

## NEUROSCIENCES AND NEUROANAESTHESIA

## Detection and differentiation of cerebral microemboli in patients undergoing major orthopaedic surgery using transcranial Doppler ultrasound

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### Abstract

**Background.** Cerebral microemboli (ME) are frequently generated during orthopaedic surgery and may impair cerebral integrity. However, the nature of cerebral ME, being either of solid or gaseous origin, is poorly investigated. Our primary aim was to determine both the frequency and nature of cerebral ME in generally anaesthetised patients undergoing major orthopaedic surgery.

**Methods.** Fifty patients (hip/knee/shoulder prosthesis, spine surgery) were enrolled. Cerebral ME and cerebral blood flow velocity (CBFV) were determined in both middle cerebral arteries for 15 min preoperatively and postoperatively, using transcranial Doppler ultrasound. Cerebral tissue oxygen index, determined by near-infrared spectroscopy, was further examined. Statistical analysis was carried out using the Wilcoxon matched-pairs signed-ranks test (median (25<sup>th</sup>; 75<sup>th</sup> percentile),  $P < 0.05$ ).

**Results.** Overall the frequency of postoperative cerebral ME rose to 600% of preoperative values. Primarily gaseous ME occurred preoperatively and postoperatively [19 (6; 63) vs 116 (24; 373),  $P < 0.001$ ], while the number of solid ME was negligibly small [1 (0; 2) vs 2 (0; 6),  $P < 0.001$ ]. CBFV and cerebral tissue oxygen index remained unaltered bilaterally before and after surgery.

**Conclusions.** Our findings indicate that cerebral ME considerably increase after major orthopaedic surgery under general anaesthesia. The predominant accumulation of gaseous ME and their preoperative occurrence, suggest that the general anaesthesia and individual patient factors may contribute to the embolic load in addition to orthopaedic surgery.

**Clinical trial registration.** NCT02340416.

**Key words:** intracranial embolism; orthopaedics; ultrasonography, Doppler, transcranial

**Editor's key points:**

- Cerebral microemboli are common during orthopaedic surgery.
- Modern transcranial Doppler technology enables accurate detection of the number and nature of emboli.
- Fifty patients undergoing major joint replacement or spinal surgery were investigated.
- Gaseous emboli were much more common than solid emboli and increased sixfold in incidence after surgery.

Cerebral microembolization regularly occurs during orthopaedic surgery.<sup>1</sup> Solid or gaseous microemboli (ME), which enter the venous circulation intraoperatively, can reach the brain through intrapulmonary shunts or right-to-left shunts within the heart. Small gaseous ME are further able to pass pulmonary capillaries.<sup>2</sup> Emboli counts during orthopaedic surgery, determined by transcranial Doppler (TCD) ultrasound, vary from low (< 10 ME/surgical procedure) to high numbers (> 100 ME/surgical procedure) in total.<sup>1</sup> But these counts may be biased, because TCD ultrasound was used intraoperatively, and both surgical manipulation and diathermy may lead to false positive ME by TCD technology.<sup>3</sup> Although cerebral microembolization is supposed to affect cerebral integrity<sup>1,4</sup> and different origins of cerebral ME are discussed (e.g. fat, thrombus, tissue, cement, gas, microbubbles), the true nature of ME, being either of solid or gaseous origin, is poorly investigated.

The primary objective of this study was to determine the amount and nature of cerebral ME in generally anaesthetised patients undergoing major orthopaedic surgery. For that, cerebral ME were detected and differentiated into solid or gaseous ones, in both middle cerebral arteries (MCAs) using TCD ultrasound. To exclude intraoperative artifacts, TCD measurements were performed preoperatively and postoperatively. Additionally, we assessed cerebral blood flow velocity (CBFV) of the MCAs by TCD ultrasound and the tissue oxygen index (TOI) of the frontal lobes by near-infrared spectroscopy (NIRS) to investigate cerebral perfusion and oxygenation.

**Methods****Ethics approval**

Our research was approved by the Ethics Committee of the Medical University of Vienna (ref: 1633/2013, chair: E. Singer) and registered with Clinicaltrials.gov (ref: NCT02340416). Written informed consent was obtained from all patients on the day before investigation and the study protocol complied with the Declaration of Helsinki. The study design was a single cohort observational clinical trial. Patients served as their own control group, as they were investigated preoperatively and postoperatively. All examinations were performed at the Medical University of Vienna between 12<sup>th</sup> August 2014 and 19<sup>th</sup> March 2015.

**Study population**

Patients aged between 50 and 90 yr, who were undergoing major orthopaedic surgery under general anaesthesia, were included. Major orthopaedic surgeries comprised the implantation of elective hip, knee, and shoulder prosthesis, or spine surgery

lasting more than three h. General anaesthesia was induced with bolus injection of fentanyl ( $2 \mu\text{g kg}^{-1}$ ) and propofol ( $2 \text{ mg kg}^{-1}$ ), and rocuronium ( $0.6 \text{ mg kg}^{-1}$ ) was used for neuromuscular paralysis. Maintenance of anaesthesia was achieved with sevoflurane (minimum alveolar concentration: 0.8-1.3) and fentanyl (by bolus injection). Mean bp was held within 25% of preoperative values using neosynephrine (by bolus injection) or noradrenaline (by syringe pump). Exclusion criteria of the study were: medical history of severe aortic or mitral valve stenosis, medical history of severe aortic or mitral regurgitation, presence of mechanical or biological heart valves, medical history of carotid stenosis > 70%, medical history of vascular dementia or Alzheimer's disease.

**Study protocol****Data collection**

Data were collected twice for 15 min, directly before patient transfer to the operating room and immediately after patient discharge from the operating room. All patients were awake and spontaneously breathing during the preoperative and postoperative examinations, which were equally performed in a supine position with 30-degree elevation of the upper body. An advanced TCD probe was used to verify whether major orthopaedic surgery under general anaesthesia leads to cerebral ME and to determine the embolic nature. CBFV of both MCAs was continuously measured to investigate cerebral perfusion.<sup>5</sup> The TOI of both frontal lobes, determined by NIRS, was assessed to examine regional cerebral oxygenation. Venous blood gas analyses were carried out preoperatively and postoperatively, to investigate laboratory changes before and after surgery.

**TCD ultrasound**

The recent generation of multifrequency pulsed TCD technology (Doppler BoxX, Compumedics Germany GmbH, DWL, Singen, Germany) was used. The MCAs were bilaterally insonated with a pulsed-wave transducer at both 2 and 2.5 MHz through the temporal acoustic window. A head frame (DiaMon, Compumedics Germany GmbH, DWL, Singen, Germany) for continuous recording of cerebral ME was applied to retain the position of the TCD probe. High-intensity transient signals were differentiated into artifacts, solid or gaseous ME by the TCD software according to the algorithm described by Devuyt and colleagues.<sup>6</sup> The algorithm is based on the fact that solid ME reflect ultrasound at lower frequencies ( $\leq 1.600 \text{ Hz}$ ) and decibel ranges ( $\leq 14 \text{ dB}$ ) than gaseous ME ( $> 1.600 \text{ Hz}$ ,  $> 18 \text{ dB}$ ). Cerebral ME were detected and differentiated in real-time automatically, and the emboli counts were subsequently reviewed off-line. The TCD examinations were carried out in compliance with the guidelines from the International Consensus Group on Microembolus detection.<sup>7,8</sup> Scale settings and power output were adjusted to provide an optimal signal-to-noise ratio. The insonation depth ranged between 55 and 65 mm. The threshold for ME registration was 9 dB, the sample volume length was 8 mm and the pulse repetition frequency was 7 kHz. CBFV (mean flow velocity) of both MCAs was determined additionally. Fast Fourier-transform spectrograms, which continuously indicate CBFV, were recorded.

**NIRS**

An ultra-rapid NIRS device (Niro-200NX, Hamamatsu, Japan) was used to determine the TOI of both frontal lobes in real-time. The TOI indicates the regional oxygen saturation level which correlates with the regional cerebral perfusion.<sup>9</sup> Detection and emission probes were laterally placed above the eyebrow. They

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