Vaporizing Thrombus With Excimer Laser Before Coronary Stenting Improves Myocardial Reperfusion in Acute Coronary Syndrome

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Background: Mechanical reperfusion has proven to be an unquestionably superior treatment strategy over that of thrombolytic therapy in patients with acute coronary syndrome (ACS). Excimer laser coronary angioplasty (ELCA) is a unique revascularization device that has a lytic effect on thrombus, in addition to its debulking effect on the atherosclerotic plaque beneath the thrombus.

Methods and Results: This single-center retrospective analysis consisted of consecutive ACS patients treated with ELCA (n=50) and age- and sex-matched ACS patients treated with manual aspiration (n=48) without use of a distal protection device. Success rate was judged by lesion crossability, procedure complications, and significant reduction of stenosis. Tissue-level perfusion was assessed on antegrade Thrombolysis In Myocardial Infarction (TIMI) flow grade, myocardial blush grade (MBG), and ST-segment elevation resolution (STR). Short-term outcome was evaluated according to occurrence of in-hospital major adverse cardiac events (MACE; myocardial infarction, target lesion revascularization, coronary artery bypass graft, and death). Lesion crossability was higher in the ELCA group than in the aspiration group (96.2% vs. 82.6%, P=0.04). Attainment of TIMI 3 flow (86.0% vs. 68.8%, P=0.04) and MBG 3 (76.0% vs. 54.2%, P=0.02) was also higher in the ELCA group than in the aspiration group. Complete STR was similar between the 2 groups. In-hospital MACE were significantly more frequent in the aspiration group.

Conclusions: ELCA is feasible, safe, and effective for the treatment of patients with ACS and appears to be useful as an adjunctive lesion preparation device. (Circ J 2013; 77: 1445–1452)

Key Words: Acute myocardial infarction; Blush score; Distal embolism; Excimer laser; ST resolution
ment of AMI by achieving maximum thrombus dissolution in lesions with extensive thrombus burden, significant increase in minimal luminal diameter, adequate restoration of antegrade Thrombolysis In Myocardial Infarction (TIMI) flow in the infarct-related artery, and a very low rate of distal embolization.¹¹

In the present study, we evaluated the safety and efficacy of ELCA as an adjunct to primary PCI in patients with ACS and compared the success rate, tissue-level perfusion, and short-term outcomes following ELCA with those of manual thrombus aspiration.

**Methods**

**Subjects**

We retrospectively analyzed consecutive patients with ACS who underwent PCI with ELCA before balloon angioplasty or stenting at Higashi Takarazuka Satoh Hospital, Japan, from January 2007 to August 2011. The patients with ACS in this analysis were diagnosed on the basis of AHA/ACC criteria, which included unstable angina, Q-wave MI, non-Q-wave MI, or recent MI (within 7 days from onset). Approximately 80% of the subjects had ST-segment elevation myocardial infarction (STEMI). ELCA was performed in the patients who accepted this advanced medical treatment, and all patients provided their written informed consent. The indication for ELCA was decided by the operator after consideration of the angiographic and intravascular ultrasound (IVUS) findings. Age-and sex-matched patients with ACS who underwent manual thrombus aspiration during the same period were randomly selected and enrolled in this comparative analysis. Patients who underwent manual thrombus aspiration combined with a distal protection device were excluded from the analysis. As a result, 50 patients who underwent ELCA (ELCA group) and 48 patients who underwent manual thrombus aspiration (aspiration group) were enrolled in the study.

This study complied with the Declaration of Helsinki in regard to investigation in humans and was approved by the institutional ethics committees at Higashi Takarazuka Satoh Hospital. There was no industry involvement in the design, conduct, financial support, or analysis of this study.

**Pre- and Post-Procedure Management and PCI**

All patients were pretreated with a loading dose of 300 mg clopidogrel or 243 mg of aspirin, and i.v. heparin boluses were given during the procedure to maintain an activated clotting time >250 s. PCI was performed according to standard techniques with the use of 7-Fr guiding catheters. Either ELCA or thrombus aspiration was performed before balloon dilation and stent deployment.

A pulsed xenon chloride excimer laser with a wavelength of 308 nm was used as the laser source (CVX-300; Spectranetics, Colorado Springs, CO, USA). Pulse duration was 135 ns and output was 200 mJ/pulse. Energy was delivered via a rapid-exchange catheter that contains flexible optical fibers. Catheters with diameters of 1.4, 1.7, and 2.0 mm, all with a concentric tip configuration, were used (Vitesse C; Spectranetics). Energy parameters for lasing were initially set at a fluency of 45 mJ/mm² and a repetition rate of 25 Hz. The diameter of the laser catheter was chosen by the operators according to target lesion morphology and degree of stenosis. At first, the guiding
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A representative patient with AMI who underwent ELCA is shown in Figure 1. Manual thrombus aspiration was performed with a TVAC aspiration catheter filled with saline immediately before lasing. The operator then initiated lasing, advancing the laser catheter at a speed of 0.5 mm/s while at the same time an assistant injected saline at 2–3 ml/s. If the thrombus was not vaporized adequately, the operator could raise the fluency and repetition rate to 60 mJ/mm² and 40 Hz maximum. A representative patient with AMI who underwent ELCA is shown in Figure 1. Manual thrombus aspiration was performed with a TVAC aspiration catheter (Nipro, Osaka, Japan), a single-lumen rapid-exchange aspiration shaft that is compatible with 7-Fr guiding catheters. Distal protection devices were not used in either group.

Most patients underwent stent deployment, and the use of bare-metal stents (BMS) or drug-eluting stents (DES) was decided by the operators. All patients also underwent IVUS. All patients received 81–100 mg aspirin once daily for life and...
75 mg clopidogrel once daily or 200 mg ticlopidine twice daily for at least 3 months after the angioplasty if BMS were implanted and for at least 6 months thereafter if DES were implanted. Thrombolytic agents and glycoprotein IIb/IIIa inhibitors were not given before the procedure. Additional optimal medications such as β-blockers, renin-angiotensin blockade agents, statins, and eicosapentaenoic acid were used at the discretion of the attending physician. Device success was defined as the ability to cross the lesion with the laser catheter or aspiration catheter, absence of major dissection, absence of perforation, and ≥20% reduction of the stenosis after lasing or aspiration. Procedure success was defined as achievement of distal flow of TIMI grade 2 or 3 without acute thrombotic occlusion of the lesion. Distal embolization was defined as a distal filling defect with an abrupt cut-off in 1 of the peripheral coronary branches of the infarct-related artery, distal to the angioplasty site. The presence of distal embolization was assessed on the angiogram done immediately following the primary coronary angioplasty by experienced investigators who were blinded to all other data apart from coronary angiogram. Procedures were considered complete after successful dilation of the target lesion with a residual stenosis <50% without major adverse cardiac events (MACE).

**Clinical Data, Electrocardiographic, and Angiographic Measurements**

Clinical data were retrospectively collected in case report forms. Coronary angiograms were obtained for angiographic analysis and reviewed off-line by 3 experienced observers. Angiographic TIMI flow grade and myocardial blush grade (MBG) were visually estimated as previously described. TIMI frame count was evaluated using the technique described by Gibson et al. Snapshot 12-lead electrocardiograms were recorded immediately before PCI and at 30–60 min after PCI and were analyzed later by 2 other observers. ST-segment elevation was measured 20 ms after the J point, the sum of ST-segment elevations was calculated, and then ST-segment elevation resolution (STR) was calculated for all patients. STR >70% was considered as complete resolution.

**Study Endpoints and Definition**

In-hospital MACE were defined as all-cause death, MI due to acute or subacute stent thrombosis, and target lesion revascularization (TLR). TLR was defined as a repeat revascularization by either PCI or coronary artery bypass graft (CABG), and stent thrombosis was classified by the Academic Research Consortium definition as definite, probable, or possible.

**Statistical Analysis**

Continuous variables are expressed as mean±SD, and categorical variables are expressed as proportions. We assessed differences between the ELCA and aspiration groups using a t-test for continuous data and chi-squared test for categorical data. P<0.05 was considered to be statistically significant.

### Results

**Baseline, Angiographic, And Procedure Characteristics**

Baseline clinical and angiographic characteristics are listed in Tables 1, 2, respectively. There were no significant differences between the 2 groups with regard to age, sex, common coronary risk factors, clinical conditions, and target vessels. Percentage of type C lesions was higher in the ELCA group, but there was no significant difference in lesion type between groups. There were also no significant differences between groups in the proportion of patients with unstable angina, Q-wave MI, non-Q-wave MI, and recent MI. Approximately half of the patients had multivessel disease, and there were no significant differences in the number of diseased vessels and prevalence of left main trunk disease between groups. Poor left ventricular function (ejection fraction <40%) was observed in 5.1% of patients. Right coronary artery lesions were the most frequent lesions in both groups because most of these lesions were suspected to contain large thrombus loads. There were no saphenous vein graft lesions. Door-to-balloon time in the case of AMI was longer in the ELCA group than in the aspiration group. Peak value and area under the curve of creatine phosphokinase were similar between both groups.

Procedural characteristics of both groups are given in Table 3. Seventeen patients were in serious condition with severe heart failure or cardiac shock. Support of PCI with intra-aortic balloon pumping (IAPB) and/or percutaneous cardiopulmonary support (PCPS) was performed in 16 patients, with no significant differences between the 2 groups (IAPB: 22.0%...
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The laser catheters could cross the lesion in 96.2% of cases, whereas the aspiration catheters could cross the lesion in 82.6% of cases (P=0.04). A ≥20% reduction of the stenosis after ELCA was achieved in 88.0% of patients, whereas this was achieved in 64.6% with the aspiration catheter (P=0.01). We performed ELCA in 8 patients in whom aspiration catheters could not cross the lesion; ELCA catheters crossed all of these lesions.

The frequency of complications was almost identical between the 2 groups, but distal embolism tended to occur less often in the ELCA group; therefore, the frequency of no-reflow/slow flow phenomena also tended to be less in the ELCA group. Coronary dissections were seen in 2 patients in the ELCA group and in 1 patient in the aspiration group. Among them, major dissection requiring implantation of additional stents occurred in 1 patient in the ELCA group.

### Procedure Success and Angiographic Results

Laser catheters of the following diameters were used: 1.4-mm diameter in 13 patients, 1.7-mm diameter in 36 patients, and 2.0-mm diameter in 1 patient. Judkins-type guiding catheters were mainly used rather than extra back-up type guiding catheters. Lesion crossability and procedural complications for the laser catheters and aspiration groups are listed in Table 4. The laser catheters could cross the lesion in 96.2% of cases, whereas the aspiration catheters could cross the lesion in 82.6% of cases (P=0.04). A ≥20% reduction of the stenosis after ELCA was achieved in 88.0% of patients, whereas this was achieved in 64.6% with the aspiration catheter (P=0.01). We performed ELCA in 8 patients in whom aspiration catheters could not cross the lesion; ELCA catheters crossed all of these lesions.

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### Table 4. Device Success and Procedural Complications

<table>
<thead>
<tr>
<th></th>
<th>ELCA (n=50)</th>
<th>ASP (n=48)</th>
<th>P-value</th>
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<tbody>
<tr>
<td><strong>Device success</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion crossability †</td>
<td>50 (96.2)</td>
<td>48 (82.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Attainment of ≥20% reduction in stenosis after procedure</td>
<td>44 (88)</td>
<td>31 (64.6)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Procedural success</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital MACE</td>
<td>0 (0)</td>
<td>5 (10.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>TLR/TVR</td>
<td>0 (0)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>MI</td>
<td>0 (0)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>CABG</td>
<td>0 (0)</td>
<td>2 (4.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>3 (6.3)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Procedural complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No reflow/slow flow</td>
<td>1 (2.0)</td>
<td>3 (6.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Distal embolism</td>
<td>6 (12.0)</td>
<td>13 (27.1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Side-branch occlusion</td>
<td>1 (2.0)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>Dissection</td>
<td>2 (4.0)</td>
<td>1 (2.1)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data given as n (%). †n=52 lesions in the ELCA group, n=58 lesions in the ASP group. MACE, major adverse cardiac events; TLR, target lesion revascularization; TVR, target vessel revascularization. Abbreviations as in Table 1.
between groups, the percentage of vessels with MBG 3 was higher in the ELCA group. There were significant differences in in-hospital MACE between the 2 groups (Table 4). Three patients died in the aspiration group, 2 due to cardiac (multiple organ failure due to sustained cardiac shock) and 1 to non-cardiac (acute pulmonary embolism) etiologies, but no patients died from procedural complications. Two patients in the aspiration group underwent CABG for a non-culprit left main trunk lesion during the chronic phase. Wall motion recovery assessed on wall motion score index ratio between baseline and 2 weeks later was similar between the 2 groups (ELCA, 0.2 ± 0.1 vs. aspiration, 0.2 ± 0.2, P=NS).

**Discussion**

The presence of a large thrombus load in a lesion increases the rate of complications during and after PCI in patients with STEMI. Thrombus dislocation during angioplasty may cause distal embolism and consequently impair tissue reperfusion. Microvascular impairment after successful PCI in AMI is associated with a poor prognosis. Failure to achieve myocardial tissue reperfusion is known to be the main complication limiting early and long-term clinical benefits of mechanical reperfusion in patients with AMI. Although reperfusion can salvage myocardium after sustained ischemia, the reperfusion itself paradoxically induces myocardial injury, named “reperfusion injury”, which attenuates the benefits of myocardial reperfusion. Among the different strategies to limit the no-reflow phenomenon, that of reducing distal embolization with a manual thrombus aspiration device is promising. Despite the logical advantage of thrombus aspiration during PCI, however, a previous early study failed to confirm superiority of this approach in reducing infarct size or death rates. A recent large, single-center, randomized trial and meta-analysis showed that manual thrombus aspiration is associated with a significant improvement in myocardial perfusion and reductions in short- and long-term mortalities in patients treated with primary PCI, but whether such improvements in myocardial reperfusion and
clinical outcome with thrombus aspiration are directly connected to better follow-up of left ventricular function and geometry have not yet been clarified.12,23 Thus, the efficacy of manual thrombus aspiration remains controversial in terms of salvage of tissue-level reperfusion.

The ELCA system was introduced more than 25 years ago as an alternative technique for the treatment of coronary and peripheral artery diseases because of the unique features of the laser system to facilitate precise tissue ablation with minimal adjacent injury.14,22 Recent clinical experience in patients presenting with acute ischemic-thermotic coronary syndromes has shown that ELCA is capable of efficient plaque debulking, thrombus vaporization, and facilitation of adjunct balloon angioplasty and stenting.10–12 In terms of tissue-level reperfusion in patients with AMI, a previous report demonstrated that the use of ELCA achieves a higher rate of STR, which is a good predictor of tissue reperfusion, than does balloon angioplasty.12 Recently, the use of manual thrombus aspiration before balloon angioplasty and stenting in patients with AMI has become common in daily clinical practice, but there are few data comparing efficacy and safety between ELCA and manual thrombus aspiration before stenting in patients with ACS. Although the present study is a retrospective and non-randomized observational investigation with a relatively small sample size, it is, to our knowledge, the first comparative study between ELCA and manual thrombus aspiration in ACS patients. The present results indicated similar feasibility and safety with both techniques, but attainment of TIMI 3 flow and MBG grade 3 after stenting was significantly more frequent in the ELCA group. The effects of manual thrombus aspiration on myocardial reperfusion in patients with AMI have been reported previously by several investigators. Attainment of TIMI 3 flow occurred in 51–91% of patients and that of MBG grade 3 occurred in 37–90% in the previous studies.9,24,28–30 In the studies in which aspiration catheter use led to superior results in attainment of TIMI 3 flow or MBG grade 3, distal protection devices also tended to be used. A notable result of the present study was that the attainment of good tissue-level reperfusion was achieved by the ELCA catheter alone without the use of distal protection devices. Thus, we regard ELCA to be not only a debulking device but also a preparation device that stabilizes unstable plaque containing large soft lipid cores and thrombi.

The other advantage of the ELCA catheter in the present study was its superior lesion crossability. In emergency cases, because the culprit lesions are thought to be soft and contain vulnerable plaque, guiding catheters with strong back-up force are not usually selected. Thus, Judkins-type guiding catheters were generally selected by the operators. Previous reports have shown that 1 potentially important factor that reduces the feasibility of manual thrombus aspiration is poorer crossability of the aspiration catheters. In previous studies, failure to reach or cross the culprit lesions occurred in approximately 4–11% of patients, and thrombotic material could not be collected in approximately 25% of patients, although the aspiration catheter was successfully delivered.5,26,31,32 In the present study, the laser catheters crossed the lesion in 96.2% of cases, whereas the aspiration catheters crossed the lesion in 82.6% of cases. Furthermore, the laser catheter crossed all lesions in the patients in whom the aspiration catheter did not cross. Several lesion-specific characteristics such as tortuosity, calcification, and bifurcation were suspected to be factors causing failure to cross the culprit lesions. Lesion characteristics in the present study were almost the same between the ELCA and aspiration groups, but the ELCA catheters showed an advantage in crossability. This would appear to be a favorable advantage in emergency settings in which weaker back-up guiding catheters tend to be used.

With regards to short-term outcome, in-hospital MACE rate was significantly higher in the manual aspiration group than the ELCA group in the present study, but all MACE were due to non-procedure-related etiologies, that is, CAGB for non-culprit lesions, acute pulmonary embolism, multiple organ failure. In contrast, wall motion recovery in the chronic phase was equal between the 2 groups. Further large-scale observations are needed to determine the advantages and disadvantages of the 2 devices in terms of prognosis.

Distal protection devices are also commonly used with manual thrombus aspiration in routine practice to reduce the occurrence of distal embolism. The efficacy of these devices, such as the GuardWire® (Medtronic, Fridley, MN, USA) or FilterWire™ (Boston Scientific, Natick, MA, USA), were recently reported, and we also realize the important role of such devices in the reduction of the no reflow phenomenon in real-world settings.31,32 The procedure, however, tends to become complicated with these devices due to the drawback of being difficult to use. In contrast, the ELCA system is a technically user-friendly device. It is readily available for urgent use in the cardiac catheterization lab, especially in unstable ACS patients requiring rapid intervention. Emission of excimer light results in adequate thrombus removal and clearance, thus contributing to rapid restoration of enhanced antegrade TIMI flow within the infarct-related vessel. The aspiration catheter is a very easy device to prepare, and door-to-balloon time in the aspiration group was significantly shorter than that in the ELCA group. The difference, however, was only 5 min, primarily due to laser console set-up time, and in contrast, attainment of TIMI 3 flow and MBG grade 3 following ELCA was superior to that following aspiration. Excimer laser energy is uniquely capable of suppressing platelet aggregation and vaporizing and debulking the underlying atherosclerotic plaque.

This study was a single-center, non-randomized, retrospective analysis and therefore has several limitations. First, selection of the devices was based on physician decision. In particular, the ELCA catheter falls into the category of advanced medical therapy in Japan, and it was not covered by Japanese Health Insurance during the study period. Thus, ELCA treatment tended to be performed only in a limited group. Second, the sample size was relatively small. Investigation through additional randomized controlled trials with larger sample sizes is necessary in the future. Third, there was a difference in frequency of DES use between the 2 groups. Selection of DES was basically by operator preference. Although this difference would probably affect mid-term outcomes, in the present study, there appeared to be no significant differences in regard to procedural and angiographic results and in-hospital MACE in patients receiving DES vs. BMS.

Conclusion

Lesion preparation with the ELCA system before stenting was feasible and safe, and we expect it to be a promising device to salvage tissue-level reperfusion in ACS patients with large thrombus load, and it might be useful in producing better outcomes in myocardial salvage. The intention of the present study was to elucidate only the safety and efficacy of ELCA compared with manual aspiration. We did not assess the long-term outcome after ELCA treatment, and further large-scale, multicenter studies are needed.
References


