JACC Vol. 30, No. 7
December 1997:1714–21

Prospective, Randomized, Multicenter Comparison of Laser-Facilitated Balloon Angioplasty Versus Stand-Alone Balloon Angioplasty in Patients With Obstructive Coronary Artery Disease

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Objectives. **The goal of this study was to examine the relative safety and efficacy of laser-facilitated percutaneous transluminal coronary angioplasty (PTCA) versus "stand-alone" PTCA.**

Background. **Plaque debulking with lasing before PTCA may result in improved lumen dimensions and decreased rates of periprocedural ischemic complications, thus improving short- and long-term outcomes after percutaneous intervention. The mid-infrared holmium:yttrium-aluminum-garnet (YAG) laser has been shown to be effective in a variety of plaque subtypes and may be particularly useful in high risk acute ischemic syndromes.**

Methods. **A total of 215 patients (mean [±SD] age 61 ± 12 years) with 244 lesions were prospectively randomized at 14 clinical centers to laser versus stand-alone PTCA. After laser treatment, all patients underwent PTCA; 148 patients (69%) had unstable angina.**

Results. **The procedural success rate without major catheterization laboratory complications was similar in patients assigned to laser treatment or PTCA alone (96.6% vs. 96.9%, p = 0.88), as was the in-hospital clinical success rate (89.7% vs. 93.9%, p = 0.27). There was no difference in postprocedural diameter stenosis after laser treatment compared with PTCA (18.3% ± 13.6% vs. 19.5% ± 15.1%, p = 0.50). However, use of the laser, versus PTCA alone, did result in significantly more major and minor procedural complications (18.0% vs. 3.1%, p = 0.0004), myocardial infarctions (4.3% vs. 0%, p = 0.04) and total in-hospital major adverse events (10.3% vs. 4.1%, p = 0.08). At a mean follow-up time of 11.2 ± 7.7 months, there were no differences in late or event-free survival in patients assigned to laser treatment versus PTCA alone.**

Conclusions. **Compared with stand-alone PTCA, laser-facilitated PTCA results in a more complicated hospital course, without immediate or long-term benefits.**

(J Am Coll Cardiol 1997;30:1714–21)

Despite advances in equipment and technique, percutaneous transluminal coronary angioplasty (PTCA) continues to be associated with an approximate 4% to 10% risk of major periprocedural complications and a 30% to 50% likelihood of angiographic restenosis within 6 months, which frequently necessitates late repeat revascularization procedures (1–5). By removing plaque before balloon dilation, debulking techniques, such as laser or atherectomy, may potentially diminish the rate of PTCA-induced major dissection and complications and improve late angiographic and clinical outcomes. In this regard, both the excimer and holmium lasers have been shown in large, prospective registry experiences to have favorable success rates in most lesion subtypes compared with balloon angioplasty (6–10). We therefore performed a prospective, randomized, multicenter trial to examine the acute and late outcomes of laser-facilitated PTCA versus standard PTCA.

Methods

Patients and clinical centers. To examine the short- and long-term outcomes of holmium laser-facilitated balloon an-

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Manuscript received June 5, 1997; revised manuscript received August 27, 1997, accepted September 2, 1997.

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0735-1097/97/$17.00
PII S0735-1097(97)00387-2

Abbreviations and Acronyms

ACC/AHA = American College of Cardiology/American Heart Association
AMRO = Amsterdam–Rotterdam (trial)
CK = creatine kinase
ECG = electrocardiogram
FDA = Food and Drug Administration
LAVA = Laser Angioplasty Versus Angioplasty (trial)
MI = myocardial infarction
OR = odds ratio
PTCA = percutaneous transluminal coronary angioplasty
TIMI = Thrombolysis in Myocardial Infarction

gioplasty versus "stand-alone" PTCA, 14 centers experienced in the use of the Eclipse Holmium 2100 laser entered patients in a prospective, randomized trial. The primary end point was the 6-month composite incidence of freedom from death, myocardial infarction (MI) or need for coronary artery bypass graft surgery or repeat PTCA. With an alpha error of 0.05 and a beta error of 0.20, 190 randomized patients with complete follow-up were required to show an improvement in the primary end point from an expected rate of 70% after stand-alone PTCA to 85% after laser-facilitated PTCA.

Entry criteria were nonrestrictive and included patients ≥18 years old, with no upper age limit, with primary or restenotic lesions in a native coronary artery or saphenous vein bypass graft. The first 10 sites enrolled patients with stable or unstable angina. After the demonstration that the holmium laser may be particularly effective in patients with acute ischemic syndromes (7,11,12), an additional four sites were added that randomized patients with unstable angina only. Patients presenting with an acute MI within 24 h of the procedure were excluded. Patients were also excluded for specific laser contraindications, including an index lesion that was on a bend >60°, if the reference segment was <2.0 mm in diameter or if excessive proximal tortuosity or heavy calcification was present, making it unlikely that the catheter could be delivered to or cross the stenosis. The presence of a chronic total occlusion was not an exclusion criteria itself; however, randomization occurred only after the lesion was successfully crossed with a guide wire, and thus nonrecanalizable total occlusions were excluded. This protocol was approved by the Food and Drug Administration (FDA) as part of the regulatory pathway for market authorization for the holmium laser. Written informed consent was obtained from all patients before enrollment after local investigational review board approval.

Study protocol. Patients were pretreated with ≥324 mg of aspirin daily for ≥24 h and calcium channel blocking agents. Other medications before cardiac catheterization were dictated by clinical presentation. After left ventriculography and coronary arteriography, if suitable coronary anatomy was present for study entry, randomization occurred by opening a sealed envelope after the index lesion was successfully wired. If multiple target lesions were present, all lesions must have met entry criteria and were approached by the assigned modality. Intravenous heparin was administered to maintain an activated clotting time >350 s. Intracoronary nitroglycerin (≥100 μg) was given before intervention. If randomization was to PTCA, balloons were chosen to approximate the reference vessel size, and dilation was performed with a goal of ≤30% residual stenosis without major dissection. If randomization was to laser treatment, lasing was performed as described in the next section, followed by PTCA in all patients to maximize the final lumen dimension. After the procedure, the sheaths were removed in 6 to 12 h, and patients were discharged when in clinically stable condition. Calcium channel blockers were prescribed for 1 month and aspirin indefinitely. Clinical follow-up was scheduled for 1, 3 and 6 months after the procedure.

Laser system and procedure. The holmium:yttrium-aluminum-garnet (YAG) Eclipse 2100 (Eclipse Surgical Technologies) is a pulsed, solid state, mid-infrared laser that has been used in 1,862 patients since 1990 under an Investigational Device Exemption (IDE) from the FDA. Laser light with a wavelength of 2.09 μm is transmitted through multiple optical low OH flexible silica fibers and emitted from the distal tip of the catheter after foot pedal activation. The device delivers 5 pulses/s with a pulse duration of 250 μs with an energy range of 250 to 1,000 mJ/pulse (1.25 to 5.0 W). The energy density (fluence) at the tip of the catheter is 125 to 500 mJ/mm^2 per pulse. The tissue penetration depth is 400 μm. Six different catheter sizes (1.2, 1.3, 1.4, 1.5, 1.7 and 2.0 mm) are manufactured that vary in diameter, number of fibers per catheter and flexibility. The 1.2- to 1.5-mm diameter catheters are compatible with an 8F guide catheter, whereas the larger devices require a 9F guide. All catheters traverse over a 0.014-in. guide wire.

The choice of laser variables (catheter size and energy range) was left to the discretion of the operator. In general, the smaller diameter catheters are initially chosen for severe lesions. The laser is prepared by flushing the central guide wire lumen and connecting the proximal end to the laser console. The device is then turned on and left in standby mode. No warm-up period or other calibrations are required. The catheter is then passed over the guide wire just proximal to the lesion and placed in active mode. The "pulse and retreat" technique is used for crossing the lesion (13), in which only a small number of pulses, usually 8 to 12 per session, are used with gentle forward pressure being applied to the catheter under fluoroscopy. The catheter is then withdrawn into the proximal artery or guide catheter for 30 to 60 s to allow heat dissipation and gas bubble dispersion. The catheter is then readvanced to the lesion, and serial passes are made with similar technique. Typically, lower energy fluences are initially selected and are then increased if adequate ablation is not occurring. Repeat arteriography, after intracoronary nitroglycerin, was performed after the last laser pass. The maximal laser catheter diameter and fluence, total number of pulses and total lasing time were recorded.

Definitions. *Unstable angina* was defined as new-onset, crescendo, rest or postinfarction angina. For the purpose of this study, *laser success* was defined as the ability of the laser to completely cross the lesion and reduce the stenosis by ≥20%. *Procedural success* was defined as <50% residual stenosis after PTCA, without major catheterization laboratory complication (death, emergency bypass surgery or sustained coronary occlusion). *Anterograde flow* was assessed by the Thrombolysis in Myocardial Infarction (TIMI) scale (14). *Lesion morphology* was characterized by the modified American College of Cardiology/American Heart Association (ACC/AHA) score (15). *Thrombus* was defined as an intraluminal filling defect, lucency or haziness refractory to intracoronary nitroglycerin. *Coronary spasm* was defined as transient reduction in blood flow with vessel caliber narrowing relieved either spontaneously or by nitroglycerin. *Abrupt closure* was defined as sustained TIMI flow grade 0 to 1 caused by obstruction of the target lesion. *Q wave MI* was defined as elevation of creatine kinase (CK) levels greater than two times above laboratory normal values with any abnormal MB fraction and the development of new pathologic Q waves on the electrocardiogram (ECG). A *non-Q wave MI* was defined as the development of similar CK elevations without Q waves. *Clinical success* was defined when a residual stenosis <50% was obtained, and the patient survived the hospital period without an MI (Q wave or non Q wave) or need for repeat PTCA or bypass surgery.

Data collection and statistical analysis. Detailed in-hospital and 1- and 6-month follow-up case report forms were prospectively completed for each patient and confirmed by review of catheterization reports, ECGs laboratory tests and discharge summaries. A study monitor traveled to each site for independent verification of case report form accuracy. Adverse events were reported to the clinical coordinating center within 24 h of occurrence. Angiograms were evaluated by individual operators using digital calipers or visual assessment. Data was entered into a computerized database, and statistical analysis was performed with commercially available packages (Statview 4.5, Abacus Concepts and JMP 3.1, SAS Institute). Intention to treat analysis was performed. Categoric variables were compared with chi-square or Fisher exact tests, and continuous variables were compared with an unpaired Student *t* test. To determine the independent correlates of procedural and clinical success, several variables known to affect outcomes were entered into a multiple logistic regression model (age, gender, diabetes, triple-vessel disease, treatment of any thrombotic lesion, any total occlusion, any ACC/AHA class C lesion, reference vessel size <3.0 mm or ≥3.0 mm in diameter, as well as randomization arm). Follow-up events were analyzed with actuarial methods, and Kaplan-Meier curves were constructed. Differences in late events among patients undergoing laser angioplasty versus stand alone PTCA were compared with the log rank test. Variables affecting late and event-free survival were examined using Cox proportional hazards regression analysis. A p value <0.05 was required for statistical significance.

Table 1. Baseline Clinical Characteristics of 215 Study Patients

	Laser (n = 117)	PTCA (n = 98)	p Value
Age (yr)	60.3 ± 11.3	62.8 ± 12.5	0.14
Female gender	31.6%	30.6%	0.78
Hypertension	59.8%	59.2%	0.87
Hypercholesterolemia	48.2%	46.8%	0.91
Diabetes mellitus	19.7%	27.6%	0.22
Cigarette use	57.2%	54.6%	0.65
Silent ischemia	3.4%	5.1%	0.76
Chronic stable angina	27.4%	26.5%	0.82
Unstable angina	69.2%	68.4%	0.89
Pain only with MI	12.0%	17.4%	0.26
Postinfarction angina	9.4%	3.1%	0.09
Prior MI	53.8%	35.7%	0.008
Prior CHF	6.0%	8.2%	0.53
Prior PTCA	27.4%	33.7%	0.29
Prior CABG	10.3%	12.2%	0.63

Data presented are mean value ± SD or percent of patients. CABG = coronary artery bypass graft surgery; CHF = congestive heart failure; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Results

Patients. A total of 215 patients were randomized at 14 centers, with 244 lesions treated. There were no major differences in baseline demographic characteristics in patients assigned to laser or standard PTCA, except for a higher incidence of previous MI in laser-treated patients (Table 1). Baseline angiographic characteristics were also well matched among the two treatment groups, except that lesions assigned to laser treatment were more likely to have thrombus present (Tables 2 and 3).

Table 2. Baseline Angiographic Characteristics of 244 Treated Lesions in 215 Patients

	Laser	PTCA	p Value
Patients	n = 117	n = 98	
LVEF (%)	55 ± 12	54 ± 11	0.41
No. of diseased epicardial vessels			
1	61.5%	66.3%	0.47
2	28.2%	19.4%	0.13
3	10.3%	14.3%	0.37
Lesions	n = 125	n = 119	
IRA distribution			
LAD	26.0%	30.7%	0.42
LCx	24.4%	42.1%	0.62
RCA	49.6%	27.2%	0.25
Infarct lesion location			
Proximal vessel	29.3%	31.6%	0.70
Midvessel	43.1%	36.8%	0.33
Distal vessel or branch	27.6%	31.6%	0.51

Data presented are mean value ± SD or number or percent of patients or lesions. IRA = infarct-related artery; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LVEF = left ventricular ejection fraction; PTCA = percutaneous transluminal coronary angioplasty; RCA = right coronary artery.

Table 3. Baseline Angiographic Lesion Morphology

	Laser (n = 125)	PTCA (n = 119)	p Value
ACC/AHA classification			
A	13.6%	25.2%	
B1	16.8%	16.8%	0.16
B2	55.2%	46.2%	
C	14.4%	11.8%	
Lesion length (mm)	11.9 ± 6.6	11.2 ± 6.7	0.46
>10 mm	43.5%	42.4%	0.79
Eccentric	52.0%	43.2%	0.17
Proximal tortuosity	27.2%	21.2%	0.52
Angulated segment >45°	6.5%	12.1%	0.27
Irregular contour	52.4%	43.6%	0.17
Calcification present	17.1%	13.6%	0.45
Total occlusion	9.6%	5.0%	0.18
Ostial location	0.8%	2.5%	0.36
Bifurcation lesion	4.0%	5.9%	0.48
Thrombus present	26.8%	14.4%	0.02
Degenerated saphenous vein graft	1.6%	0%	0.55

Data presented are mean value ± SD or percent of lesions. ACC/AHA = American College of Cardiology/American Heart Association; PTCA = percutaneous transluminal coronary angioplasty.

Procedural outcome. Among patients randomized to laser angioplasty, the laser catheter reached the lesion and was activated in 122 (98%) of 125 lesions. Laser success was achieved in 117 lesions (93.6%), whereas the laser partially penetrated the lesion in 3 lesions (2.4%). Mean (±SD) catheter size was 1.3 ± 0.2 mm, and a mean of 1.1 ± 0.3 catheters were used per patient. A mean of 103 ± 294 pulses were applied per lesion, at maximal mean energy of 3.1 ± 0.5 W. PTCA was performed in all patients assigned to laser treatment. Reference vessels were judged to be slightly larger in the laser-treated patients than the PTCA-treated patients. This difference was compensated for by use of larger balloons in patients assigned to laser treatment, and thus the balloon/artery ratio was identical between the two groups (Table 4). There were no other significant differences in PTCA variables in patients randomized to laser-facilitated versus stand-alone PTCA (Table 4).

The results of the quantitative angiographic analysis are shown in Table 5. By on-site assessment, baseline lesion severity was slightly worse in patients assigned to laser angioplasty than in those with stand-alone PTCA. However, there was no difference in the final post-PTCA residual stenosis between the two groups, although the absolute minimal lumen diameter was slightly greater in the laser-treated patients, given the larger baseline mean reference vessel diameter. Dissection was noted in only 5.6% of patients immediately after laser treatment. However, the frequency of dissection after laser-facilitated PTCA was similar to that after stand-alone PTCA (16.8% vs. 15.9%, respectively, p = 0.85).

Procedural success without major catheterization laboratory complications was obtained in 96.6% of laser-treated patients versus 96.9% of PTCA-treated patients (p = 0.88). The only variable independently predictive of procedural failure in the multivariate model was the presence of triple-vessel disease (odds ratio [OR] 6.3, p = 0.03). However, as shown in Table 6, procedural complications were significantly

Table 4. Coronary Angioplasty Variables for 244 Lesions

	Laser (n = 125)	PTCA (n = 119)	p Value
Balloons/lesion	1.4 ± 06	1.5 ± 0.9	0.30
Inflations/lesion	3.1 ± 2.1	3.3 ± 2.8	0.55
Ref seg diam (mm)	3.1 ± 0.4	2.9 ± 0.4	0.008
Max balloon size (mm)	3.1 ± 0.5	2.9 ± 0.4	0.009
Balloon/artery ratio	1.0 ± 0.1	1.0 ± 0.1	0.79
Total inflation time (min)	7.8 ± 7.0	8.6 ± 7.7	0.50
Max pressure (atm)	7.7 ± 2.9	7.9 ± 2.6	0.48

Data presented are mean value ± SD. Max = maximal; PTCA = percutaneous transluminal coronary angioplasty; Ref seg diam = reference segment diameter.

Table 5. Quantitative Angiographic Analysis

	Laser (n = 125)	PTCA (n = 119)	p Value
Ref seg diam (mm)	3.1 ± 0.4	2.9 ± 0.4	0.008
MLD (mm)			
Before intervention	0.3 ± 0.3	0.4 ± 0.4	0.01
After laser	1.0 ± 0.6	—	—
After PTCA	2.5 ± 0.5	2.3 ± 0.6	0.04
%DS			
Before intervention	89.6 ± 9.0	85.8 ± 11.7	0.005
After laser	67.0 ± 16.5	—	—
After PTCA	18.3 ± 13.6	19.5 ± 15.1	0.50

Data presented are mean value ± SD. MLD = minimum lumen diameter; %DS = percent diameter stenosis; — = not applicable; other abbreviations as in Table 4.

Table 6. Periprocedural Complications in 215 Patients

	Laser (n = 117)	PTCA (n = 98)	p Value
Major complications			
Coronary occlusion	5.1%	2.0%	0.30
Emergency CABG	1.7%	0	0.50
Sustained VT/VF	0.9%	0	0.65
Cardiopulmonary arrest	0	0	—
Free perforation with tamponade	0	0	—
Stroke	0	0	—
Death	0	0	—
Any major complication	6.8%	2.0%	0.11
Minor complications			
Coronary artery spasm	9.4%	1.0%	0.007
New thrombus formation	4.3%	1.0%	0.10
Distal thromboembolism	0.9%	0	0.65
Localized perforation without tamponade	1.7%	0	0.50
Any minor complication	14.0%	2.0%	<0.0001
Any procedural complication (major or minor)	18.0%	3.1%	0.0004

Data presented are percent of patients. VT/VF = ventricular tachycardia/ventricular fibrillation; other abbreviations as in Tables 1 and 5.

Table 7. Major In-Hospital End Points (includes cardiac catheterization laboratory events)

	Laser (n = 117)	PTCA (n = 98)	p Value
Death	1.7%	0%	0.50
CABG	2.6%	3.1%	0.83
Emergent	1.7%	0%	0.50
Urgent	0.9%	2.1%	0.59
Elective	0%	1.0%	0.46
MI	4.3%	0%	0.04
Q wave	0.9%	0%	0.65
Non-Q wave	3.4%	0%	0.12
Repeat PTCA	7.0%	3.1%	0.19
Any major adverse event*	10.3%	4.1%	0.08
Duration of hospital stay (days)	5.1 ± 3.9	4.3 ± 3.8	0.15

*Death, Q wave or non-Q wave myocardial infarction (MI), coronary artery bypass graft surgery (CABG) or repeat percutaneous transluminal coronary angioplasty (PTCA). Data presented are mean value ± SD or percent of patients.

more frequent in patients undergoing laser treatment than stand-alone PTCA. By multivariate analysis, the only correlate predictive of procedural complications was randomization to laser treatment (OR 7.5, p = 0.002).

In-hospital and late clinical events. Overall clinical success in patients randomized to laser-facilitated PTCA was similar to that in patients with stand-alone PTCA (89.7% vs. 93.9%, respectively, p = 0.39). In-hospital adverse events are presented in Table 7, and tended to occur more frequently in the laser-treated group. Postprocedural MI was more common in laster-treated patients than in those managed with PTCA only.

Late follow-up was available in 209 (99%) of 212 patients discharged alive at a mean time of 11.2 ± 7.7 months. By actuarial analysis, there was no difference in long-term rates of mortality, MI or reintervention in patients treated with laser versus PTCA alone, whether adverse in-hospital events were included (Fig. 1) or excluded (Fig. 2) in the determination. By Cox regression analysis, only the presence of triple-vessel disease was identified as an independent correlate of late death, MI or repeat revascularization (OR 2.4, p = 0.009).

Patients with previous MI and thrombus-containing lesions. Because patients randomized to laser treatment had a higher baseline incidence of previous MI and lesions containing thrombus than did patients randomized to PTCA only, separate analyses were performed in these subgroups. When considered independently of the randomization arm, previous MI was not a correlate of cumulative 6-month adverse events (death, MI, bypass surgery or repeat PTCA) (24.5% in patients with vs. 28.2% in those without a previous MI, p = 0.90). Similarly, treatment of a thrombus-containing lesion had no effect on the occurrence of cumulative 6-month adverse events (29.0% in patients undergoing treatment of one or more lesions with thrombus vs. 25.7% in patients with no lesions with thrombus, p = 0.68). Furthermore, no major differences in acute or late outcomes in patients treated with laser versus stand-alone PTCA substratified by these baseline differences were identified (Table 8).

Discussion

Previous studies. Only one prospective, randomized study (16) has been previously published in which the strategy of plaque debulking with a laser before PTCA was directly compared with stand-alone PTCA. In the multicenter Amsterdam–Rotterdam (AMRO) trial (16), 308 patients with stable angina and lesions visually >10 mm in length were randomized to excimer laser angioplasty (followed by PTCA in 98% of patients) versus PTCA only (16). There were no differences in acute or late major clinical events between the two groups. By

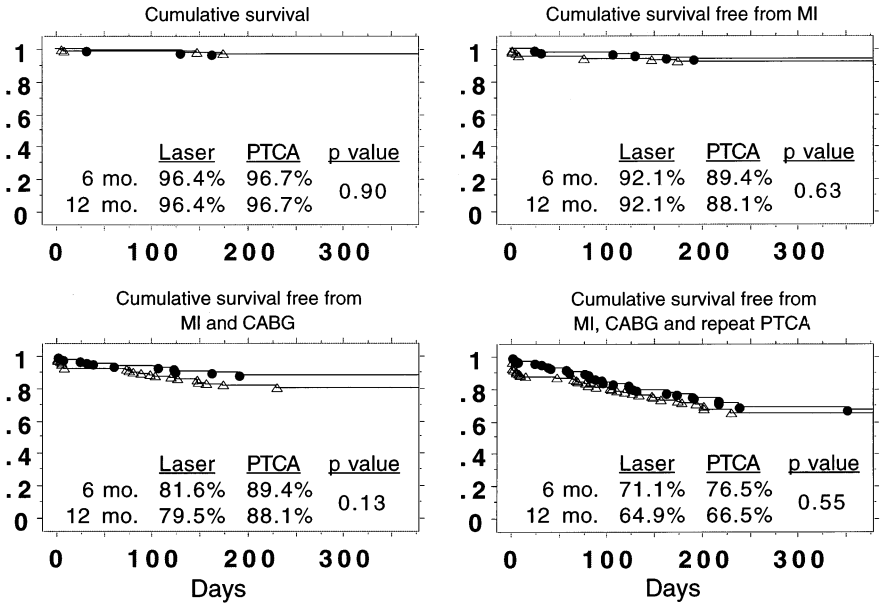

Figure 1. Kaplan-Meier curves displaying cumulative survival and event-free survival in patients randomized to undergo laser-facilitated PTCA (**triangles**) versus stand-alone PTCA (**circles**). Outcomes include in-hospital and late events. Inset in each graph are the 6- and 12-month survival rates by actuarial analysis, with the corresponding p values by the log rank test. CABG = coronary artery bypass graft surgery.

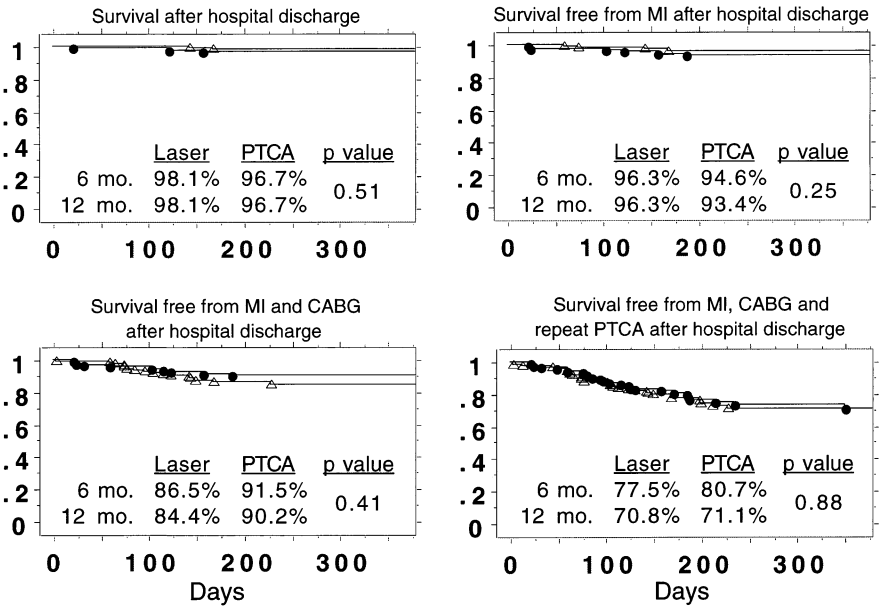

Figure 2. Kaplan-Meier curves displaying survival and event-free survival after hospital discharge (excluding in-hospital events) in patients randomized to undergo laser-facilitated PTCA (**triangles**) versus stand-alone PTCA (**circles**). Format as in Figure 1. CABG = coronary artery bypass graft surgery.

quantitative coronary analysis, similar acute gain was realized after both strategies, but late loss was greater in the laser-treated patients. As a result, restenosis tended to be greater after laser angioplasty than after PTCA alone (52% vs. 41%, $p = 0.13$).

Compared with the ultraviolet excimer laser, the mid-infrared holmium laser offers several advantages that warranted a second randomized trial of somewhat different design:

1. The holmium laser may result in less arterial damage than the excimer laser, a contention supported by registry data (6–9,17). Both the excimer and holmium lasers produce photoacoustic trauma by the creation, rapid expansion and dispersion of vapor gas bubbles that can result in arterial dissection or perforation (18–20). Although the extent of dissection may be reduced by replacing the blood field with saline before excimer treatment (21), a histologic comparative in vitro study (22), in which presently available catheters at clinically relevant energy levels and pulse strategies were used, found that the holmium laser resulted in fewer arterial cleavage planes (dissections) than did the excimer laser, despite lasting in a saline field.

2. Thrombi, which possess a high water content, avidly absorb light in the mid-infrared region (23). As a result, the holmium laser has been found to be particularly effective in thrombus-containing lesions and acute ischemic syndromes (7,11,12). In contrast, lower success and greater complication rates have been reported after treatment of thrombotic lesions with the excimer laser (24). These observations were incorporated into the design of both the AMRO and Laser Angioplasty Versus Angioplasty (LAVA) trials. Whereas the AMRO study excluded patients with unstable angina and thrombus-containing lesions, the present trial was specifically weighted to capture these patient subgroups. The solid state design of the mid-infrared laser confers other advantages of this system compared with the excimer, including short warm-up times, minimal maintenance, a smaller footprint, no toxic gases to vent and lower cost (6,23,24).

Results of the present study. Despite these considerations, no acute or late benefits of holmium laser-facilitated PTCA versus stand-alone PTCA were found in the present randomized trial, either by univariate or multivariate analysis. Laser success was relatively improved when treating thrombus-containing lesions but still did not surpass PTCA alone. In contrast, procedural complications were significantly increased

Table 8. Comparison of Outcomes in Laser- and Coronary Angioplasty-Assigned Patients Substratified by Presence of Previous Myocardial Infarction and Lesional Thrombus

	Previous MI			No Previous MI			≥1 Lesion With Thrombus			No Lesion With Thrombus		
	Laser (n = 63)	PTCA (n = 35)	p Value	Laser (n = 54)	PTCA (n = 63)	p Value	Laser (n = 32)	PTCA (n = 17)	p Value	Laser (n = 85)	PTCA (n = 81)	p Value
Procedural success	96.8%	97.1%	0.93	96.3%	96.8%	0.88	96.9%	100%	0.65	96.5%	96.3%	0.95
Clinical success	90.5%	97.1%	0.22	88.9%	92.1%	0.55	87.5%	88.2%	0.94	90.6%	95.1%	0.26
6-mo EFS	73.9%	78.8%	0.78	67.8%	75.3%	0.49	71.7%	69.3%	0.99	70.8%	78.0%	0.46

Data presented are percent of patients. EFS = event-free survival (survival free from myocardial infarction [MI], bypass surgery or repeat percutaneous transluminal coronary angioplasty [PTCA]; includes in-hospital events).

by lasing before PTCA, especially the occurrence of spasm, with trends noted for greater abrupt coronary occlusion and new thrombus formation. As a result, the rate of periprocedural MI was increased, and trends were present for greater overall major complications and a longer hospital stay. Thus, the present trial does not support the use of laser angioplasty as an everyday tool, even in high risk patients with unstable angina or thrombus-containing lesions (2,25), especially when the high costs of the system and single-use catheters are factored into account. The negative results of the LAVA and AMRO trials, in direct contradiction to the earlier favorable registry experiences, reconfirm the essential importance of performing prospective, multicenter, randomized trials before the widespread adoption of new methodologies can be recommended.

Limitations of the study. Several limitations of this study must be acknowledged: 1) Given the relatively small sample size, the study was powered to show only major differences between the two treatment arms. Lesser degrees of benefit favoring laser-assisted PTCA or stand-alone PTCA may have gone undetected. However, given the higher rate of complications and slightly worse long-term outcomes with lasing in this trial, it is unlikely that enrolling a larger population would have revealed significant long-term benefits in the laser arm. 2) Although the two treatment arms were well matched for most baseline characteristics, several differences were present between the two groups, including the frequency of previous MI and the presence of thrombus-containing lesions. However, when analyzed separately and adjusted for by multivariate analysis, these factors had no bearing on acute or late event-free survival. 3) Some degree of selection bias cannot be excluded, especially in investigator reporting of clinical events and angiographic results. However, the participating physicians were dedicated laser investigators, suggesting that bias, if present, would have been directed toward more favorable laser results. 4) The results of the angiographic analysis must be cautiously regarded, given the lack of a central core laboratory. However, the lack of any difference in the site-assessed final percent diameter stenoses between the laser and stand-alone PTCA groups suggests that no true angiographic benefit of laser is likely to exist. Furthermore, the equivalent 6-month clinical outcomes between the two treatment groups are consistent with the nearly identical acute lumen outcomes observed (26).

Finally, and perhaps most importantly, the size of the laser catheters used in the present trial (and the AMRO study), in concert with the observation that laser angioplasty results in minimal plaque debulking, may have made the comparative late outcomes after laser-facilitated angioplasty versus stand-alone PTCA a fait accompli. Recent studies have demonstrated that if debulking is to reduce restenosis and improve late clinical events, it is likely to do so by improving the acute result obtained (26). However, studies with intravascular ultrasound imaging have shown that with present-day catheters and techniques, laser debulking of plaque contributes only a small percentage of the lumen gain realized after adjunctive PTCA (27). In the present trial, with a mean catheter size of 1.3 mm used, the average cross-sectional area stenosis after laser alone would be expected to be 81% (assuming 100% ablation efficiency and no significant vessel remodeling). However, given the high rate of procedural complications noted with the small diameter catheters utilized in this study, it is doubtful that the use of larger catheters to achieve more complete plaque removal would be safe. The important issue of whether maximal plaque debulking improves long-term outcomes after percutaneous intervention is being addressed with regard to high speed rotational atherectomy in the ongoing Study to Determine Rotablator and Transluminal Angioplasty Strategy (STRATUS) trial.

Present role of laser coronary angioplasty. In view of the results of the present trial, which confirm and extend the AMRO study findings, the routine use of laser angioplasty before PTCA is unwarranted. Whether laser facilitation of balloon angioplasty is or is not useful for lesions that are known to respond poorly to PTCA, such as ostial lesions, bifurcation stenoses, undilatable lesions and in-stent restenosis (10,28), cannot be answered by these trials because too few patients with these lesion characteristics were included. However, many of these lesion subtypes also respond well to high speed rotational atherectomy, which is potentially a more cost-effective alternative, given the high up-front costs of the laser system. A unique role for lasers in coronary artery disease may yet be found with the laser wire application to recanalize chronic total occlusions that cannot be traversed by conventional guide wires (29).

Appendix

Participating Institutions and Investigators for the Laser Angioplasty Versus Angioplasty Trial

Clinical Coordinating Center. *The Cardiovascular Institute, El Camino Hospital, Mountain View, California*: Gregg W. Stone (Primary Investigator), JoAnn McDonnell, Nancy Richardson.

Clinical Centers and Principal Investigators. *The University of Miami/Jackson Memorial Hospital, Miami, Florida*: Eduardo de Marchena. *Audubon Hospital, Louisville, Kentucky*: David Dageforde, Richard Allen. *St. Francis Hospital, Evanston, Illinois*: Alberto Foschi, Alan Kogan. *LDS Hospital, Salt Lake City, Utah*: Joseph B. Muhlestein. *All Children's Hospital, St. Petersburg, Florida*: Michael McIvor. *Scottsdale Memorial Hospital, Scottsdale, Arizona*: David Rizik. *Blodgett Memorial Medical Center, Grand Rapids, Michigan*: Ronald Vanderlann, Ray Roden. *The Cleveland Clinic Foundation, Cleveland, Ohio*: Joe Sutton. *Episcopal Heart Institute, Philadelphia, Pennsylvania*: Vidya Banka, Peter Fail. *Maimonides Medical Center, Brooklyn, New York*: Robert Frankel, Jacob Shani. *Methodist Hospital, Indianapolis, Indiana*: Kirk Parr. *Rex Hospital, Raleigh, North Carolina*: Daryl Emery. *Texas Heart Institute, Houston, Texas*: Emerson Perin. *University Medical Center, Tucson, Arizona*: Samuel Butman.

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