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Measurements of Cerebrospinal Fluid Concentrations of S100β Protein During and After Thoracic Endovascular Stent Grafting☆

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Objectives. *Thoracic endovascular aortic repair is associated with postoperative spinal cord ischemia in approximately 1 to 12.5% of all cases.*

S100β is a protein that is released during acute damage of the central nervous system. This study was performed to determine the concentration of S100β in cerebrospinal fluid during and after stenting of the thoracic aorta in patients at high risk for spinal cord ischemia.

Design. *Prospective clinical study.*

Materials and methods. *Eight patients who underwent elective thoracic aortic stent grafting underwent lumbar spinal fluid drainage. These patients were at high risk to develop spinal cord ischemia.*

Methods. *CSF samples for analysis of S100β protein were drawn after induction of anesthesia, during stenting, once every hour the following six hours and 20 hours after repair.*

Results. *No significant increase in S100β protein could be detected in CSF and no neurological deficits were detected postoperatively.*

Conclusions. *The results of this study show us that there is no significant release of S100β protein in CSF during stenting of the thoracic aorta in this subgroup of patients at high risk for spinal cord ischemia, consistent with clinical exam that there was no significant damage to the central nervous system.*

Keywords: S-100β; Endovascular; Aneurysm; Paraplegia; Paraparesis; Stent.

Introduction

Surgical treatment of thoracic and thoracoabdominal aortic aneurysms may be associated with a significant risk of perioperative morbidity, including paraplegia and paraparesis. The risk to develop paraplegia or paraparesis has been reported to be 4 to 21%.[1] In selected thoracic aneurysms, there is a possibility for endovascular aortic repair, which is accompanied with far less morbidity and mortality. The risk to develop postoperative paraplegia or paraparesis however remains 1 to 12.5% with an average of 2.7%.[2,3] Probable risk factors for paraplegia include previous abdominal aortic aneurysm repair,[4] longer length of the thoracic aorta being covered by prosthetic material,[2] the location of the endograft[5] and postoperative hypotension.[6]

Cerebrospinal fluid (CSF) drainage theoretically can improve the blood supply to the spinal cord. CSF drainage reduces the risk of postoperative paraplegia after open surgical repair of thoracic and thoracoabdominal aneurysms.[1,7,8]

The use of biochemical markers may be a sensitive detection method to detect spinal cord ischemia.[9,10] The S100β protein is such a marker: it is a calcium binding protein which is found in high concentrations in glial and Schwann cells and is unique to the central nervous system. The S100β protein is released during acute damage of the central nervous system such as spinal cord ischemia due to hypoperfusion.[11] A rise in S100β protein concentration in CSF correlates with a decrease in the amplitude of transcranial motor evoked potentials[12] and may be a sensitive marker for detection of damage to the central nervous system.[9] S100β protein concentrations in CSF are probably more sensitive in detecting damage to the central nervous system than

☆ This study was performed at St. Antonius Hospital in Nieuwegein, The Netherlands.

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serum concentrations.[13,14] Baseline values of S100β protein in CSF range from approximately 0.9 to 1.7 μg/L and may rise to approximately 4.0 μg/L during surgical thoracoabdominal aortic replacement without postoperative neurological deficits.[11]

This study was performed to determine the concentration of S100β protein in CSF during and after stenting of the thoracic aorta in patients at high risk for spinal cord ischemia.

Materials and Methods

Eight patients, three men and five women, aged 58 to 76 years (mean, 68 years) who underwent elective thoracic aortic stent grafting participated in the study. All patients were free from any neuromuscular disorder. The spinal fluid drainage and S100β measurements were approved by the Institutional Ethics Committee.

All stent grafts were inserted for treatment of thoracic aortic aneurysms. The studied patients were considered at a higher risk than the previously mentioned 2.7% to develop postoperative paraplegia or paraparesis. This assumption was made because the aneurysms involved critical intercostal arteries (T8-L2), the total thoracic descending aorta was to be covered or the patient had a history of previous abdominal aortic aneurysm repair. For these reasons patients underwent lumbar spinal fluid drainage in order to keep the spinal fluid pressure at a maximal level of 10 mm Hg. The catheter (Integra NeuroSciences Implants S.A., Sophia Antipolis, France) was left in place for 20 hours postoperatively.

In one patient critical intercostal arteries (T8-L2) were covered, after previous surgical treatment of an abdominal aortic aneurysm. The other seven patients received stents covering the total thoracic descending aorta. Four of these seven patients also had a history of abdominal aneurysm repair.

CSF samples for analysis of S100β protein were drawn after induction of anesthesia, during stenting, once every hour the following six hours and 20 hours after repair.

One patient was considered to run a higher risk of developing postoperative paraplegia or paraparesis compared to the other patients. This assessment was made because of this patient's history of infrarenal and thoracoabdominal aortic replacement. The final part of his native descending aorta was going to be excluded by stenting. For these reasons the decision was made to continue CSF drainage for 48 hours postoperatively and an extra CSF sample was taken after 48 hours.

The CSF concentrations of S100β protein were analyzed with a commercially available enzyme-linked immunosorbent assay kit (Sangtec_100 ELISA kit, Sangtec Molecular Diagnostics AB, Bromma, Sweden). All samples were analyzed in duplicate, with a variation of less than 10%. A measurement takes approximately two hours.

Results

No significant increase in S100β protein during the procedures could be demonstrated in CSF and no central or peripheral neurological deficits were detected postoperatively.

However in the one patient, who was considered to have the highest risk for developing postoperative paraplegia or paraparesis, we found a more than three fold increase in the S100β concentration in CSF. This relative increase normalized during the second postoperative day (Fig. 1). Despite this temporary relative increase the absolute value of S100β protein stayed within the normal range. This patient showed no clinical signs of neurological damage postoperatively.

Discussion

The results of this study show that there is no significant release of S100β protein in CSF during stenting of the thoracic aorta in this small subgroup of patients at high risk for spinal cord ischemia. This correlated with the absence of postoperative neurological deficits and suggests that there may have been no significant damage to the central nervous system.

The normal range of S100β protein in CSF however may differ per person and it remains unknown whether one should focus on absolute or relative increases in S100β protein when monitoring damage to the central nervous system.

Postoperative neurologic deficits are caused by interruption of sufficient duration of spinal cord blood supply. A CT angiography was performed in all patients in order to accurately size the stents needed, however, in our hospital it was not accurate enough to reliably identify all intercostal arteries supplying the spinal cord. Preoperative spinal cord angiography was not performed. Angiographic localization itself can cause serious complications such as emboli. Furthermore paralysis after elective open repair still occurs among those with preoperative detailed spinal cord blood supply.

Important may be the fact that measuring the S100β protein concentration in CSF in this small group of patients meant that we also took a protective measure.

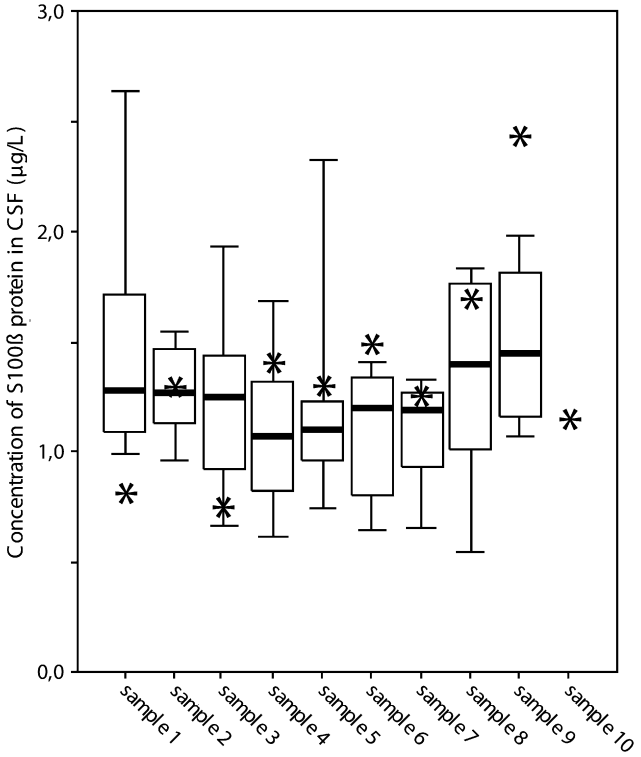

Fig. 1. Vertical axis: Boxplots show the median, interquartile range and extremes of the concentration (µg/L) of S100β protein in CSF. The asterisk shows the samples of the extreme high risk patient, while the boxplots represent the samples of the other seven patients.
Horizontal axis: the different samples taken:
Sample 1: After induction of anesthesia
Sample 2: During placement of the stent
Sample 3: One hour after stent placement
Sample 4: Two hours after stent placement
Sample 5: Three hours after stent placement
Sample 6: Four hours after stent placement
Sample 7: Five hours after stent placement
Sample 8: Six hours after stent placement
Sample 9: Twenty hours after stent placement
Sample 10: Forty-eight hours after stent placement

All patients underwent CSF drainage to keep the spinal fluid pressure at 10 mm of Hg or less to help prevent damage to the spinal cord. Perfusion pressure of the spinal cord is equal to mean arterial blood pressure less venous pressure or CSF pressure, whichever is higher. Therefore keeping the CSF pressure low may improve perfusion of the spinal cord. For these reasons the release of S100β might have been altered by our treatment. It was considered unethical though not to keep the spinal fluid pressure at safe levels.

The value of 10 mm Hg was chosen because it has been proven that keeping the CSF pressure at 10 mm Hg or less helps to protect against ischemic damage to the spinal cord during and after surgical replacement of the thoracoabdominal aorta.[1,7,8,15,16] However, values below 10 mm Hg may be associated with a rise in complications like intracerebellar hematoma[17] or subdural hematoma.[18,19]

In addition to these complications persistent CSF leakage,[20] hematoma formation around the cauda equina[18] and bacterial meningitis[21] may also occur.

Whether there is an indication for CSF drainage in a subgroup of patients at high risk to develop neurological deficits after endovascular repair has never been defined.

Following endovascular thoracic aortic aneurysm repair, there are several case reports that show reversal of postoperative paraplegia after institution of cerebrospinal fluid drainage.[22–24] Patients after endovascular repair can be neurologically examined directly postoperative. Immediate postoperative CSF drainage may possibly be almost as effective as preoperative institution of CSF drainage, because of the short duration of preventable spinal cord ischemia.

The complications of CSF drainage can be life threatening, which is why its management should not be taken lightly. Considering the fact that lumbar CSF drainage is not without risks[25] the indications for its use during thoracic endovascular stent grafting remain to be studied, since even in this small subgroup of patients at high risk to develop postoperative paraplegia or paraparesis there was no rise in S100β protein in the CSF.

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