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Direct observation during surgery shows preservation of cerebral microcirculation in patients with traumatic brain injury

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ABSTRACT

Objective: To describe the alterations of the cortical microcirculation of the brain (blood flow and vessel density) in TBI patients who and compare them with a control group.
Methods: Prospective and observational study in a third-level university hospital. Cortical microcirculation in the brain was directly observed using sidestream dark-field (SDF) imaging in 14 patients who underwent surgery: 5 subdural hematomas (SDH) and 9 parenchymal lesions (contusions/hematomas). In this last set of patients, images were recorded in the "pericontusional" areas and in the "surrounding" brain (areas that were as far from the lesion as the craniotomy allowed). These patients were compared to five patients who underwent craniotomy for a disease that did not affect the cortex.
Results: There were fewer "pericontusional" images that could be analyzed due to the presence of subarachnoid hemorrhage. The proportion or perfused vessels was similar in all groups: control 99.5% ± 1.3%; SDH 98.6% ± 2.4%; "pericontusional" area 98.2% ± 2.4%; "surrounding" area 98.4% ± 2.5% ($p = 0.145$). The perfused vessel density index was smaller in the "pericontusional" area: control 6.5 ± 1.6 l/mm; SDH 6.5 ± 2.5 l/mm; "pericontusional" area 5.4 ± 2.6 l/mm; "surrounding" 6.6 ± 2.1 l/mm ($p = 0.07$).
Conclusions: Although the analysis of pericontusional zone was difficult, there were fewer vessels than in the controls and there was no change in the flow. In the surrounding zone and in patients with SDH, we did not document alterations in the microcirculation. Direct imaging of cerebral microcirculation in TBI patients showed that despite serious brain injury the cerebral microcirculation was remarkably well preserved.

1. Introduction

Following traumatic brain injury (TBI), its management has generally focused on the prevention or attenuation of cerebral hypoxia [7]. However, despite the common observation of ischemic neuropathologic changes in fatal head injury [13,14], efforts to demonstrate when, where, and why true ischemia occurs in the brain have been in vain.

Initial studies demonstrated that >30% of patients exhibit global cerebral blood flow below accepted ischemic thresholds (<18 ml·100 g^{-1}·min^{-1}) within 12 h of head injury [3]. However, classic concepts in cerebrovascular physiology dictate that viable brain tissue with critically low cerebral blood flow (CBF) must increase oxygen extraction to maintain cerebral metabolism. When these criteria are applied, it is difficult to conclude that CBF reductions in head injury represent global ischemia. In addition, global metabolic data derived from oxygen-15 positron emission tomography PET show a mean oxygen extraction (OEF) of 31%, suggesting the absence of global ischemia [9]. This conjunction of low CBF and low OEF is more in keeping with hypometabolism rather than ischemia.

These contradictory findings, coupled with the incontrovertible evidence of ischemia in postmortem studies, raise the possibility that there may be mechanisms of tissue hypoxia that are not characterized by the classic physiologic profile seen in conventional macrovascular

Abbreviations: CBF, cerebral blood flow; ICP, intracranial pressure; MAP, mean arterial pressure; MFI, mean flow index; OEF, oxygen extraction fraction; OPS, orthogonal polarization spectral imaging; PPC, cerebral perfusion pressure; PPV, proportion of perfused vessels; PVD, perfused vessel density; SDF, sidestream dark-field; SDH, subdural hematomas; TBI, traumatic brain injury.

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ischemia. One of these explanations could include the alteration of the microcirculation, as it has been suggested by some authors [16,17,24].

Most of the knowledge related to the pathophysiology at the microcirculation level in TBI patients comes from experimental research or from biopsies of patients who were operated or died. Unfortunately, in vivo data on microcirculation in the human brain is limited, partially due to the lack of appropriate investigational techniques. Recently, the sidestream dark-field (SDF) system and its technical predecessor, orthogonal polarization spectral (OPS) imaging, have been introduced in the field of cerebrovascular microcirculation study. These non-invasive techniques enable the continuous observation and assessment of the small blood vessels on the cortical surface of the brain during surgery [15,18–21].

The objective of the present study was to describe the alterations of the cortical microcirculation in TBI patients. Specifically, using SDF, we assessed the blood flow and vessel density of brain microcirculation in TBI patients with subdural hematomas (SDH) and parenchymal lesions. These patients were compared to a control group who underwent elective surgery for other reasons.

2. Methods

2.1. Patient population

The intraoperative use of SDF imaging on the brain surface was approved by the Local Ethics Committee, and written informed consent was obtained from each patient or their closest relative.

Our study population included adults (over 18 years of age) with traumatic brain injury. We included patients with SDH and parenchymal lesions. Traumatic parenchymal lesions are a heterogenous group, traditionally divided into focal and nonfocal lesions [6]. Focal lesions included in this study were basically intracerebral hematomas and contusions. The neurosurgical treatment was performed within the first 24 h after the head trauma and the indications were based on current surgical guidelines [6].

The control group was composed by 5 patients who underwent craniotomies to treat small brain tumors or unruptured aneurysms, not expected to affect the cortical microcirculation.

2.2. Clinical protocols

The general management of all patients with severe TBI was standardized according to the Brain Trauma Foundation Guidelines [4]. In summary, the focus of the critical care of patients with severe TBI was to maintain a cerebral perfusion pressure (CPP) above 60 mmHg, an intracranial pressure (ICP) below or equal to 20 mmHg. Patients were maintained in a euvolemic state and blood pressure maintained at a mean arterial pressure (MAP) above 80 mmHg by using volume replacement and/or vasopressor support. The vasopressor of choice in these patients was noradrenaline. Intracranial hypertension was managed with a stepwise protocol that included sedation (morphine, midazolam, or propofol, or a combination), head elevation (20°-30°), maintenance of normothermia, intermittent drainage of cerebrospinal fluid, osmotherapy with mannitol or hypertonic saline, or both and muscle paralysis with cisatracurium. Barbiturates and/or decompressive craniotomy were optional therapies used in refractory intracranial hypertension.

2.3. Anesthesia

General anesthesia was induced with midazolam or propofol and fentanyl. Intubation was facilitated with rocuronium. Anesthesia was maintained with a 0.4% sevofluorane/O_2 air mixture. A central venous line and an arterial catheter were inserted for continuous hemodynamic monitoring. Arterial blood samples were drawn to determine blood gases and hemoglobin levels.

2.4. Microcirculatory measurements and analysis

SDF imaging (Microscan™, Microvision Medical, Amsterdam, The Netherlands) is a stroboscopic light-emitting diode ring-based imaging modality based on an early introduced optical technique for observing the microcirculation [1] incorporated into a handheld device. The device consists of a light guide with a magnifying lens, which can be placed on an area of interest illuminating it and capturing images by use of an analogue camera in the device. It has been successfully validated against its technical predecessor, OPS imaging [12]. Illumination is achieved by green light of a wavelength chosen for absorption by hemoglobin (e.g., 530 nm) so that red blood cells appear dark globules in a white background. The vessel walls thus are not visualized directly but instead the red blood cells filling them are imaged

Video recording was performed by the neurosurgeons in all cases. After performing the craniotomy, the duramater was opened in a standard fashion. In those patients belonging to the control group and for those harboring traumatic parenchymal lesions, images were acquired before starting the corticectomy or the arachnoid dissection. In the group of patients with traumatic parenchymal lesions, a first set of images within 1 cm from the contusion/hematoma core were recorded ("pericontusion area") (Fig. 1C) and also a second group of videos were obtained as far from the contusion/hematoma as the craniotomy allowed ("surrounding brain") (Fig. 1D). Previous studies that examined cerebral blood flow in contusions, observed hypoperfusion, and gradual normalization with increasing distance from the ischemic center of the contusion. This alteration of the cerebral flood flow was normalized after a distance of approximately 1 cm from the ischemic center, albeit with considerable individual variations [22,27]. In SDH patients, video recording was performed after hematoma evacuation from different sites.

Ten-second duration video clips were obtained avoiding pressure artifacts and stored using a portable computer and an analog digital video converter (ADVC110, Canopus Co, San Jose, CA, USA). Video clips were stored as AVI files to allow frame-by-frame image analysis. Adequate focus and contrast adjustment were verified.

Offline data analysis was performed using a semi-automated microvascular image analysis software platform developed specially for this purpose [10]. Vascular density measurements of blood vessels <25 μm were quantified to determine the perfused vessel density (PVD; mm vessel/mm^2) and the microvascular flow index (MFI; based on the predominant flow type in four quadrants and defined as being absent (0), intermittent (1), sluggish (2), or normal (3)). The proportion of perfused vessels (PPV) was calculated as the percentage of vessels in which perfusion was observed to total number of vessels [2,8].

2.5. Statistical analysis

Statistical analysis was undertaken using SPSS version 19 (SPSS Inc, Chicago, IL). All data are expressed and displayed as mean ± SD, unless otherwise stated. As we have compared more than one group (control, subdural hematomas, "pericontusions," and "surrounding"), we used the nonparametric Kruskal–Wallis one-way analysis of variance.

3. Results

The control group was composed of 5 patients who underwent neurosurgery for 2 meningiomas, 2 nonruptured aneurysm, and one patient with a tumor of the 3rd ventricle. Overall, 20 good-quality movie images were analyzed with 4 images per patients. In normal brains, the cortical vessels were regularly shaped and pulsating with a continuous flow (MFI of 3) in small, medium, and large vessels. SDF images of the cerebral microcirculation in a healthy cortex (small [10–25 μm], medium [26–51 μm], and large [51–100 μm] vessels) were seen with continuous blood flow (Supplemental Video 1). Clinical and demographic data of the patients studied are summarized (Table 1). Physiologic data at