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INNOVATION

Neuropsychological outcomes after pulmonary endarterectomy using moderate hypothermia and periodic circulatory arrest

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KEYWORDS:
chronic thromboembolic pulmonary hypertension;
moderate hypothermia;
circulatory arrest;
pulmonary endarterectomy;
neuropsychological dimensions

BACKGROUND: In this prospective, single-center, observational study, we investigated the association between repeated short periods of circulatory arrest with moderate hypothermia during pulmonary endarterectomy (PEA) in patients with chronic thromboembolic pulmonary hypertension (CTEPH) and different neuropsychological dimensions.

METHODS: We examined 70 patients with CTEPH, >18 to 80 years of age, who had been treated with PEA. Neuropsychological testing was performed.

RESULTS: Learning ability and delayed memory remained well within the normal range for patients' age. We found a statistically significant post-surgical improvement in motor speed, which was accompanied by a better quality of life and reduced symptoms of depression and anxiety.

CONCLUSION: PEA with repeated short periods of circulatory arrest in CTEPH did not result in any neuropsychological complications and may even lead to post-surgical psychological improvements.

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Chronic thromboembolic pulmonary hypertension (CTEPH) is a significant source of morbidity and mortality.[1–3] However, the condition is amenable to treatment with pulmonary endarterectomy (PEA), without having to resort to lung transplantation.[4] The clinical outcomes of PEA are dependent both on post-operative hemodynamic results and the occurrence of surgical complications.[5] In this regard, neurologic complications after PEA can potentially occur as result of brain ischemia during surgery.[4] Consequently, improved PEA protocols with advanced cerebral protection strategies are paramount to ensure optimal post-surgical neurologic and neuropsychological outcomes.[6] The surgical goal of PEA is the

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removal of all thromboembolic materials in the pulmonary artery. To achieve this goal, circulatory arrest is mandatory to have a bloodless surgical field, and hypothermia is required to reduce metabolic activity and protect vital organ function.

Vuylsteke et al[7] compared the changes in cognitive function at 12 weeks after PEA in 74 patients who were randomized either to maintenance of antegrade cerebral perfusion or deep hypothermic circulatory arrest (DHCA). All patients had improved cognitive function at 12 weeks post-operatively, without significant differences between the 2 treatment groups.[7] Although their preliminary data suggest that the use of DHCA did not have a detrimental impact on cognition, detailed neuropsychological results on PEA with short periods of moderate hypothermic circulatory arrest (MHCA) in CTEPH have not been fully elucidated. Therefore, we designed a pilot study to investigate the effect of repeated short periods of MHCA during PEA on different neuropsychological dimensions in patients with CTEPH. Specifically, we compared the neuropsychological parameters of the study participants before PEA and at 3 months post-operatively.

Methods

Patients and surgery

This study was designed as a prospective, single-center, observational investigation. Between February 2014 and June 2016, a total of 183 patients with CTEPH underwent PEA. Exclusion criteria were as follows: age <18 or >80 years; pregnancy or breastfeeding; previous history of neurologic or psychiatric disorders; inability or unwillingness to complete neuropsychological tests before PEA; lack of adherence to the protocol; and language barrier. Thus, the final study cohort included 70 patients with CTEPH undergoing PEA (Figure 1). The standard PEA technique, developed by Jamieson et al,[8] was modified with the ultimate goal of reducing the degree of hypothermia and the duration of the single circulatory arrest.[9] In the standard technique, PEA of each side (right and left lung) is performed in a 20-minute period of deep hypothermia (18° to 20°C).[10] Our anesthesiologic and surgical methods have been reported elsewhere.[9] Briefly, we used 7 to 10 minutes of repeated MHCA, each followed by short periods (5 to 7 minutes) of reperfusion. During circulatory arrest and reperfusion periods, cerebral oxygen saturation was monitored using near-infrared spectroscopy. When the target temperature of 24°C was reached, thiopental was administered before starting PEA both to induce anesthesia and for cerebral protection during cardiopulmonary bypass.[9,11]

The study was carried out in accordance with the tenets of the Declaration of Helsinki and approved by the local ethics committee. Written informed consent was obtained from all participants.

Neuropsychological assessment

Neuropsychological testing was performed at baseline (i.e., before surgery) and at 3 months post-operatively. The neuropsychological tests selected for the study allowed assessing key cognitive domains, included: (1) global cognitive functioning (Mini-Mental State Examination)[12]; (2) short- and long-term verbal memory (Forward Digit Span, Rey 15 Words Test)[13,14]; (3) selective attention (Attentional Matrices)[15]; (4) fine motor speed, visuomotor speed, and eye–hand coordination (Grooved Pegboard Test)[16]; (5) verbal fluency (Phonological and Semantic Verbal Fluency Test)[17]; (6) divided attention, processing speed, planning, and flexibility (Trail Making Test A, B, and B-A)[18]; and (7) executive functioning (Frontal Assessment Battery).[19] Symptoms of anxiety (Hospital Anxiety and Depression Scale—Anxiety [HADS-A]) and depression (Hospital Anxiety and Depression Scale—Depression [HADS-D]),[20] as well as quality of life (36-item Short Form [SF-36]) were also assessed.[21] All neuropsychological tests were corrected for age and education with scores calculated according to published manuals (see Table S1 in Supplementary Material available online at www.jhltonline.org/).

Statistical analysis

We summarized continuous data by mean and standard deviation or median and 25th to 75th percentiles, and categorical variables by number and percent. We compared the baseline characteristics of patients who were included in the 3-month evaluation with those not included by using the Mann–Whitney *U*-test and Fisher's exact test (see Table S2 in Supplementary Material online). We used generalized linear models to assess changes in cognitive/psychological characteristics at 3 months. We computed Huber–White

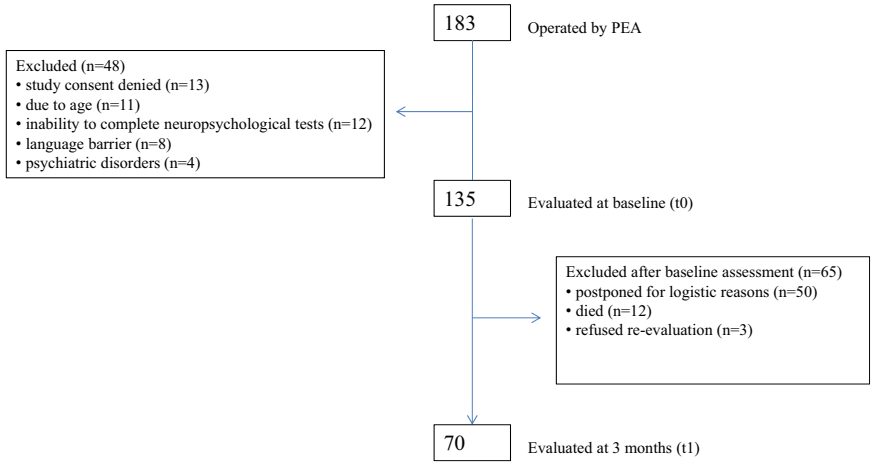

Figure 1 Study Consort flowchart: initial and final patient sample.