ten men with normal coronary arteries. CFR (peak/basal mean velocity) was measured, immediately after angioplasty, a few days, one month and four months later, with a NO. 3F coronary Doppler catheter placed immediately proximal to the lesion and an intracoronary injection of 12.5 mg papaverine. All 16 patients had no coronary restenosis at follow up angiography.

Results: CFR and hemodynamic data (heart rate: HR (bpm). left ventricular end-diastolic pressure: LVEDP (mmHg) are reported below. In patients with AMI undergoing direct angioplasty, CFR showed slowly progressive improvement after angioplasty. However, even after four months CFR was impaired significantly as compared with CFR in the normal region.

	immediately after	a few days later	one month later	four months later	control (n = 10)
CFR	1.4 ± 0.3	1.8 ± 0.6*	2.5 ± 0.8**	2.9 ± 0.9**+	4.0 ± 1.0
HR	79 ± 12	78 ± 10	72 ± 10	71 ± 8	70 ± 5
LVEDP	23 ± 7	19 ± 7	16 ± 4*	16 ± 6*	10 ± 4

*P < 0.05, **P < 0.01 vs immediately after, +P < 0.01 vs control

Conclusion: In patients with acute myocardial infarction undergoing direct angioplasty, impaired coronary flow reserve is present for at least one month after coronary reperfusion. This "vascular stunning" must be considered when exercise tolerance in patients with acute myocardial infarction is assessed within one month.

957-111 Time Course of Impaired Coronary Vasodilatory Reserve After Reperfusion in Acute Myocardial Infarction

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We have previously reported that coronary vasodilatory reserve is severely impaired immediately after reperfusion in patients with acute myocardial infarction. To investigate the time course of impaired coronary vasodilatory reserve after reperfusion, we studied 11 patients with a first acute anterior myocardial infarction who underwent coronary angioplasty (PTCA) within 6 hours after the onset of symptom. After PTCA, a coronary Doppler guide wire was positioned beyond the infarct related coronary lesion. Dipyridamole (0.56 mg/kg) was administered intravenously over 4 minutes and coronary flow velocity was measured for 10 minutes. Coronary vasodilatory reserve was calculated as the ratio of hyperemic average peak velocity (APV) / resting APV. These measurements were repeated at 2 weeks (n = 9) and 6 months (n = 6) after PTCA. Additional 10 patients with normal angiograms served as control.

Results:

	After PTCA (n = 11)	2 weeks (n = 9)	6 months (n = 6)	Control (n = 10)
resting APV (cm/s)	27 ± 17	24 ± 7	29 ± 9	20 ± 4
hyperemic APV (cm/s)	35 ± 22#	46 ± 13#	69 ± 19#	61 ± 11#
vasodilatory reserve	1.36 ± 0.28§	1.89 ± 0.31§	2.46 ± 0.36§	3.02 ± 0.25

#p < 0.01 vs resting APV, §p < 0.01 vs control, *p < 0.01

Conclusion: Coronary vasodilatory reserve is severely impaired immediately after reperfusion. The coronary vasodilatory reserve gradually improves over 2 weeks but the impairement persists at 6 months after acute myocardial infarction.

957-112 The Incidence and Clinical Implication of Acute Hemorrhagic Myocardial Infarction Detected by MRI

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There has been no data available on the incidence of acute hemorrhagic myocardial infarction (AHMI) until now except for autopsied heart. The purpose of this study is to evaluate the incidence of AHMI after reperfusion therapy with Gd-DTPA enhanced MRI (Gd-MRI) in beating heart. We studied 53 patients of acute myocardial infarction. All patients underwent successful reperfusion therapy by PTCA on admission and ECG gated Gd-MRI with 1.5 Tesla system within 1 week after reperfusion. 18 patients supplemented gradient echo acquisition (GEA) MRI. GEA MRI depicts hemorrhage as low signal intensity (SI) zones due to paramagnetic susceptibility effect of deoxyhemoglobin. Our preliminary study demonstrated that intramyocardial hemorrhage was depicted as low SI areas within high SI zone in risk area by Gd-MRI. The location of low SI areas by Gd-MRI corresponded to low SI zones by GEA MRI and macroscopic intramyocardial hemorrhage in autopsied heart. The definition of AHMI is the enhancement pattern which is depicted as low SI areas within high SI zone in risk area by Gd-MRI. Patients were classified into 2 groups according to duration from occlusion to reperfusion (early reperfusion (ER) group less than 6 hour, late reperfusion (LR) group more than 6 hour) and each group was classified into 2 subgroups according to Gd-DTPA enhancement pattern (hemorrhagic (H) and non hemorrhagic (N) pattern). Results are shown in Table.

	Gd-MRI	n (%)	Duration of occlusion	peak CK	EF (admission)	EF (1 month)
ER	H	4 (28)	3.9 ± 0	4707 ± 913*	55 ± 11	54 ± 12*
	N	14 (72)	4.4 ± 1.1	1452 ± 896	53 ± 8	61 ± 10†
LR	H	14 (66)	20 ± 24	3412 ± 2100*	45 ± 10	47 ± 12*
	N	21 (34)	24 ± 18	1458 ± 1413	52 ± 12	58 ± 9

EF: left ventricular ejection fraction, *P < 0.05 vs. non-hemorrhagic myocardial infarction, †P < 0.05 vs. EF (admission)

The incidence of AHMI was 28% in ER group and 66% in LR group. AHMI demonstrated higher peak serum creatine kinase (CK) level and poorer improvement of left ventricular function even in ER group than non-hemorrhagic AMI. *Conclusion:* (1) Gd-MRI can only detect AHMI in vivo. (2) AHMI occurs even in ER group. (3) The incidence of AHMI increase markedly in LR group.

958 Silent Myocardial Ischemia

Tuesday, March 21, 1995, Noon–2:00 p.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: Noon–1:00 p.m.

958-92 A Randomized, Double-Blind, Placebo-Controlled Trial of Zatebradine and Diltiazem SR in Chronic Stable Angina: Efficacy and Safety

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Zatebradine is a member of a new class of compounds, sinus node inhibitors, that may be useful for the management of chronic stable angina. To test this concept, 188 pts with mild to moderate angina in 17 Canadian centers were enrolled in a parallel-design trial with placebo and diltiazem comparison groups; 143 of them completed a placebo run-in period that required reproducible exercise-induced angina and ST depression. They were then randomized to placebo, zatebradine or diltiazem SR. Study drugs were uptitrated (2.5, 5 and 7.5 mg BID for zatebradine and 60, 90 and 120 mg BID for diltiazem SR) at weekly intervals if the exercise test remained positive. The highest dose was reached by 24 of 47 zatebradine pts and 28 of 49 diltiazem pts. Pts took no other anti-anginal drugs except sublingual NTG to relieve angina. The primary endpoint of the trial was the change from baseline in total exercise time, measured at 12 hours post-dose, after at least 2 weeks at the optimum dose. The table lists the differences from baseline, ±1 SD:

	Placebo	Zatebradine	Diltiazem
Completed Pts	49	47	47
Total exercise time (sec)	43 ± 56	56 ± 69	79 ± 56*
Time to angina (sec)	30 ± 82	63 ± 76*	76 ± 65*
Time to ↓ ST (sec)	12 ± 94	59 ± 87*	60 ± 90*
Heart rate at rest (bpm)	0 ± 10	−13 ± 11*	−6 ± 10*

*p < 0.05 versus placebo

The improvement in exercise time with diltiazem, but not with zatebradine, was significantly better than with placebo. The number of responders, defined as pts whose total exercise time improved by >20% or by >60 sec, was higher with diltiazem (p < 0.01), but not with zatebradine, compared to placebo. Both drugs improved time to angina and time to 1 mm ST depression. Visual phenomena, described as wavy lines or flashes in peripheral visual fields, were reported by 26% of the zatebradine pts.

Conclusion: Although zatebradine has anti-anginal efficacy, as shown in this trial, visual adverse effects will limit its clinical utility for this indication. However, drugs like zatebradine that slow heart rate but have no other cardiac effects may play a role in the management of angina.