Postoperative cognitive dysfunction after shoulder surgery in beach chair position: a pilot study

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Promotor 2: Dr. Tom Jacobs

Masterproef voorgedragen in de master in de specialistische geneeskunde
Anesthesie - Reanimatie
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Abstract

Background/Goal

Major shoulder surgery in beach chair position has been associated with severe adverse neurologic events even in healthy middle-aged patients. This has been attributed to the beach chair position itself as it reduces cerebral oxygenation. The aim of the present study is to identify whether intra-operative episodes of cerebral desaturation are associated with postoperative cognitive decline.

Methods and Materials

After obtaining ethics committee approval and informed consent, 11 adult patients (4 males and 7 females with mean age=65;0y, SD=12.4y) without prior neurological and psychiatric disorder were enrolled prospectively. Neurocognitive function was assessed preoperatively, at the 3rd postoperative day and at 3 months postoperatively. Memory and attention performance were evaluated by means of the Auditory Verbal Learning Test (AVLT), the Stroop Color Word Test (SCWT) and the Symbol Digit Modalities Test (SDMT). Near-infrared spectroscopy (NIRS) was used to determine intra-operative episodes of cerebral desaturation, defined as a decrease in cerebral tissue oxygen saturation ($rScO_2$) of more than 20% compared to the baseline value. Routine anesthesia was applied. A repeated measures multivariate analysis of variance with time as within-subject variable (pre-surgery, post-surgery, and follow up assessment) was performed.

Results

Cerebral desaturation occurred in all patients. No significant changes in overall cognitive test performance was observed over time, neither was there any significant interaction between time and age or cerebral desaturation. A significantly increased performance was observed between the postoperative and the follow-up assessment on the AVLT ($p=.014$), which may possibly be attributed to a test-retest effect.

Conclusion

These preliminary results suggest no association between episodes of cerebral desaturation and postoperative cognitive dysfunction. The current sample is yet too
small to come to definite conclusions, and confirmation in an adequate sample-sized study population (as is planned in this ongoing study) is mandatory.
Introduction

Beach chair position

Surgery on the shoulder joint is one of the most common surgical procedures performed by orthopedic specialists. Since its introduction in the early eighties beach chair position is the most frequently preferred position for both open and arthroscopic shoulder surgery. Patients are positioned sitting up more than 70 degrees upright with the operative arm draped free to be manipulated by either a mechanical arm rest or a surgical assistant. The head rests on a well-padded head block.

Figure 1: Classical beach chair position (picture copyrighted by Ao Foundation)

The advantages of the classic beach chair position include easier access to the joint, lack of brachial plexus strain, less risk for neurovascular trauma and if necessary an easy conversion from arthroscopic to open procedure (Skyhar et al., 1988; Gelber et al., 2008).
The safety of this position has been well established. Most patients who undergo shoulder surgery in this position do not show adverse sequelae (Friedman et al., 2009). Nonetheless severe adverse neurologic events have occurred in a relatively healthy middle-aged population supposedly not at risk for severe cerebrovascular incidents. A case of visual loss and ophthalmoplegia has been described after a surgically uneventful rotator cuff repair in 2003 (Bhatti and Enneking, 2003). Pohl and Cullen have reported four cases of ischemic brain damage and spinal cord injury, resulting in a permanent vegetative state and death in two cases (Pohl and Cullen, 2008). The American Shoulder and Elbow Surgeon’s Association has reported eight cases of cerebrovascular events during shoulder surgery in beach chair position (Friedman et al., 2009). The etiologic mechanisms are largely unknown. It is postulated that the upright position induces unfavorable hemodynamic changes. In healthy awake volunteers, assuming a sitting position induces a sympathetic nervous system response. Heart rate and systemic vascular resistance rise to maintain adequate mean arterial pressure and cardiac output (Smith et al., 1994; Edgell et al., 2004). This autonomous effect does not diminish with increasing age (Edgell et al. 2004; Murell et al., 2011). During general anesthesia these sympathetic responses are diminished due to the vasodilation effect and blunting of the baroreceptor reflex of anesthetics, resulting in an attenuated increase in system vascular resistance, decrease in mean arterial pressure and a decreased cardiac output. A high incidence of severe hypotension is not surprising during general anesthesia in a sitting position (Potter et al., 1999). These profound physiological changes may lead to undetected cerebral hypotension. This reduction in cerebral perfusion pressure below a critical threshold of duration and severity may induce neurological damage. This threshold is felt to be the lower limit of cerebral autoregulation, which according to recent publications is a subject of physiological heterogeneity. While it attempts to maintain a constant cerebral perfusion pressure over a wide range of mean arterial pressures, both lower and upper limits are subject of interpatient variability, taking patient’s age, comorbidities and pharmacologic therapies in consideration (Drummond, 1999; Sanders et al, 2011). Cerebral hypotension may go unnoticed using standard intraoperative monitoring. Cerebral perfusion pressure can be estimated using mean arterial pressure (MAP) (Murphy and Szokol, 2011). However cerebral perfusion pressure can be severely underestimated using brachial cuff readings, due to hydrostatic pressure differences between head and
arm/heart level. This difference can be as much as 20 to 40 mmHg depending on the elevation of the head (Koh et al, 2012)

Near-infrared spectroscopy: technical aspects and clinical use

Near-infrared spectroscopy (NIRS) is a non-invasive technique allowing measurements of tissue oxygenation, including brain oxygenation. It became possible to measure regional cerebral oxygen saturation (rScO₂) after the innovative work of Jöbsis. He demonstrated that light in the near-infrared spectrum can penetrate the bone of the cranium, allowing measurements of oxyhemoglobin and deoxyhemoglobin inside the brain (Jöbsis, 1977). Non-invasive, self-adhesive optical sensors are applied to the skin of the forehead. These optodes emit a light in the near-infrared spectrum. Its reflection is measured by sensors at fixed distances from the light source. The strength of the reflected light detected by these sensors is inversely related to the concentration of light-absorbing molecules in the underlying tissue. Oxyhemoglobin and deoxyhemoglobin absorb light at a wavelength of 800 nm in the near infrared spectrum, but they both have a different characteristic peak absorption. Using a modified Beer-Lambert law, NIRS provides a measurement of the concentration of oxygenated and deoxygenated hemoglobin to total hemoglobin concentration. Algorithms are used to distract absorption of superficial extracranial tissue from that obtained from deeper cerebral tissue to obtain a cerebral saturation value of the superficial frontal cortex (Zheng et al., 2013). Traditional pulse oximetry, which uses light in the red and infrared spectrum, distinguishes between venous and arterial blood. NIRS does not make this differentiation. Approximately 70 to 80 % of cerebral blood is venous blood, consequently rScO₂ provides an indication of the regional oxygen supply and demand (McCormick et al, 1991; Murking and Arango, 2009). Continuous measurements of cerebral oxygenation allow for an accurate recognition of episodes of cerebral desaturation. NIRS is used extensively in major surgery at high risk for adverse neurologic outcome. It has found its way into the arsenal of the cardiac anesthesiologist. NIRS may predict postoperative neurological dysfunction after cardiac surgery and allows detection of intraoperative cannula misplacement during cardiopulmonary bypass (Zheng et al, 2013). During pediatric cardiac surgery, NIRS
is the most widely applied and accepted tool in multimodal neuromonitoring. Some evidence exists in the pediatric population that decreased cerebral oxygen values are associated with brain abnormalities on postoperative MRI scans, though no conclusive evidence exists on the neurologic outcome after perioperative intervention solely based on NIRS values (Clark et al., 2012). NIRS not only has its part in cardiac surgery, but it is widely used during major vascular procedures. NIRS offers the possibility to predict neurologic events during carotid endarterectomy. About ten percent of patients suffer from postoperative neurologic changes triggered by carotid clamping. A decrease in rScO₂ is related to potential postoperative neurologic deterioration and might imply the need for a different anesthetic approach (Pennekamp et al., 2009), using deliberate hypertension, or surgical approach, using a carotid shunt (Nielsen, 2014). NIRS also opens the possibility to predict a hyperperfusion syndrome in the immediate postoperative period after releasing the carotid clamp (Pennekamp et al. 2012). Similar applications of NIRS are performed during abdominal surgery, both laparoscopic and open. Inducing a head up position for laparoscopic procedures induces a decrease in rScO₂, up to 80% of baseline value in 20% of patients (Gipson et al., 2006). Similar results were found during laparoscopic gynecological procedures (Lee et al., 2006). Clamping the inferior caval vein during orthotopic liver transplantation, induces a decrease in rScO₂. A cerebral desaturation of 13% has been associated with release of neuron specific enolase, a biomarker of neuronal damage (Plachky et al., 2004). This makes NIRS a viable option for monitoring cerebral autoregulation and subsequently hemodynamic management during major abdominal and transplantation procedures.

Few studies exist assessing events of cerebral desaturation and their neurocognitive sequelae. A systematic review by Zheng and colleagues only cited low-level evidence that interventions to improve cerebral saturation could prevent stroke or post-operative cognitive dysfunction during cardiac surgery with cardiopulmonary bypass (Zheng et al., 2013). Two studies examine the effects of cerebral desaturation and occurrence of neurocognitive dysfunction in abdominal surgery. They both associated cerebral desaturation with postoperative cognitive decline, as evidenced by a lower mini-mental state examination (MMSE) score or the occurrence of postoperative delirium (Casati et al, 2007; Morimoto et al., 2009). This association was also confirmed during thoracic surgery (Tang et al., 2012). Several observational
studies have investigated the use of NIRS during shoulder surgery in different positions. During arthroscopic procedures in lateral decubitus rScO₂ is maintained. On the other hand beach chair position may induce a dramatic decrease in rScO₂ (Fisher et al., 2009; Dippmann et al. 2010, Tange et al, 2010; Lee et al. 2011; Yadeau et al., 2011; Jeong et al., 2012; Ko et al., 2012; Moerman et al. 2012; Salazar et al, 2013; Pant et al, 2014). Lowered cerebral saturation corresponded with a decreased MAP. A restoration of MAP to preoperative value restored rScO₂ (Lee et al., 2011).

Postoperative decline in cognitive function

Postoperative decline in cognitive function is becoming increasingly recognized in Postoperative cognitive dysfunction (POCD) is broadly defined as a decline in cognition temporally associated with surgery. Cognitive function is a rather 'simple' name for a broad and elaborate spectrum of capabilities such as learning, understanding, perception, attention, verbal abilities, executive functions and abstract thinking. Unlike delirium, no elaborate definition exists to accurately describe cognitive dysfunction. It is considered a mild neurocognitive disorder and, according to DSM IV criteria, it can only be identified as an exclusion diagnosis. Other neurocognitive disorders such as delirium, dementia and other amnestic disorders have to be excluded first (Alcover et al, 2013). While it is categorized as a trivial brain dysfunction, it has been associated with an increased one year mortality, impairment of daily functioning, risk of leaving the labor market or early retirement, increased health care cost and dependency on government support payments (Deiner and Silverstein, 2009).

Cognitive deterioration after cardiac surgery has been described in about three to eight patients out of ten, with ongoing cognitive deficits after six months in up to 60% of these patients. POCD had been described in one out of four elderly patients in the first seven days after major non-cardiac surgery. The cognitive symptoms persist in about ten to twenty percent following major surgery after six months. Incidence is lower in younger patients and minor surgery (Steinmetz and Rasmussen, 2016).
The pathophysiologic mechanisms leading to POCD after surgery are poorly understood. Animal studies attribute an extensive role to the immune system succeeding surgical ‘trauma’. Peripheral surgery in a mice model activates the inflammatory TNFα/NF-κB pathways with cytokines release. In turn these cytokines disrupt the integrity of the blood-brain barrier, which allows macrophages to invade the hippocampal formation more easily, impairing memory formation. Cognitive functioning remains preserved when cytokine release is blocked by activation of the anti-inflammatory cholinergic pathways (Terrando et al., 2011). POCD has been extensively studied in cardiac surgery. Longer duration of cardiopulmonary bypass, poor left ventricular function, manipulation of an atherosclerotic aorta, cerebral hyperthermia and valve surgery have all been associated with postoperative cognitive deterioration (Tomotko and Maekawa, 2014). Although cognitive dysfunction has been less comprehensively studied and identified in non-cardiac surgery, numerous risk factors have been identified in more recent studies. Table 1 gives an overview of the most common risk factors (Rundshagen, 2014).

Table 1: Risk factors for POCD

<table>
<thead>
<tr>
<th>Patient</th>
<th>Advanced age; pre-existing cerebral, cardiac or vascular disease; preoperative mild cognitive impairment; low educational level; history of alcohol abuse; genetic predisposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>Extensive surgical procedure; intra- or postoperative surgical complications; secondary surgery; cardiac surgery (long cardiopulmonary bypass, poor cardiac function, valve surgery and atherosclerotic aorta handling)</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>Long-acting anesthetics; marked disturbances of homeostasis (hypoxemia, hypotension), intra- or postoperative anesthesia complications</td>
</tr>
</tbody>
</table>

Several observational studies have revealed an association between extensive surgery, secondary surgery and postoperative complications and an increased incidence of POCD (Steinmetz and Rasmussen, 2016). Age is a major risk factor for
POCD. Increasing age implies a decreased cognitive performance and ability to compensate for cognitive deficits. This coincides with the ‘brain reserve’ theory, which shows a greater vulnerability for POCD in brains with a lower reserve. This also includes patients with a pre-existing mild cognitive impairment (Deiner and Silverstein, 2009). A low educational level is a further risk factor for POCD. Several studies have presumed the expression of the APOE 4 allele as a risk factor (Alcover et al, 2013). Hudetz et al showed that patients with a positive history for alcohol abuse had worse cognitive impairment after surgery. A severe disruption of homeostasis, such as severe hypotension or hypoxemia, have been blamed for postoperative cognitive deterioration (Steinmetz and Rasmussen, 2016; Rundshagen, 2014). Even though general anesthesia has often been blamed for causing neurotoxicity, currently no sufficient evidence exists to link POCD to general anesthesia. The residual effect of the anesthetics solely depends on its pharmacokinetic properties. A shorter duration of action implies a shorter impairment of cognitive function in the postoperative period.

Diagnosis of postoperative cognitive dysfunction requires a preoperative baseline cognitive function analysis and a determination of what will be defined as a significant decline in cognitive functioning. Cognitive deterioration is a subtle process and can only be detected using a combination of neuropsychological tests. Current test batteries for POCD have several issues. First there is the flooring effect, i.e. what is the correct technical approach for a patient with an already low baseline score. Secondly there is currently no real consensus about which tests have to be used to diagnose POCD. A 1995 recommendation lists four essential tests to diagnose POCD: Rey Auditory Verbal Learning test (a word learning test), Trail Making test (ability to perform combined tasks), Groove Pegboard test (manual dexterity) and Digit Span test (ability to remember a sequence of numbers) (Murkin et al., 1995). This variety of tests may be due to the absence of theoretically substantiated model that accurately describes causes and outcomes of cognitive changes due to surgical trauma. This confusing recommendation resulted in a lot of combinations of different tests have being in clinical studies, making data interpretation and comparison a real challenge.

A possible explanation is the duration of these combinations of tests. A comprehensive neuropsychological examination takes about three hours, which is not always suitable in a perioperative setting. Currently diagnosis of POCD implies testing
in the following domains: learning and memory, attention, executive functioning and language, supplemented by a decline in perception and abstract thinking (Tsai et al, 2010). Finally, there is no clear agreement about the optimal timing when to test patients at risk for POCD. Patients undergoing their preoperative cognitive assessment may not score as well as expected due to pre-procedural anxiety or effects of premedication. Patients who are tested shortly after surgery may have substandard scoring due to residual effect of the medication or anesthetics, pain and general health status. Trials requiring long-term follow-up may experience loss to follow up in patients suffering from POCD, leading to confounding by attrition.

Postoperative cognitive decline had been extensively tested in cardiac surgery, but less in non-cardiac surgical patients. Several studies have tried to associate the occurrence of POCD with various adjustable surgical and anesthetic factors. Currently only two clinical studies have addressed the association between cerebral desaturation during shoulder surgery in beach chair position and postoperative cognitive dysfunction. One study did not find any significant change in postoperative MMSE score (Salazar et al., 2013). The other study combined both executive function tests and serum biomarkers of brain injury. No differences in cognitive outcome were found between the beach chair group and supine position control group (Laflam et al, 2015).
Goal of the study

This study aims to identify episodes of cerebral desaturation using NIRS during shoulder surgery in beach chair position and will try to associate these episodes to potential postoperative neurocognitive dysfunction using a combination of neurocognitive tests. These will test executive functions mediated by the frontal lobe, i.e. the location where NIRS is used to measure cerebral oxygenation. Considering the underlying shoulder pathology, all tests will be motor free. Furthermore patient risk factors for events of cerebral desaturation and postoperative neurocognitive dysfunction will be investigated. We hypothesize that events of cerebral desaturation are connected to neurocognitive dysfunction in the postoperative period.
Materials and methods

Approval from the local ethics committee was obtained. Written informed consent was obtained from study candidates. All consecutive patients planned for total shoulder arthroplasty, were screened for inclusion after referral to the preoperative consultation. The average time interval between this consultation and date of surgery was ten days. Exclusion criteria were age younger than 18, prior neurologic event, amourosis fugax, apparent cognitive dysfunction, carotid stenosis, previous head and neck surgery, cervical disc herniation, recent acute myocardial infarction and syncope. Elderly patient aged 75 or more were screened using a mini-mental state examination for gross neurocognitive deficit prior to inclusion in the study. A score lower than 24 is compatible with a preoperative existing neurocognitive deficit, thus these patients were excluded. Collected demographic data included age, gender, level of education, smoking status, prior health problems (diabetes mellitus, chronic obstructive pulmonary disease, metabolic syndrome, pre-existing cardiovascular disease), length, weight, body mass index (BMI) and current medication use. Education level was defined as years in any form of education (primary education, secondary education, college/university, doctorate, night classes). A baseline preoperative neurocognitive function was assessed using the ‘Auditory Verbal Learning Test’ (AVLT), ‘Stroop Color Word Test’ (SCWT) and ‘Symbol Digit Modalities Test’ (SDMT). All neurocognitive tests evaluate frontal lobe mediated executive functions. All tests were motor free, considering the underlying shoulder pathology. Patients did not receive any psychoactive medications (e.g. anxiolytics) before performing this neurocognitive assessment.

No premedication or anxiolytics were administered pre-operatively. After arrival in the operating room, the standard protocol for shoulder surgery was followed. An intravenous line was placed and normal saline was used as a standard. A three or five leads ECG, depending on the cardiovascular status of the patient, was applied to the patient. A pulse oximeter was secured to the index finger of the non-operated hand. A blood pressure cuff was positioned on the non-operated arm. Non-invasive blood pressure was measured every three minutes. All three were connected to the anesthesia monitor. Before induction of general anesthesia an ultrasound guided interscalene block was placed using a mixture of plain levobupivacaine 0.5% and
mepivacaine 2%. Two INVOS sensors (Covidien, Medtronic, Minneapolis, USA) and a bispectral index (BIS) sensor (Covidien, Medtronic, Minneapolis, USA) were applied on the patient’s forehead. Anesthesia was induced with sufentanil (0.1 µg/kg), propofol (2 – 3 mg/kg) and cisatracurium (0.1 mg/kg). After reaching adequate depth of anesthesia and neuromuscular blockade an endotracheal tube was placed. Anesthesia was maintained with a mixture of 50% air and 50% inspired oxygen and sevoflurane (age corrected MAC value of 1) and adapted to obtain BIS values between 40 and 60. Additional doses of muscle relaxants and opiates were at the discretion of the treating anesthesiologist. An oral thermometer was placed and patient’s temperature was kept at a minimum of 35.5°C using forced air warming. A baseline cerebral oximetry value was obtained after obtaining adequate depth of anesthesia and before positioning. Afterwards the patient was positioned in the beach chair position. Patients were raised to a 60 to 70 degrees sitting position with the head fixed in midline position. Continuous cerebral oximetry was obtained during the entire anesthetic and surgical procedure. All personnel in the operating room was blinded for cerebral oximetry measurements. Likewise all auditory signals of the device were disabled.

Cerebral desaturation was defined as a decline in cerebral oxygen saturation of 20%, compared to baseline value. An area under the curve combining the duration and severity of cerebral desaturation (AUCrScO2) was calculated. Intraoperative hypotension was defined as systolic blood pressure lower than 80 mmHg. Bradycardia was defined as a heart rate below 45 beats per minute. They were treated with ephedrine and atropine respectively, according to current standard of care guidelines in our operating theatre. In view of the current debate concerning the use of phenylephrine and its effect on cerebral oxygenation, this drug was not our first choice of medication. Standard postoperative nausea and vomiting and pain protocols were followed. The amount of blood loss and fluids given to the patient as well as the doses of all drugs administered, were recorded. After the surgical procedure, the patient was awakened and transported to the postoperative care unit, where they were discharged after reaching discharge criteria (Aldrete score > 8).

The first postoperative testing took place on the third postoperative day (concordant with the day of hospital discharge in the majority of standard cases). The ‘Auditory Verbal Learning Test’ (AVLT), ‘Stroop Color Word Test’ (SCWT) and ‘Symbol
Digit Modalities Test’ (SDMT) were repeated using alternative versions where appropriate to minimize test-retest effects.

The second postoperative testing took place three months post-surgery. This coincided with a follow-up consultation with the treating orthopedic surgeon in the outpatient clinic. The ‘Auditory Verbal Learning Test’ (AVLT), ‘Stroop Color Word Test’ (SCWT) and ‘Symbol Digit Modalities Test’ (SDMT) were assessed again. After this follow-up moment, the study was ended. All neurocognitive tests were performed by the same person.

Statistical analysis was performed using the SPSS Statistics version 23 (2015) (IBM, New York, USA). Data were tested for normal distribution using the Shapiro – Wilk test. Normally distributed data are reported as mean and standard deviation (SD). The incidence of cerebral desaturation in patients older than 65 and patients suffering from hypertension was analyzed using the Fisher Exact test. Correlation were calculated using Pearson correlation coefficient. The pre-surgery, post-surgery and follow-up test results were analyzed using a repeated multivariate analysis of variance (repeated ANOVA). Age and degree of cerebral oxygen desaturation were included as covariates. A p-value lower than 0.05 was considered statistically significant.
Results

21 consecutive patients, planned for total shoulder arthroplasty, were screened for inclusion. After medical evaluation 12 (57.1%) were included in the study. One patient did not complete the second postoperative neurocognitive evaluation and was considered lost to follow-up. Table 2 shows relevant demographic data of included patients. Consequently statistical analysis was performed on the data of 11 patients, who completed all three neurocognitive evaluations after surgery. Two patients (18.2%) required additional surgery in beach chair position because of surgical complications. One patient required shoulder reduction under general anesthesia two months postop after prosthesis luxation. The other patient required evacuation of a hematoma at the surgical site under general anesthesia four days after the initial surgery.

Table 2: Patients characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sex, male/female (n (%))</th>
<th>Age, years (mean ± SD)</th>
<th>Education level, years (mean ± SD)</th>
<th>Hypertension, yes/no (n (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4 (36.4%) / 7 (63.6%)</td>
<td>65 ± 12.39</td>
<td>10.6 ± 3.8</td>
<td>5 (45.5%) / 6 (54.5%)</td>
</tr>
</tbody>
</table>

Table 3 shows relevant information about anesthesia and surgery. All patients received crystalloid solutions. Following current controversy about fluid administration, colloids were only used in severe blood loss, which none of our patients suffered from. The surgical procedure did not necessitate deliberate hypotension, so current standard practice in case of low blood pressure was followed. The use of phenylephrine as first-line treatment of hypotension was discouraged. 7 out of 11 patients (63.63%) received ephedrine (6 – 33 mg) and 2 patients (18.2%) received phenylephrine (100 – 700 µg) for systolic blood pressure lower than 80 mmHg. Phenylephrine was only used as a second line agent in hypotension refractory to ephedrine. Two patients (18.2%) received a fluid bolus of crystalloids for the treatment of hypotension. No patients received atropine for a heart rate lower than 45 beats per minute.
**Table 3:** Anesthesia and surgical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Duration BCP, min (mean ± SD) (min – max)</th>
<th>Blood loss, ml (mean ± SD) (min – max)</th>
<th>Total fluids, ml (mean ± SD) (min – max)</th>
<th>Drugs use, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>110 ± 32 (48 – 192)</td>
<td>325 ± 352 (120 – 1200)</td>
<td>789 ± 487 (360 – 2250)</td>
<td></td>
</tr>
<tr>
<td>Drugs use, n (%)</td>
<td>Atropine: 0 (0%)</td>
<td>Ephedrine: 7 (63.63%)</td>
<td>Phenylephrine: 2 (18.2%)</td>
<td>Fluid bolus: 2 (18.2%)</td>
</tr>
</tbody>
</table>

The descriptive statistics of the neurocognitive tests at the three different points in time are displayed in table 4. The AVLT score represents a learning score. The total score represents the number of correct answer during the first five AVLT test runs. The SCWT is scored as the number of correct answers. The SDMT represent the time in seconds to finish the entire test.

**Table 4:** Descriptive statistics of the neurocognitive tests

<table>
<thead>
<tr>
<th>SCWT, n (mean ± SD)</th>
<th>T1</th>
<th>55.52 ± 35.67</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T2</td>
<td>64.74 ± 43.89</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>56.35 ± 45.0</td>
</tr>
<tr>
<td>AVLT, n (mean ± SD)</td>
<td>T1</td>
<td>38.18 ± 10.27</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>38.18 ± 12.41</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>48.73 ± 13.07</td>
</tr>
<tr>
<td>SDMT, s (mean ± SD)</td>
<td>T1</td>
<td>42.36 ± 14.73</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>42.18 ± 15.79</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>47.64 ± 10.45</td>
</tr>
</tbody>
</table>

No patient experienced gross neurological complications. Mean baseline rScO₂ before induction was 60.9% and 62.4%, respectively on the left and right side. Before positioning mean rScO₂ on the left side was 71.2% and 75.2% on the right side. After positioning to beach chair positioning, there was a relative decrease of rScO₂ of more
than 20% in 3 patients (27.3%). During the overall surgical procedure in beach chair position there was a relative decrease of rScO₂ of more than 20% in all eleven patients (100%). The mean AUCrScO₂ during the entire surgical procedure in beach chair position was 73.42 %*sec on the left side and 180.92 %*sec on the right side. Age older than 65 did not appear to be a significant risk factor for cerebral desaturation after positioning in beach chair (χ² = 0.244; P = 0.62). Likewise, adequately treated hypertension did not appear to be a risk factor for cerebral desaturation after positioning (χ² = 0.749; P = 0.39). Similarly no correlation was found between age and AUCrScO₂ on the right (r = 0.081, P = 0.81) and left side (r = -0.040, P = 0.91).

A repeated measures multivariate analysis of variance with a Greenhouse-Geisser correction with time as within-subject variable (pre-surgery, post-surgery, and follow up assessment) was performed. Age and degree of rScO₂ desaturation were included as covariates and SCWT, SDMT and AVLT as measures. The analysis revealed no significant changes in overall cognitive test performance over time. In addition, no significant interaction between time and age or rScO₂ desaturation was unveiled. Post-hoc tests only revealed a significant rise in score between the postoperative and follow-up assessment on the AVLT performance (P = 0.014), which can be attributed to a test-retest effect.
Discussion

To our knowledge, this is the first study to examine the incidence of cerebral desaturation and its association with postoperative neurocognitive sequelae in such a homogenous surgical group. All patient underwent the same surgical procedure, a total shoulder arthroplasty, with a similar amount of surgical time and duration of beach chair position. As demonstrated in previous research, a high incidence of cerebral desaturation occurs when a patient’s position is changed from supine to beach chair. Our results confirmed a cerebral desaturation during the surgical procedure in beach chair position in all of our patients. This corresponds with previous research (Fisher et al., 2009; Dippmann et al. 2010, Tange et al, 2010; Lee et al. 2011; Yadeau et al., 2011; Jeong et al., 2012; Ko et al., 2012; Moerman et al. 2012; Salazar et al, 2013; Pant et al, 2014). Episodes of cerebral desaturation were similar in patients with and without chronic hypertension. Finally our study showed no decline in cognitive outcome after shoulder surgery in beach chair position.

The exact frequency of neurologic complications in patients undergoing surgery in beach chair position is unknown. Major stroke occurs in 0.0004% of patients according to a survey of the American Shoulder and Elbow Surgeons (Friedman et al., 2009). When the treating anesthetist fails to appreciate the effect of hemodynamic changes caused by the gravitational effect of the head-up position, cerebral hypoperfusion may ensue. Blood pressure decreases proportionally to the weight of the ‘fluid’ column. A subtraction of 1.35 mmHg per cm of head elevation is advised to estimate the actual blood pressure at the brain. Although we were not able to provide beat-to-beat blood pressure measurements and link them directly to episodes of cerebral desaturation, several previous studies have shown the connection between cerebral desaturation and hypotension. Not all patients will subsequently develop cerebral ischemia, if compensatory mechanism such as a higher oxygen extraction reserves are sufficient. At risk are patients with altered cerebral autoregulation (such as untreated hypertension), cerebral atheromatosis and other problems with the circle of Willis.
Cerebral desaturation was not associated with neurocognitive deficit in our study population. In the majority of studies trying to find an association between neurocognitive dysfunction and operations in beach chair position, no systematic neuropsychological testing was performed. This is the second study that uses a test battery of validated neuropsychological tests. Although our neuropsychological testing is compatible with the 1995 consensus guideline and subsequent revisions, we chose not to include motor testing, thus disabling some executive functions and frontotemporal interactions. We opted to retest our patient on the third postoperative day to reduce the possibility of residual effect of medication and anesthesia, which could affect test scores negatively. Postoperative cognitive dysfunction may not always be apparent during the hospital stay. We opted to retest at the third month postoperative. A significant retesting effect was found in the AVLT, a test with memory forming and recall as prime goal. Substitution to a more difficult test could possibly eliminate this effect and improve test quality. A possible addition to our neurocognitive testing could be the use of specific enzymatic markers of cerebral damage. Neuron-specific enolase (NSE) is a neuronal isoform of the glycolytic enzyme enolase and is more specific for grey matter lesions. Protein S100B is an intracellular calcium-binding dimer, implicated in the proliferation and differentiation of neurons. It is more specific for white matter. Considering the different characteristics, the more prudent approach would be to analyze both, though current evidence has yet to define a clear consensus about cut-off values compatible with neuronal damage, especially in the case of the more subtle neurocognitive dysfunction. Other biomarkers of brain damage are currently under investigation in a post-resuscitation and traumatic brain injury setting (Tomaszewski, 2015) Only two studies show an association between POCD and elevated serum markers of brain damage (Xie et al., 2013; Lagram et al., 2015). Another possible option is the electroencephalogram (EEG). Patients who develop cognitive dysfunction show less burst suppression and states of deep sleep during anesthesia (Deiner et al., 2015). Thus far no study has investigated the use of EEG in the postoperative diagnosis of POCD.

Our study has several limitations. The small sample size and lack of power could explain the absence of a statistically significant result. This has several implications. Our smaller study population did not allow for any proper subgroup analysis. Perhaps the effect of cerebral desaturation does not have significant cognitive implications in
healthy patients, but may prove to be important in patients with cardiovascular risk factors, such as peripheral artery atheromatosis, diabetes mellitus with associated autonomous neuropathy, severe untreated hypertension and coronary artery disease. No analysis was possible in the group of older patients (> 65 years old), who might be at increased risk for the development of neurocognitive dysfunction. Our inclusion criteria were strict. We chose not to admit any patients with a pre-existing neurocognitive deficit or psychiatric disorder to the study protocol. Nonetheless both patients group have an impaired cerebral reserve and are especially at risk for the development of POCD. Another limitation is the lack of control group. We did not compare our beach chair group with a similar non-beach chair group. Prolonged shoulder surgery in lateral decubitus or other major joint surgery could be considered as a control group in later study protocols.

In conclusion, a large fraction of our study patients undergoing shoulder surgery in beach chair position are prone to experience episodes of cerebral desaturation at positioning and during surgery. In our patient population, this cerebral lack of oxygen was not correlated with any development of postoperative cognitive dysfunction. In patients at risk for cerebral desaturation, specific monitoring and appropriate hemodynamic interventions seems warranted as long as a potential relation between cerebral desaturation and POCD has not been definitively excluded.
References


DRUMMOND J.C.: The lower limit of cerebral autoregulation: time to revise our thinking. Anesthesiology, 197, 1481-1483.


Nederlandse samenvatting

Achtergrond/doel
Majeure schouderchirurgie in strandstoelhouding is geassocieerd met ernstige neurologische gevolgen, zelfs in een gezonde patiëntenzorgpopulatie van middelbare leeftijd. De strandstoelhouding zelf wordt vaak aangehaald, aangezien deze de cerebrale oxygenatie in het gedrang kan brengen. Deze studie heeft als doel de associatie aan te tonen tussen peroperatieve episodes van cerebrale desaturatie en postoperatieve cognitieve dysfunctie.

Materialen en methoden
Na toestemming van het Ethisch Comité en het afnemen van geïnformeerde toestemming, werden 11 volwassen patiënten (4 mannen, 7 vrouwen met gemiddelde leeftijd van 65 jaar met een SD van 12.4 jaar) zonder voorafgaande neurologische of psychiatrische pathologie op prospectieve wijze geïncludeerd. Zowel preoperatief, als op de derde dag en drie maanden postoperatief werd de neurocognitieve functie beoordeeld. Geheugen en aandacht werden geëvalueerd door middel van de ‘Auditory Verbal Learning Test (AVLT)’, de ‘Stroop Color Word Test (SCWT)’ en de ‘Symbol Digit Modalities Test (SDMT)’. Nabij-infrarood spectroscopie (NIRS) werd gebruikt om peroperatieve episodes van cerebrale desaturatie op te sporen, gedefinieerd als een daling van de basiswaarde met meer dan 20%. Standaard anesthesiologische zorg werd verleend. Een herhaalde meting multivariaat analyse van variantie met tijd als ‘within-subject’ variabele werd uitgevoerd.

Resultaten
Cerebrale desaturatie kwam voor bij alle patiënten tijdens de chirurgische procedure. Er werden geen significante veranderingen in cognitief vermogen gevonden tijdens de drie evaluatiemomenten. Eveneens was er geen significante interactie tussen tijd en leeftijd met cerebrale desaturatie. Een significante verbetering in test score voor de AVLT test postoperatief werd opgemerkt. Dit is meer dan waarschijnlijk het gevolg van een belangrijk test-hertest effect.
Conclusie

Deze voorlopige resultaten tonen geen associatie tussen episodes van cerebrale desaturatie en postoperatieve cognitieve dysfunctie. De huidige patiëntenpopulatie is echter nog te klein om tot definitieve conclusies te komen. Bevestiging van de bekomen resultaten in een grotere populatie is noodzakelijk.