 +/- 167 to 515 +/- 149/mm3, p < 0.01). The maximum monocyte count after stent implantation showed a significant positive correlation with in-stent neointimal volume at six-month follow-up (r = 0.44, p < 0.0001). Other fractions showed neither significant serial changes nor a correlation with in-stent neointimal volume. Multiple regression analysis revealed that in-stent neointimal volume was independently correlated with stent volume immediately after implantation (r = 0.45, p < 0.0001) and maximum monocyte count (r = 0.35, p < 0.001). Angiographic restenosis, defined as percent diameter stenosis >50%, was observed in 22 patients (21%), and these patients showed a significantly larger maximum monocyte count than patients without restenosis (642 +/- 110 vs. 529 +/- 77/mm3, p < 0.01). CONCLUSIONS: Circulating monocytes increased after coronary stent implantation, and the peak monocyte count related to in-stent neointimal volume. Our results suggest that circulating monocytes play a role in the process of in-stent neointimal hyperplasia.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14715176

Circulation (2004);109:487-93
Inhibition of restenosis with a paclitaxel-eluting, polymer-free coronary stent: the European evaLUation of pacliTaxel Eluting Stent (ELUTES) trial
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BACKGROUND: The use of a stent to deliver a drug may reduce in-stent restenosis. Paclitaxel interrupts the smooth muscle cell cycle by stabilizing microtubules, thereby arresting mitosis. METHODS AND RESULTS: On the basis of prior animal studies, the European evaLUation of the pacliTaxel Eluting Stent (ELUTES) pilot clinical trial (n=190) investigated the safety and efficacy of V-Flex Plus coronary stents (Cook Inc) coated with escalating doses of paclitaxel (0.2, 0.7, 1.4, and 2.7 microg/mm2 stent surface area) applied directly to the abluminal surface of the stent in de novo lesions compared with bare stent alone. The primary efficacy end point was angiographic percent diameter stenosis at 6 months. At angiographic follow-up, percent diameter stenosis was 33.9+/-26.7% in controls (n=34) and 14.2+/-16.6% in the 2.7-microg/mm2 group (n=31; P=0.006). Late loss decreased from 0.73+/-0.73 to 0.11+/-0.50 mm (P=0.002). Binary restenosis (> or =50% at follow-up) decreased from 20.6% to 3.2% (P=0.056), with no significant benefit from intermediate paclitaxel doses. Freedom from major adverse cardiac events in the highest (effective) dose group was 92%, 89%, and 86% at 1, 6, and 12 months, respectively (P=NS versus control). No late stent thromboses were seen in any treated group despite clopidogrel treatment for 3 months only. CONCLUSIONS: Paclitaxel applied directly to the abluminal surface of a bare metal coronary stent, at a dose density of 2.7 microg/mm2, reduced angiographic indicators of in-stent restenosis without short- or medium-term side effects.
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Am Heart J (2004);147:1071-7
Preprocedural inflammatory markers do not predict restenosis after successful coronary stenting
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BACKGROUND: Levels of C-reactive protein (CRP), serum amyloid A protein (SAA), and interleukin-6 (IL-6) can predict coronary restenosis following angioplasty and stent deployment in patients with unstable angina. We investigated whether measurement of periprocedural inflammatory markers predicted the angiographic outcome at 6 months in stable angina patients undergoing coronary stenting. METHODS: We prospectively studied 182 patients; 152 patients underwent elective and successful stenting procedure for de novo lesions in native and nongrafted coronary arteries and 30 individuals in the control group underwent diagnostic angiography alone. CRP, SAA, and IL-6 were determined by high-sensitivity immunoassays. RESULTS: At 6 months, quantitative computer-assisted angiographic analysis in 133 patients with stents showed a binary restenosis rate of 33.8%. Statins were being taken by 80% of the patients. There were no significant differences between the pre- or postprocedure values of CRP, SAA, or IL-6 in patients with or without in-stent restenosis. CONCLUSIONS: Preprocedural inflammatory markers in stable angina subjects undergoing coronary artery stent deployment did not correlate with the development of in-stent restenosis. Differences in pathobiology between stable and unstable coronary syndromes, the widespread use of statins with anti-inflammatory activity in our cohort of patients, along with different mechanisms underlying the early angiographic appearances of restenosis as compared to clinical end points, most likely explain our findings.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15199358

Circulation (2004);110:790-5
Randomized, double-blind, placebo-controlled trial of oral sirolimus for restenosis prevention in patients with in-stent restenosis: the Oral Sirolimus to Inhibit Recurrent In-stent Stenosis (OSIRIS) trial
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BACKGROUND: Despite recent advances in interventional cardiology, including the introduction of drug-eluting stents for de novo coronary lesions, the treatment of in-stent restenosis (ISR) remains a challenging clinical issue. Given the efficacy of systemic sirolimus administration to prevent neointimal hyperplasia in animal models and to halt and even reverse the progression of allograft vasculopathy, the aim of the present double-blind, placebo-controlled study was to evaluate the efficacy of a 10-day oral sirolimus treatment with 2 different loading regimens for the prevention of recurrent restenosis in patients with ISR. METHODS AND RESULTS: Three hundred symptomatic patients with ISR were randomly assigned to 1 of 3 treatment arms: placebo or usual-dose or high-dose sirolimus. Patients received a cumulative loading dose of 0, 8, or 24 mg of sirolimus 2 days before and the day of repeat intervention followed by maintenance therapy of 2 mg/d for 7 days. Angiographic restenosis at

6-month angiography was the primary end point of the study. Restenosis was significantly reduced from 42.2% to 38.6% and to 22.1% in the placebo, usual-dose, and high-dose sirolimus groups, respectively (P=0.005). Similarly, the need for target vessel revascularization was reduced from 25.5% to 24.2% and to 15.2% in the placebo, usual-dose, and high-dose groups, respectively (P=0.08). The sirolimus blood concentration on the day of the procedure correlated significantly with the late lumen loss at follow-up (P<0.001). CONCLUSIONS: In patients with ISR, an oral adjunctive sirolimus treatment with an intensified loading regimen before coronary intervention resulted in a significant improvement in the angiographic parameters of restenosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15302787

Circulation (2004);109:634-40
Analysis of 1-year clinical outcomes in the SIRIUS trial: a randomized trial of a sirolimus-eluting stent versus a standard stent in patients at high risk for coronary restenosis
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BACKGROUND: This study evaluated a large group of patients enrolled in a double-blind randomized trial of the sirolimus-eluting stent to document whether the initial clinical improvement seen in previous smaller series is maintained out to 12 months and to study the potential treatment effect in patient subsets known to be at increased risk of restenosis. METHODS AND RESULTS: A total of 1058 patients with de novo native coronary stenosis undergoing clinically indicated percutaneous coronary intervention were randomly assigned to sirolimus-eluting stent (533) or control bare stent (525). Procedural success and in-hospital outcomes were excellent and did not differ between the 2 groups. At 9 months, clinical restenosis, defined as target-lesion revascularization, was 4.1% in the sirolimus limb versus 16.6% in the control limb (P<0.001). At 12 months, the absolute difference in target-lesion revascularization continued to increase and was 4.9% versus 20% (P<0.001). There were no differences in death or myocardial infarction rates. In high-risk patient subsets, defined by vessel size, lesion length, and presence of diabetes mellitus, there was a 70% to 80% reduction in clinical restenosis at 1 year. CONCLUSIONS: Placement of the sirolimus-eluting stent results in continued clinical improvement at 1 year after initial implantation, with significant reduction in clinical restenosis as defined by target-lesion revascularization. Between 9 and 12 months, the absolute reduction of clinical restenosis continues to increase. Even in high-risk subsets of patients, there is a 70% to 80% relative reduction in clinical restenosis at 12 months with this drug-eluting stent.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14769686

Am J Cardiol (2004);94:1050-4

The investigators tested whether abciximab-coated stents prevent neointimal hyperplasia (NIH) formation in coronary de novo lesions. Abciximab-coated stents were compared with control stents. All patients underwent follow-up coronary angiography and intravascular ultrasound (IVUS). All stents were successfully deployed, and patients were discharged home without clinical events. At follow-up coronary angiography, the restenosis rate and late loss were 14% and 0.33 +/- 0.28 mm in the abciximab-coated stent group and 28.6% and 0.64 +/- 0.32 mm in the control stent group (p = 0.099 and p = 0.014, respectively). At follow-up IVUS, the intrastent luminal area and intrastent NIH area were 5.7 +/- 1.6 and 2.0 +/- 1.6 mm(2), respectively, in the abciximab-coated stent group and 4.2 +/- 0.8 and 3.4 +/- 1.7 mm(2), respectively, in the control stent group (p = 0.001 and p = 0.001, respectively). Abciximab-coated stents are feasible and significantly inhibit NIH, with potential therapeutic benefit in preventing stent restenosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15476624

J Am Coll Cardiol (2004);43:1954-8
Significant reduction in restenosis after the use of sirolimus-eluting stents in the treatment of chronic total occlusions
A. Hoye*, et al.*
Department of Interventional Cardiology, Erasmus MC, Rotterdam, the Netherlands.
OBJECTIVES: The aim of this study was to assess sirolimus-eluting stent (SES) implantation for the treatment of chronic total coronary occlusions (CTO).
BACKGROUND: Long-term results after percutaneous coronary intervention (PCI) in the treatment of CTOs is hindered by a significant rate of restenosis and reocclusion. In the treatment of relatively simple nonocclusive lesions, SESs have shown dramatically reduced restenosis rates compared with bare metal stents (BMS), but whether these results are more widely applicable is unknown. METHODS: From April 2002, all patients at our institution were treated with SES as the device of choice during PCI. During the first six months, 563 patients were treated solely with SES, with treatment of a de novo CTO in 56 (9.9%). This CTO cohort was compared with a similar group of patients (n = 28) treated in the preceding six-month period with BMS. RESULTS: At one year, the cumulative survival-free of major adverse cardiac events was 96.4% in the SES group versus 82.8% in the BMS group, p < 0.05. At six-month follow-up, 33 (59%) patients in the SES group underwent angiography with a binary restenosis rate (>50% diameter stenosis) of 9.1% and in-stent late loss of 0.13 +/- 0.46 mm. One patient (3.0%) at follow-up was found to have reoccluded the target vessel. CONCLUSIONS: The use of SESs in the treatment of chronic total coronary occlusions is associated with a reduction in the rate of major adverse cardiac events and restenosis compared with BMS.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15172397

Am J Cardiol (2004);94:351-4
Effectiveness of sirolimus-eluting stent implantation for treatment of in-stent restenosis after brachytherapy failure
I. Iakovou*, et al.*
EMO Centro Cuore Columbus, Milan, Italy.
The impact of the use of sirolimus-eluting stents (SESs) in the treatment of in-stent

restenosis in previously irradiated sites has not been adequately evaluated. Fifteen consecutive patients who underwent percutaneous coronary interventions using SESs in lesion sites previously intervened with intracoronary radiation therapy were identified. All stents were implanted successfully, and there were no major in-hospital complications. At 30-day follow-up, there was 1 case of subacute thrombosis that led to target lesion revascularization (TLR). At 6 months, 2 patients underwent TLR because of recurrent angina with angiographic restenosis, and 1 patient underwent target vessel revascularization distally to the SES site; no other major adverse cardiac events occurred at long-term follow-up (mean 17 +/- 8 months).
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15276103

Catheter Cardiovasc Interv (2005);64:129-33
Is overdilatation of 3.0 mm sirolimus-eluting stent associated with a higher restenosis rate?
I. Iakovou*, et al.*
EMO, Centro Cuore Columbus, Milan, Italy.
We evaluated the safety and effectiveness of postdilating a 3.0 mm sirolimus-eluting stents (SESs; six cells) with a 3.5-4.0 mm balloon. We identified 254 consecutive patients who underwent percutaneous coronary interventions using SESs with a nominal diameter of 3.0 mm (six cells). Patients were divided into two groups based on whether they were subsequently postdilated with a 3.0 mm (group 1: 168 patients, 251 lesions) or a 3.5-4 mm balloon (group 2: 86 patients, 102 lesions). There were no significant differences regarding the incidence of in-hospital and long-term follow-up. Angiographic follow-up was available in 72% and 74% of groups 1 and 2, respectively. The two groups had no significant differences regarding late lumen loss (0.51 +/- 0.36 vs. 0.52 +/- 0.33; P = 0.3) and binary restenosis rates (10.7% vs. 8.8%; P = 0.1). Six-month clinical follow-up was available in all patients. At long-term follow-up (mean: 10.6 +/- 3.7 for group 1 and 11.3 +/- 3.9 months for group 2), there were no significant differences between the two groups regarding major adverse cardiac events (8.9% vs. 9.2%; P = 0.9). Implantation of a 3.0 mm SES with postdilation with a 3.5-4 mm balloon did not result in any significant difference in complications, in-hospital non-Q-wave myocardial infarction, binary restenosis, or target lesion revascularization. These data should lessen concern that overdilation may dilute the beneficial effects of SESs. Catheter Cardiovasc Interv 2005;64:129-133. (c) 2005 Wiley-Liss, Inc.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15678464

J Am Coll Cardiol (2004);44:1408-14
Cilostazol 5.1(of)-5

inhibits alpha-granule release of P-selectin in platelets. The P-selectin-mediated platelet-leukocyte interaction promotes activation and upregulation of leukocyte Mac-1 after coronary stenting, which plays a key role on the mechanism of restenosis. Thus, cilostazol's potential inhibition of this process may lead to prevention of restenosis. METHODS: Using flow cytometric analysis of whole blood obtained from the coronary sinus, the expression of platelet membrane glycoproteins and neutrophil adhesion molecules was observed in 70 consecutive patients undergoing coronary stenting. The patients were randomly assigned to either a cilostazol or ticlopidine group before stent placement. RESULTS: The restenosis rate was lower (15% vs. 31%, p < 0.05) in the cilostazol group (n = 34) than in the ticlopidine group (n = 32). A stent-induced increase in platelet P-selectin (CD62P) expression and an increase in neutrophil Mac-1 (CD11b) expression were suppressed in the cilostazol group compared with the ticlopidine group. Angiographic late lumen loss was correlated with the relative changes in platelet P-selectin and neutrophil Mac-1 at 48 h after coronary stenting. CONCLUSIONS: Cilostazol may have effects on suppression of P-selectin-mediated platelet activation, platelet-leukocyte interaction, and subsequent Mac-1-mediated leukocyte activation, which might lead to a reduced restenosis rate after coronary stent implantation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15464320

Catheter Cardiovasc Interv (2005);64:28-34
Sirolimus- and paclitaxel-eluting stents in comparison with balloon angioplasty for treatment of in-stent restenosis
E. Iofina*, et al.*
Medical Clinic I, University RWTH Aachen, Aachen, Germany.
This study evaluated the acute and follow-up effectiveness of sirolimus-eluting stents (SESs) and nonpolymer-based paclitaxel-eluting stents (PESs) in comparison will balloon angioplasty for treatment of complex in-stent restenosis (ISR) lesions. Drug-eluting stents have been demonstrated to be highly effective for treatment of de novo lesions. The use of drug-eluting stents for treatment of complex ISR is less well defined. Eighty one lesions with in-stent restenosis (lesion length < 30 mm in a native coronary artery) were treated with either PTCA alone (n = 26 lesions in 25 patients), PES (n = 27 lesions in 24 patients; Achieve, Cook; 3,1 mug paclitaxel/mm(2) nonpolymer-based coating), SES (n = 28 lesions in 28 patients; Cypher, Cordis; 140 mug sirolimus/cm(2) metal surface area). Nine-month MACE rates were 32%, 8%, and 14% (all due to repeated revascularization procedures, except one death in the SES group) in the PTCA, PES, and SES group, respectively. Postintervention minimal lumen diameter in stent was significantly greater in the SES and the PES group in comparison with the PTCA group (2.37 +/- 0.26, 2.54 +/- 0.42, 1.78 +/- 0.23 mm; P < 0.001). At 6-month angiographic follow-up, late loss in stent was 0.77 +/- 0.45, 0.43 +/- 0.53, and 0.29 +/- 0.52 mm for the PTCA, PES, and SES group, respectively (P = 0.005). In-lesion restenosis rate was 61% for the PTCA group, 20% for the PES group, and 13% for the SES group (P = 0.042). The implantation of SES as well as nonpolymer PES proved to be effective for treatment of ISR. The combination of improved acute gain and reduced late loss results in a significantly improved angiographic follow-up result in comparison with PTCA. Catheter Cardiovasc Interv 2005;64:28-34. (c) 2004 Wiley-Liss, Inc.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citatio

n&list_uids=15619307

Am J Cardiol (2004);94:199-201
Comparison of neointimal formation in polymer-free paclitaxel stents versus stainless stents (from the ASPECT and ELUTES randomized clinical trials)
G. L. Kaluza*, et al.*
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The investigators examined 326 pairs of angiograms from 2 randomized dose-finding (0.2 to 3.1 microg paclitaxel/mm(2) of stent surface area) clinical trials of polymer-free paclitaxel-eluting stents in de novo lesions (the ASian Paclitaxel-Eluting stent Clinical Trial [ASPECT] and the European evaLUation of Taxol Eluting Stent [ELUTES]). A dose-dependent effect was observed: the largest dose of paclitaxel in the 2 trials resulted in a significantly larger proportion of lesions at follow-up with <10% diameter stenosis (54% vs 16%, p = 0.00012 in ASPECT; 53% vs 21%, p = 0.013 in ELUTES) and with minimal luminal diameter located outside the stent compared with control stents (62% vs 20% in ASPECT, 48% vs 18% in ELUTES; p <0.05). Also, significantly shorter lesion lengths at 6-month follow-up were observed for the doses of 0.7 to 3.1 microg/mm(2) (p <0.03) relative to their respective lengths before the procedure compared with control stents.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15246901

Lancet (2004);363:751-6
Effects of intracoronary infusion of peripheral blood stem-cells mobilised with granulocyte-colony stimulating factor on left ventricular systolic function and restenosis after coronary stenting in myocardial infarction: the MAGIC cell randomised clinical trial
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Cardiovascular Laboratory, Clinical Research Institute, Seoul National University Hospital, Seoul, Republic of Korea.
BACKGROUND: Bone-marrow stem-cell transplantation has been shown to improve cardiac function in patients with myocardial infarction. We examined the feasibility and efficacy of granulocyte-colony stimulating factor (G-CSF) therapy and subsequent intracoronary infusion of collected peripheral blood stem-cells (PBSCs) in such patients. METHODS: We prospectively randomised 27 patients with myocardial infarction who underwent coronary stenting for the culprit lesion of infarction into three groups; cell infusion (n=10), G-CSF alone (n=10), and control group (n=7). Changes in left ventricular systolic function and perfusion were assessed after 6 months. By December, 2003, seven patients from the cell infusion group, three from the G-CSF group, and one from the control group had been assessed. FINDINGS: G-CSF injection and intracoronary infusion of the mobilised PBSC did not aggravate inflammation and ischaemia during the periprocedural period. Exercise capacity (mean treadmill exercise time: 450 s [SD 178] at baseline vs 578 s [168] at 6 months' follow-up, p=0.004), myocardial perfusion (perfusion defect 11.6% [9.6] vs 5.3% [5.0], p=0.020) and systolic function (left ventricular ejection fraction 48.7% [8.3] vs 55.1% [7.4], p=0.005) improved significantly in patients who received cell infusion. However, we noted an unexpectedly high rate of in-stent restenosis at culprit lesion in patients who received G-CSF, and

therefore we stopped enrollment. INTERPRETATION: G-CSF therapy with intracoronary infusion of PBSC showed improved cardiac function, and promoted angiogenesis in patients with myocardial infarction. However, aggravation of restenosis could be a serious problem. In future studies with G-CSF based stem-cell therapy, patients should be carefully monitored for unexpected effects.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15016484

Jama (2005);293:165-71

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15644543

J Am Coll Cardiol (2004);44:733-9
Role of the endothelium in modulating neointimal formation: vasculoprotective approaches to attenuate restenosis after percutaneous coronary interventions
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Restenosis at the site of an endoluminal procedure remains a significant problem in the practice of interventional cardiology. We present current data on intimal hyperplasia, which identify the major role of endothelial cells (ECs) in the development of restenosis. Considering endothelial denudation as one of the most important mechanisms contributing to restenosis, we focus more attention on methods of accelerating restoration of endothelial continuity. Prevention of restenosis may be achieved by promoting endothelial regeneration through the use of growth factors, EC seeding, vessel reconstruction with autologous EC/fibrin matrix, and the use of estrogen-loaded stents and stents designed to capture progenitor ECs.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15312851

N Engl J Med (2004);350:2673-81
Folate therapy and in-stent restenosis after coronary stenting
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BACKGROUND: Vitamin therapy to lower homocysteine levels has recently been recommended for the prevention of restenosis after coronary angioplasty. We tested the effect of a combination of folic acid, vitamin B6, and vitamin B12 (referred to as folate therapy) on the risk of angiographic restenosis after coronary-stent placement in a double-blind, multicenter trial. METHODS: A total of 636 patients who had undergone successful coronary stenting were randomly assigned to receive 1 mg of folic acid, 5 mg of vitamin B6, and 1 mg of vitamin B12 intravenously, followed by daily oral doses of 1.2 mg of folic acid, 48 mg of vitamin B6, and 60 microg of vitamin B12 for six months, or to receive placebo. The angiographic end points (minimal luminal diameter, late loss, and restenosis rate) were assessed at six months by means of quantitative coronary angiography. RESULTS: At follow-up, the mean (+/-SD) minimal luminal diameter was significantly smaller in the folate group than in the placebo group (1.59+/-0.62 mm vs. 1.74+/-0.64 mm, P=0.008), and the extent of late luminal loss was greater (0.90+/-0.55 mm vs. 0.76+/-0.58 mm, P=0.004). The restenosis rate was higher in the folate group than in the placebo group (34.5 percent vs. 26.5 percent, P=0.05), and a higher percentage of patients in the folate group required repeated target-vessel revascularization (15.8 percent vs. 10.6 percent, P=0.05). Folate therapy had adverse effects on the risk of restenosis in all subgroups except for women, patients with diabetes, and patients with markedly elevated homocysteine levels (15 micromol per liter or more) at baseline. CONCLUSIONS: Contrary to previous findings, the administration of folate, vitamin B6, and vitamin B12 after coronary stenting may increase the risk of in-stent restenosis and the need for target-vessel revascularization.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15215483

Circulation (2004);109:1366-70
Clinical, angiographic, and procedural predictors of angiographic restenosis after sirolimus-eluting stent implantation in complex patients: an evaluation from the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) study
P. A. Lemos*, et al.*
Erasmus Medical Center, Thoraxcenter, Rotterdam, The Netherlands.
BACKGROUND: The factors associated with the occurrence of restenosis after sirolimus-eluting stent (SES) implantation in complex cases are currently unknown. METHODS AND RESULTS: A cohort of consecutive complex patients treated with SES implantation was selected according to the following criteria: (1) treatment of acute myocardial infarction, (2) treatment of in-stent restenosis, (3) 2.25-mm diameter SES, (4) left main coronary stenting, (5) chronic total occlusion, (6) stented segment >36 mm, and (7) bifurcation stenting. The present study population was composed of 238 patients (441 lesions) for whom 6-month angiographic follow-up data were obtained (70% of eligible patients). Significant clinical, angiographic, and procedural predictors of post-SES restenosis were evaluated. Binary in-segment restenosis was diagnosed in 7.9% of lesions (6.3% in-stent, 0.9% at the proximal edge, 0.7% at the distal edge). The following characteristics were identified as independent multivariate predictors: treatment of in-stent restenosis (OR 4.16, 95% CI 1.63 to 11.01; P<0.01), ostial location (OR 4.84, 95% CI 1.81 to 12.07; P<0.01), diabetes (OR 2.63, 95% CI 1.14 to 6.31; P=0.02), total stented length (per 10-mm increase; OR 1.42, 95% CI 1.21 to 1.68; P<0.01), reference diameter (per 1.0-mm increase; OR 0.46, 95% CI 0.24 to 0.87; P=0.03), and left anterior descending artery (OR 0.30, 95% CI 0.10 to 0.69; P<0.01). CONCLUSIONS: Angiographic restenosis after SES implantation in complex patients is an infrequent event, occurring mainly in association with lesion-based characteristics and diabetes mellitus.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14993127

Circulation (2004);109:2500-2
Post-sirolimus-eluting stent restenosis treated with repeat percutaneous intervention: late angiographic and clinical outcomes
P. A. Lemos*, et al.*
Erasmus Medical Center, Thoraxcenter, Rotterdam, The Netherlands.
BACKGROUND: We evaluated the clinical and angiographic outcomes of patients presenting with restenosis after sirolimus-eluting stent (SES) implantation treated with repeated percutaneous intervention. METHODS AND RESULTS: A total of 24 cons-5.15u.-17.5.1(ed-)0.6(a)4.7(inc79tG ict5,0.6(t)-3t1 Twon)5.6(u:)-5.1.14.6(pt)(mellitus.).1(me,e0

follow-up of 279 days from the post-SES treatment. The overall recurrent restenosis rate was 42.9%. The risk of recurrent restenosis was increased for patients with hypercholesterolemia, previous angioplasty, failed brachytherapy, post-SES restenosis needing early (<6 months) treatment, and post-SES restenosis treated with balloon dilatation. The recurrent restenosis rate of originally de novo lesions re-treated with drug-eluting stents was 18.2%. CONCLUSIONS: Even though de novo lesions treated with SES at baseline and re-treated with drug-eluting stents had reasonably better outcomes than other lesion types and strategies, our study shows that the treatment of post-SES restenosis is currently suboptimal and warrants further investigation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15148279

Eur Heart J (2004);25:2040-7
Utility of the fractional flow reserve in the evaluation of angiographically moderate in-stent restenosis
R. Lopez-Palop*, et al.*
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AIMS: The evaluation of in-stent restenosis (ISR) is usually based on angiographic quantification. This evaluation is sometimes difficult and it has not an accurate clinical correlation. Fractional flow reserve (FFR) measured by intracoronary pressure wire has demonstrated its value in determining the functional repercussion of coronary stenosis. The aim of this study was to evaluate the relation between quantitative angiography-FFR in borderline in-stent restenotic lesions and the accuracy of FFR in deciding the treatment of ISR. METHODS AND RESULTS: Quantitative angiographic values of 65 lesions in 62 patients with angiographically moderate ISR are compared with the FFR value obtained by pressure wire. An FFR value<0.75 was considered significant. Patients with non-revascularized ISR (FFR > or = 0.75) were clinically followed during a year. An FFR value > or = 0.75 was obtained in 41 lesions (63%), 21 of them with stenosis > or = 50%. The co-efficient of correlation between parameters of quantitative angiography and FFR value was <0.5. No events related to the non-treated lesions were observed. CONCLUSIONS: A poor correlation between angiographic quantification and FFR of moderate ISR was found. Conservative management of moderate 40-70% in-stent restenotic lesions with FFR value > or = 0.75 is safe avoiding unnecessary revascularizations based solely on the angiography.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15541841

Am J Cardiol (2004);93:1340-6, A5
Effects of stent length and lesion length on coronary restenosis
L. Mauri*, et al.*
Division of Clinical Biometrics, Brigham & Women's Hospital, 1620 Tremont Street, Boston, MA 02120, USA.
The choice of drug-eluting versus bare metal stents is based on costs and expectations of restenosis and thrombosis risk. Approaches to stent placement vary from covering just the zone of maximal obstruction to stenting well beyond the lesion boundaries (normal-to-normal vessel). The independent effects of stented lesion length, nonstented

lesion length, and excess stent length, on coronary restenosis have not been evaluated for bare metal or drug-eluting stents. We analyzed the angiographic follow-up cohort (1,181 patients) from 6 recent bare metal stent trials of de novo lesions in native coronary arteries. Stent length exceeded lesion length in 87% of lesions (mean lesion length 12.4 +/- 6.3 mm, mean stent length 20.0 +/- 7.9 mm, mean difference 7.6 +/- 7.9 mm). At 6- to 9-month follow-up, the mean percent diameter stenosis was 39.1 +/- 20.1%. In an adjusted multivariable model of percent diameter stenosis, each 10 mm of stented lesion length was associated with an absolute increase in percent diameter stenosis of 7.7% (p <0.0001), whereas each 10 mm of excess stent length independently increased percent diameter stenosis by 4.0% (p <0.0001) and increased target lesion revascularization at 9 months (odds ratio 1.12, 95% confidence interval 1.02 to 1.24). Significant nonstented lesion length was uncommon (12.5% of cases). In summary, stent length exceeded lesion length in most stented lesions, and the amount of excess stent length increased the risk of restenosis independent of the stented lesion length. This analysis supports a conservative approach of matching stent length to lesion length to reduce the risk of restenosis with bare metal stents.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15165911

Catheter Cardiovasc Interv (2004);61:190-5
Intracoronary stenting and angiographic results: Restenosis after direct stenting versus stenting with predilation in patients with symptomatic coronary artery disease (ISAR-DIRECT trial)
J. Mehilli*, et al.*
Deutsches Herzzentrum, Munich, Germany. mehilli@dhm.mhn.de
The objective of this randomized study was to assess whether direct stenting leads to less restenosis than does conventional stenting (CS) with predilation in clinical practice. We included 910 patients who were randomly assigned to undergo either direct stenting (DS; n = 456) or CS (n = 454). No significant difference was observed in the incidence of angiographic restenosis (primary endpoint): 23.6% for DS and 21.0% for CS (P = 0.41; relative risk = 1.1; 95% CI = 0.8-1.5). The incidence of target vessel revascularization was 17.3% among DS and 14.8% among CS patients (P = 0.29; relative risk = 1.2; 95% CI = 0.8-1.6). The combined incidence of death or myocardial infarction at one year was 9.0% in the DS group and 7.0% in the CS group (P = 0.28). In conclusion, direct stenting is not associated with any reduction of thrombotic and restenotic complications as compared to the conventional stenting.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14755810

Heart (2004);90:1189-93
Influence of alcohol consumption on restenosis rate after percutaneous transluminal coronary angioplasty and stent implantation
F. Niroomand

angioplasty (PTCA) and stent implantation. DESIGN: Retrospective cohort study. PATIENTS: 225 consecutive male patients underwent PTCA and stent implantation. All patients had a control angiography and were contacted for a questionnaire regarding their drinking habits. MAIN OUTCOME MEASURES: Mean late loss of luminal diameter, rate of coronary restenosis of 50% or more within the stented segment, and rate of repeat angioplasty. RESULTS: 53 patients (with 80 stents) consumed < 50 g of alcohol a week and 172 (with 266 stents) consumed more (50-700 g a week). Baseline characteristics were similar in both groups except for a higher prevalence of reduced cardiac function and multivessel disease and a lower high density lipoprotein cholesterol concentration among patients who consumed little or no alcohol. Patients who consumed > or = 50 g alcohol a week had a lower mean late loss of the luminal diameter (1.1 (0.79) mm v 1.45 (0.82) mm, p = 0.002), a lower rate of coronary restenosis within the stented segment (33.7% v 48.8%, p = 0.001), and a lower rate of repeat angioplasty (23.3% v 42.5%, p = 0.002). In multivariate analysis, only alcohol consumption and diabetes were independent and significant discriminators for late loss of luminal diameter (p = 0.005 and p = 0.01, respectively), restenosis (odds ratio 0.54 and 2.08, respectively), and repeat angioplasty (odds ratio 0.39 and 2.18, respectively). CONCLUSION: Alcohol intake is associated with reduced restenosis after PTCA and stent implantation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15367521

Circulation (2004);110:3773-80
Quantitative assessment of angiographic restenosis after sirolimus-eluting stent implantation in native coronary arteries
J. J. Popma*, et al.*
Department of Internal Medicine, Cardiovascular Division, Brigham and Women's Hospital, 75 Francis St, Boston, Mass 02115, USA. jpopma@partners.org
BACKGROUND: Sirolimus-eluting stents (SESs) reduce angiographic restenosis in patients with focal, native coronary artery stenoses. This study evaluated the usefulness of SESs in complex native-vessel lesions at high risk for restenosis. METHODS AND RESULTS: Angiographic follow-up at 240 days was obtained in 701 patients with long (15- to 25-mm) lesions in small-diameter (2.5- to 3.5-mm) native vessels who were randomly assigned to treatment with SESs or bare-metal stents (BMSs) in the SIRIUS trial. Quantitative angiographic measurements of minimal lumen diameter and percent diameter stenosis were obtained within the treated segment, within the stent, and within its 5-mm proximal and distal edges. Patients treated with SESs had lower rates of binary (>50% diameter stenosis) angiographic restenosis within the segment (8.9% versus 36.3% with the BMS; P<0.001) and within the stent (3.2% versus 35.4% with the BMS; P<0.001). SESs were associated with significantly less late lumen loss within the treated segment, within the stent, and within its 5-mm proximal and distal edges (all P<0.001). The reduction of restenosis with the SES was consistent in patients at risk for restenosis, including those with small vessels, long lesions, and diabetes mellitus. The frequency of late aneurysms was similar in the 2 groups. CONCLUSIONS: Compared with BMSs, SESs reduced angiographic late lumen loss within the stent and its adjacent 5-mm margins in patients with complex native-vessel lesions.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citatio

n&list_uids=15596568

Eur Heart J (2004);25:920-5
Treatment of in-stent restenosis using a paclitaxel-eluting stent: acute results and long-term follow-up of a matched-pair comparison with intracoronary beta-radiation therapy
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AIMS: Intracoronary radiation therapy (ICR) has significantly improved the long-term outcome after treatment of diffuse in-stent restenosis (ISR). The efficacy of drug eluting stents in this setting remains less well defined. This matched-pair analysis compared the procedural and long-term clinical and angiographic outcome after treatment of diffuse ISR using a paclitaxel-eluting stent (PES) with intracoronary beta-radiation therapy. METHODS AND RESULTS: Twenty-two patients receiving 25 PES (ACHIEVE, Cook, 3.1 microg paclitaxel per square millimeter, non-polymer based coating) for ISR underwent 6-month angiographic and 12-month clinical follow-up. From a database including 141 patients (174 lesions) undergoing intracoronary beta-radiation for ISR, 25 lesions (25 patients) were pair-matched with the former group for lesion length and vessel size. PES implantation and ICR were successful in all patients with a significantly lower postprocedural in-stent diameter stenosis in the PES group (8+/-12% vs. 18+/-8%, $p < 0.01$). Angiographic binary in-lesion restenosis at 6 month was 20% (5/25 lesions) in the PES group and 16% (4/25) in the ICR group ($p = 1.0$). PES implantation resulted in significantly higher in-stent MLD at FU (2.10+/-0.71 vs. 1.75+/-0.36, $p = 0.03$) and a higher in-stent net gain (PES: 1.19+/-0.69, ICR: 0.84+/-0.49, $p = 0.04$). Two patients in the PES group and 6 patients in the ICR group experienced a target lesion revascularisation at 12-month follow-up ($p = 0.25$). CONCLUSION: Implantation of a non-polymer based paclitaxel-elution stent and conventional ICR therapy for complex ISR lead to comparable acute and long-term clinical and angiographic follow-up results.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15172463

Am J Cardiol (2004);93:1271-5
Incidence of thrombotic stent occlusion during the first three months after sirolimus-eluting stent implantation in 500 consecutive patients
E. Regar*, et al.*

for the thrombosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15135702

Am J Cardiol (2004);93:477-80
Impact of strut thickness on late luminal loss after coronary artery stent placement
S. Z. Rittersma*, et al.*
Department of Cardiology, Academic Medical Center, Amsterdam, The Netherlands.
To determine the influence of coronary artery stent strut thickness on angiographic late luminal loss, 663 patients were included in a single-center observational cohort after receiving an ACS Multilink stent in a native coronary vessel. At 6- to 10-month follow-up, 287 patients treated with a thin-strut stent (50 microm) had significantly less late luminal loss than 376 patients treated with a thick-strut stent (> or =90 microm) (mean 0.92 +/- 0.59 vs 1.06 +/- 0.71 mm, p = 0.011); on multivariate regression analysis, strut thickness was found to be an independent predictor for late luminal loss.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14969629

Eur Heart J (2004);25:2026-33
Soft plaque detected on intravascular ultrasound is the strongest predictor of in-stent restenosis: an intravascular ultrasound study
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AIMS: Although various predictors of in-stent restenosis (ISR) have been reported, the subject of parameters relating to ISR on intravascular ultrasound (IVUS) still leaves room for discussion. The aim of this study was to clarify the strongest predictors of ISR using IVUS. METHODS AND RESULTS: Ninety-two native coronary lesions undergoing single bare-metallic stent implantation were investigated retrospectively. We classified them into the ISR (n=46) and non-ISR (n=46) groups using quantitative coronary angiography. On serial IVUS studies, plaque morphology, and areas and volumes of each component in vessel were evaluated. Among all parameters, diabetes mellitus and soft plaque appearing hypoechoic on IVUS were associated with ISR. By multivariate analysis, soft plaque was the only independent predictor of ISR (p=0.0057). Compared with non-soft plaque, soft plaque had a larger plaque reduction rate (-7.1% vs. -1.6%, p=0.0613) and smaller percent plaque volume (53.0% vs. 55.5%, p=0.0273) after stenting. Conversely, soft plaque had a larger neointimal area (4.39 vs. 3.33 mm2, p=0.0437) and percent plaque area (80.5% vs. 75.1%, p=0.0503) at follow-up. CONCLUSION: Soft plaque detected on IVUS was the strongest predictor of ISR. Soft plaque was compressed more easily by stenting, however, causing more proliferation of neointima subsequently and resulted in a worse prognosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15541839

Heart (2004);90:1183-8
Routine sirolimus eluting stent implantation for unselected in-stent restenosis: insights from the rapamycin eluting stent evaluated at Rotterdam Cardiology Hospital

(RESEARCH) registry
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OBJECTIVE: To assess the effectiveness of routine sirolimus eluting stent (SES) implantation for unselected patients with in-stent restenosis and to provide preliminary information about the angiographic outcome for lesion subgroups and for different in-stent restenosis patterns. DESIGN: Prospective, single centre registry. SETTING: Tertiary referral centre. PATIENTS: 44 consecutive patients (53 lesions) without previous brachytherapy who were treated with SES for in-stent restenosis were evaluated. Routine angiographic follow up was obtained at six months and the incidence of major adverse cardiovascular events was evaluated. RESULTS: At baseline, 42% of the lesions were focal, 21% diffuse, 26% proliferative, and 11% total occlusions. Small vessel size (reference diameter < or = 2.5 mm) was present in 49%, long lesions (> 20 mm) in 30%, treatment of bypass grafts in 13%, and bifurcation stenting in 18%. At follow up, post-SES restenosis was observed in 14.6%. No restenosis was observed in focal lesions. For more complex lesions, restenosis rates ranged from 20-25%. At the one year follow up, the incidence of death was 0, myocardial infarction 4.7% (n = 2), and target lesion revascularisation 16.3% (n = 7). The target lesion was revascularised because of restenosis in 11.6% (n = 5). CONCLUSIONS: Routine SES implantation is highly effective for focal in-stent restenosis and appears to be a promising strategy for more complex patterns of restenosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15367519

Am J Cardiol (2004);94:1037-40
Mechanism of coronary artery restenosis after stenting for acute myocardial infarction
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In this intravascular ultrasound study, the mechanism of restenosis after stenting in acute myocardial infarction (AMI) was investigated in 33 patients 6 months after primary coronary intervention for AMI. Restenosis after stenting for AMI was primarily caused by stent underexpansion, not by neointima formation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15476620

Circulation (2004);110:810-4

based on angioplasty balloons. METHODS AND RESULTS: Stainless steel stents (n=40; diameter, 3.0 to 3.5 mm; length, 18 mm) were implanted in the left anterior descending and circumflex coronary arteries of domestic pigs. Both conventional uncoated and 3 different types of paclitaxel-coated, percutaneous transluminal coronary angioplasty balloons (contact with vessel wall for 1 minute) were used. No difference in short-term tolerance between coated and uncoated balloons and no signs of thrombotic events were observed. Quantitative angiography and histomorphometry of the stented arteries asserted the statistical equality of the baseline parameters between the control and the 3 treatment groups. Paclitaxel balloon coating led to a marked, dose-dependent reduction of parameters characterizing in-stent restenosis (reduction of neointimal area up to 63%). Despite the marked reduction in neointimal proliferation, endothelialization of stent struts was present in all samples. There was no evidence of a significant inflammatory response in the neighborhood of the stent struts. CONCLUSIONS: Paclitaxel balloon coating is safe, and it effectively inhibits restenosis after coronary angioplasty with stent implantation in the porcine model. The degree of reduction in neointimal formation was comparable to that achieved with drug-eluting stents.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15302790

Am Heart J (2004);147:317-22
Restenosis detected by routine angiographic follow-up and late mortality after coronary stent placement
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BACKGROUND: Routine 6-month follow-up angiography (FU angio) is the most sensitive tool to detect restenosis. Thus, FU angio protocols have been a pivotal part of trials on long-term efficacy of stents. However, it is unclear if such protocols supply data relevant for the prognosis of individual patients. The purpose of this study was to assess the impact of angiographic restenosis detected by FU angio on late mortality after coronary stent placement. METHODS AND RESULTS: We analyzed 2272 consecutive patients with successful stent placement performed from May 1992 through December 1996. All patients were scheduled for 6-month FU angio and contacted again after 4 years. FU angio was performed in 1958 patients. Of those, 557 patients (28.4%) had restenosis. After 4 years, 8.8% of patients with restenosis died, compared to 6.0% without (P =.02). There were several significant differences in clinical and angiographic characteristics between the 2 groups. In a multivariate analysis including those characteristics plus restenosis, only older age and restenosis were independent risk factors for late mortality. In patients with severe restenosis (>75% of lumen diameter; n = 231), late mortality was 7.6% in those with target vascular revascularization, compared to 14.9% without (P = not significant). CONCLUSIONS: In this analysis, mortality 4 years after stent placement was higher in patients with angiographic restenosis. Restenosis was an independent risk factor for late mortality, with a potential benefit after target vessel revascularization in severe restenoses. These data suggest that routine FU angio after stenting provides data relevant for long-term prognosis of patients.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citatio

n&list_uids=14760331

Am J Cardiol (2004);93:920-2
Usefulness of insulin resistance measured by homeostasis model assessment in predicting restenosis after coronary stent placement in nondiabetic patients
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The homeostasis model assessment enabled us to evaluate insulin resistance easily and accurately in the clinical setting. The restenosis rate of coronary stenting was significantly higher among patients with high values for the homeostasis model assessment. Our findings suggest that insulin resistance measured by the homeostasis model assessment predicts restenosis after coronary stent placement in nondiabetic patients.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15050499

Am Heart J (2004);147:16-22
Randomized trial of Rotational Atherectomy Versus Balloon Angioplasty for Diffuse In-stent Restenosis (ROSTER)
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BACKGROUND: Various autopsy and intravascular ultrasound (IVUS) studies have shown neointimal proliferation as the main mechanism of in-stent restenosis (ISR) responsible for >95% of luminal narrowing while stent struts are not compressed. ISR of diffuse type has a high incidence of recurrence (up to 70%) after balloon angioplasty (PTCA). Tissue ablation with percutaneous rotational coronary atherectomy (PRCA) may be more efficacious compared to tissue compression or extrusion after PTCA for the interventional treatment of diffuse ISR. METHODS: The Rotational Atherectomy Versus Balloon Angioplasty for Diffuse In-Stent Restenosis (ROSTER) trial is a single-center, randomized trial comparing PRCA to PTCA (both with IVUS guidance) in the treatment of diffuse ISR in 200 patients. In the PRCA group (n = 100), rotablation was performed using a burr-to-artery ratio >0.7 followed by adjunctive balloon dilatation at low pressure (4-6 atm). In the PTCA group (n = 100), high-pressure (>12 atm) balloon dilatation was performed using an optimal size balloon. The study's primary end point was target lesion revascularization (TLR) at 9 months and secondary end points included clinical events at 1 year and angiographic restenosis in a substudy of the last 75 patients enrolled. RESULTS: Baseline clinical and angiographic variables were comparable between the 2 groups with similar procedural and angiographic success, but a higher rate of repeat stenting occurred in the PTCA group (31% vs 10%; P <.001). Although the angiographic acute luminal gain was similar between the 2 groups, IVUS analysis revealed lower residual intimal hyperplasia area after PRCA versus PTCA (2.1 +/- 0.9 mm2 vs. 3.3 +/- 1.8 mm2; P =.005). At a mean follow-up of 12 +/- 2 months, there were 2 deaths, 3 myocardial infarctions, and 3 coronary artery bypass graft procedures in each group. TLR incidence was 32% in the PRCA group and 45% in the PTCA group (P =.042), with a similar trend noted in the angiographic substudy.

CONCLUSION: The ROSTER trial for diffuse ISR revealed both PRCA and PTCA to be safe and effective, but PRCA resulted in less residual intimal hyperplasia, lower repeat stent use, and decreased TLR.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14691413

Am J Cardiol (2004);93:953-8
Comparison of directional coronary atherectomy and stenting versus stenting alone for the treatment of de novo and restenotic coronary artery narrowing
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Late lumen loss after directional coronary atherectomy (DCA) is mainly determined by arterial remodeling. We hypothesized that stent implantation after optimal lesion debulking could be an effective approach to reduce restenosis. A total of 753 patients with de novo or restenotic coronary lesions were prospectively randomized to DCA plus stenting (n = 381) or stenting alone (n = 372). The patients were followed for 12 months. Procedural success was achieved in 91.5% versus 97.3% (p = 0.0007) of patients treated with DCA plus stent versus stent alone. Optimal atherectomy (<20% residual stenosis) was achieved in 26.5% of patients. The final minimal luminal diameter and the acute gain were similar in the 2 groups. There was no increase in 30-day major adverse cardiac events in the DCA plus stent group (3.9% vs 2.4%, p = 0.30). The primary end point, angiographic restenosis at 8 months, occurred in 26.7% of patients treated with DCA plus stents and in 22.1% of patients treated with stents alone (p = 0.237). Clinical follow-up to 1 year showed no difference in mortality (1.3% vs 0.8%, p = 0.725), acute myocardial infarction (4.2% vs 3.5%, p = 0.706), and target vessel failure (composite of death, Q-wave myocardial infarction, and target vessel revascularization) (23.9% vs 21.5%, p = 0.487) between patients with DCA plus stents and those with stents alone. This study failed to support the hypothesis that DCA before stenting lowers the angiographic restenosis rate compared with stents alone. At 12-month follow-up, there were no significant differences between the 2 groups in rates of death, reinfarction, or target vessel failure.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15081434

Circulation (2004);109:481-6
High plasma heparin cofactor II activity is associated with reduced incidence of in-stent restenosis after percutaneous coronary intervention
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BACKGROUND: Thrombin plays an important role in the development of atherosclerosis and restenosis after percutaneous coronary intervention. Because heparin cofactor II (HCII) inhibits thrombin action in the presence of dermatan sulfate, which is abundantly present in arterial wall, HCII may affect vascular remodeling by modulating thrombin action. We hypothesized that patients with high plasma HCII activity may show a reduced incidence of in-stent restenosis (ISR). METHODS AND
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implantation in 134 patients were evaluated before, immediately after, and at 6 months after percutaneous coronary intervention. Patients were divided into the following groups: high HCII (> or =110%, 45 lesions in 36 patients), normal HCII (> or =80% and <110%, 81 lesions in 66 patients), and low HCII (<80%, 40 lesions in 32 patients). Percent diameter stenosis at follow-up in the high-HCII group (18.7%) was significantly lower (P=0.046) than that in the normal-HCII group (30.3%) or the low-HCII group (29.0%). The ISR rate in the high-HCII group (6.7%) was significantly lower than that in the low-HCII group (30.0%) (P=0.0039). Furthermore, multivariate analysis demonstrated that high plasma HCII activity is an independent factor in reducing the incidence of angiographic restenosis (odds ratio, 0.953/1% increase of HCII; 95% CI, 0.911 to 0.998). CONCLUSIONS: The results demonstrate that HCII may have a hitherto unrecognized effect in inhibiting ISR. The effect of HCII may be mediated by inactivating thrombin in injured arteries, thereby inhibiting vascular smooth muscle cell migration and proliferation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14744972

Am Heart J (2004);147:E9
Frequency and time course of reocclusion and restenosis in coronary artery occlusions after balloon angioplasty versus Wiktor stent implantation: results from the Mayo-Japan Investigation for Chronic Total Occlusion (MAJIC) trial
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BACKGROUND: Compared with balloon angioplasty, stent implantation has been shown to reduce restenosis and reocclusion after treatment of chronic total coronary artery occlusions (CTOs). However, little is known about the time course of restenosis and reocclusion after the 2 procedures. The purpose of this study was to examine the frequency and time course of restenosis and reocclusion after treatment of CTOs with balloon angioplasty and Wiktor stent implantation. METHODS AND RESULTS: A total of 221 patients with successfully recanalized CTOs were randomly assigned to either treatment with a coil stent implantation (Wiktor stent, n = 110) or standard balloon angioplasty (n = 111). Repeat angiography was performed the day after treatment and at 6 months. Patients undergoing balloon angioplasty showed 29.8% restenosis and 1.1% reocclusion the following day versus 2% restenosis and no reocclusion in stent patients the following day. The cumulative reocclusion rate was significantly lower in the stent group than in the balloon group at 6 months (2.1% versus 9.3%, P <.05). As a result of the more frequent need of target vessel revascularization (49.5% in the balloon group and 30.6% in the stent group, P <.005) and earlier final follow-up angiography in the balloon group, the frequency of angiographic restenosis at 6 months was similar in both groups (57.3% in the stent group and 54.5% in the balloon group). CONCLUSIONS: The frequency and time course of reocclusion and restenosis after balloon angioplasty and stent placement differ within 24 hours of the procedure and remain different on angiography at 6 months.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14999211

Am J Cardiol (2004);94:115-8
Restenosis rates following bifurcation stenting with sirolimus-eluting stents for de novo narrowings
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The percutaneous treatment of coronary bifurcation stenoses is hampered by an increased rate of subsequent restenosis. The present study reports on the outcomes of a consecutive series of 58 patients with 65 de novo bifurcation stenoses treated with sirolimus-eluting stent implantation in both the main vessel and side branch. At 6 months, the incidence of major adverse cardiac events was 10.3% (1 death and 5 target lesion revascularizations) with no episodes of acute myocardial infarction or stent thrombosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15219520

Eur Heart J (2004);25:1679-87
Inflammation and restenosis after percutaneous coronary interventions
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The role of inflammation in the development of restenosis after percutaneous coronary interventions has been investigated in several studies. There is an interaction of inflammatory activation and vascular wall response to injury leading to intimal hyperplasia. Percutaneous interventions trigger inflammatory reactions leading to the development of intimal hyperplasia. This reaction is even more prominent in atheromatic plaques in which inflammatory cells have already been activated. In the clinical setting there are several methods for the recognition of the inflammatory activation. In this article we review the data for the role of inflammatory process in restenosis and the significance of identifying the inflamed lesions prior to the intervention. Moreover, the therapeutic implications for the inhibition of inflammatory activation are mentioned.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15451145

J Am Coll Cardiol (2004);44:1386-92
Oral rapamycin to inhibit restenosis after stenting of de novo coronary lesions: the Oral Rapamune to Inhibit Restenosis (ORBIT) study
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OBJECTIVES: The aim of this study was to establish safety and feasibility of oral Rapamycin at two doses-2 mg and 5 mg-in achieving low rates of repeat target lesion revascularization (TLR) in de novo native coronary artery lesions. BACKGROUND: Drug-eluting stents have shown the ability to limit restenosis. Oral Rapamycin is an alternative strategy that can target multiple coronary lesions suitable for treatment with any approved metal stent and at potentially lower cost. METHODS: The Oral Rapamune to Inhibit Restenosis (ORBIT) study is an open-label study of 60 patients with de novo lesions treated with bare metal stents in up to two vessels. After a loading

days. Six-month angiographic, intravascular ultrasound (IVUS), and clinical follow-up were conducted. RESULTS: Baseline clinical and procedural characteristics were similar: 10% of patients in the 2-mg group and 30% in the 5-mg group did not complete the course; 43% in the 2-mg group and 66% in the 5-mg group had side effects. At six-month follow-up, late loss (0.6 +/- 0.5 mm vs. 0.7 +/- 0.5 mm; p = NS), in-stent binary restenosis (7.1% vs. 6.9%; p = NS), in-stent percent volume obstruction by IVUS (29% vs. 24%; p = NS), and clinically driven TLR (14.3% vs. 6.9%; p = NS) were similar in 2-mg and 5-mg groups. CONCLUSIONS: Oral Rapamycin for the prevention of restenosis is safe, feasible, and associated with low rates of repeat revascularization. Although associated with certain side effects, it may be considered for patients undergoing multivessel stents if proven in larger randomized studies.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15464317

Circulation (2004);109:340-4
Five-year follow-up after intracoronary gamma radiation therapy for in-stent restenosis
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BACKGROUND: The Washington Radiation for In-Stent Restenosis Trial is a double-blinded randomized study evaluating the effects of intracoronary radiation therapy (IRT) in patients with in-stent restenosis (ISR). METHODS AND RESULTS: One hundred thirty patients with ISR (100 native coronary and 30 vein grafts) underwent percutaneous transluminal coronary angioplasty, laser ablation, rotational atherectomy, or additional stenting (36% of lesions). Patients were randomized to either 192-Iridium IRT or placebo, with a prescribed dose of 15 Gy to a 2-mm radial distance from the center of the source. Angiographic restenosis (27% versus 56%, P=0.002) and target vessel revascularization (26% versus 68%, P<0.001) were reduced at 6 months in patients treated with IRT. Between 6 and 60 months, patients treated with IRT compared with placebo had more target lesion revascularization (IRT, 21.6% versus placebo, 4.7%; P=0.04) and target vessel revascularization (IRT, 21.5% versus placebo, 6.1%; P=0.03). At 5 years, the major adverse cardiac event rate was significantly reduced with IRT (46.2% versus 69.2%, P=0.008). CONCLUSIONS: In the Washington Radiation for In-Stent Restenosis Trial, patients with ISR treated with IRT using 192-Iridium had a reduction in the need for repeat target lesion and vessel revascularization at 6 months and 5 years.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14732756

Catheter Cardiovasc Interv (2004);63:259-64
Sirolimus-eluting stents for the prevention of restenosis in a worst-case scenario of diffuse and recurrent in-stent restenosis
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For recurrent in-stent restenosis (ISR), surgical revascularization or brachytherapy is still the principal therapeutic options. The present investigation explores the efficacy of a

sirolimus-eluting stent to prevent restenosis in these lesions with a high risk of recurrence. In 22 consecutive patients with a recurrent and diffuse ISR, a sirolimus-eluting stent was implanted to cover the restenotic lesion. All patients were followed clinically for at least 1 year and underwent a repeat angiography after 7 months. A quantitative coronary angiographic analysis was done. The target vessel failure was 14% in the sirolimus-eluting stent group, with an angiographic late loss of only 0.39 +/- 0.54. No subacute stent thrombosis was observed, and the 1-year event-free survival was 86%. The three cases with restenosis were all focal and could be successfully treated by additional drug-eluting stent implantation. This study showed the efficacy of a sirolimus-eluting stent for the prevention of restenosis in a worst-case scenario of recurrent and diffuse ISR. The observed restenosis rate is lower than that reported after brachytherapy and suggests that sirolimus-eluting stents are a promising treatment option for ISR.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15505841

Circulation (2004);109:867-73
Clinical and angiographic predictors of restenosis after stent deployment in diabetic patients
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BACKGROUND: Restenosis and consequent adverse cardiac events are increased in diabetics undergoing percutaneous coronary intervention. Use of intracoronary stents may ameliorate such risks; however, factors influencing the likelihood of restenosis after stent deployment in this high-risk patient subgroup are unknown. METHODS AND RESULTS: We retrospectively analyzed all stented diabetic patients in 16 studies of percutaneous coronary intervention, all of which underwent core angiographic analysis at Cardialysis, Rotterdam. Univariate and multivariate analyses, with 37 clinical and angiographic variables, compared those with and without restenosis and predicted restenosis rates calculated through the use of reference charts derived from angiographic data. Within the studies, 418 of 3090 (14%) stented patients with 6-month angiographic follow-up had diabetes. Restenosis (> or =50% diameter stenosis at follow-up) occurred in 550 of 2672 (20.6%) nondiabetic and 130 of 418 (31.1%) diabetic patients (P<0.001). Univariate predictors of restenosis in diabetics were smaller vessel reference diameter (RD) (P<0.001), smaller minimal luminal diameter before stenting (P=0.01), smaller minimal luminal diameter and percent diameter stenosis after stenting (P<0.001, P=0.04), greater stented length of vessel (P<0.001), and reduced body mass index (BMI) (P=0.04). With the use of multivariate analysis, only smaller RD (P=0.003), greater stented length of vessel (P=0.04), and reduced BMI (P=0.04) were associated with restenosis. Reference charts demonstrated an incremental risk of restenosis that appears solely dependent on vessel RD. CONCLUSIONS: Restenosis after stent