Journal of the American College of Cardiology
Published by Elsevier Science Inc.
Vol. 39, No. 9, 2002
ISSN 0735-1097/02/$22.00
PII S0735-1097(02)01793-X

Coronary Hemodynamics of Stent Implantation After Suboptimal and Optimal Balloon Angioplasty

Michiel Voskuil, MD,* Rob A. M. van Liebergen, MD,* Mariano Albertal, MD,† Eric Boersma, PHD,† Jan G. P. Tijssen, PHD,* Patrick W. Serruys, MD,† Jan J. Piek, MD,* on behalf of the DEBATE II Investigators

Amsterdam and Rotterdam, The Netherlands

OBJECTIVES This study was performed to evaluate hemodynamic alterations of stent implantation after Doppler flow–guided balloon angioplasty (BA).

BACKGROUND There is controversy regarding the effect of stent implantation on coronary hemodynamics after suboptimal and optimal BA.

METHODS A total of 523 of 620 patients underwent Doppler-guided BA in the setting of a multicenter study and were analyzed before and after additional stent implantation. Balloon angioplasty was considered optimal when the diameter stenosis (DS) was ≤35% and coronary flow reserve (CFR) was >2.5 and suboptimal if these two criteria were not met. Coronary flow reserve was also measured in an angiographically normal artery to determine relative CFR. Patients were followed for 12 months to document major adverse cardiac events (MACE).

RESULTS The main difference between patients with suboptimal BA (n = 195 [51%]) and optimal BA (n = 184 [49%]) was a more pronounced increase in baseline blood flow velocity (15 ± 8 to 22 ± 11 vs. 14 ± 8 to 16 ± 10 cm/s, p < 0.01). Coronary flow reserve improved after stent implantation in both patient groups, owing to a reduction in residual lumen obstruction, as determined by angiographic (%DS) and Doppler flow criteria (hyperemic blood flow velocity, relative CFR), and was associated with a decrease in MACE (16% vs. 7% in optimal BA group, p = 0.08; and 27% vs. 11% in suboptimal BA group, p = 0.007).

CONCLUSIONS Stent implantation enhances CFR after suboptimal and optimal Doppler-guided BA, owing to a reduction in residual lumen obstruction—determined by angiographical and Doppler flow criteria—as the underlying mechanism for an improved clinical outcome. (J Am Coll Cardiol 2002;39:1513–7) © 2002 by the American College of Cardiology Foundation

The effectiveness of balloon angioplasty (BA) is hampered by the relatively high incidence of restenosis. The introduction of stents in the beginning of the 1990s for the treatment of procedural complications has led to a reduction of coronary renarrowing after percutaneous transluminal coronary angioplasty (PTCA) (1,2). The exponential growth in the use of stent implantation has resulted in an increasing number of patients with in-stent restenosis, which is difficult to treat with current percutaneous techniques, except for brachytherapy (3). It has been suggested that an optimal outcome after BA is similar to the clinical outcome of stenting (4). The results of the Doppler Endpoints Balloon Angioplasty Trial Europe (DEBATE I) study support this hypothesis (5). Patients with both a diameter stenosis (DS) ≤35% and coronary flow reserve (CFR) >2.5 after BA showed a "stent-like" clinical outcome. Other studies confirmed these findings—that is, optimized BA using angiography (6) or vascular ultrasound imaging (7,8) results in a clinical outcome similar to stent implantation. These studies suggest that a substantial number of patients fare well without stent implantation. In the DEBATE II study, the cost-effectiveness of provisional BA, guided by Doppler flow velocity and angiography, was compared to that of elective stent implantation. The unique design of this study provided the setting for a more detailed evaluation of hemodynamic alterations after stent implantation subsequent to suboptimal or optimal BA.

From the *Academic Medical Center, Amsterdam; and †Thoraxcenter, Rotterdam, The Netherlands. Prof. Dr. J. J. Piek is a clinical investigator sponsored by the Netherlands Heart Foundation (grant nos. D96.020 and 2000.090).

Manuscript received May 4, 2001; revised manuscript received January 24, 2002, accepted February 6, 2002.

METHODS

Patient selection. The study group included in this subanalysis consisted of 523 of 620 patients who underwent guided BA (with angiography and Doppler flow velocity measurements) to treat stable or unstable angina pectoris (excluding Braunwald classification III) or documented myocardial ischemia due to a single primary coronary stenosis potentially amenable to stent implantation, or both, in the setting of a multicenter study (DEBATE II). The details of this multicenter study have been described elsewhere (9). Briefly, patients scheduled for PTCA of one major native coronary artery, with normal left ventricular function, were included. The exclusion criteria were multivessel disease, previous Q-wave myocardial infarction in the territory distributed by the vessel to be dilated, acute myocardial infarction less than one week before PTCA, total or functional coronary occlusion, lesions >25 mm in length, extreme tortuosity of the vessel to be dilated or

JACC Vol. 39, No. 9, 2002
May 1, 2002:1513–7

Abbreviations and Acronyms

BA	= balloon angioplasty
CFR	= coronary flow reserve
DEBATE	= Doppler Endpoints Balloon Angioplasty Trial Europe
DS	= diameter stenosis
MACE	= major adverse cardiac events
OR	= odds ratio
PTCA	= percutaneous transluminal coronary angioplasty

vessels that were previously bypassed or contained a thrombus. The study protocol was approved by the Institutional Review Board of the participating centers. The study was performed according to the principles in the Declaration of Helsinki. All patients gave written, informed consent.

Angioplasty procedure and blood flow velocity assessment. In the DEBATE II study, 620 patients were first randomized to either guided BA (n = 523) or direct stent implantation (n = 97). In the guided BA arm, the operators were urged to obtain an optimal result, defined as DS ≤35% and CFR >2.5. A result was considered suboptimal when these two criteria were not met (DS ≤35% and CFR ≤2.5 or DS >35% and/or CFR ≤2.5). This approach resulted in bail-out stenting in 129 patients, which was allowed according to the protocol in the presence of residual stenosis >50%; dissection type D, E or F; persistent myocardial ischemia with dissection type C; a reduction of Thrombolysis in Myocardial Infarction (TIMI) flow grade by 1; or the existence of TIMI flow grade 0 or 1. The study group consisted of the remaining 379 patients who underwent a second randomization toward stent implantation or completion of the procedure. Briefly, the study protocol included Doppler flow measurements distal to the lesion under baseline and hyperemic conditions, using a 0.014-in. (0.035-cm) Doppler-tipped guide wire (FloWire by Endosonics, Rancho Cordova, California). Maximal hyperemia was induced by an intracoronary bolus injection of adenosine—12 μg in the right coronary artery and 18 μg in the left coronary artery—or as an intravenous infusion (140 μg/kg body weight per min).

Quantitative coronary angiography. Cine angiography was performed after the intracoronary administration of 0.1 to 0.3 mg of nitroglycerin or 1 to 3 mg of isosorbide dinitrate to achieve maximal coronary vasodilation. At least two cine angiograms, in the orthogonal projections, were obtained before coronary angioplasty and at the end of the procedure. All cine films were analyzed by an independent core laboratory, whose investigators had no knowledge of the clinical or Doppler flow data. Matched views and frames were selected for off-line quantitative computer-assisted analysis.

Blood flow velocity analysis. During the angioplasty procedure, the Doppler flow velocity signals were recorded continuously on videotape, using a Doppler flow spectral analyzer (FloMap by Endosonics). The blood flow velocity measurements were used to calculate, by means of the time-averaged peak velocity (normalized to the cardiac cycle), the distal blood flow velocity reserve, defined as the ratio between the adenosine-induced hyperemic blood flow velocity and the baseline blood flow velocity. Relative CFR was defined as the ratio between the CFR in the target and reference vessels. The appropriateness of the Doppler flow measurements was verified by an independent core laboratory.

End points. Patients were followed for 12 months to document the major adverse cardiac events (MACE), defined as death from any cause, nonfatal myocardial infarction or the need for target lesion revascularization. Myocardial infarction was defined as the development of a new Q wave or a rise in serum creatine kinase, with an abnormal plasma concentration of myocardial isoenzymes. Enzymes were sampled twice in the first 24 h. Patients visited the outpatient clinic 1, 6 and 12 months after hospital discharge. At each visit, records were kept on the patient's anginal status, cardiac medications, 12-lead electrocardiogram and complete physical examination. No follow-up angiogram was obtained, unless clinically indicated.

Statistical analysis. Continuous variables are expressed as the mean value ± SD. Chi-square analysis was used to detect a difference in categorical patient characteristics. A two-tailed unpaired *t* test (or Mann-Whitney *U* test for nonparametric data) was used to assess differences in continuous variables. The Holms-Sidak method was performed to control the family error rate. All relevant clinical, hemodynamic and flow velocity variables were subsequently entered in a univariate binary logistic regression analysis to determine the predictors of CFR <2.5 after BA. Contributing factors ($p < 0.1$) were entered into a multivariate regression analysis to determine independency. A p value <0.05 was considered to be statistically significant.

RESULTS

A total of 523 of 620 patients who underwent guided BA in the setting of the DEBATE II trial were included in this subanalysis. Fifteen patients (3%) were excluded because of technical and logistical problems. A total of 129 patients (25%) underwent bail-out stenting. Consequently, 379 patients (73%) remained for analysis. Of these 379 patients, 184 (49%) appeared to have an optimal BA result (DS ≤35% and CFR >2.5) after PTCA. A total of 195 patients (51%) did not meet these criteria. The majority of the patients with a suboptimal BA result were characterized by CFR ≤2.5 and DS ≤35% (n = 178 [91%]), whereas 14 patients (7%) had CFR ≤2.5 and DS >35%, and 4 patients (2%) had CFR >2.5 and DS >35%. The baseline characteristics of both groups are depicted in Table 1. The group of patients with an optimal result after PTCA appeared to be younger, predominantly male and less frequently diag-

Table 1. Baseline Characteristics of the 379 Study Patients

	Optimal (n = 184)	Suboptimal (n = 195)	p Value
Age (yrs)	57 ± 10	60 ± 11	0.001
Male	149 (81%)	136 (69%)	0.008
Systemic hypertension	62 (34%)	77 (39%)	NS
Cigarette smokers	55 (30%)	51 (26%)	NS
Total cholesterol >6.5 mmol/l	108 (59%)	109 (56%)	NS
Diabetes mellitus	12 (7%)	21 (11%)	NS
Previous myocardial infarction	15 (8%)	22 (11%)	NS
Unstable angina pectoris	52 (28%)	74 (38%)	0.05
Medications			
Aspirin	162 (88%)	169 (87%)	NS
Beta-blocker	121 (66%)	125 (64%)	NS
Calcium antagonist	92 (50%)	94 (48%)	NS
Nitrates	121 (66%)	123 (63%)	NS
Coronary artery dilated			
LAD	96 (52%)	98 (50%)	NS
RCA	57 (31%)	56 (29%)	NS
LCx	31 (17%)	40 (21%)	NS
CCS classification			
1	7 (4%)	9 (5%)	NS
2	58 (32%)	58 (30%)	NS
3	48 (26%)	31 (16%)	NS
4	5 (3%)	4 (2%)	NS

Data are presented as the mean value ± SD or number (%) of patients. Values are n (%).
CCS = Canadian Cardiovascular Society; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; RCA = right coronary artery

nosed with unstable angina pectoris, as compared with the group of patients with a suboptimal result.

Hemodynamic, angiographic and Doppler flow variables in the suboptimal and optimal groups before and after BA. Heart rate was slightly higher before (70 ± 12 vs. 67 ± 12 beats/min, $p < 0.05$) and after (72 ± 12 vs. 67 ± 11 beats/min, $p < 0.05$) the procedure in the patients with a suboptimal result. In the suboptimal and optimal groups, DS improved after guided BA, from 70 ± 11% and 68 ± 11% to similar values of 23 ± 10% and 22 ± 8%, respectively (Table 2). Baseline blood flow velocity increased after BA in the suboptimal group, although it remained unchanged in the optimal group (15 ± 8 to 22 ± 11 vs. 14 ± 8 and 16 ± 10 cm/s, respectively; $p < 0.01$). Increased hyperemic blood flow velocity was observed in both groups after BA. Coronary flow reserve was already low before the procedure in patients who showed a suboptimal result after BA, as compared with patients with an optimal result (1.47 ± 0.5 vs. 1.72 ± 0.6, $p < 0.01$), whereas relative CFR was equal in both patient groups. An impaired relative CFR was observed after BA in the suboptimal group, as compared with the optimal group (0.80 ± 0.2 vs. 1.06 ± 0.4, $p < 0.01$).

Hemodynamic, angiographic and Doppler flow variables in the suboptimal and optimal BA groups after stent implantation. Percent DS further diminished from 22 ± 9% to 7 ± 8% and 22 ± 8% to 8 ± 8% after stent implantation in both suboptimal and optimal groups, respectively (Table 2). After stent implantation, baseline blood flow velocity remained elevated (22 ± 11 cm/s) in the suboptimal group, although it remained low in the optimal

Table 2. Quantitative Coronary Angiographic and Coronary Blood Flow Velocity Data of the Patients With an Optimal and Suboptimal Result After Balloon Angioplasty

	Optimal BA Group (n = 184)	Suboptimal BA Group (n = 195)	p Value	
			Before GBA	Gain*
DS (%)				
Before GBA	68 ± 11	70 ± 11	0.15	
After GBA	22 ± 8	23 ± 10		0.95
After stenting	8 ± 8	7 ± 8		0.60
b-APV (cm/s)				
Before GBA	14 ± 8	15 ± 8	0.49	
After GBA	16 ± 10	22 ± 10		<0.01†
After stenting	17 ± 7	22 ± 11		0.20
h-APV (cm/s)				
Before GBA	23 ± 15	22 ± 12	0.21	
After GBA	46 ± 18	41 ± 18		0.20
After stenting	52 ± 24	49 ± 26		0.28
CFR				
Before GBA	1.72 ± 0.6	1.47 ± 0.5	<0.01†	
After GBA	3.10 ± 0.6	1.95 ± 0.4		<0.01†
After stenting	3.30 ± 0.7	2.36 ± 0.7		0.56
Relative CFR				
Before GBA	0.59 ± 0.3	0.59 ± 0.2	0.97	
After GBA	1.06 ± 0.4	0.80 ± 0.2		<0.01†
After stenting	1.12 ± 0.4	0.95 ± 0.3		0.11

*The upper p value is for the comparison of the gain of GBA (relative to that before GBA) between patients with an optimal (n = 184) and suboptimal (n = 195) result. The lower p value is for the comparison of the gain of stent implantation (relative to that after GBA) between patients with an optimal (n = 77) and suboptimal result (n = 110). †Statistically significant according to the Holm-Sidak method. Data are presented as the mean value ± SD.
BA = balloon angioplasty; b-APV and h-APV = baseline and hyperemic average peak flow velocity, respectively; CFR = coronary flow reserve; DS = diameter stenosis; GBA = guided balloon angioplasty.

group (17 ± 7 cm/s). Hyperemic blood flow velocity further increased after stent implantation, to a value of 49 ± 26 cm/s in the suboptimal group and 52 ± 24 cm/s in the optimal group. In the suboptimal and optimal groups, CFR in the target artery further improved after stent implantation, to a value of 2.36 ± 0.7 and 3.30 ± 0.7, respectively. After stent implantation, relative CFR also remained low in the suboptimal group, as compared with the optimal group (0.95 ± 0.3 vs. 1.12 ± 0.4).

Univariate and multivariate analyses of predictors of post-procedural CFR. A binary logistic regression analysis of all relevant clinical, hemodynamic and flow velocity variables revealed baseline CFR in the target vessel, baseline CFR in the reference vessel, family history, male gender, lesion length, lesion eccentricity, height, weight, age, baseline percent DS and smoking as predictors of CFR <2.5 after PTCA. A multivariate analysis of these variables revealed that CFR before angioplasty (odds ratio [OR] 2.32, $p = 0.001$), reference CFR (OR 2.59, $p < 0.001$) and family history (OR 2.36, $p = 0.002$) were the only independent predictors of CFR <2.5 directly after PTCA.

Clinical outcome in groups with an optimal or suboptimal result after PTCA. In Table 3, the frequencies of all MACE are shown. The incidence of MACE at one-year follow-up was lower in the total study group (disregarding a

Table 3. Frequency of Major Adverse Cardiac Events

	Optimal BA Group (n = 184)		Suboptimal BA Group (n = 195)	
	BA (n = 107)	Stenting (n = 77)	BA (n = 85)	Stenting (n = 110)
Death	1 (0.9%)	2 (2.6%)	2 (2.3%)	1 (0.9%)
Myocardial infarction	2 (1.8%)	0	3 (3.5%)	4 (3.6%)
TLR rate	14 (13%)	3 (4)	18 (21%)	7 (6.3%)
Total MACE	17 (16%)	5 (6.5%)	23 (27%)	12 (11%)

Data are presented as the number (%) of patients.
BA = balloon angioplasty; MACE = major adverse cardiac events; TLR = target lesion revascularization.

suboptimal or optimal result) with stent implantation in addition to guided BA, as compared with patients who underwent BA only (9% vs. 21%, p = 0.002). The incidence of MACE in the suboptimal group that had stent implantation in addition to guided BA was 11%, as compared with 27% in patients who had guided BA only (p = 0.007). A similar trend was seen in the patients with an optimal result after PTCA (7% vs. 16%, p = 0.08).

DISCUSSION

The results of this analysis of the DEBATE II study demonstrate that the clinical benefit of stent implantation after suboptimal and optimal BA is related to a reduction in residual lumen obstruction, as determined by angiographic and Doppler flow indexes.

Suboptimal guided BA and additional stent implantation. The unique design of the DEBATE II study allowed the evaluation of the effect of stent implantation after BA on coronary hemodynamics in a large number of patients. The data show that a suboptimal result of BA, defined by angiographic and Doppler flow criteria, is due to both an enhanced baseline blood flow velocity and, presumably, residual lumen obstruction, as reflected by impaired relative CFR, as compared with an optimal result after BA. In the group of patients who did not meet the criteria for optimal BA, baseline blood flow velocity appeared to be elevated after the procedure, which confirms earlier studies (10–12). Coronary flow reserve was already impaired before PTCA in the subgroup of patients with a suboptimal result directly after PTCA, along with a normal relative CFR (and an equal degree of angiographic severity of epicardial stenosis in both groups). Moreover, multivariate analysis showed that CFR before the intervention and reference CFR were predictors of CFR after PTCA, suggesting that hemodynamic factors before the intervention are responsible for the impaired CFR after PTCA, rather than procedure-related factors, such as particulate embolization and reactive epicardial vasoconstriction at the site of the guide wire tip (13,14). Several other mechanisms have been suggested to explain an impaired CFR, due to an enhanced baseline flow velocity directly after guided BA, including a temporarily disturbed autoregulation, microvascular stunning and diffuse disease, as reported in previous studies (10–12,15). The baseline flow velocity remained unchanged after stent implantation, whereas CFR improved, owing to a reduction in residual lumen obstruction, as determined by angiographic (diminished %DS) and Doppler (enhanced hyperemic blood flow velocity and relative CFR) criteria. This improved hemodynamic status after stent implantation was associated with an improved clinical outcome, as reported before (9).

Optimal guided BA and additional stent implantation. An optimal result after BA was achieved in approximately half of the patients. These patients were characterized by a baseline blood flow velocity that remained unchanged after guided BA, whereas the hyperemic blood flow velocity increased significantly as a result of the diminished residual lumen obstruction. This optimal result after BA led to a low incidence of MACE (16%) during follow-up, which is in accordance with DEBATE I, the Doppler Endpoint Stenting Interventional Investigation (DESTINI) and the French Randomized Optimal Stenting Trial (FROST). This indicates that potentially half of the patients show a good clinical outcome after optimal BA (incidence of MACE varying between 15% and 19%). This treatment strategy, to avoid additional stent implantation, prevents the risk of the patient developing in-stent restenosis, which is currently still difficult to treat (5,16,17). Nevertheless, additional stent implantation in this subgroup of patients resulted in a further increase in CFR and relative CFR, owing to an enhancement of hyperemic blood flow velocity. The incidence of MACE in the group of patients with additional stent implantation after optimal BA was 7%, whereas that in patients who had primary stent implantation in the main study was 13% (p = 0.08). This trend toward significance suggests that physiologically guided stent implantation, either based on intracoronary blood flow velocity or pressure measurements (18), may be better than primary stent implantation. However, this hypothesis should be tested in a larger group of patients. Furthermore, it should be noted that the excellent clinical outcome after Doppler-guided stent implantation could also be related to a selection bias of the study patients, consisting predominantly of patients with single-vessel disease and those with a presumably normal or mildly diseased microvasculature.

Study limitations. This study is a post-hoc analysis of a multicenter study. The changes in arterial dimensions were assessed by quantitative coronary angiography; intravascular ultrasound imaging was not mandatory for appropriate evaluation of epicardial remodeling, estimation of coronary volume flow changes or shear stress analysis. Furthermore, a substantial number of patients were excluded from this analysis because of bail-out stent implantation. Finally, this study involved a selected cohort of patients with single-vessel disease and normal left ventricular function, thus limiting the extrapolation of the present findings to other patient groups.

Clinical implications. The operators pursued an aggressive approach to obtain an optimal angiographic result, as demonstrated by the percent DS after BA. The present study shows that intracoronary hemodynamic guidance of a coronary intervention, in addition to angiography, results in an additional improvement in the patient's clinical outcome. Approximately 50% of the patients in the provisional stenting arm of the DEBATE II study showed an unsatisfactory result, despite Doppler-guided BA, which is in accordance with the DESTINI and FROST trials. This subset of patients requires stent implantation to improve the direct hemodynamic and late clinical outcomes. However, this indicates that the remaining 50% of the patients showed a good "stent-like" clinical outcome after optimal BA. From a clinical point of view, this is an essential observation, because a restenotic lesion can be treated easily with a stent, whereas the treatment of in-stent restenosis is still cumbersome (3). The provocative low rate of target lesion revascularization in the subgroup of patients with an optimal result after BA, followed by additional stent implantation, suggests the usefulness of hemodynamic guidance of stent implantation, which is in contrast to the current clinical practice of direct stenting.

Reprint requests and correspondence: Dr. Jan J. Piek, Department of Cardiology, B2-108, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. E-mail: j.j.piek@amc.uva.nl.

REFERENCES

1. Serruys PW, de Jaegere P, Kiemeneij F, et al., the BENESTENT Study Group. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery. N Engl J Med 1994;331:489–95.
2. Fischman DL, Leon MB, Baim DS, et al., the Stent Restenosis Study Investigators. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 1994;331:496–501.
3. Mintz GS, Mehran R, Waksman R, et al. Treatment of in-stent restenosis. Semin Interv Cardiol 1998;3:117–21.
4. Foley DP, Serruys PW. Provisional stenting—stent-like balloon angioplasty: evidence to define the continuing role of balloon angioplasty for percutaneous coronary revascularization. Semin Interv Cardiol 1996;1:269–73.
5. Serruys PW, di Mario C, Piek J, et al. Prognostic value of intracoronary flow velocity and diameter stenosis in assessing the short- and long-term outcomes of coronary balloon angioplasty: the DEBATE (Doppler Endpoints Balloon Angioplasty Trial Europe) study. Circulation 1997;96:3369–77.
6. Rodriguez A, Ayala F, Bernardi V, et al. Optimal coronary balloon angioplasty with provisional stenting versus primary stent (OCBAS): immediate and long-term follow-up results. J Am Coll Cardiol 1998;32:1351–7.
7. Fitzgerald PJ, Oshima A, Hayase M, et al. Final results of the Can Routine Ultrasound Influence Stent Expansion? (CRUISE) study. Circulation 2000;102:523–30.
8. Suzuki T, Hosokawa H, Katoh O, et al. Effects of adjunctive balloon angioplasty after intravascular ultrasound-guided optimal directional coronary atherectomy: the result of Adjunctive Balloon Angioplasty following Coronary Atherectomy Study (ABACAS). J Am Coll Cardiol 1999;34:1028–35.
9. Serruys PW, de Bruyne B, Carlier S, et al. Randomized comparison of primary stenting and provisional balloon angioplasty guided by flow velocity measurement. Circulation 2000;102:2930–7.
10. Nanto S, Kodama K, Hori M, et al. Temporal increase in resting coronary blood flow causes an impairment of coronary flow reserve after coronary angioplasty. Am Heart J 1992;123:28–36.
11. Kern MJ, Deligonul U, Vandormael M, et al. Impaired coronary vasodilator reserve in the immediate postcoronary angioplasty period: analysis of coronary artery flow velocity indexes and regional cardiac venous efflux. J Am Coll Cardiol 1989;13:860–72.
12. van Liebergen RA, Piek JJ, Koch KT, de Winter RJ, Lie KI. Immediate and long-term effect of balloon angioplasty or stent implantation on the absolute and relative coronary blood flow velocity reserve. Circulation 1998;98:2133–40.
13. Erbel R, Heusch G. Coronary microembolization. J Am Coll Cardiol 2000;36:22–4.
14. Gregorini L, Fajadet J, Robert G, Cassagneau B, Bernis M, Marco J. Coronary vasoconstriction after percutaneous transluminal coronary angioplasty is attenuated by antiadrenergic agents. Circulation 1994; 90:895–907.
15. Kern MJ, Puri S, Bach RG, et al. Abnormal coronary flow velocity reserve after coronary artery stenting in patients: role of relative coronary reserve to assess potential mechanisms. Circulation 1999;100: 2491–8.
16. Lafont A, Dubois-Rande JL, Steg PG, et al., the FROST Study Group. The French Randomized Optimal Stenting Trial: a prospective evaluation of provisional stenting guided by coronary velocity reserve and quantitative coronary angiography. J Am Coll Cardiol 2000;36:404–9.
17. Di Mario C, Moses JW, Anderson TJ, et al. Randomized comparison of elective stent implantation and coronary balloon angioplasty guided by online quantitative angiography and intracoronary doppler. Circulation 2000;102:2938–44.
18. Hanekamp CE, Koolen JJ, Pijls NH, Michels HR, Bonnier HJ. Comparison of quantitative coronary angiography, intravascular ultrasound, and coronary pressure measurement to assess optimum stent deployment. Circulation 1999;99:1015–21.