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Effects of Selective α_1- and α_2-Adrenergic Blockade on Coronary Flow Reserve After Coronary Stenting

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Background—Coronary flow reserve (CFR) is not normalized shortly after coronary stenting. We hypothesized that α-adrenergic coronary vasoconstriction acts to limit CFR.

Methods and Results—We assessed flow velocity by Doppler wires and cross-sectional area by angiography in 46 patients undergoing coronary culprit lesion stenting ($81\pm4\%$ stenosis). Hyperemia was induced by adenosine (24 μg IC or 140 μg/kg per minute IV) before and after stenting. Finally, either the α_1-antagonist urapidil (10 mg IC) or the α_2-antagonist yohimbine (3 mg IC) was randomly combined with adenosine. In 8 subjects with angiographically normal coronary arteries, CFR was increased from 3.21 ± 0.30 to 3.74 ± 0.43 by yohimbine and to 4.58 ± 0.65 by urapidil, respectively ($P=0.0001$). Patients were divided according to the cutoff of CFR ≥3.0 (n=18) or <2.5 (n=28). Revascularization per se did not change CFR. However, 15 minutes after stenting, CFR decreased to 2.05 ± 0.55 from CFR 3.64 ± 0.58, whereas in patients with CFR 2.39 ± 0.51, it remained unchanged. Yohimbine improved CFR to 3.26 ± 0.42 and to 3.41 ± 0.58 in patients with >3.0 and $<2.05\pm0.55$ baseline CFR, respectively. Urapidil improved CFR to 3.52 ± 0.30 and 3.98 ± 1.07, respectively.

Conclusions—Urapidil and yohimbine attenuated the CFR impairment occurring after revascularization by increasing both the epicardial vasodilator effect of adenosine and the blood flow velocity, thus suggesting that the adrenergic system plays an important role in limiting the capacity of the coronary circulation to dilate. (***Circulation***. 2002;106:2901-2907.)

Key Words: adenosine ■ blood flow ■ microcirculation ■ nervous system, sympathetic ■ receptors, adrenergic, alpha

A fter stenting, coronary flow reserve is not immediately normalized.[1–3] We have recently shown that angioplasty and stenting induce a diffuse α-adrenergic coronary vasoconstriction in the epicardial vessels and in the microcirculation that acts to limit coronary blood flow and contractile function.[4–6] Such α-adrenergic coronary vasoconstriction was antagonized by intracoronary phentolamine and intravenous urapidil, a selective α_1-antagonist. α-Adrenergic microvascular coronary constriction is predominantly mediated by α_2-adrenoceptors in dogs[7,8] and in humans.[9,10] Therefore, in the present study, we analyzed the effects of selective α_1- and α_2-antagonists on the recovery of coronary flow reserve (CFR) in patients after stenting. We divided patients according to the cutoff value of CFR >3.0 or <2.5, because a value >3.0 is considered normal in clinical practice.[1–3]

Methods

Patients

We enrolled 46 patients with unstable or effort angina who had the indication for coronary revascularization and underwent coronary stenting. Patients with CFR >3.0 and <2.5 were 54 ± 8 and 56 ± 9 years of age, respectively (NS). Six patients were female. Patients with CFR >3.0 had a severe effort angina. Twenty-three subjects with angiographically normal coronary arteries (age 48 ± 7 years) served as controls. Fifteen controls had a 4.77 ± 0.58 CFR and had 3 consecutive CFR measurements over 15 minutes to assess its reproducibility. Eight controls with a 3.10 ± 0.35 CFR (age, 53 ± 8 years) underwent the full protocol. All patients and controls gave informed written consent to the study. The Clinique Pasteur Ethical Committee previously approved the study.

Calcium antagonists, long-acting nitrates, and ACE inhibitors were discontinued 12 hours before angioplasty. Low-molecular-weight heparin (Enoxaparin, Rhône-Poulenc Rorer, 2 mg/kg per day in 2 divided subcutaneous doses) was given before the procedure to 20 patients for 3 days. Intravenous nitrates were discontinued 30
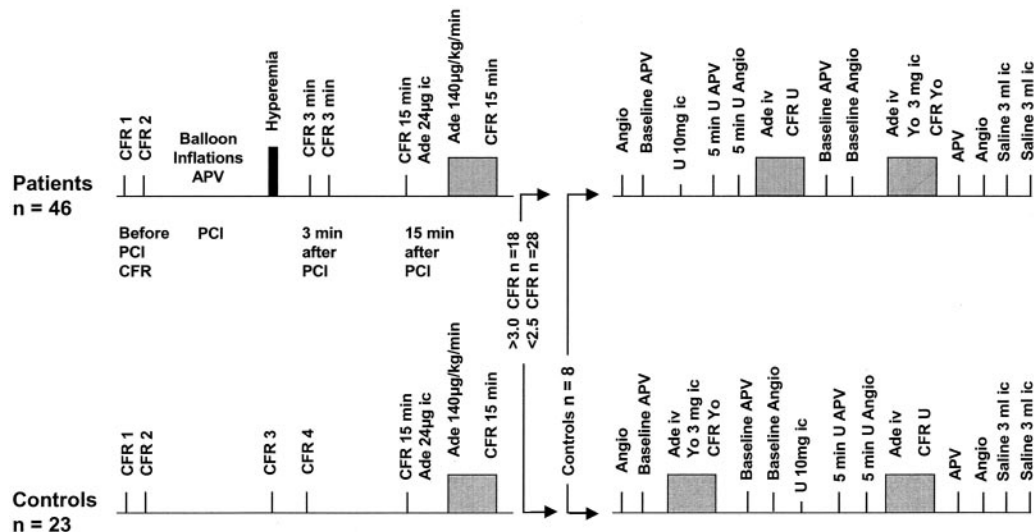
Figure 1. Protocol scheme and time course of CFR measurements during revascularization (PCI). APV was continuously acquired. Adenosine (Ade) was given intracoronary (24-μg IC bolus) or intravenously (140 μg/kg per minute for 5 minutes). Patients and subjects with apparently normal coronary arteries were randomized to receive urapidil (U) or yohimbine (Yo). CFR was calculated by dividing hyperemic by baseline blood flow. In each condition, an angiogram (angio) was performed to obtain the cross-sectional area.

minutes before the procedure. In all patients, the baseline flow velocity measurements were repeated at the end of the revascularization procedure (60 minutes) to investigate the time effect.

Angiographic Analysis Methods
Automatic contour detection was performed in duplicate in the catheterization laboratory and offline by quantitative angiography, as previously described.[4–6] An angiogram was performed at each step of the procedure. The cross-sectional area (CSA) measured at the Doppler guidewire tip was used to calculate coronary blood flow.

Coronary Flow Velocity, Coronary Blood Flow, and Coronary Flow Reserve
Coronary blood flow velocity (CBFV) was measured as average peak velocity in centimeters per second (APV) using a Doppler-tipped guidewire of 0.014-inch diameter with a 12-MHz piezoelectric ultrasound transducer at its tip (Cardiometrics JOMED).[11] The guidewire was positioned in a distal epicardial vessel (2.34±0.22-mm diameter) at the beginning of the procedure and left in place until the end of the study. APV was continuously recorded, because the Doppler guidewire was only shortly disconnected for insertion of balloons or stents.

Coronary blood flow velocity reserve (CFVR) was calculated as the ratio of maximal coronary flow velocity to baseline flow velocity with the search option of the maximal hyperemic APV that is supplied with the Cardiometrics software. A blinded reader measured offline the peak effect on flow velocity induced by α_1- and α_2-adrenergic blockade superimposed on top of adenosine infusion. CBF (mL/min) was calculated by multiplying APV and CSA of the vessel just distal to the flow wire tip, assuming a parabolic flow velocity profile. CFR was calculated as the ratio of maximal hyperemic coronary blood flow to baseline blood flow.

Coronary Stenting
Coronary stenting was performed in our patients both to reduce restenosis rate[12] and to avoid residual stenosis that may in part be responsible for the limitation of CFR.[1] Stent delivery was performed either by the transfemoral (25% of cases) or the transradial approach (75% of cases). The angiographic images were acquired with a Philips-Integris H 3000 single-plane system. Unfractionated heparin (100 IU/kg) was given intravenously as anticoagulant. In addition, patients were pretreated with 250 mg/d aspirin for ≥7 days and 250 mg/BID ticlopidine or 75 mg/d clopidogrel for 72 hours preceding

the procedure. Meglumine ioxaglate (64 g iodine/200 mL) was used as a nonionic contrast medium. Neuroleptic analgesia was given at the beginning of the procedure (droperidol 2 to 10 mg IV and phenoperidine 0.6 to 1 mg IV), as previously reported.[4–6] Isosorbide dinitrate (1.5 mg IC) was administered to measure the normal reference diameter in an angiographically normal segment adjacent to the lesion and to calculate the percent diameter stenosis. Repeated balloon inflations were performed to optimize the stent expansion.

Protocol
The study protocol is shown in Figure 1. In all patients the baseline CFR was obtained in duplicate with intracoronary bolus injection of 24 μg adenosine.[13] CFR measurements were repeated 3 minutes after coronary stenting and 15 minutes later, when coronary vasoconstriction and LV dysfunction had been previously documented.[4–6] Fifteen minutes after stenting in 38 patients, the CFR measurements were repeated to compare the effects of intracoronary adenosine (24-μg bolus) with the intravenous infusion (140 μg/min in 5 minutes). As previously reported,[13,14] these doses of adenosine induced identical blood flow velocity responses.

Two ECG leads were continuously recorded. Systolic, diastolic, and mean blood pressures were measured through the guiding catheter at the coronary ostium.

Patients received an intracoronary bolus of both the selective α_1-antagonist urapidil (10 mg, Ebrantil, 50-mg vials, Byk Gulden)[5,6] and the selective α_2-antagonist yohimbine (3 mg, Streuli G & Co)[4,15] in randomized sequence on top of or before intravenous adenosine. Urapidil and yohimbine were diluted in 3 mL saline. A second bolus of 3 mL saline was given to wash the guiding catheter. In the 28 patients with a basal CFR <2.5, the α_1-antagonist urapidil was injected 5 minutes before adenosine instead of on top of adenosine to test the effect of the drug on basal APV. We have previously observed that urapidil (10 mg IC) achieves maximal coronary dilation 5 to 8 minutes after intracoronary injection.[16] Accordingly, the adenosine infusion (140 μg/kg per minute over 5 minutes) was started 5 minutes after urapidil injection and after measuring the effects induced by urapidil per se on blood flow velocity and coronary diameters.

Warm saline as vehicle or angiographic contrast media[17] per se has a vasodilator action when injected into the coronary circulation. Accordingly, in our patients, we evaluated the changes in blood flow velocity induced both by contrast medium (meglumine ioxaglate, 6

TABLE 1. Coronary Flow Reserve

Time	Condition	≥3.0 CFR Patients n=18				<2.5 CFR Patients n=28				≥3.0 CFR Controls n=8			
		APV	CSA	BF	CFR	APV	CSA	BF	CFR	APV	CSA	BF	CFR
Before	Baseline	11.1±5.0‡	4.9±0.9	33.7±21.3‡		14.7±4.7§†‡	3.0±1.1*	26.6±11.6		10.8±2.5‡	5.5±0.4	35.8±9.5‡	
PCI	Adenosine	35.5±16.3‡	5.5±0.9	119.9±71.6‡	3.64±0.58§‡	29.8±9.0	3.5±1.2	59.5±21.9§	2.39±0.51§	29.4±5.6†	6.2±0.5	110.1±25.4‡	3.10±0.35‡
3 min after	Baseline	12.3±5.1‡	5.0±1.0	37.6±21.1‡		26.8±5.5‡	3.8±1.4†	59.8±21.3†		10.4±1.8‡	5.4±0.4	33.9±6.1‡	
Stenting	Adenosine	39.3±16.6‡	5.4±1.1	129.1±67.3§	3.55±0.54§‡	52.8±17.4§	4.4±1.4	135.6±57.6	2.27±0.46	29.8±5.1†‡	6.2±0.3	109.9±19.3‡	3.26±0.34‡
15 min after	Baseline	15.9±4.6§‡	4.4±1.2	43.2±20.6		27.2±6.7‡	2.9±1.3†	47.4±26.9		10.4±1.6‡	5.5±0.4	34.2±5.8‡	
Stenting	Adenosine	31.8±14.1‡	4.6±1.2	91.8±55.7‡§	2.05±0.55§	50.6±13.8‡	3.5±1.5	110.0±62.6	2.35±0.39	29.4±4.2†‡	6.2±0.3	109.0±16.1†‡	3.21±0.30†‡
>15 min after	Baseline	15.9±4.6*‡	4.4±1.2	43.2±20.6		24.9±6.2†	2.9±1.7†	42.2±22.5		10.8±2.5†‡	5.5±0.4	35.7±8.7	
Stenting	Adenosine	35.7±12.5*‡				48.8±11.1†‡	3.5±1.5	135.0±63.8		29.5±4.6†‡	6.2±0.3	109.0±16.1	
α₂Block and	Adenosine	45.2±14.2§‡	5.0±1.2	138.4±70.5	3.26±0.42§	60.8±14.4‡	3.9±1.8	142.1±77.0	3.41±0.58§	33.6±5.3‡	6.5±0.3	131.7±23.6	3.74±0.43†‡
5 min α₁ Block	Urapidil 5		5.7±1.4			20.7±4.7	4.0±1.7	49.1±26.6		8.4±1.6‡	6.2±0.4	31.0±6.3	
8 min α₁ Block	Adenosine	49.3±12.0§‡	6.2±1.6	186.4±70.6‡§	3.52±0.30§‡	65.6±19.1†	4.9±2.1	499.7±123.6	3.98±1.07§†	35.7±4.6†‡	7.5±0.6†‡	160.0±28.6†‡	4.58±0.65†‡

Between groups: †P<0.05 vs ≥3.0 CFR, ‡P<0.05 vs CFR <2.5, §P<0.05 vs Controls.
Within groups: *P<0.05, **P=0.001, ***P=0.0001.

to 8 mL) and by vehicle saline. Saline was injected intracoronary both at baseline and on top of intravenous adenosine infusion.

Statistical Analysis

Results are expressed as mean±SD. One- or two-way ANOVA for repeated measures was performed with the commercially available package SPSS version 11.0 (SPSS Inc). To assess statistical significance between controls and patients, Scheffé F tests were applied, and a value of $P<0.05$ was considered significant. Covariance analysis was used to account for different baseline cross-sectional areas. Agreement between the two observers' readings was evaluated estimating the consistent bias between measurements, as recommended by Bland and Altman.[18]

Results

Coronary Stenting

Patients with CFR >3.0 and <2.5 had an 80±3% and 82±6% diameter stenosis, respectively (NS). No residual in-stent stenosis was present after coronary stenting.

Adverse Adenosine Effects

Adenosine infusion induced atrial fibrillation in 2 patients and transient complete AV block in 5. These patients were not included in the study.

Coronary Blood Flow Velocity

The mean difference in blood flow velocity responses to intracoronary and intravenous adenosine in 38 patients 15 minutes after stenting was 0.03±2.219 cm/s or 5.6±4.2%, respectively.[17] The intracoronary injection of 3 mL saline on top of intravenous adenosine infusion elicited an additional 19.9±7.5% increase in APV ($P<0.05$). This increase was limited to the injection time and lasted 2.9±1.5 seconds. The intracoronary injection of saline in the absence of adenosine elicited an APV increase of 27.4±8.2% ($P<0.05$). The effect lasted for 5.4±1.5 seconds.

Before revascularization, APV was 11.1±5.0 and 14.7±4.7 cm/s in patients with CFR >3.0 and CFR <2.5,

respectively ($P<0.05$, Table 1). Soon after balloon deflation, a short-lasting hyperemia was observed. Hyperemic APV was 46.1±8.0 and 32.6±3.6 cm/s, respectively. Three minutes after balloon deflation, APV decreased to 12.3±5.1 ($P=$NS versus before percutaneous coronary intervention [PCI]) and to 26.8±5.5 cm/s ($P=0.001$ versus before PCI). These values were unchanged at the end of the study, when the effect of drugs had vanished.

In the group with CFR <2.5, in which urapidil was injected before adenosine, urapidil decreased APV to 20.7±4.7 cm/s ($P=0.001$ versus 3 minutes stenting), whereas the adenosine infusion given on top of urapidil's peak effect potentiated the hyperemia, reaching 65.6±19.1 cm/s.

When urapidil was injected before adenosine in control subjects, no major changes in APV were observed. In both patient groups, yohimbine superimposed on top of adenosine additionally potentiated the effect of adenosine alone ($P=0.001$).

Cross-Sectional Area

Before revascularization, adenosine significantly increased epicardial CSA from 4.9±0.9 to 5.5±0.9 mm² and from 3.0±1.1 to 3.5±1.2 mm² in patients with CFR >3.0 and <2.5, respectively. Also in controls, adenosine significantly increased CSA from 5.7±1.0 to 7.2±1.1 mm² and from 5.5±0.4 to 6.2±0.5 mm² in subjects with CFR 4.77±0.58 ($P=0.0001$) and with CFR 3.10±0.35 ($P<0.05$), respectively. When yohimbine was superimposed on top of adenosine, CSA increased from 4.4±1.2 to 5.0±1.2 mm² and from 2.9±1.7 to 3.9±1.8 mm² ($P=0.0001$) in patients with CFR >3.0 and <2.5, respectively. Also, in controls who underwent the full drug protocol, yohimbine increased CSA from 5.5±0.4 to 6.5±0.3 mm² ($P=0.0001$). As previously reported,[5,6] urapidil increased coronary CSA from 4.4±1.2 to 5.7±1.4 mm² and from 2.9±1.7 to 4.0±1.7 mm² in the 2 groups of patients, respectively. When adenosine was super-
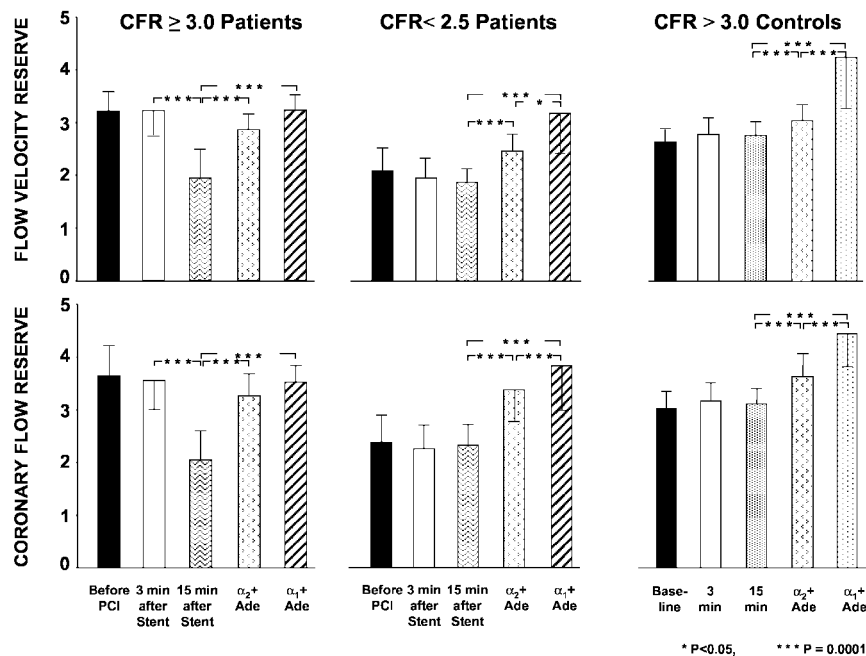
Figure 2. The bars show coronary flow velocity reserve and coronary flow reserve in patients and in controls after superimposing yohimbine or urapidil on top of adenosine.

* P<0.05,   *** P = 0.0001

imposed on top of urapidil, the vasodilator effects were combined and consequently greater. In fact, CSA was increased to 6.2 ± 1.6 and 4.9 ± 2.1 mm² in patients with basal CFR >3.0 and <2.5, respectively. The vasodilator effect of urapidil combined with adenosine was present also in controls, and CSA increased from 5.5 ± 0.4 to 7.5 ± 0.6 mm². (Table 1).

Coronary Blood Flow

Blood flow changes induced by adenosine were significantly greater in patients with CFR >3.0 than in patients with CFR <2.5. Three minutes after revascularization, adenosine significantly improved flow, but 15 minutes later this hyperemia was reduced, reaching the lowest value observed during the study (Table 1). The reduction in blood flow paralleled the previously observed vasoconstriction and reduction in LV function.[4–6] Both α_1- and α_2-adrenergic blockers, combined with adenosine, increased CBF.

Coronary Flow Reserve

In controls with CFR 4.77 ± 0.58, two consecutive CFR measurements during the protocol duration were reproducible with CFR 4.67 ± 0.85 and 4.81 ± 0.87, respectively. Reproducible were also the measurements obtained in controls with CFR 3.10 ± 0.35, who were subsequently given α-antagonists (Table 1). Coronary revascularization left CFR immediately unchanged in patients, whereas 15 minutes later, when postischemic LV dysfunction is described to occur,[5,6] in patients with CFR >3.0 it decreased from 3.55 ± 0.54 to 2.05 ± 0.55 ($P=0.0001$). Yohimbine and urapidil combined with adenosine restored almost normal values in both groups of patients (Figures 2 and 3 and Table 1). In control subjects, CFR was increased from 3.21 ± 0.30 to 4.58 ± 0.65 by urapidil and to 3.74 ± 0.43 by yohimbine, respectively.

Hemodynamics

The changes in blood pressure and in heart rate are reported in Table 2. Adenosine transiently reduced systolic blood pressure and mean pressure when given alone and when combined with α-adrenergic blockade. Yohimbine and adenosine did not reduce SBP in patients and controls with >3.0 CFR. No heart rate changes were observed, except when α_1-blockers were combined with adenosine.

Discussion

In the present study, α_1- and α_2-adrenergic blockade combined with adenosine exerted an additional vasodilation and, counteracting the α-adrenoceptor–mediated vasoconstriction, normalized coronary flow reserve. Several mechanisms are hypothesized to play a role in the CFR decrease observed after coronary stenting. The ischemia induced by balloon inflations and the stretch of the artery elicit a reflex[19] sympathetic increase of α-adrenergic constrictor tone, leading to an increase previously described in animals[19,20] and in humans.[4–6,9,10] Both α_1- and α_2-adrenergic receptors are present in the human coronary circulation, with α_2-adrenoceptors predominant in the microcirculation.[4–6,9,10] Also, in the present study, selective blockade of α_1- and α_2-adrenergic receptors had different effects on conduit and resistance vessels. In fact, urapidil mainly dilated conduit coronary arteries and even decreased blood flow velocity in patients with CFR <2.5 in the absence of adenosine. Yohimbine increased blood flow mainly by increasing the flow velocity over that observed with adenosine alone, thus indicating an additional vasodilatation of the microcirculation.[7,8] Urapidil combined with adenosine acted by increasing both epicardial CSA and hyperemic APV (Table 1). Our data are in agreement with the functional distribution of α_1- and α_2-adrenergic receptors along the coronary tree previously described in animal models.[7,8]

Coronary Blood Flow Velocity

Baseline APV was lower in patients with CFR >3.0 than in patients with a CFR<2.5 in all conditions. Soon after coronary stenting, a short-lasting hyperemia was observed in
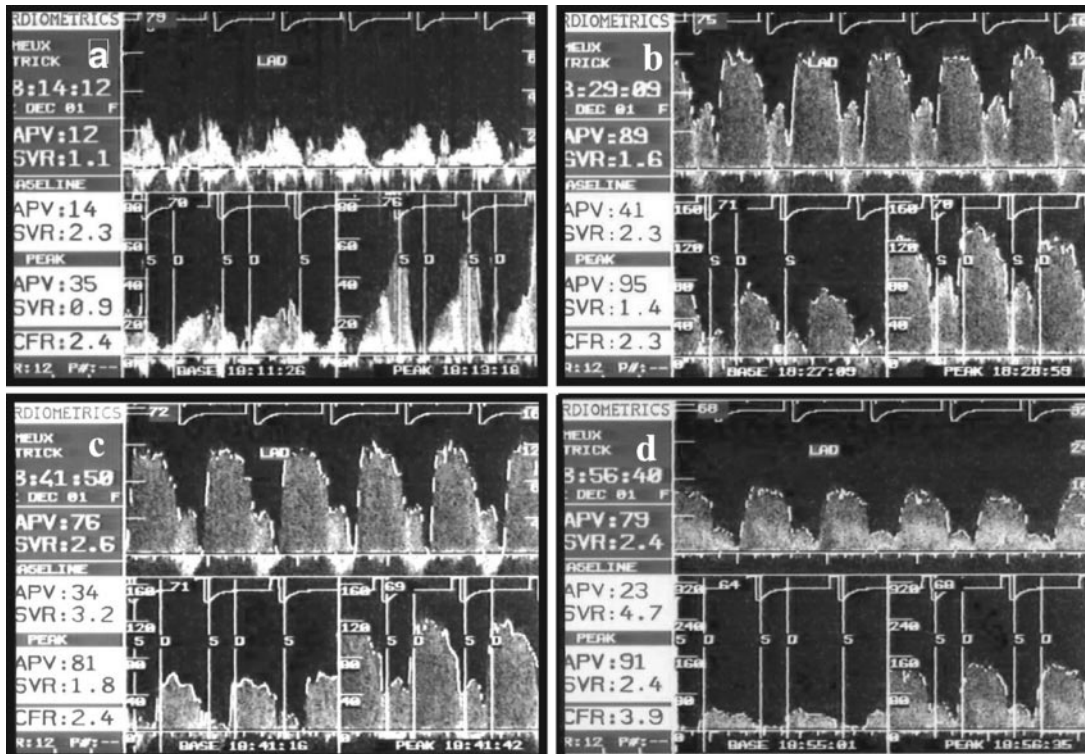
Figure 3. Coronary flow velocity reserve before revascularization (PCI) (a), 3 minutes after stenting (b), 15 minutes after stenting (c), and 8 minutes after urapidil and adenosine (d). APV was measured with a Doppler flow-wire. The IC urapidil injection decreased baseline APV from 34 cm/s to 23 cm/s and increased CFVR from 2.4 to 3.9.

all patients. This hyperemia was greater in patients with CFR >3.0. As previously reported by other authors,[1–3] baseline APV was increased after revascularization. Indeed, the higher baseline coronary blood flow velocity was in part responsible for the CFR reduction[2] in our patients with CFR <2.5. Such APV increase might be the consequence of distal embolization of plaque debris after the manipulation of the plaque.[21,22]

In fact, Hori et al[23,24] have previously described in dogs that acute embolization of the coronary microcirculation by microspheres and subsequent release of adenosine into adjacent nonembolized vessels is responsible for hyperemia. In the past, distal embolization was considered an uncommon phenomenon both in angioplasty and in coronary stenting procedures.[25] More recently, the use of protective intravascular

TABLE 2. Blood Pressure and Heart Rate

Time	Condition	≥ 3.0 CFR Patients n = 18				< 2.5 CFR Patients n = 28				>3.0 CFR Controls n = 8			
		SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR
		mm Hg			b/min	mm Hg			b/min	mm Hg			b/min
Before	Baseline	107±14	69±11	81±6	75±10	109±14	69±11	82±11	75±10	122±8†	75±4†	91±4†	71±3
PCI	Adenosine	106±12	67±10	79±7	78±9	103±12	67±10	79±10	78±9	117±8†	73±3†	88±4†	72±3†
3 min after	Baseline	109±12	69±11	82±5	76±9	107±12	69±11	82±10	76±9	116±7††	69±3	85±4	73±4
Stenting	Adenosine	104±11	67±10	79±5	77±9	103±11	67±10	80±9	77±9	113±†	66±2	82±3	70±2
15 min after	Baseline	108±14	69±11	82±5	77±9	111±14	69±11	82±10	77±9	117±7††	69±2	85±3	73±4†
Stenting	Adenosine	102±13	66±7	78±4	76±6	105±13	66±7	79±7	76±6	113±6†	66±2	82±3	70±2†
α2Block and	Adenosine	118±12	68 ±9	85±9	77±10	104±12	68 ±9	80±9	77±10	117±4†	67 ±7	80±9	77±10
8 min α1 Block	Adenosine	104 ±12	67±8	80±8	73±6	106 ±12	67±8	80±8	73±6	108 ±3†	69±6	82±5	67±5

Between groups: †P<0.05 vs Controls.

Within groups: *P<0.05.

filters has confirmed that an unsuspected amount of plaque debris can be retrieved[26] after revascularization. In support of the hypothesis that distal microembolization is responsible for the sustained hyperemia occurring after coronary stenting, urapidil administered 5 minutes before adenosine significantly attenuated the APV increase measured after coronary stenting. The α_1-adrenergic blocker urapidil may share with prazosin the capacity of inhibiting adenosine release[23] and accordingly decrease APV. The APV increase was greater in patients with unstable angina and lower baseline CFR, whereas the patients with >3.0 CFR who had a more stable clinical situation and likely a more stable plaque had only a minor APV increase. Unstable plaques are known to be frequently ulcerated and more inclined to embolize.[25] These findings support the idea of coronary microembolization.

In our study, the combination of urapidil and high doses of exogenous adenosine significantly dilated the coronary circulation. Apparently, when in the presence of exogenous adenosine, urapidil's effect on endogenous adenosine release becomes negligible; the blockade of α_1-adrenergic coronary vasoconstriction prevails in both epicardial conduit vessels and in the microcirculation.

Both the baseline APV decrease and the CSA increase improved the coronary flow reserve (Figures 2 and 3 and Table 1). In subjects with apparently normal coronary arteries, a minor APV reduction was observed with urapidil injection (from 10.8 ± 2.5 to 8.4 ± 1.6 cm/s), whereas the combination of urapidil and adenosine induced an increase in CFR. This effect is in agreement with the observation of Lorenzoni et al[27] in healthy human volunteers with positron emission tomography. In this study, the α_1 adrenoreceptor antagonist doxazosin led to a 30% to 40% increased in dipyridamole-induced hyperemia, thus suggesting that also in a normal setting α_1-mediated coronary vasoconstriction limits dipyridamole-hyperemia. These data in humans are in agreement with a previous study in dogs demonstrating a tonic α-mediated vasoconstrictor tone that limited hyperemia by 30%.[28] A greater vasoconstrictor effect is likely to occur in the presence of ischemia or of distal embolization, when the α-mediated constrictor tone is increased.[4–6,9,10]

The effect of yohimbine on top of adenosine is expected, because coronary blood flow was previously reported to be increased in animal studies with high doses of yohimbine.[29]

Although all of our patients were pretreated with the full doses of anticoagulants and antiplatelets, the sustained vasodilation may also have reduced platelet microaggregates in arterioles or leukocyte plugging.[30] The impaired production of NO by the atherosclerotic endothelium,[31] ie, of a vasodilator mechanism that competes with α_1- and α_2-adrenergic constriction and contributes to the vasodilator effect of adenosine,[32–34] likely also plays a role in the observed CFR reduction.

Conclusions and Perspective

In patients undergoing coronary revascularization, an additional increase in coronary blood flow can be obtained by superimposition of α_1- or α_2-adrenoceptor blockade on top of adenosine, and coronary reserve is normalized. Whether the effects of α-blockade in patients undergoing revascularization are actually greater than in controls depends on the parameter used. Coronary reserve in patients undergoing revascularization remains somewhat, although not significantly, lower than in controls, whereas the increment in coronary reserve by α-blockade is clearly greater (Figure 2). Certainly, the functional importance of α-adrenergic coronary vasoconstriction in patients during revascularization is greater than in controls, as previously evidenced by the α-blockade–associated improvement in contractile function.[5,6] The more long-term functional consequences of peri-interventional α-blockade remain to be determined.

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