Defect size and method of repair affect cerebral oxygenation in patients with atrial septal defects

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Masterproef voorgedragen in de master in de specialistische geneeskunde
Anesthesie en reanimatie
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List of abbreviations

ASD = atrial septal defect
bpm = beats per minute
CO₂ = carbon dioxide
CPB = cardiopulmonary bypass
Hb = hemoglobin
mmHg = millimeters of mercury
NIRS = near-infrared spectroscopy
PFO = patent foramen ovale
Qp = pulmonary blood flow, Qs = systemic blood flow
S₉O₂ = cerebral oxygen saturation
SpO₂ = peripheral tissue oxygen saturation
Abstract

Defect size and method of repair affect cerebral oxygenation in patients with atrial septal defects.

Background and goal of the study:
Despite being a minor heart defect, neuropsychological impairment has been demonstrated after repair of atrial septal defects (ASD). The underlying etiology is unclear, but increased preoperative cerebral vulnerability or acute cerebral alterations during repair have been suggested. Therefore, the aim of this study is to assess cerebral oxygen saturation ($S_cO_2$) in order to determine if ASD patients have preoperatively low $S_cO_2$, or if major changes in $S_cO_2$ occur during repair.

Materials and methods:
After approval by the local ethics committee and written informed consent, patients scheduled for surgical or transcatheter repair of ASD or patent foramen ovale (PFO) were recruited prospectively. Hemodynamic data and $S_cO_2$ measured with near-infrared spectroscopy (NIRS) (NIRO-200NX) were recorded throughout the procedure. Data was compared with analysis of variance and posthoc Tukey test for pairwise comparisons. Correlation analysis was performed by Pearson $\rho$ testing. Statistical significance was accepted at $p<0.05$.

Results and discussion:
Sixteen patients were included: 7 undergoing surgical ASD repair, 5 transcatheter ASD repair and 4 transcatheter PFO repair. Mean age was $6\pm4$, $22\pm23$ and $52\pm15$ years respectively, ($p=0.001$). Defect sizes did not differ between groups ($17\pm4$, $17\pm7$ and $13\pm2$ mm respectively, ($p=0.273$)). No differences in preoperative hemodynamic parameters and baseline $S_cO_2$ were found between groups.

The $S_cO_2$ values were significantly lower during closure in the surgical group compared to the transcatheter groups ($49\pm10\%$ vs $72\pm4\%$ and $72\pm7\%$ for transcatheter ASD and PFO respectively, $p<0.001$). A strong correlation was observed between defect size and baseline $S_cO_2$ ($r=0.9$, $p=0.037$ and $r=0.6$, $p=0.29$, for left and right respectively).

We do not regard the lower $S_cO_2$ values during surgical repair as clinically relevant, as it has been demonstrated that the method of treatment does not affect neuropsychological outcome. More interestingly, our finding that larger defect sizes were correlated with higher baseline $S_cO_2$ suggests that further studies are warranted to determine if the risk of neuropsychological impairment is associated with defect size.

Conclusion:
Lower $S_cO_2$ values were observed during surgical repair of an ASD compared to a transcatheter approach. Larger defect sizes were correlated with higher baseline $S_cO_2$.

Reference:
1 Sarrechia et al. J Pediatr 2015; 166(1):31-8
1. Introduction

1.1 Background

An atrial septal defect (ASD) is an abnormal communication between the left and right atrium resulting in shunting of oxygenated blood from the left atrium to deoxygenated blood to the right atrium. Atrial septal defects are the third most common type of congenital heart disease with an estimated incidence of 564 per million live births. An ASD can be either surgically repaired by open heart surgery or minimally invasive via catheterisation. If the heart defect is repaired before the age of 25, the patients retain the same life expectancy as their healthy peers.

A foramen ovale is a normal temporarily heart defect during fetal life, permitting blood to pass from the right atrium to the left atrium. Usually this foramen ovale closes right after birth, if not, it is called a patent foramen ovale (PFO).

Although an ASD and a PFO are considered to be less severe heart defects, neurocognitive changes have been reported in patients who underwent an ASD or PFO repair. Alterations in executive functions, language proficiency, memory and learning skills have been demonstrated.

A few theories attempt to explain these alterations. It is possible that, due to their heart defect, these patients suffer of an impaired cerebral blood flow resulting in neurocognitive changes even before undergoing the corrective procedure. On the other hand, the corrective procedure itself may induce changes in the brain either by the sudden interruption of the left to right shunt or by specific peri-operative factors, such as the use of cardiopulmonary bypass (CPB) or release of micro embolisms.
1.2 Neurocognitive impairment

Predictors of neurocognitive impairment

Over the years, identifying possible predictors of adverse neurocognitive outcome after surgery for congenital heart defects has gained significance. So far, research revealed complex interactions of pre-, intra- and postoperative factors which might be responsible for neurocognitive impairment after surgery. Preoperative factors are often not preventable and/or are irreversible. Genetics, prematurity, severity of the disease and age at repair have been proven to influence neurocognitive outcome. Research on intraoperative factors is less abundant, generating often conflicting or inconclusive results.

Miatton et al. summarised some intraoperative techniques which have been investigated in relation to neuropsychological consequences. Hemodilution during CPB, deep hypothermic circulatory arrest and micro embolisms (bubbles or small particulate matter) occurring during CPB have been associated with neurocognitive changes. Postoperative factors include the number of operations, length of stay in intensive care, occurrence of postoperative seizures and age at the moment of neuropsychological testing.

Neurocognitive impairment in patients with ASD

Significant lower scores in neurodevelopmental and behavioural tests have been observed in children after ADS closure. To date, this cannot be attributed to the type of technique used. Although Newman et al. demonstrated a high prevalence of persistent cognitive decline after CPB for coronary artery bypass grafting in adults, several research groups could not confirm the causal association between the implementation of CPB and postoperative cognitive impairment after ASD repair in children.

Compared to a matched healthy control group, Sarrechia et al. found significant differences on both neurodevelopmental and behavioural features in patients treated for ASD by surgical or interventional techniques. Both patients and their healthy controls scored equally on the Wechsler Intelligence Scale, however significant differences were found during neuropsychological assessment (attention and executive functioning, language, working memory, sensorimotor functioning, social cognition and visuospatial information processing). The differences were not related to the type of technique used (open vs. transcatheter ASD...
However due to the low power of the study, these differences might not have achieved statistical significance.

Furthermore, correlational analysis showed that length of stay in intensive care and defect size were associated with lower scores on neuropsychological testing.3

1.3 Near-infrared spectroscopy

Adequate tissue oxygenation during surgery is of utmost importance to maintain aerobic metabolism. Several techniques have been validated to monitor systemic tissue oxygenation, among which pulse oximetry and blood gas analysis. Regional measurement of tissue oxygenation on the other hand has remained a challenge for many years. Conventional hemodynamic monitoring during anesthesia usually adequately represents systemic tissue oxygenation but is often insensitive to regional hypoxia. Since tissue hypoxia might be a contributing factor to perioperative morbidity and mortality, additional monitoring is warranted. Using near-infrared light, near-infrared spectroscopy (NIRS) enables a real time estimation of regional tissue oxygenation.

The NIRS technique is based on the law of Lambert-Beer, which describes that the attenuation of light is directly proportional to characteristics of the substance through which the light travels (Figure 1A).

![Diagram illustrating the various ways that light can interact with organic samples.](image)

Figure 1A: Diagram illustrating the various ways that light can interact with organic samples.8
Several light absorbing chromophores are identified in human tissue. However only hemoglobin is present in both a sufficient level and in two different light absorbing optical spectra, enabling differentiation between oxy- and deoxyhemoglobin (Figure 1B).

Figure 1B: Distinct absorption spectra of oxygenated and deoxygenated hemoglobin (Hb). Moerman et al.⁹

The probe consists of an emitter of near-infrared light and a receiver of reflected light, usually utilizing wavelengths between 690 and 880 nanometre. In contrast to visible light, near-infrared light can penetrate several centimetres into tissue and even into bone. This characteristic is essential for transcranial cerebral tissue oxygenation monitoring. When placing one probe on each side of the forehead, near-infrared light travels in a boomerang shaped pathway from the emitter through the tissue. Two different receiving probes are located adjacent to each other and to the emitter, one capturing light from superficial tissue via a small banana shaped pathway and a more distant probe capturing light from the deeper tissue (region of interest) (Figure 1C).

By using a mathematical formula, which has not been made public, NIRS devices generate a percentage representing the deep tissue oxygen saturation. In case of cerebral oxygen saturation, NIRS provides an estimation of the balance between oxygen delivery and oxygen consumption mostly obtained from the cerebral cortex.

However, a potential pitfall while using NIRS is interference of visible light when the probes are poorly shielded from the surroundings.¹⁰
Research demonstrated that regional tissue oxygenation measured by NIRS correlates well with jugular venous bulb saturation which is considered an indirect assessment of cerebral oxygen supply and demand. Because probe positioning and interindividual anatomic variations (e.g. age, skull thickness, tissue characteristics) make it unfavourable to compare NIRS values between patients, it is recommended to analyse the individual trend.

An association has been demonstrated between intraoperative low cerebral saturations and postoperative cognitive dysfunction, stroke and prolonged length of stay in intensive care. NIRS values below 45% increase this risk threefold and a decline of more than 25% in NIRS value compared to baseline is considered a critical threshold for unfavourable neurological outcome.

1.4 Aim

The aim of this study was to assess cerebral oxygen saturation ($S_cO_2$) using NIRS during both surgically and transcatheater ASD/PFO closure, in order to determine if patients have preoperatively low $S_cO_2$, or if major changes in $S_cO_2$ occur during repair.
2. Materials and methods

After approval of the local research ethics committee (EC/2017/1064), written informed consent was obtained from the adult patients, from the parents or the guardian of children under the age of 18 and from children between the age of 12 and 18 years old. Patients with other associated cardiac defects were excluded from this study.

The original methodology of this study consisted of a prospective, observational study, comparing three different groups (surgical closure of an ASD, transcatheter closure of an ASD and transcatheter closure of a PFO).

2.1 Basic protocol setup

All patients were asked to follow the standard fasting guidelines according to the local preoperative fasting protocol. Patients were allowed to continue their routine medication. Standard monitoring was used throughout the procedure, including electrocardiography, peripheral oxygen saturation (SpO₂), non-invasive blood pressure measurement every three minutes in case of transcatheter repair, temperature measurement (oral and/or rectal) and end-tidal oxygen-, carbon dioxide- (CO₂) and sevoflurane concentrations (Dräger Infinity C700, Dräger Medical GmbH, Lübeck Germany).

In case of surgical repair, invasive arterial and central venous pressure measurements were also implemented.

Two NIRS sensors (NIRO-200NX, Hamamatsu Photonics, Tokyo, Japan) were placed symmetrically on the left and right forehead for continuous registration of S₂O₂ of the corresponding frontal cerebral cortex.

Before induction of general anesthesia, patients were preoxygenated with 100% oxygen enriched air. General anesthesia was induced with fentanyl up to 3 µg kg⁻¹, propofol up to 2 mg kg⁻¹, and rocuronium up to 1 mg kg⁻¹. Mechanical ventilation with fractional inspired oxygen 0.6 was adapted to keep the end-tidal CO₂ around 35 mmHg. General anesthesia was maintained throughout the procedure with sevoflurane at a minimum end-tidal concentration of 1.5%.
2.2 Protocol measurement setup

Measurements were done at 11 stages during the repair which are common in all procedures and of which the registered parameters would be compared between surgical and transcatheter closure of an ASD/PFO. Assessments were implemented at baseline (1), during preoxygenation (2), induction (3), intubation (4), two minutes after intubation (5), start of procedure (6), preparation of the transcatheter closure device vs. moment of administering heparin (7), mean value and lowest value during deployment of the closure device vs. mean and lowest values during CPB (8), after deployment of the closure device vs. end of CPB (9), start of weaning from general anesthesia vs. administration of protamine (10), and extubation vs. end of surgical procedure (11).

2.3 Sample size calculation and statistical analysis

Since there are currently no data available which document changes in cerebral oxygen saturation during ASD/PFO repair, a preliminary sample size was determined. Approximately 30 patients are scheduled for this type of repair in our institution each year, whereby a 3-year cohort was chosen, taking into account loss of data due to unavailability of the investigators. We aimed for a total of 60 patients (20 patients in every group).

Statistical analysis was performed by using the statistical software SPSS Statistics 22 (SPSS Inc., Chicago, IL). All registered parameters were analysed by using a two-way ANOVA for repeated measurements or the Friedman’s test, depending on normality of data distribution, and with posthoc Tukey test for pairwise comparisons. Distribution of the data was tested for normality using the Shapiro-Wilk test. The level of statistical significance was set at a corrected 2-sided p-value < 0.05.
3. Results

3.1 Comparison of the three groups

The initial design of this study consisted of analysing and comparing data collected during surgical ASD closure, transcatheter ASD closure and transcatheter PFO closure. The aim was to include 20 patients in each group (surgical closure of an ASD, a transcatheter closure of an ASD or a transcatheter closure of a PFO).

So far, sixteen patients have been included; seven patients in the surgical ASD group, five patients in the transcatheter ASD group, and four patients scheduled for a transcatheter PFO closure.

Demographic data are presented in table 1. There was a significant difference in age, length and weight between the three groups. Mean defect size was comparable between groups (p=0.273).

<table>
<thead>
<tr>
<th></th>
<th>Surgical ASD closure</th>
<th>Transcatheter ASD closure</th>
<th>Transcatheter PFO closure</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6 ± 4</td>
<td>22 ± 23</td>
<td>53 ± 15</td>
<td>0.001</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>115 ± 21</td>
<td>136 ± 35</td>
<td>167 ± 9</td>
<td>0.017</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>21 ± 8</td>
<td>43 ± 35</td>
<td>73 ± 21</td>
<td>0.009</td>
</tr>
<tr>
<td>Defect size (mm)</td>
<td>17.4 ± 3.9</td>
<td>16.6 ± 6.9</td>
<td>12.5 ± 1.9</td>
<td>0.273</td>
</tr>
</tbody>
</table>

Table 1: Demographic data. Data are presented as mean ± standard deviation. ASD: atrial septal defect; PFO: patent foramen ovale.

Hemodynamic data are presented in table 2. Analysis of the hemodynamic data revealed a significant difference in blood pressure between the three groups. This difference was not yet present at baseline but remained significant throughout the procedure. The difference was only observed when comparing the surgical group with both transcatheter groups, not in between these last two groups (p<0.05).

Values of SpO2, and end tidal values of CO2 and sevoflurane were not significantly different between the three groups.
<table>
<thead>
<tr>
<th></th>
<th>Surgical ASD closure</th>
<th>Transcatheter ASD closure</th>
<th>Transcatheter PFO closure</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline SpO₂ (%)</td>
<td>99 ± 1</td>
<td>99 ± 1</td>
<td>99 ± 2</td>
<td>0.83</td>
</tr>
<tr>
<td>Baseline blood pressure (mmHg)</td>
<td>68 ± 11</td>
<td>93 ± 17</td>
<td>89 ± 25</td>
<td>0.09</td>
</tr>
<tr>
<td>Baseline heart rate (bpm)</td>
<td>99 ± 17</td>
<td>89 ± 17.3</td>
<td>77 ± 9.3</td>
<td>0.10</td>
</tr>
<tr>
<td>During closure SpO₂ (%)</td>
<td>97 ± 3</td>
<td>99 ± 1</td>
<td>98 ± 1</td>
<td>0.57</td>
</tr>
<tr>
<td>During closure blood pressure (mmHg)</td>
<td>48 ± 10</td>
<td>61 ± 10</td>
<td>77 ± 11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>During closure lowest value blood pressure (mmHg)</td>
<td>34 ± 8</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>During closure heart rate (bpm)</td>
<td>/</td>
<td>76 ± 18</td>
<td>68 ± 9</td>
<td>0.78</td>
</tr>
<tr>
<td>During closure end-tidal CO₂ (mmHg)</td>
<td>35 ± 6</td>
<td>35 ± 3</td>
<td>35 ± 4</td>
<td>0.99</td>
</tr>
<tr>
<td>During closure end-tidal sevoflurane (%)</td>
<td>2.2 ± 0.5</td>
<td>2.3 ± 0.3</td>
<td>1.8 ± 0.4</td>
<td>0.16</td>
</tr>
<tr>
<td>After closure SpO₂ (%)</td>
<td>99 ± 1</td>
<td>98 ± 1</td>
<td>98 ± 2</td>
<td>0.40</td>
</tr>
<tr>
<td>After closure blood pressure (mmHg)</td>
<td>65 ± 14</td>
<td>60 ± 11</td>
<td>85 ± 16</td>
<td>0.04</td>
</tr>
<tr>
<td>After closure heart rate (bpm)</td>
<td>/</td>
<td>70 ± 17</td>
<td>66 ± 8</td>
<td>0.96</td>
</tr>
<tr>
<td>After closure end-tidal CO₂ (mmHg)</td>
<td>31 ± 3</td>
<td>35 ± 3</td>
<td>35 ± 4</td>
<td>0.11</td>
</tr>
<tr>
<td>After closure end-tidal sevoflurane (%)</td>
<td>2.2 ± 0.2</td>
<td>2.3 ± 0.3</td>
<td>1.8 ± 0.4</td>
<td>0.05</td>
</tr>
<tr>
<td>End of procedure SpO₂ (%)</td>
<td>99 ± 2</td>
<td>99 ± 1</td>
<td>100 ± 0</td>
<td>0.39</td>
</tr>
<tr>
<td>End of procedure blood pressure (mmHg)</td>
<td>67 ± 8</td>
<td>89 ± 15</td>
<td>103 ± 20</td>
<td>0.005</td>
</tr>
<tr>
<td>End of procedure heart rate (bpm)</td>
<td>110 ± 18</td>
<td>96 ± 39</td>
<td>95 ± 5</td>
<td>0.49</td>
</tr>
</tbody>
</table>

Table 2: Hemodynamic data at baseline, during and after closure of the defect, and at the end of the procedure. Data are presented as mean ± standard deviation. ASD: atrial septal defect; PFO: patent foramen ovale; SpO₂: peripheral oxygen saturation; CO₂: carbon dioxide.

NIRS data are presented in table 3. There was no significant difference in baseline S_cO₂ between the three groups. During closure of the defect, a significant difference was observed in S_cO₂ values between the surgical and the transcatheter groups. There was no difference in S_cO₂ between both transcatheter groups.
Surgical ASD closure & Transcatheter ASD closure & Transcatheter PFO closure & P-value \\
Baseline $S_cO_2$ left (%) & 69 ± 2 & 69 ± 5 & 72 ± 3 & 0.66 \\
Baseline $S_cO_2$ right (%) & 69 ± 8 & 70 ± 3 & 69 ± 8 & 0.91 \\
During closure $S_cO_2$ left (%) & 61 ± 6 & 73 ± 5 & 74 ± 6 & <0.001 \\
During closure $S_cO_2$ right (%) & 59 ± 9 & 70 ± 5 & 69 ± 8 & 0.003 \\
After closure $S_cO_2$ left (%) & 68 ± 6 & 74 ± 5 & 74 ± 6 & 0.25 \\
After closure $S_cO_2$ right (%) & 70 ± 8 & 71 ± 5 & 70 ± 7 & 0.94 \\
End of procedure $S_cO_2$ left (%) & 71 ± 6 & 78 ± 4 & 82 ± 4 & 0.39 \\
End of procedure $S_cO_2$ right (%) & 70 ± 6 & 77 ± 7 & 77 ± 7.7 & 0.15 \\

Table 3: NIRO values at baseline, during and after closure of defect, and at the end of the procedure. Data are presented as mean ± standard deviation. ASD: atrial septal defect; PFO: patent foramen ovale; $S_cO_2$: cerebral oxygen saturation.

3.2 Comparison of surgical and transcatheter closure

Posthoc, a secondary analysis was performed, comparing surgical ASD closure versus transcatheter ASD/PFO closure.

Demographic characteristics were significantly different in the categories of age, length and weight (Table 4). Mean defect size was comparable between surgical and transcatheter group.

<table>
<thead>
<tr>
<th></th>
<th>Surgical ASD closure</th>
<th>Transcatheter ASD/PFO</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6 ± 4</td>
<td>35 ± 25</td>
<td>0.007</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>115 ± 21</td>
<td>149 ± 30</td>
<td>0.023</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>21 ± 8</td>
<td>57 ± 32</td>
<td>0.013</td>
</tr>
<tr>
<td>Defect size (mm)</td>
<td>17.4 ± 3.9</td>
<td>14.8 ± 5.4</td>
<td>0.298</td>
</tr>
</tbody>
</table>

Table 4: Demographic data. Data are presented as mean ± standard deviation. ASD: atrial septal defect; PFO: patent foramen ovale.
Hemodynamic data of the two groups are presented in table 5. Significant differences in blood pressure were observed at baseline and throughout the procedure. No significant differences in SpO2, end tidal CO2 and sevoflurane were registered.

<table>
<thead>
<tr>
<th></th>
<th>Surgical ASD closure</th>
<th>Transcatheter ASD/PFO closure</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline SpO2 (%)</td>
<td>99 ± 1</td>
<td>99 ± 1</td>
<td>0.77</td>
</tr>
<tr>
<td>Baseline blood pressure (mmHg)</td>
<td>68 ± 11</td>
<td>91 ± 20</td>
<td>0.03</td>
</tr>
<tr>
<td>Baseline heart rate (bpm)</td>
<td>99 ± 17</td>
<td>84 ± 15</td>
<td>0.07</td>
</tr>
<tr>
<td>During closure SpO2 (%)</td>
<td>97 ± 3</td>
<td>98 ± 1</td>
<td>0.34</td>
</tr>
<tr>
<td>During closure blood pressure (mmHg)</td>
<td>48 ± 10</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>During closure lowest value blood pressure (mmHg)</td>
<td>34 ± 8</td>
<td>68 ± 13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>During closure heart rate (bpm)</td>
<td>/</td>
<td>72 ± 14</td>
<td>/</td>
</tr>
<tr>
<td>During closure end-tidal CO2 (mmHg)</td>
<td>35 ± 6</td>
<td>35 ± 3</td>
<td>0.99</td>
</tr>
<tr>
<td>During closure end-tidal sevoflurane (%)</td>
<td>2.2 ± 0.5</td>
<td>2.1 ± 0.4</td>
<td>0.62</td>
</tr>
<tr>
<td>After closure SpO2 (%)</td>
<td>99 ± 1</td>
<td>98 ± 1</td>
<td>0.17</td>
</tr>
<tr>
<td>After closure blood pressure (mmHg)</td>
<td>65 ± 14</td>
<td>71 ± 18</td>
<td>0.52</td>
</tr>
<tr>
<td>After closure heart rate (bpm)</td>
<td>/</td>
<td>68 ± 13</td>
<td>/</td>
</tr>
<tr>
<td>After closure end-tidal CO2 (mmHg)</td>
<td>33 ± 3</td>
<td>35 ± 4</td>
<td>0.14</td>
</tr>
<tr>
<td>After closure end-tidal sevoflurane (%)</td>
<td>2.2 ± 0.2</td>
<td>2 ± 0.4</td>
<td>0.49</td>
</tr>
<tr>
<td>End of procedure SpO2 (%)</td>
<td>99 ± 2</td>
<td>99 ± 1</td>
<td>0.40</td>
</tr>
<tr>
<td>End of procedure blood pressure (mmHg)</td>
<td>67 ± 8</td>
<td>95 ± 18</td>
<td>0.003</td>
</tr>
<tr>
<td>End of procedure heart rate (bpm)</td>
<td>111 ± 18</td>
<td>95 ± 28</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Table 5: Hemodynamic data at baseline, during and after closure of the defect, and at the end of the procedure. Data are presented as mean ± standard deviation. ASD: atrial septal defect; PFO: patent foramen ovale; SpO2: peripheral oxygen saturation; CO2: carbon dioxide.

NIRS data for the surgical versus transcatheter closure groups are presented in table 6. Baseline $S_c$O2 values did not differ significantly between both groups. During closure of the defect and at the end of the procedure, $S_c$O2 values were significantly lower in the surgical closure group.
Table 6: NIRO values at baseline, during and after closure of defect, and at the end of the procedure. Data are presented as mean ± standard deviation. ASD: atrial septal defect; PFO: patent foramen ovale; $S_cO_2$: cerebral oxygen saturation.

### 3.3 Correlation analysis

Correlation analysis was performed exclusively with ASD patients. A strong correlation of 0.90 was found between defect size and baseline left sided $S_cO_2$ values (p= 0.037). The correlation with right sided $S_cO_2$ was less strong (r= 0.60) and not significant (p= 0.29).
4. Discussion

The aim of the present study was to assess if patients with ASD/PFO have preoperatively low \( S_cO_2 \) or if major changes in \( S_cO_2 \) occur during repair of the defect. Our data demonstrates that baseline \( S_cO_2 \) were within normal ranges.\(^9\) Interestingly, a positive correlation between size of the ASD and baseline \( S_cO_2 \) was found. Patients with larger defect sizes had significantly higher baseline \( S_cO_2 \). We also demonstrated that during repair of the defect, changes in \( S_cO_2 \) were significantly more pronounced in patients undergoing surgical repair.

Significantly lower \( S_cO_2 \) values were observed during surgical repair compared with transcatheter closure. During CPB in the surgical repair group, the \( S_cO_2 \) values decreased to 61 ± 6 % and 59 ± 9% at the left and right side, respectively. Previous research showed that \( S_cO_2 < 45\% \) or a 25% drop in \( S_cO_2 \) compared to the baseline value, might be considered as a critical threshold for unfavourable neurological outcome. These critical changes were never observed in our patient population. Previous studies in adults revealed that the use of CPB implicates a potential risk for future neurocognitive difficulties. However, investigation by Sarrechia et al. could not reproduce a difference in neurocognitive outcome between surgical and transcatheter ASD closure in children.\(^10\)

Another hypothesis for the adverse neurocognitive impairment after ASD closure is the influence of the pre-existing left-right shunt.

Patients with a left-right shunt have an increased circulating blood volume, resulting in an increased cardiac output. It is now recognized that changes in cardiac output affect the cerebral autoregulation mechanism.\(^13\) If cardiac output increases, the autoregulation curve shifts upwards, so cerebral blood flow will increase. Vice versa, if cardiac output decreases, the curve is shifted downwards and cerebral blood flow will also decrease. It is assumed that the autoregulation curve itself remains unaffected, but actually this is still unknown (Figure 2).

Cerebral function and development is dependent on a sufficient and constant cerebral blood flow. Although the influence of hypoperfusion is already well established, little is known about the effect of hyperperfusion. Recent evidence suggests that hyperperfusion might be as deleterious as hypoperfusion.\(^14\) Further studies should consider using transcranial doppler to thoroughly evaluate possible increased cerebral blood flow in patients with an ASD.
The positive correlation we found in the present study between the defect size and baseline $S_cO_2$ is in accordance with the assumption that these patients have a higher cardiac output, and consequently a higher cerebral blood flow. As demonstrated in other population groups, higher cerebral blood flows might adversely affect the brain. Therefore, it is worthwhile to explore the association between defect size and neurological outcome in patients with left-right shunting. If there is indeed an association, it should be considered to correct these type of defects at an earlier age.\textsuperscript{13,15}

Interestingly, data showed a difference in correlation between left sided and right sided $S_cO_2$ baseline values. Only left sided values shared a strong and significant correlation. Fluctuations in cerebral hemodynamics have been demonstrated by using NIRS\textsuperscript{16} but it remains unclear if this sufficiently explains our findings.

Lastly, major hemodynamic differences were observed between the surgical and the transcatheter groups. However, these differences can actually be brought back to three main characteristics. First, the age difference between the groups, resulting in dissimilarity in hemodynamic reference values. Secondly, whether the patient was woken up (transcatheter approach) or left asleep (surgical approach) at the end of the procedure. And thirdly, the difference in procedure, with the use of CPB in the surgical repair group. Of note, there was no difference in $SpO_2$ between the groups, underscoring that peripheral oxygen saturation is not a reliable indicator for cerebral oxygenation.\textsuperscript{10}
Some limitations have to be taken into account. First of all, due to the low sample size, the present data have to be regarded as very preliminary. Secondly, estimation of the severity of the left-right shunt is ideally performed by using a Qp/Qs ratio measured during echocardiography. Future studies should focus on investigating a potential correlation between the Qp/Qs ratio and S_cO_2.

5. Conclusion

The present study demonstrated that changes in cerebral saturation were significantly more pronounced in patients undergoing surgical repair of an ASD. However, these changes remained within acceptable ranges. More importantly, a positive correlation between defect size and baseline cerebral saturation was revealed. It seems worthwhile to explore if the defect size, and a fortiori the shunt fraction, is a risk factor for adverse neurocognitive outcome.
6. References


7. Samenvatting

Onderzoek naar de veranderingen in cerebrale oxygenatie na chirurgisch versus transkatheter sluiten van een atriaal septum defect

Achtergrond en doelstelling:
Hoewel een atriaal septum defect (ASD) beschouwd wordt als een mineure hartafwijking, werden er toch belangrijke neurocognitieve problemen opgemerkt na correctie. De onderliggende oorzaken hiervoor blijven tot nu toe grotendeels ongekend. Zowel verhoogde perioperatieve cerebrale kwetsbaarheid als acute cerebrale veranderingen tijdens herstel werden hier reeds mee in verband gebracht. In deze studie willen we de cerebrale zuurstof saturatie $S_cO_2$ in kaart brengen om te bepalen of ASD patiënten preoperatief lagere $S_cO_2$ hebben of er belangrijke veranderingen zich voordoen tijdens herstel.

Methodiek:
Na goedkeuring door de ethische commissie werden patiënten, gepland voor een chirurgisch of transkatheter herstel van ASD of een patent foramen ovale (PFO), prospectief gerekruteerd. Doorheen de procedure werden $S_cO_2$, gemeten aan de hand van nabije-infrarood spectroscopie (NIRS) (NIRO-200NX), en hemodynamische parameters geregistreerd. Data werd geanalyseerd voor variantie en de groepen werden onderling vergeleken aan de hand van de posthoc Tukey test. Onderzoek naar correlatie werd uitgevoerd met de Pearson p test. Statistische significantie werd vastgelegd op $p<0.05$.

Resultaten en discussie:
Zestien patiënten werden geïncludeerd: 7 gepland voor chirurgisch herstel van een ASD, 5 voor transkatheter ASD herstel en 4 voor een transkatheter PFO herstel. De gemiddelde leeftijd in deze groepen was $6\pm4$, $22\pm23$ en $52\pm15$ jaar respectievelijk, ($p=0.001$). De grootte van het defect was niet verschillend tussen de groepen ($17\pm4$, $17\pm7$ en $13\pm2$ mm respectievelijk, ($p=0.273$)). Er was geen verschil in pre-operatieve hemodynamische parameters en baseline $S_cO_2$ tussen de groepen.

Tijdens het herstel daarentegen, was de $S_cO_2$ significant lager in patiënten die een chirurgisch herstel ondergingen vergeleken met de transkatheter groepen ($49\pm10\%$ vs $72\pm4\%$ en $72\pm7\%$ voor transkatheter ASD en PFO respectievelijk, $p<0.001$). Een sterke en significante correlatie werd waargenomen tussen grootte van het defect en basis $S_cO_2$ waarden ($r=0.9$, $p=0.037$ and $r=0.6$, $p=0.29$, voor links en rechts respectievelijk).
Lagere $S_cO_2$ waarden tijdens chirurgisch herstel werden als niet signifiant beschouwd omdat deze waarden nooit de kritisch lage drempel bereikten. Daarnaast kon er in onderzoek tot nu toe geen link gelegd worden tussen het soort herstel en neurocognitieve veranderingen.\(^1\) Aangezien hogere basis $S_2O_2$ waarden gecorreleerd werden aan een groter defect, zijn verdere studies nodig om te kijken of deze defect grootte ook kan gelinkt worden aan neurocognitieve problemen achteraf.

**Conclusie:**

Lagere $S_cO_2$ waarden werden waargenomen tijdens chirurgisch herstel vergeleken met transkatheter herstel van een ASD. Daarnaast werden grotere defecten gecorreleerd met hogere basis ScO2 waarden.

**Referentie:**

\(^1\) Sarrechia et al. J Pediatr 2015; 166(1):31-8