Laser Endarterectomy: A Comparison of Thrombotic Potential Following CO₂ Laser vs Surgical Endarterectomy

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SUMMARY Although laser endarterectomy has recently been suggested as useful in the treatment of arteriosclerotic obstructions, the "in vivo" clotting effects have not been well delineated. In this study, the common carotid and femoral arteries of ten mongrel dogs were exposed, and alternating 1 cm segments of each artery were treated with surgical endarterectomy and low-powered CO₂ laser endarterectomy. Segments were then harvested, and subjected to histologic examination and vascular prostacyclin synthesis determinations, as measured by 6-keto PFG₁α radioimmunoassay.

Gross examination and light and scanning electron microscopy showed increased platelet aggregation and more extensive damaging of the underlying media of the laser compared to the surgical segments. Six-keto PFG₁α levels were significantly lower (p = 0.001) in the laser compared to surgical sites (mean 232 ± 72 pg/mg vs 515 ± 144 pg/mg), or controls (895 ± 337 pg/mg). These findings suggest that laser endothelial evaporation leads to increased thrombotic potential in the early post-operative period in comparison to surgical endarterectomy.

LASER ENDARTERECTOMY, using a multiple portal co-axial catheter delivery system, has recently been proposed as a method to recanalize partially or totally occluded coronary arteries. This technology also has great theoretical attractiveness in the treatment of arteriosclerotic cerebrovascular disease, as at least one-third of patients with carotid-distribution ischemic symptoms have obstructive lesions that are inaccessible to direct surgical correction (i.e. carotid endarterectomy). The specific effects of laser on vessel luminal surfaces have been largely limited to morphologic studies of small discrete (i.e. less than 1 mm diameter) lesions. As most clinically significant carotid or vertebro-basilar stenoses represent considerably greater luminal surface area, the direct application of these results in the treatment of cerebrovascular lesions may not be appropriate. Furthermore, the alterations of the clotting mechanism induced by intimal and media exposure to laser energy have not been well delineated. Since many untoward events in the cerebrovascular circulation are related to clotting abnormalities (i.e. thrombosis and embolism), the laser-induced effects on these mechanisms must be thoroughly analyzed before application to cerebral lesions can be safely considered.

In this study, the effects of low power CO₂ laser intimal and partial medial vaporization (herein termed laser endarterectomy) were investigated, both by light and scanning electron microscopy and by prostacyclin biosynthesis. These results were then compared to those changes induced by surgical endarterectomy, to evaluate the differences in clotting alterations induced by both treatments.

Materials and Methods

Ten mongrel dogs (15–25 kg) were anesthetized with intravenous pentobarbital (35 mg/kg), intubated, and placed on a large animal ventilator (Harvard venti-
lator model 613, Harvard Apparatus Co., S. Natick, Ma.). Standard operating techniques were used to expose 19 common carotid and 4 femoral arteries. After systemic heparinization (125 mg/kg intravenously), a long segment of each artery was isolated between vascular clamps, and a 5 cm linear arteriotomy was made. Using the operating microscope, each vessel was then subjected to both microsurgical endarterectomy (END) and CO$_2$ laser endarterectomy (LAS) in alternating 1.0 cm segments. An intact 1–2 cm arterial segment was interposed between the two endarterectomy sites to provide a control (CON) specimen.

Laser endarterectomy was accomplished utilizing continuous CO$_2$ laser energy delivered through a microscope-mounted mirrored delivery system (Cooper LaserSonic, Inc., Santa Clara, CA). The parameters of the laser energy applied to the vessel intima induced a power setting of 1–2 watts (as measured proximal to the delivery system), 100 millisecond pulse increments, and a defocused spot size (0.7 to 1.0 mm in diameter). These settings resulted in an approximate radiant exposure of 13 to 52 joules/cm$^2$. The vessel was kept moist with heparinized saline without allowing excess fluid to accumulate on the surface. These parameters were sufficient to superficially vaporize a 1 cm$^2$ segment of luminal surface without significant char formation.

Eight common carotid arteries were subjected to both laser and standard microsurgical endarterectomy, and were not thereafter exposed to blood flow. After immediate sacrifice, 1 cm segments of the LAS, END, and CON areas were gently washed and harvested. The segments subjected to light microscopy were fixed with 10% buffered formalin, and those for scanning electron microscopy (SEM) with Trump’s solution. Specimens for light microscopy were then paraffin-embedded, cut in 10 micron sections, and stained with hematoxylin-eosin, trichrome, and phosphotungstic acid hematoxylin. SEM specimens were examined and photographed on the Hitachi S-450 scanning electron microscope.

In four carotids, the linear arteriotomies were closed with 8-0 nylon suture, and blood flow was re-established for 60 to 75 minutes. The arteries were then perfusion-fixed at physiologic pressures with 100 ml of either 10% buffered formalin (for light microscopy), or Trump’s solution (for scanning electron microscopy). The fixed segments were then prepared for light microscopy or SEM with standard techniques, as outlined above.

The remaining seven carotid and 4 femoral arteries were harvested immediately for determination of 6-keto PGF$_{1\alpha}$ biosynthesis determination. Control, laser-treated, and surgically endarterectomized segments of each artery were separated, trimmed, and placed immediately in ice-cold Ca$^{++}$ and Mg$^{++}$ free phosphate buffered saline. The tissue was washed several times, placed in Hank’s Buffered Salt Solution (HBSS) containing Ca$^{++}$ and Mg$^{++}$, and incubated with 0.1 mM arachidonic acid for 15 minutes at 37°C. Six-keto PGF$_{1\alpha}$ was then measured in the supernatant by radioimmunoassay. Supplies for the radioimmunoassay were obtained from New England Nuclear, Boston, MA. Detailed description of methods and materials utilized in radioimmunoassay and cross-reactivities of 6-keto PGF$_{1\alpha}$ have been reported elsewhere. 

**FIGURE 1.** Light microscopic examination of canine carotid arteries, longitudinal section with intraluminal surface oriented superiorly. A: Control segment with all arterial layers intact. (H & E, ×40). B: Surgically endarterectomized segment. Note superficial accumulation of leukocytes (arrow) and intact deep layers of media. (H & E, ×100). C: Laser endarterectomized segment. Darkly staining superficial laser coagulum (arrow) with underlying hemorrhagic lakes is evident. Graded cellular damage marked by tissue separation and pyknotic nuclei can be seen to extend deep into media. Note absence of inflammatory infiltrate. (H & E, ×100).
Results

Light microscopic examination (fig. 1) revealed several important differences between laser and surgically treated arterial segments. Surgical endarterectomy removed the intima, elastic lamina, and approximately 10% of the media. Deeper layers of the media and adventitia were largely unaffected by the procedure. After exposure to blood flow, the media uniformly exhibited an inflammatory infiltrate consisting predominately of polymorphonuclear leukocytes. Hemorrhagic pockets in the adventitia were occasionally noted and attributed to the dissection of the carotid sheath.

Laser endarterectomized segments were found to have a smooth superficial coagulum situated slightly deeper than the internal elastic lamina of contiguous normal arterial wall. Although the full thickness of the underlying media was maintained, graded cellular damage characterized by pyknotic nuclei and tissue separation was evident below the surface. This damage was worst immediately under the coagulum, and in several places extended through the full thickness of the media. Hemorrhagic lakes were commonly incorporated into or just beneath the coagulum within the superficial layers of the media. Inflammatory cells were rarely noted.

Of those arteries in which blood flow was re-established, none developed complete luminal occlusion. Gross examination of the treated segments revealed a variable but consistently greater degree of thrombus formation on the LAS surfaces as compared to the END group. No cases of subintimal dissection were observed following either treatment type.

SEM disclosed striking differences between the surgical and laser endarterectomy segments. In arteries unexposed to blood flow, tightly woven bands of collagen or elastin were visible in the surgically endarterectomized vessels, compared to a glassy, smooth surface of coagulum in the laser-treated segments (fig. 2).

After exposure to blood flow for 60 to 75 minutes, platelet adhesion and aggregation into irregular monolayers was commonly encountered in the surgical specimens (fig. 3). Thrombus formation, when evident, had an equal mix of platelets and fibrin, with an occasional red or white blood cell. In contrast, laser endarterectomized segments were noted to have large, thick, irregular clumps of platelets covering most of the surface, interspersed occasionally with thrombus exhibiting a nearly equal mix of fibrin and platelets. Between the large clumps of platelets, the surface coagulum could occasionally be seen, and was sprinkled with elongated adherent platelets. No platelet monolayers could be identified.

The data representing prostacyclin biosynthesis is presented in figure 4. Six-keto PGF1α levels in the supernatant (mean pg/mg ± tissue standard error) were 895 pg/mg ± 337 in the CON group, 515 pg/mg ± 144 in the END group, and 232 pg/mg ± 72 in the LAS segments. Significant differences (p > .001) in 6-
keto PFG1α levels were found between all groups, as assessed by the paired Student's t-test. The relatively tight clustering of the data within each group suggests excellent uniformity of the analysis technique between samples.

**Discussion**

Our study demonstrates that application of low power CO₂ laser to the endovascular surface causes substantial damage to deeper tissue layers, potentially resulting in increased thrombosis risk to the vessel thus exposed. Similar findings were reported by Weichert et al, who reported that the Argon laser induces endovascular damage leading to platelet adhesion, transformation, and aggregation in rat mesenteric vessels. The clotting complications could potentially be ameliorated with the use of platelet aggregation inhibitors such as dipiridamole. Multiple other variables related to the laser energy itself could also be adjusted to reduce overall endovascular damage and its attendant risk. The ratio of exposure time to power density, utilization of pulsed rather than continuous energy (allowing for greater heat dispersion), mechanical cellular damage from vaporization shock, and the various types of laser media and delivery systems are each important technical considerations, and remain to be further explored.

Prostacyclin, a prostaglandin synthesized from the action of prostacyclin synthetase on the cyclic endoperoxides PGG2 and PGH2, is a potent inhibitor of platelet aggregation, disaggregates platelet clumps, and acts as a vasodilator. It is unstable in aqueous solution, and hydrolyzes rapidly to the stable product 6-keto PFG1α, which can be measured by radioimmunoassay. In our study, synthesis of prostacyclin, as determined by 6-keto PFG1α radioimmunoassay, was significantly decreased in arterial segments subjected to laser endarterectomy when compared to control or microsurgical endarterectomized segments of the same vessel. This alteration correlates well with the microscopic findings of vessel wall damage induced by LAS treatment.

Since prostacyclin is produced both by vascular endothelium and by the smooth muscle of the arterial wall underlying the endothelial surface, surgical or laser removal of the vessel intima (endarterectomy) would be expected to reduce its synthesis. In this study, surgical endothelial removal left intact the deeper medial layers, thus preserving some residual prostacyclin synthesis and platelet aggregation inhibition. Conversely, laser endarterectomy led to more extensive medial damage, further reducing prostacyclin activity, and was followed by increased platelet aggregation on the exposed surface. These findings indicate that laser endarterectomy, even with the application of low radiant energy, induces greater injury to arterial wall than surgical endarterectomy. This increased damage, even when mild, can reduce prostacyclin biosynthesis and enhance the potential for thrombotic complications in the early post-laser-treatment period. With deeper vessel wall injury, perforation is possible, and aneurysm formation may occur over a longer time interval. These consequences emphasize the importance of minimizing deep cellular damage from heat spread or vaporization if the laser is to become a clinically useful tool in the treatment of obstructive cerebrovascular disease.

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Evaluation of a Scoring System for Extracranial Carotid Atherosclerosis Extent With B-Mode Ultrasound

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SUMMARY We have developed a scoring system to quantify extent of extracranial carotid artery atherosclerosis using real-time ultrasound (B-mode). To evaluate repeatability of this scoring system we correlated repeat scores obtained within a short interval of one another (6 months) in 52 individuals. We compared repeatability of extent measurements with repeatability of a measure of severity (single most severe lesion). Correlations between first and second studies for severity were weak ($r^2 = 0.20$) but significant ($p < 0.001$). Extent scores correlated much better ($r^2 = 0.77$, $p < 0.001$). In another group of 22 patients we found that the extent of atherosclerosis decreased following endarterectomy. We used this method to determine changes in extent of carotid atherosclerosis with age in two sets of individuals. One consisted of a cohort of 22 patients who underwent repeat B-mode studies separated by 1½–3 years. This cohort demonstrated an increase in carotid score with age ($p < 0.05$). In a second group of volunteers undergoing cardiac catheterization and B-mode evaluation of the carotid system, carotid scores could be compared in individuals with age differences that averaged 15 years. Extent of carotid atherosclerosis was significantly greater in older individuals ($p < 0.01$) and differences in extent with age were exaggerated in patients with coronary disease compared to coronary disease free controls.

METHODS FOR QUANTITATION OF SEVERITY* of individual atherosclerotic plaques in the carotid arterial system are of great clinical importance for following patients longitudinally. A single strategically placed lesion may be the source of cerebral emboli or the cause of a hemodynamic reduction of flow and pressure.1–10 However, little is known about the significance of the extent of carotid artery disease. Because extensive carotid atherosclerosis that results in modest luminal stenosis may have no recognized clinical correlate, and because evaluation of extent is more difficult than evaluation of severity of individual lesions, extent is only rarely studied in the clinical setting.11,12 However, by analogy with coronary atherosclerosis, statistical strength may be gained by considering atherosclerosis extent as well as severity as a response variable.13 Coronary atherosclerosis extent may be evaluated by counting the number of coronary arteries with stenosis of 50% or more14–18 or by more sophisticated scoring systems such as that suggested by the American Heart Association Grading Committee19 or others20–23 that include lesions at multiple sites in the coronary system.

Using evaluation systems for coronary artery atherosclerosis as a model we have developed a scoring system for extent of extracranial carotid artery disease. We have employed this system to evaluate change in extent with age and in patients with and without coronary artery atherosclerosis and change in

*In this discussion severity refers to the axial thickness (by B-mode) of a single luminal obstruction while extent refers to the sum (or average) of axial thicknesses for a number of such obstructions.

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Supported by Specialized Center of Research in Arteriosclerosis Grant HL-14164 from the NHLBI and Cerebrovascular Research Center Grant NS06655 from the NINCDS.

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Received February 26, 1985; revision #1 accepted June 12, 1985.
Laser endarterectomy: a comparison of thrombotic potential following CO2 laser vs surgical endarterectomy.

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Stroke. 1986;17:266-270
doi: 10.1161/01.STR.17.2.266

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