J Cardiol 2005 Aug; 46(2): 43–51

Effect of Rotational Atherectomy on the Coronary Microcirculation in Patients With Angina Pectoris

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Abstract

Objectives. The coronary microcirculation can be impaired by ablated debris just after a rotational atherectomy procedure, but the specific effects of rotablation on the microcirculation have not been investigated. The present study examined the effects of rotational atherectomy on the coronary microcirculation by analyzing coronary flow reserve(CFR)and the component parameters of the coronary flow-pressure loop.

Methods. This study included 31 patients with angina pectoris who underwent stent implantation after rotational atherectomy and with＜50% diameter stenosis at 6-month follow-up(*i.e.* without clinical restenosis). The CFR, the flow-pressure slope index(FPSI)and zero-flow pressure were measured using the FloWire^{TM} Doppler guidewire in both treated and untreated reference vessels without stenosis immediately after and on 6 months from the rotational atherectomy procedure.

Results. CFR and FPSI in the treated vessels were significantly lower than in the untreated reference vessels without stenosis just after rotational atherectomy(CFR: 2.1±0.5 vs 2.6±0.7, $p<0.05$; FPSI: 1.61±0.8 vs 2.35±0.9 cm/sec/mmHg, $p<0.05$), but no significant differences were observed in CFR or FPSI between these same sets of arteries at follow-up. There was also a significant correlation between the extent of attenuation of CFR and total ablation time($r=-0.54$, $p<0.01$).

Conclusions. Rotational atherectomy attenuates CFR by reducing coronary artery conductance, probably due to coronary microvessel obstruction with the debris ablated during the procedures of rotational atherectomy.

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Key Words

■**Atherectomy(rotational)** ■**Coronary artery disease** ■**Angina pectoris**
■**Coronary microcirculation**

INTRODUCTION

The application of the intracoronary Doppler guidewire for the measurement of coronary flow velocity has been extensively validated in the clinical setting[1–3]. In addition to the main, larger coronary conduit vessels, the coronary microvasculature plays a key role in the regulation of coronary arterial blood flow. Coronary flow reserve(CFR), which has been shown to reflect coronary microvascular function[4–10], is the ratio of coronary flow velocity at baseline and during maximal hyperemia after the administration of a coronary vasodilator[11]. CFR measurement provides important diagnostic information about cardiovascular disease, but recent reports illustrate that there are theoretical limita-

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Manuscript received December 14, 2004; revised March 30, 2005; accepted April 1, 2005

tions to the CFR concept[12,13]. One limitation is that maximal hyperemic coronary blood flow is strongly pressure-dependent, whereas auto-regulated basal coronary flow does not remain at a constant level. The flow-pressure slope index (FPSI) is determined by measuring the slope of the linear diastolic segment of the relationship between instantaneous aortic pressure and hyperemic coronary flow. In the late-diastolic phase, under maximal hyperemia, the relationship between these indices become linear and permits measurement of the slope, the FPSI. FPSI is independent of changes in heart rate, preload, aortic pressure, and cardiac contractility[14−17]. Coronary vessel conductances estimated by this index correlate with those obtained in the experimental study using microspheres[18]. Zero-flow pressure or pressure at zero-flow (Pzf) also reflects conditions of the coronary microcirculation tone, which may also be used as an index of coronary circulation[19].

The mechanism of the action of rotational atherectomy is the pulverizing of the atherosclerotic plaque by the blades of the atherectomy device. The technique is recommended for the treatment of long lesions, bifurcation lesions, and diffuse calcified lesions[20,21]. One major drawback to rotational atherectomy is the debris created by the procedure, which contains atheromatous and platelet-rich tissue that can easily embolize distally, clog the distal coronary vasculature and microcirculation, cause microcirculatory plugging, and result in slow flow[22−25]. The immediate post-procedural phase is therefore very important in rotational atherectomy, as the phase when the coronary microcirculation may be impaired by ablated debris. The present study assessed the influence of rotational atherectomy on the coronary microcirculation by analyzing CFR and the different parameters of the CFR loop.

SUBJECTS AND METHODS

Study population

Our population consisted of 31 stable angina pectoris patients who underwent rotational atherectomy, adjunctive balloon angioplasty and stent implantation and also were evaluated by intracoronary flow velocity with Doppler flow wire during the procedures and at mean follow-up of 6 months. None of the patients showed $>50\%$ diameter stenosis, or clinical restenosis at follow-up. The exclusion criteria used in this study included prior myocardial infarction, severe valvular heart disease, hypertrophic or dilated cardiomyopathy, triple vessel coronary disease, and left ventricular ejection fraction $<30\%$. Patients were further excluded by angiographic evidence of visible thrombus, lesion length >40 mm, presence of a chronic total occlusion, or evidence of good collateral supply to the target vessel. Prior to catheterization, all patients gave written informed consent to the study protocol, which had been approved by the Ethics Committee of the Showa General Hospital.

Rotational atherectomy and adjunctive coronary angioplasty

All rotational atherectomy procedures were performed in accordance with established techniques and a conventional anti-thrombotic strategy. A standard 7F or 8F angioplasty guiding catheter was positioned at the vessel ostium, and a 0.014-inch angioplasty guidewire advanced across the lesion. The guidewire was next exchanged for the rigid 0.009-inch rotational atherectomy guide wire using a 2.3F infusion catheter. Once the rotational atherectomy guidewire was in the correct position, the rotablator was advanced along the guiding catheter until in position at the lesion. The burr, rotating at 180,000−220,000 rpm, was then used to ablate the lesion. Generally, between 2 and 5 passes were used. Following ablation, adjunctive balloon angioplasty was performed, where necessary, to achieve optimal pre-stent conditions. All patients were then underwent stent placement. All patients received anti-platelet therapy of 100 mg of aspirin and 200 mg of ticlopidine a day for 6 months. Quantitative coronary angiography (QCA) data was analyzed using a computerized QCA system (QCA-CMS, Medis Medical Imaging System Co., Ltd.) before and after successful coronary dilation, and at mean follow-up of 6 months.

Doppler evaluation

After successful coronary dilation, a 0.014-inch Doppler guidewire (FloWire™, Volcano Therapeutics) was advanced into the treated vessel through a guiding catheter, and used to monitor the flow velocity pattern on a video display. Coronary flow velocities were measured in this way from single-cycle images using a FloMap™ (Volcano Therapeutics). Under the stable state, when the influence of ischemic reactive hyperemia by stenting was negligible, the Doppler velocities were obtained at both baseline levels and at peak hyper-

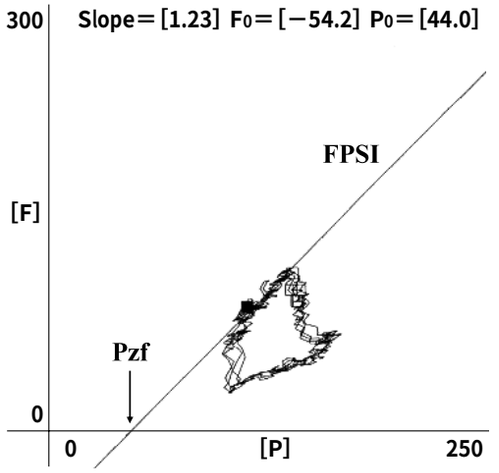

Fig. 1 Instantaneous assessment of the flow-pressure relationship
Pzf＝zero-flow pressure; FPSI＝flow-pressure slope index.

emia induced by bolus intracoronary injection of 25 to 50 μg adenosine. CFR was calculated as the ratio of hyperemic-to-baseline averaged peak velocity. We also calculated CFR in another untreated reference vessel without stenosis using identical methods, as a reference. Blood pressure, heart rate, and surface electrocardiographic leads were monitored continuously throughout the procedure.

Instantaneous assessment of the flow-pressure relationship

Coronary flow velocity and aortic pressure signals were digitized, and analyzed using a computer system (CORDYNAS, Research Institute of Cardiovascular Technology). The graph of coronary flow velocity versus aortic pressure was plotted (the flow-pressure loop), and Pzf and FPSI were calculated using the methods previously described[17]. As has been stated above, FPSI (cm/sec/mmHg) was defined as the slope of the regression of the linear portion of the flow-pressure loop in the late diastolic phase. The flow-pressure loop in the diastolic phase was analyzed using linear regression analysis to extrapolate the point where zero flow intercepted the pressure axis (Pzf). Data were recorded from the diastolic phases of at least four cardiac cycles for analysis and for calculating FPSI and Pzf (**Fig. 1**).

Statistical analysis

All data were expressed as mean ± SD. Comparisons of variables used Student's *t*-test. Correlations between total ablation times and CFR were evaluated using linear regression analysis. A p value < 0.05 was considered statistically significant.

Table 1 Patient characteristics

Age (yr)	67±9
Sex (male / female)	27 / 4
Coronary risk factor	
Diabetes mellitus	23 (74)
Hypertension	18 (58)
Hyperlipidemia	13 (42)
Smoking	13 (42)
ACC/AHA type	
A	0
B	27 (87)
C	4 (13)
Target vessel	
LAD	24 (77)
LCX	2 (6)
RCA	5 (16)
Lesion length (mm)	26±13
Reference diameter (mm)	2.70±0.60
Minimum lumen diameter (mm)	
Acute post-stenting	2.66±0.59
Follow-up	2.36±0.38
Total ablation time (sec)	61±21
Burr size (mm)	1.78±0.17
Slow-flow / no-reflow during RA	2 / 0
Significant ST elevation after RA	2
Stents used (including overlapping stents)	
Multi-Link	17
NIR	6
S670	15

Continuous values are mean±SD. ( ): %.
ACC/AHA＝American College of Cardiology/American Heart Association; LAD＝left anterior descending artery; LCX＝left circumflex artery; RCA＝right coronary artery; RA＝rotational atherectomy.

RESULTS

Patient characteristics

Baseline clinical and angiographic data are shown in **Table 1**. There were no differences in hemodynamics between just after rotational atherectomy and at follow-up (**Table 2**).

Table 2 Hemodynamics

	Just after rotational atherectomy	Follow-up	*p* value
Heart rate (beats/min)	77±10	72±12	NS
Systolic blood pressure (mmHg)	138±27	140±25	NS
Diastolic blood pressure (mmHg)	79±12	82±15	NS
Mean blood pressure (mmHg)	99±17	103±18	NS

Values are mean±SD.

Table 3 Coronary flow reserve, flow-pressure slope index, and zero-flow pressure in treated and untreated reference vessels without stenosis after rotational atherectomy

	Treated vessel	Untreated reference vessel without stenosis	*p* value
CFR	2.1±0.5	2.6±0.7	<0.05
FPSI (cm/sec/mmHg)	1.61±0.8	2.35±0.9	<0.05
Pzf (mmHg)	39.3±18	44.6±13	NS
APV (cm/sec)			
Baseline	29±12	23±10	<0.05
Hyperemia	59±13	62±15	NS

Values are mean±SD.
CFR=coronary flow reserve; APV=averaged peak flow velocity. Other abbreviations as in Fig. 1.

Coronary flow reserve, flow-pressure slope index, and zero-flow pressure in treated and untreated vessels without stenosis immediately after rotational atherectomy (Table 3)

CFR and FPSI in treated vessels were both significantly lower than those in untreated vessels without stenosis just after rotablation (CFR: 2.1±0.5 vs 2.6±0.7, $p<0.05$, FPSI: 1.61±0.8 vs 2.35±0.9 cm/sec/mmHg, both $p<0.05$), but there were no significant differences in Pzf between target and reference arteries. Baseline coronary flow velocities in the treated vessels were also higher than those in the untreated vessels without stenosis (29±12 vs 23±10, $p<0.05$), but there were no differences in coronary flow velocity during hyperemia.

Correlation between total ablation time and coronary flow reserve

There was a significant positive correlation between total ablation time and CFR just after rotational atherectomy ($r=-0.54$, $p<0.01$). Details are shown in **Fig. 2**.

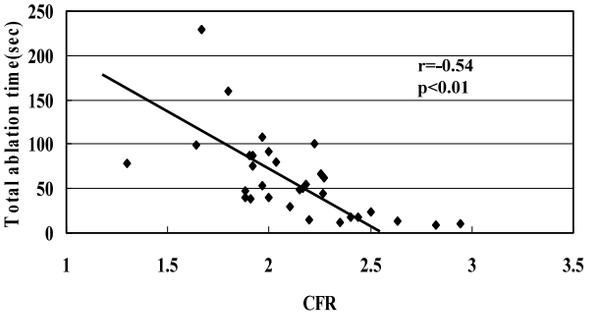

Fig. 2 Correlation between total ablation time and coronary flow reserve
Abbreviation as in Table 3.

Coronary flow reserve, flow-pressure slope index, and zero-flow pressure in treated and untreated vessels without stenosis at follow-up (Table 4)

At mean 6 months follow-up, we observed no significant differences in CFR, FPSI or Pzf between treated and untreated vessels without stenosis. Similarly, there were no differences in coronary flow velocity at baseline and at hyperemia between the treated vessels and untreated vessels without stenosis.

Table 4 Coronary flow reserve, flow-pressure slope index, and zero-flow pressure in treated and untreated reference vessels without stenosis at follow-up

	Treated vessel	Untreated reference vessel without stenosis	*p* value
CFR	2.4±0.5	2.6±0.6	NS
FPSI (cm/sec/mmHg)	1.96±0.7	2.29±0.8	NS
Pzf (mmHg)	41.3±16	39.7±15	NS
APV (cm/sec)			
Baseline	25±11	24±12	NS
Hyperemia	61±15	63±16	NS

Values are mean±SD.
Abbreviations as in Fig. 1, Table 3.

DISCUSSION

Our findings in this study suggest that rotational atherectomy may be detrimental to coronary microvascular function, as reflected by impaired CFR and coronary conductance.

Rotational atherectomy works by pulverizing the atherosclerotic plaque, and the resultant debris can embolize distally, causing microcirculatory plugging. Experimental studies have suggested that the debris is usually small enough to pass right through into the capillary circulation to be subsequently removed by the reticulo-endothelial system[26]. In the clinical setting, however, angiography following rotational atherectomy has indicated the slow flow or the no-reflow phenomenon in 7−8% of patients, in turn associated with myocardial infarction, electrocardiographic evidence of ischemia and creatine kinase-myocardial band elevation[23,27].

Investigation of the effect of rotational atherectomy on coronary blood flow concluded that rotational atherectomy and adjunctive balloon angioplasty in the conduit coronary vessels significantly improved coronary flow velocity[24]. Although CFR increased to some extent, it was still impaired despite excellent luminal enlargement by angiography, therefore, adjunctive balloon angioplasty could contribute significantly to the overall physiological benefit of combined procedure. The present study examined mainly the effects on coronary microcirculation. We also analyzed FPSI and Pzf, the parameters which could evaluate coronary conductance just after rotational atherectomy and at follow-up.

In this study, CFR in the treated stenotic vessels was significantly lower than that in the untreated vessels without stenosis just after rotablation. This decrease in CFR could be explained mostly by the statistically significant increase in the baseline flow velocity in the ablated vessel, because we could not show any statistically significant difference between hyperemic flow velocities in treated vessels and those in untreated vessels without stenosis just after rotational atherectomy. Animal studies[28,29]demonstrated that coronary blood flow increased linearly to about 175% of its control level by embolizing the coronary vascular bed with 15 μm microspheres, about the same diameter as the particles ablated by a rotablator burr[26]. About 37% of the total material ultimately embolized, but thereafter decreased almost linearly as the degree of embolized material increased. In their study, embolization with 300 μm microspheres minimally increased coronary blood flow. The hyperemic coronary blood flow, however, remained unchanged under this condition. A marked increase in adenosine concentration of blood samples obtained from the coronary vein was also observed. We estimate that minimal microvascular embolism with small particles such as ablated debris might induce only slight reduction of the hyperemic flow velocity as found in our study.

In the present study, we also observed a correlation between total ablation time and CFR just after rotational atherectomy, which may reflect linearly-increasing baseline flow velocities. Therefore, the potential mechanism of reduced CFR after rotational atherectomy would seem to be micro-embolization of the ablated particles, in concert with a hyperemic response in terms of baseline flow velocity, probably due to the release of adenosine from the ischemic myocardium.

The hyperemic response induced by transient ischemia during stenting could not be the reason for the increased baseline flow velocity. Although we

did not examine the effect of ischemia induced by stenting on the baseline flow velocity in this study, our previous study demonstrated that hyperemic response to ballooning without visible slow flow by angiography did not last more than several minutes[30].

FPSI is the index most closely related to subendocardial coronary conductance during hyperemia, and is almost independent of perfusion pressure[14–17]. In the present study, FPSI in treated vessels was lower than that in our untreated vessels without stenosis, which may indicate a reduction in coronary conductance during hyperemia. Embolization of coronary artery with repeated injection of small microspheres decreased the mean reactive hyperemic flow slightly, but the reduction was not statistically significant[29]. We also observed this slight but not statistically significant reduction in hyperemic flow velocity in the treated vessels compared with those in the untreated vessels without stenosis. So one of the mechanisms by which FPSI was reduced just after rotational atherectomy might be increased microvascular resistance because of micro-embolization of the debris generated during debulking of the lesion.

In this study, hyperemic FPSI was lower in treated coronary vessels with rotational atherectomy than that in control vessels without stenosis despite the higher basal coronary flow velocity in the treated vessels, indicating that the coronary artery conductance might be increased transiently after debulking with rotational atherectomy. Because we did not measure the basal FPSI in this study, we expect that the debris might have slightly increased the conductance transiently as a result of adenosine release. However, we could not neglect the possibility that residual focal stenosis, which could not be detected by angiography in the treated epicardial coronary artery even just after rotablation, might have contributed to the reduced FPSI. As we used aortic pressures instead of intracoronary pressures to determine FPSI, values of FPSI could be lower in the presence of coronary stenosis as the pressure-flow loop would be modified because intracoronary pressure might be lower than that in aorta. FPSI should be determined ideally by measuring intracoronary pressure in patients with coronary stenosis and even in patients with coronary luminal narrowing as indicated by the luminal reduction from 2.66 to 2.36 mm at follow-up. There was significant positive correlation between total ablation time and CFR, but there was no significant correlation between baseline coronary flow velocity and total ablation time ($r = 0.22$), as the decrease in CFR was probably due not only to the increased basal coronary flow velocity but also to the reduced hyperemic coronary flow velocity.

Pzf is an index of coronary circulation which might reflect coronary microvascular tone and is obtained as the intercept of the PFSI slope at zero flow. Pzf increases when the perfusion bed mass decreases, as in a patient with acute myocardial infarction[18,19]. In our study, we could not demonstrate an increase in Pzf just after rotational atherectomy compared with that in the non-stenotic coronary artery. One of the reasons might be that the Pzf index is not so sensitive unless corrected with cardiac mass, especially if values of FPSI are low as in our study. Another reason is that we used aortic pressures instead of intracoronary pressures for the detection of Pzf as in determining FPSI, so the intercept of the FPSI slope might have shifted to the left if FPSI is low in the presence of residual coronary artery stenosis even after atherectomy, so Pzf might reveal lower than the real values.

The exact effects of rotational atherectomy on FPSI and Pzf are therefore somewhat unclear, but increased microvascular resistance due to platelet aggregation, activation of neutrophils, micro-embolization of the debris generated by lesion debulking, and microvascular spasm would seem to be critical.

We experienced two patients with coronary slow flow just after rotational atherectomy. Coronary slow flow was not so serious as ST elevation was transient, and neither patient showed a significant rise in creatin phosphokinase levels. CFR just after rotational atherectomy was 1.9 and 2.0, and FPSI was 1.58 and 2.01, respectively. There were no significant differences in coronary flow velocity pattern between these patients and the others.

We could not neglect the possibility that rotational atherectomy might induce micro-vascular spasm, which had an effect on coronary blood flow as shown in our study, although nitroglycerin was continuously administered during the procedures of rotational atherectomy. Recently, the effectiveness of nicorandil on preventing flow disturbance during rotational atherectomy was reported[22]. Nicorandil improved coronary microcirculation and also dilated epicardial coronary arteries, so relieved refractory coronary spasm. In this study, we used nitroglyc-

erin for coronary dilation, so we cannot say whether nicorandil administration is more suitable than nitroglycerin to prevent coronary spasm after rotational atherectomy. Further study is necessary to evaluate this point.

Limitations

Coronary microcirculation is affected by the stenosis of epicardial blood vessels as was proved using the pressure wire[31]. In this study, we removed the local stenosis by stenting in all cases. However, the focal epicardial coronary artery stenosis, which can be evaluated only with pressure wire or intracoronary ultrasonography, might have affected the CFR to some extent. To exclude the influences of stent implantation on coronary flow velocity, we have to measure flow velocities in the two vessels in the same patient after stenting with and without rotational atherectomy. Relative CFR[32], a new index which is defined as the ratio of the CFR in treated vessel to the reference CFR measured in the coronary artery without stenosis, is considered to be a good predictor for the long-term result. Relative CFR is the index based on the premise that CFR in the treated vessel and untreated reference vessel were similar. Therefore, we chose the untreated vessels without stenosis as the reference vessel in this study.

CONCLUSIONS

Rotational atherectomy may attenuate CFR as a result of a reduction in coronary artery conductance immediately following rotablation. The mechanism would seem to be microvessel obstruction by the debris ablated during rotational atherectomy.

要　　約

狭心症患者における高速回転式アテレクトミーの冠微小循環に与える影響

田中　茂博　　清 水　寛　　石原有希子

矢野　幸平　　定　利 勝　　吉良　有二

目　的: 高速回転式アテレクトミーによる粥腫切削後，その切削片が冠微小循環に悪影響を及ぼす可能性があるという報告はあるが，高速回転式アテレクトミーが冠微小循環にいかなる影響を与えるかについての報告はない．本研究は，冠予備能および冠血流速度−圧ループの解析から高速回転式アテレクトミーが冠微小循環に与える影響を検討した．

方　法: 高速回転式アテレクトミー施行後にステントを留置し，6ヵ月後の慢性期の冠動脈造影により残存狭窄が50%以下で再狭窄が認められなかった狭心症患者31例を対象とした．高速回転式アテレクトミー施行後および6ヵ月後に，治療対象冠動脈および狭窄を有さない対照冠動脈にそれぞれドプラーガイドワイヤーを挿入して冠予備能を測定した．さらに，冠血流速度−圧ループの解析からflow-pressure slope index（FPSI）およびzero-flow pressureを求めた．

結　果: 高速回転式アテレクトミー後における治療対象冠動脈の冠予備能とFPSIは，対照冠動脈に比べて有意に低値であった（冠予備能 2.1±0.5 vs 2.6±0.7，$p<0.05$; FPSI: 1.61±0.8 vs 2.35±0.9 cm/sec/mmHg，$p<0.05$）．しかしながら，6ヵ月後には治療対象冠動脈と対照冠動脈間で冠予備能とFPSIに差は認められなかった．また，冠予備能と総切削時間では有意な負の相関関係が認められた（$r=-0.54$，$p<0.01$）．

結　論: 高速回転式アテレクトミー後に冠予備能が低下する機序として，高速回転式アテレクトミー直後に生じた切削片により冠末梢血管が閉塞し，冠動脈のコンダクタンスが低下する可能性が示唆された．

J Cardiol 2005 Aug; 46(2): 43−51

References

1) Doucette JW, Corl PD, Payne HM, Flynn AE, Goto M, Nassi M, Segal J: Validation of Doppler guide wire for intravascular measurement of coronary artery flow velocity. Circulation 1992; **85**: 1899−1911
2) Serruys PW, di Mario C, Piek J, Schroeder E, Vrints C, Probst P, de Bruyne B, Hanet C, Fleck E, Haude M, Verna E, Voudris V, Geschwind H, Emanuelssen H, Muhlberger V, Danzi G, Peels HO, Ford AJ Jr, Boersma E: Prognostic value of intracoronary flow velocity and diameter stenosis in assessing the short- and long-term outcomes of coronary balloon angioplasty: The DEBATE Study (Doppler Endpoints Balloon Angioplasty Trial Europe). Circulation 1997; **96**: 3369−3377
3) Baumgart D, Haude M, Liu F, Ge, J, Goerge G, Erbel R: Current concepts of coronary flow reserve for clinical decision making during cardiac catheterization. Am Heart J 1998; **136**: 136−149
4) Lepper W, Hoffmann R, Kamp O, Franke A, de Cock CC, Kuhl HP, Sieswerda GT, vom Dahl J, Janssens U, Voci P, Visser CA, Hanrath P: Assessment of myocardial reperfusion by intravenous myocardial contrast echocardiography and coronary flow reserve after primary percutaneous transluminal coronary angioplasty in patients with acute myocardial infarction. Circulation 2000; **101**: 2368−2374
5) Palombo C, Kozakova M, Magagna A, Bigalli G, Morizzo C, Ghiadoni L, Virdis A, Emdin M, Taddei S, L'Abbate A, Salvetti A: Early impairment of coronary flow reserve and increase in minimum coronary resistance in borderline hypertensive patients. J Hypertens 2000; **18**: 453−459
6) Yokoyama I, Ohtake T, Momomura S, Nishikawa J, Sasaki Y, Omata M: Reduced coronary flow reserve in hypercholesterolemic patients without overt coronary stenosis. Circulation 1996; **94**: 3232−3238
7) Nahser PJ Jr, Brown RE, Oskarsson H, Winniford MD, Rossen JD: Maximal coronary flow reserve and metabolic coronary vasodilation in patients with diabetic mellitus. Circulation 1995; **91**: 635−640
8) Chauhan A, Mullins PA, Petch MC, Schofield PM: Is coronary flow reserve in response to papaverine really normal in syndrome X? Circulation 1994; **89**: 1998−2004
9) Hamasaki S, Suwaidi JA, Higano ST, Miyauchi K, Holmes DR Jr, Lerman A: Attenuated coronary flow reserve and vascular remodeling in patients with hypertension and left ventricular hypertrophy. J Am Coll Cardiol 2000; **35**: 1654−1660
10) Reis SE, Holubkov R, Lee JS, Sharaf B, Reichek N, Rogers WJ, Walsh EG, Fuisz AR, Kerensky R, Detre KM, Sopko G, Pepine CJ: Coronary flow velocity response to adenosine characterizes coronary microvascular function in women with chest pain and no obstructive coronary disease: Results from the pilot phase of the Women's Ischemia Syndrome Evaluation (WISE) study. J Am Coll Cardiol 1999; **33**: 1469−1475
11) Jeremias A, Filardo SD, Whitbourn RJ, Kernoff RS, Yeung AC, Fitzgerald PJ, Yock PG: Effects of intravenous and intracoronary adenosine 5′-triphosphate as compared with adenosine on coronary flow and pressure dynamics. Circulation 2000; **101**: 318−323
12) Hoffman JIE: Maximal coronary flow and the concept of coronary vascular reserve. Circulation 1984; **70**: 153−159
13) Klocke FJ: Measurements of coronary flow reserve: Defining pathophysiology versus making decisions about patients care. Circulation 1987; **76**: 1183−1189
14) Di Mario C, Krams R, Gil R, Serruys PW: Slope of the instantaneous hyperemic diastolic coronary flow velocity-pressure relation: A new index for assessment of the physiological significance of coronary stenosis in humans. Circulation 1994; **90**: 1215−1224
15) Di Mario C, Gil R, Sunamura M, Serruys PW: New concepts for interpretation of intracoronary velocity and pressure tracings. Br Heart J 1995; **74**: 485−492
16) Kondo M, Azuma A, Yamada H, Kohno H, Kawata K, Tatsukawa H, Ohnishi K, Kohno Y, Asayama J, Nakagawa M: Estimation of coronary flow reserve with the instantaneous coronary flow velocity versus pressure relation: A new index of coronary flow reserve independent of perfusion pressure. Am Heart J 1996; **132**: 1127−1134
17) de Bruyne B, Bartunek J, Sys SU, Pijls NHJ, Heyndrickx GR, Wijns W: Simultaneous coronary pressure and flow velocity measurements in humans: Feasibility, reproducibility, and hemodynamic dependence of coronary flow velocity reserve, hyperemic flow versus pressure slope index, and fractional flow reserve. Circulation 1996; **94**: 1842−1849
18) Mancini GBJ, Cleary RM, DeBoe SF, Moore NB, Gallagher KP: Instantaneous hyperemic flow-versus-pressure slope index: Microsphere validation of an alternative to measures of coronary resreve. Circulation 1991; **84**: 862−870
19) Shimada K, Sakanoue Y, Kobayashi Y, Ehara S, Hirose M, Nakamura Y, Fukuda D, Yamagishi H, Yoshiyama M, Takeuchi K, Yoshikawa J: Assessment of myocardial viability using coronary zero flow pressure after successful angioplasty in patients with acute anterior myocardial infarction. Heart 2003; **89**: 71−76
20) Warth DC, Leon MB, O'Neill W, Zacca N, Polissar NL, Buchbinder M: Rotational atherectomy multicenter registry: Acute results, complications and 6-month angiographic follow-up in 709 patients. J Am Coll Cardiol 1994; **24**: 641−648
21) Ellis SG, Popma JJ, Buchbinder M, Franco I, Leon MB, Kent KM, Pichard AD, Satler LF, Topol EJ, Whitlow PL: Relation of clinical presentation, stenosis morphology, and operator technique to the procedural results of rotational atherectomy and rotational atherectomy-facilitated angioplasty. Circulation 1994; **89**: 882−892
22) Tsubokawa A, Ueda K, Sakamoto H, Iwase T, Tamoki S: Effect of intracoronary nicorandil administration on preventing no-reflow / slow flow phenomenon during rotational atherectomy. Circ J 2002; **66**: 1119−1123
23) Kini A, Reich D, Marmur JD, Mitre CA, Sharma SK: Reduction in periprocedual enzyme elevation by abciximab after rotational atherectomy of type B2 lesions: Results of the Rota ReoPro randomized trial. Am Heart J 2001; **142**: 965−969
24) Bowers TR, Stewart RE, O'Neill WW, Reddy VM, Safian RD: Effect of Rotablator atherectomy and adjunctive balloon angioplasty on coronary blood flow. Circulation 1997; **95**: 1157−1164
25) Williams MS, Coller BS, Vaananen HJ, Scudder LE,

Sharma SK, Marmur JD: Activation of platelets in platelet-rich plasma by rotablation is speed-dependent and can be inhibited by abciximab (c7E3 Fab; ReoPro). Circulation 1998; **98**: 742−748
26) Hansen DD, Auth DC, Vracke R, Ritchie JL: Rotational atherectomy in atherosclerotic rabbit iliac arteries. Am Heart J 1988; **115**: 160−165
27) Safian RD, Niazi KA, Strzelecki M, Lichtenberg A, May MA, Juran N, Freed M, Ramos R, Gangadharan V, Grines CL, O Neill WW: Detailed angiographic analysis of high-speed mechanical rotational atherectomy in human coronary arteries. Circulation 1993; **88**: 961−968
28) Hori M, Tamai J, Kitakaze M, Iwakura K, Gotoh K, Iwai K, Koretsune Y, Kagiya T, Kitabatake A, Kamada T: Adenosine-induced hyperemia attenuates myocardial ischemia in coronary microembolization in dogs. Am J Physiol 1989; **257**: H244−H251.
29) Hori M, Inoue M, Kitakaze M, Koretsune Y, Iwai K, Tamai J, Ito H, Kitabatake A, Sato T, Kamada T: Role of adenosine in hyperemic response of coronary blood flow in microembolization. Am J Physiol 1986; **250**: H509−H518
30) Tanaka T, Nonogi H, Miyazaki S, Goto Y, Itoh S, Daikoku S, Yamamoto Y: Enhancement of coronary reactive hyperemia in patients with ischemic myocardial tolerance during angioplasty. Heart Vessels 1996; **11**: 242−247
31) De Bruyne B, Hersbach F, Pijls NHJ, Bartunek J, Bech JW, Heyndrickx GR, Gould LK, Wijns W: Abnormal epicardial coronary resistance in patients with diffuse atherosclerosis but "Normal" coronary angioplasty. Circulation 2001; **104**: 2401−2406
32) van Liebergen RAM, 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**: 2133−2142