Transmyocardial Laser Revascularization Induces Cerebral Microembolization

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Background: Transmyocardial laser revascularization may vaporize fluid in the left heart, allowing bubbles to form. This study aimed to determine whether the laser pulse resulted in cerebral emboli and to examine changes in middle cerebral artery flow velocity and jugular bulb oxygen saturation (SjO₂) during transmyocardial laser revascularization.

Methods: Twelve patients (American Society of Anesthesiologists' physical status III) were studied after the authors received institutional review board approval and the patients' informed consent. Monitored variables included mean arterial blood pressure (measured in millimeters of mercury), heart rate (measured as beats/min), and partial pressure of carbon dioxide (measured in millimeters of mercury). A 5-MHz transesophageal-sonography system was used to record intraventricular events after laser injection. Mean blood flow velocity (Vm, measured in centimeters per second) was monitored in the middle cerebral artery using transcranial Doppler sonography, and SjO₂ (expressed as a percentage) was measured using a fiberoptic thermocatheter placed in the right jugular bulb. Data were recorded before, during, and for 4 min after laser injection.

Results: After laser injection, intraventricular echogenic contrast was seen in transesophageal-sonography, and 2–4 s later high-intensity signals (microemboli) appeared in the transcranial Doppler sonography spectra. As long as mean arterial pressure remained stable during the observation period, Vm, and SjO₂ did not change.

Conclusions: These data show that microemboli can be detected after laser injection in the middle cerebral artery, although they do not affect Vm, and SjO₂. The results suggest that these microemboli do not induce a global oxygen imbalance. (Key words: Anesthesia: cardiovascular, Brain: embolization. Blood flow. Jugular bulb oxygen saturation. Transcranial Doppler sonography. Surgery: transmyocardial laser revascularization.)

TRANSMYOCARDIAL laser revascularization is an alternative treatment for patients with symptomatic coronary artery disease who are refractory to maximal medical therapy but unsuitable for coronary artery bypass graft.1,2 A carbon dioxide laser is used to create transmyocardial channels to initiate neovascularization and thereby improve myocardial blood supply. Complete perforation of the myocardial wall is assessed by determining laser-induced intraventricular bubble formation using transesophageal echocardiography monitoring.2

It is unclear whether these bubbles embolize to the cerebral circulation or if they impair cerebral oxygen delivery. Emboli in the middle cerebral artery can be detected by transcranial Doppler sonography (TCD).3,4 In addition, fiberoptic jugular bulb oximetry can assess the ratio of global cerebral oxygen delivery and demand.5,7 The purpose of the study, therefore, was to investigate the effects of laser-induced embolization on cerebral blood flow velocity and jugular bulb oxygen saturation (SjO₂).

Materials and Methods

After receiving approval of the ethics committee and informed patient consent, we enrolled 12 patients (American Society of Anesthesiologists' physical status III) who were undergoing transmyocardial laser revascularization. We excluded patients with preexisting neurologic dysfunction. All patients were premedicated with flurazepam (1 mg/kg given orally) on the evening before surgery. 60 min before induction, dehydrobenzperidol (0.07 mg/kg) and fentanyl (1.5 μg/kg) were given by subcutaneous injection. Anesthesia was in-
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duced with fentanyl (15 µg/kg), etomidate (50 µg/kg), both administered intravenously, and neuromuscular blockade was conducted using pancuronium (100 µg/kg given intravenously). After endotracheal intubation, all patients were ventilated to normocapnia with oxygen in air (fractional inspired oxygen tension, 0.3–0.5), and anesthesia was maintained with fentanyl; midazolam, as clinically required; and continuous infusion of etomidate. The radial artery was cannulated to permit measurement of mean arterial pressure and blood sampling. Total length of the procedure was 60–90 min.

Transesophageal echocardiography was used to monitor the transmural cardiac laser pulse (Vingmed 750; Sonotron, Vingmed, Horten Norway). Complete perforation of the myocardium was shown by the detection of laser-induced echogenic contrast. The ejection of laser-induced emboli into the aortic root was demonstrated using the two-dimensional mode.

Cerebral blood flow velocity was monitored through a transtemporal approach to the proximal segment (M1) of the left middle cerebral artery using a bidirectional 2-MHz TCD system (Neuroguard; Medasonics, Fremont, USA). The TCD probe was fixed in a frame to keep the depth and angle of insonation constant over time. The flow velocity profiles are presented in real time on an integrated video monitor after flow direction discrimination and calculation of the Doppler frequency shift. The mean flow velocity (Vmean measured in centimeters per second) was recorded continuously throughout the procedure.

SjO2 (expressed as a percentage) and jugular bulb temperature (expressed as degrees centigrade) were measured using a fiberoptic thermocatheter (Opticath F 5.5; Abbott Critical Care Systems, Abbott Park, IL) placed in the left jugular bulb via the left internal jugular vein because the patient was turned to the right lateral decubitus position. Appropriate catheter position was verified radiographically before measurements were taken. The catheter was calibrated in vitro before insertion according to the colorimetric method supplied by the manufacturer. Immediately after insertion, and during the observation period, accurate fiberoptic saturation values were verified by drawing blood samples from the catheter and measuring the oxygen saturation rate using a co-oximeter (Radiometer, model OSM 3, Copenhagen, Denmark). If the catheter- and co-oximeter-derived values differed by more than 5%, the catheter was recalibrated in vitro. The catheter display provided a value for reflected light intensity at 5-s intervals.

Table 1. Demographic and Intraoperative Data

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<tr>
<td>Patients (n)</td>
<td>12</td>
<td>Gender (male/female)</td>
<td>9/3</td>
<td>Age (yr)</td>
<td>64 ± 9</td>
<td>Weight (kg)</td>
<td>77 ± 8</td>
<td>Height (cm)</td>
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<td>Ejection fraction (%)</td>
<td>48 ± 13</td>
<td>Laser pulse (n)</td>
<td>37 ± 5</td>
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Applicable data are mean ± SD.

In each patient, three to eight periods of laser application with three to seven laser pulses per period were obtained. Before, during, and 4 min after administration of laser pulses, Vmean, SjO2, heart rate (expressed as beats/minute), mean arterial pressure, and jugular bulb temperature were monitored continuously and recorded every minute. Arterial blood gas analyses were performed before and 4 min after laser injection. In each patient, one period was evaluated during stable hemodynamic conditions. Data were not collected when systemic hemodynamic parameters were unstable (mean arterial pressure < 60 mmHg) due to surgical manipulation.

A complete neurologic examination was performed by a neurologist in all patients on the day before and on the first day after operation.

Statistics

Data are presented as means ± SD. Physiologic variables at given time intervals were tested for Gaussian distribution using the Kolmogorov-Smirnov test. Analysis of variance for repeated measurements was used to test for significant differences over time. Post hoc data were analyzed using paired t tests with Bonferroni corrections for repeated measurements. Statistical significance was assumed at probability values less than 0.05.

Results

Table 1 shows demographic data and the number of laser pulses administered. Figure 1 depicts a representative transesophageal echocardiography recording after successful transmural perforation. Intraventricular contrast ("snow") rapidly develops after the pulses representing a high concentration of emboli; this is subsequently ejected through the aortic valve. Between 2 and 4 s after the laser pulse, high-frequency signals (indi-
cating emboli) are detected in the middle cerebral artery for a period of 20–60 s by TCD (fig. 2). This typically lasts 20–60 s.

These observations were made in each patient during each laser pulse period. Heart rate (82 ± 11 beats/min), mean arterial pressure (80 ± 8 mmHg), partial pressure of carbon dioxide (37.9 ± 2.0 mmHg), and jugular bulb temperature (35.7 ± 0.4°C) did not change in the 4 min after the laser pulse. The $V_{\text{mean}}$ (36 ± 6 cm/s) and $\text{SjO}_2$ (56 ± 8%) also remained unchanged. All patients were awake and oriented on the first postoperative day. No neurologic abnormalities were noted.

**Discussion**

Ultrasonic echo monitoring can detect solid or gaseous microemboli. In dogs, the sensitivity of echocardiography was high, with values for specificity that were reduced by as much as the size of the emboli decreased. The studies cited show that the snow-like clouds observed in the present study are likely to correspond to embolic material that is transported into the systemic circulation. As with transesophageal echocardiography in the heart, TCD can detect intraluminal emboli in cerebral vessels. Russel et al. have shown in rabbits that intravascular injection of particles was invariably followed by the appearance of high-intensity signals on the screen. In vivo Markus and Brown found a linear relation between the embolus size and the duration of the high amplitude and a relation between the embolus size and the maximum amplitude of the Doppler signal. The regression lines differed for different embolic materials. However, according to Russel et al., identification of the material embolized, judging from the signal characteristics of the Doppler tracing, will barely be possible. Furthermore, TCD is prone to movement artifacts and electromagnetic disturbances, both of which may cause high-intensity signals, thus mimicking embolization episodes. In our study, the sequential appearance of laser pulse, “snow clouds” in transesophageal echocardiography, and acoustic phenomena in TCD after a trans-time of 2–3 s strongly suggest the existence of arterial emboli, ruling out artifacts as a source of the signals.

Van Leeuwen et al. noted the possibility of the formation of intravascular emboli after the use of laser. In a hemoglobin solution, those authors demonstrated photographically that an excimer laser pulse (using the radiation of an electronically "excited dimer" molecule) formed a fast-expanding (2.3 mm in diameter...
within 100 μs) and imploding vapor bubble (within 250 μs after the laser pulse). The bubble reexpanded and disappeared at 500 μs, but some small bubbles remained long after the laser pulse. The same group of researchers observed the formation of vapor bubbles in vivo in rabbits during laser angioplasty of the femoral artery. In the vicinity of the site of vapor bubble formation, severe arterial wall lesions, including media-necrosis and vascular dissection, were observed and appeared not to be due to the effect of the laser pulse itself. The authors ascribed their observations to the potential formation of vapor bubbles. Absorption of the energy of the laser pulse thus would have lead to vaporization of blood due to energy absorption by hemoglobin and tissue proteins. Freed et al. found that during implosion of vapor bubbles, violent peak pressure gradients occur, which along with local damage of blood particles and vessel walls leads to formation of bubbles from gases dissolved in blood (oxygen, nitrogen, and carbon dioxide). In addition, those authors have shown that cavitation after implosion fragmented circulating microbubbles into many gaseous microemboli (measuring <15 μm) that may persist briefly in the circulation. These mechanisms may serve, in part, to explain the observations that we made in our study: The emboli detected are likely to be due to vaporization of blood, particles, and solutes after the impact of the carbon dioxide laser. Thus they probably consist of vapor and gas. Recently researchers have shown that microbubbles in flowing blood are not absorbed very quickly. However, Feinstein et al. found that only arterial emboli larger than 15 μm lead to temporary occlusion of more than 1 min, whereas emboli of less than 10 μm in diameter pass the capillary vasculature unrestricted. Thus many small emboli may cause the phenomena observed without leading to clinical neurologic abnormalities.

The laser pulse may cause the formation of cell debris and toxic photoproducts, which both may contribute to the occurrence of emboli. In dogs after Argon-laser angioplasty, Gal et al. found levels of carboxyhemoglobin and hydrogen cyanide that were much less than accepted clinical toxic limits, but microparticulate debris was not detected. Therefore the occurrence of debris and toxic photoproducts due to the incineration of organic material may play only a minor role for cerebral embolization.

Our finding that SjO2 remained largely constant over time indicates that the global cerebral oxygen balance is not grossly impaired by embolic events. Jugular bulb oxygen saturation does not detect regional cerebral ischemia based on microembolization. Only occlusion of a major vessel or diffuse occlusion of about 10% of the arterial vascular volume with an increase of oxygen extraction would induce a change in SjO2. In our study, the latter remained unchanged in the observation periods, suggesting that an impairment of cerebral oxygen balance may occur only on a regional basis, undetectable by SjO2.

We detected no major neurologic complications, probably because of the small sample size of 12 patients studied. However, measures should be taken clinically to reduce the risk of cerebral embolization during transmyocardial laser revascularization. Because oxygen bubbles dissolved about ten times faster than nitrogen bubbles, use of oxygen (fractional inspired oxygen tension, 1.0) 10 min before the procedure may be beneficial. Use of nitrous oxide appears to be potentially harmful because its high diffusion capacity into preformed bubbles. In addition, systemic hemodynamic variables should be adjusted to an optimum level to prevent cerebral hypoperfusion that may aggravate effects of the emboli on the cerebral circulation.

Our results show that transmyocardial laser revascularization leads to cerebral embolization. The ratio of global cerebral oxygen delivery and oxygen demand remains unchanged if perfusion pressure is maintained within sufficient limits. Based on the assumption that the emboli observed by transesophageal echocardiography and TCD consist of gas, nitrogen and nitrous oxide should be discontinued before the laser pulse is administered. We did not perform neuropsychiatric tests in this study. However, none of the 12 patients exhibited major neurologic deficits on the first day after operation, indicating that transmyocardial laser revascularization did not cause significant cerebral ischemia. Further studies should evaluate the potential influence of the embolic events on postoperative neuropsychiatric performance using more meticulous methods of testing.

References

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