Doppler Ultrasound Monitoring for Detection of Microembolic Signals in Peripheral Arteries

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Objective: to use Doppler ultrasound to detect peripheral microembolization.

Methods: standard Transcranial Doppler equipment was used to detect peripheral high intensity transient signals (HITSs) in a pig model following injection of microparticles and atheroma, and in 23 patients who underwent open repair of an abdominal aortic aneurysm (AAA), six patients with blue toe syndrome and 10 age matched healthy subjects.

Results: the pig study showed increasing signal intensity with particle size. Particles of 100 (n = 24), 200 (n = 17), and 400 μm (n = 31) elicited 14, 25, 33 dB signals, respectively (p < 0.05). During AAA surgery, the intensity (median) of HITSs before clamping (n = 226) and after declamping (n = 1216) were 14, and 20 dB, respectively (p < 0.001). Quite a few HITSs were detected after surgery. In patients with blue toe syndrome, a total of 63 HITSs could be detected, and the frequency of HITSs (median: 5.72/30 min) was significantly higher than that in patients with AAA before surgery (0.065/30 min) (p < 0.001).

Conclusions: Doppler ultrasound technique may be a clinically useful test to guide the treatment of patients at risk of distal atheroembolic events.

Key Words: Microembolus; Doppler ultrasound; High intensity transient signal (HITS); Peripheral artery.

Introduction

Transcranial Doppler ultrasound (TCD) scanning is often used for embolus detection in the middle cerebral artery of patients with symptoms of cerebral ischemia. Blue toe syndrome (BTS) is primarily an observed diagnosis and an objective examination is needed for diagnosis and treatment. Intraoperative monitoring for emboli in the peripheral arteries could be useful to prevent thromboemboli and to revise operative technique.

The aim of this study was two-fold. First, we validated whether microemboli could be detected as high intensity transient signals (HITSs) in the peripheral arteries in the pig model. Second, intraoperative Doppler ultrasound monitoring was applied in patients undergoing aortic surgery and in those diagnosed with BTS.

Materials and Methods

Experimental model

Male swine (32 kg) were intubated under general anesthesia with isoflurane. A 10-cm pararectal abdominal incision was made, and the aorta exposed via a retroperitoneal approach. The Doppler examination was carried out continuously on the right common femoral artery (diameter 3.0 mm). Artificial embolic materials comprised 100, 200 and 400 μm diameter microspheres (polystyrene; catalog number 4310A, polystyrene DVB (divinylbenzene, 4–8%); catalog number 4320A, 4340A, Duke Scientific Co., Palo Alto, CA, U.S.A.). Human atheroma was diced into 0.2–0.5 mm cubes. Embolic materials were then suspended in saline (10 ml) and injected directly into the abdominal aorta. Great care was taken to and the introduction of air.

Doppler setup was based upon previous work. A commercially available Doppler ultrasound machine (EME Pioneer, Nicolet Biomedical, Madison, WN, U.S.A.) was used with a 2-MHz transducer. An intensity threshold of ≥3 dB and a 128-point fast Fourier
transform (FFT) with a time-window overlap of 67% was used for spectral analysis. Both leading columns and trailing columns were 250. Scale setting was -50–100 cm/s, and a high-pass filter was set at 106 Hz. The sample volume was 10 mm and it was kept constant for all recordings in this study. Amplitude was reduced to 44%. Gain was adjusted to make the common femoral arterial signal have a pale blue color, corresponding to a background intensity of 3–9 dB. All Doppler audio signals were recorded onto hard disc of the same Doppler ultrasound machine for off-line analysis. The SoundTrak software was supplied with this machine (Nicolet Biomedical). The following identification criteria as HITS was used for off-line analysis: intensity increase ≥3 dB above background, short duration (<300 milliseconds), unidirectional, random appearance in the cardiac cycle, and with characteristic sound on the audible output according to a recent consensus (Fig. 1).

**Human studies**

**AAA patients**

Twenty-three patients (18 men and five women) with AAA (Group A) were studied before, during, and after an elective aortic aneurysmectomy and a bifurcated graft replacement. They had a median age of 73 years with ranging from 62 to 86 years. All abdominal aneurysms were infrarenal type and the median diameter of the aneurysm was 55 mm with ranging from 40 to 85 mm. No patient had embolic symptoms and findings at their foot, and ankle brachial pressure index (ABI) was more than 1.0 in all patients.

Patients, who had cardiac arrhythmia, prosthetic valves, or atherosclerotic occlusive disease, or who received anticoagulation therapy, were excluded from this study. Recordings were possible in all subjects, and all subjects completed the study protocol. All patients gave signed informed consent.

All procedures were performed with the patients under general anesthesia with epidural analgesia. The transperitoneal approach (n = 10) and the retroperitoneal approach (n = 13) were applied for an aneurysmectomy and a bifurcated knitted Dacron® graft replacement. Clamps were preferentially placed on the iliac arteries before proximal aortic clamping was performed. On completion of the proximal anastomosis, the graft was flushed with heparinised saline (heparin 2500 units/saline 500 ml) in order to wash out debris. Before the distal anastomosis was completed, the iliac arteries were back-bleed and the air was fully vented in the prosthetic graft.

Doppler ultrasound recordings were performed with the patient supine. A specially designed holder fixed the probe to the medial aspects of the calf part and adjusted an insonation angle to about 60° to detect the tibioperoneal trunks (Fig. 2). Depth was determined to obtain optimal Doppler flow wave of the artery, and the depth was 40 mm with ranging from 32 to 48 mm. Monitoring duration was prolonged for 60 min (30 min for each side of the lower limbs) before and after surgery, and for 80 min (range: 47–116 min, before clamping) and 121 min (range: 84–191 min after declamping) during surgery to monitor MESs.
Age matched healthy controls
A group of 10 age-matched healthy subjects served as controls (Group C, 8 men and two women) and were also studied at the supine position. The recordings were obtained for 60-min duration (30 min for each side of the lower limbs).

Patients with blue toe syndrome
Six patients (all men, 11 limbs) with BTS (Group B) were studied. Emboli were considered to be originated from AAA (n = 3), shaggy aorta (n = 2), stenotic lesion with ulceration of the left iliac artery (n = 1). They had a median age of 70 with ranging from 65 to 80 years. In these patients, we also monitored two cases after aneurysmectomy and one case after stenting for iliac stenosis. The same settings and technique mentioned above were applied. Monitoring duration was prolonged for 60 min (30 min for each side of the lower limbs) before and after surgery or iliac stenting.

Statistical analysis
Results are expressed as median value with ranges. A p-value < 0.05 is used to define statistical significance. Statistics for between-group differences were calculated with the Mann–Whitney test.

Results

Experimental study
A total of 89 emboli (24 100-μm sized particles: 17 200-μm sized particles: 31 400-μm sized particles: 17 human atheroma) were detected in the Doppler spectrum and by their characteristic “chirping” sounds as they passed the Doppler probe.

The intensity of embolic signals depended on the embolic size and character. The intensity increase was shown in Figure 3. The signal intensity of 200-μm sized particles (median: 25 dB, range: 8–37 dB) was significantly higher than that of 100-μm sized particles (median: 14 dB, range: 5–38 dB) (p = 0.032), and that of 400-μm sized particles (median: 33 dB, range: 14–39 dB) was also significantly higher than that of 200-μm sized particles (p = 0.030).

Atheroma emboli were also detected as HITSs, which contained various sized particles. The median intensity of atheroma emboli was 29 dB (range: 11–41 dB), which ranged between that of 200-μm sized particles and 400-μm sized particles.

Human studies with AAA

In group A (n = 23), a total of three HITSs were detected before surgery, and its frequency was 0.065 HITSs/30 min at each insonated site.

A total of 1442 HITSs (226 HITSs before aortic cross clamping, 1216 HITSs after declamping the iliac artery) was detected during surgery in group A (Figs 4, 5). Before the aortic cross-clamping, the median intensity and the median frequency of HITSs were 14 dB (range: 3–35 dB), 3 counts (range: 0–46 counts)/limb, respectively. After declamping the iliac artery, the median intensity and the median frequency of HITSs were 20 dB (range: 3–41 dB), 27 counts (range: 5–256 counts)/limb, respectively. More than 70% of HITSs were detected less than 5 min after declamping. The intensity of HITSs after declamping...
was significantly higher than that of HITSs before clamping ($p < 0.001$).

A total of 12 HITSs (0.26 HITSs/30 min), and two HITSs (0.043 HITSs/30 min) were detected 4 h, and 24 h after surgery, respectively. It demonstrated that quite few HITSs were detected four hours after surgery although a lot of HITSs were detected immediately after declamping and blood restoration to the lower extremity intraoperatively. No case showed blue toe in the postoperative period. In group C ($n = 10$), no HITS were detected.

Human studies with blue toe syndrome

In group B ($n = 6$), a total of 63 HITSs were detected. The median intensity and the median frequency of HITSs were 14 dB (range: 3–19 dB), 5.72 HITSs/30 min (range: 3–9), respectively (Fig. 6).

The frequency of HITSs in group B was significantly higher than that of HITSs in group A before surgery ($p < 0.001$). On the other hand, there was no significant difference of the signal intensity of HITSs between group B and group A before clamping during surgery ($p = 0.77$).

No HITS could be detected after aneurysmectomy in two cases and after iliac stenting in one case. In one patient with AAA, the right third and fourth digits finally became demarcated and amputated naturally about 6 months after the surgery. Microscopic findings demonstrated cholesterin crystals in the arterioles (200 mm in a diameter) at the both amputated digits. Blue toe was also cured in other two patients, who underwent aneurysmectomy or iliac stenting. The remaining three cases should be followed with conservative therapy because their general conditions were poor.

Discussion

TCD scanning is now routinely used for embolus detection in the intracranial vasculature of patients with symptoms of cerebral ischemia. Microemboli can also be detected as MESs in the peripheral arteries. The results showed the intensity of the MESs depended on the embolic size. Although signal intensities were significantly different among different particle size, relatively higher signal intensities in MESs were detected even if 100 and 200 μm particles were injected into the abdominal aorta. It could be considered that a couple of particles could pass through the detecting window of the introducer at the same time. At least four papers described that Doppler ultrasound could be applied to detect the MESs in the peripheral arteries. Recording parameters including insonated arteries, sample volume, amplitude, and frequency of the transducer were different (Table 1). There has been no guideline for embolus detection in the peripheral arteries.

Clinical experience showed that embolus detection might be difficult when Doppler ultrasound settings were inappropriate. Doppler apparatus settings should be optimized for detection of MESs in the peripheral arteries because there were some differences between embolus detection in the intracranial
The embolus to blood ratio (EBR) increases with decreasing vessel diameter.11 The tibioperoneal trunks are about 4 mm in diameter to make background signal a pale blue color. Sufficient depth is necessary for optimal embolus detection because intensity attenuation is little at monitoring in the peripheral arteries. It is possible to obtain appropriate depth at monitoring in the tibioperoneal trunks, which was located at 40 mm (range: 32±48 mm). A small sample volume in the tibioperoneal trunks, which was located at is possible to obtain appropriate depth at monitoring beam.8 2-MHz, 4-MHz, or 8-MHz probes were commercially available with TCD machine, and 2-MHz probe was chosen in this study because lower frequency improved signal/noise ratio.

The embolus to blood ratio (EBR) increases with decreasing vessel diameter. It is possible to obtain appropriate depth at monitoring in the tibioperoneal trunks, which was located at 40 mm (range: 32–48 mm). A small sample volume produces the best embolic signal-background differentiation.7 As sample volume setting 10 mm is considered to be adequate to insonate the tibioperoneal trunks because of peak systolic velocity, vessel diameter, and signal/noise ratio. Because intensity attenuation is much lesser in the peripheral arteries due to absence of any intervening bone between the transducer and the insonated artery, and the insonated arterial configuration. On the basis of the previous documentations7–8 and experimental validations, the following settings were considered to be appropriate for embolus detection with Doppler ultrasound apparatus in the peripheral arteries.

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Inadequate degrees of FFT time-window overlap results in failure to detect MESs by the current Doppler ultrasound apparatus. Time-window overlap 67% is an adequate degrees to detect and not to overlook MESs in this study, because no MESs were missed with an approximately 57%.6 Threshold was determined 3 dB due to the identification criteria of HITS in the guidelines for proper use of TCD monitor.4 This technique was also applied to patients with BTS, and MESs were successfully detected, which vanished right after surgery or stenting in three patients. The embolic source could be removed or covered in these patients because clinical symptoms including painful toe and gangrene were cured. Because the typical clinical symptoms, radiological findings, postoperative improvement, as well as the cholesterin crystals of the amputated digits were recognised in the patients, the cholesterin emboli could be successfully detected as HITs by the above-mentioned settings. It seemed to be validated that Doppler apparatus settings and monitoring were reliable in the study because HITs vanished in accordance with clinical improvement after surgical or interventional therapy.

To theoretically describe the detectability of microemboli, Moehring and Klepper11 investigated EBR by observing how it changed with its constituent variables, i.e. the carrier frequency, the embolus diameter, and the vessel diameter, for both red-cell aggregate emboli and air emboli in the in-vitro model. The EBR was 10–15 dB when carrier frequency was 2 MHz, vessel diameter was 4 mm, and red-cell aggregated embolus size was 200 μm. It was really similar to our result except the embolic materials were pathologically different.

In the current study, no patient showed blue toe in the postoperative period in group A although a lot of HITs were detected by the intraoperative monitoring in all cases. On the other hand, quite few HITs were detected four hours after surgery. It might be suggested that temporal microemboli didn’t cause blue toe. In addition, it might be suggested that there was the tolerance of the digit of the foot as well as the brain to microemboli.12 It is necessary to study the pathophysiologic importance of microemboli to blue toe. This technique will be helpful in study of microemboli.

Table 1. The settings for embolus detection in the peripheral arteries in the previous documentations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Subject</th>
<th>Insonated artery</th>
<th>SV</th>
<th>Amplitude</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Al-Hamali et al.</td>
<td>PTBA</td>
<td>CFA</td>
<td>4 mm</td>
<td>2%</td>
<td>2 MHz</td>
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<tr>
<td>Thompson et al.</td>
<td>AAA, stent graft</td>
<td>SFA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Abraham et al.</td>
<td>Angiography</td>
<td>PTA or DPA (ankle level)</td>
<td>NA</td>
<td>10%</td>
<td>2 MHz</td>
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<tr>
<td>Nicholls et al.</td>
<td>Case report</td>
<td>PTA (distal part)</td>
<td>NA</td>
<td>NA</td>
<td>3 MHz</td>
</tr>
<tr>
<td>Kudo et al.</td>
<td>AAA</td>
<td>Tibioperoneal trunks</td>
<td>10 mm</td>
<td>44%</td>
<td>2 MHz</td>
</tr>
</tbody>
</table>

AAA, abdominal aortic aneurysm; PTBA, percutaneous transluminal balloon arterioplasty; CFA, common femoral artery; SFA, superficial femoral artery; DPA, dorsalis pedis artery; PTA, posterior tibial artery; SV, sample volume; NA, not available.

Eur J Vasc Endovasc Surg Vol 24, July 2002
in the peripheral circulation and as a clinical test to guide medical and surgical treatment for patients at risk of BTS.

References


Accepted 17 April 2002