The role of Willis circle variations during unilateral selective cerebral perfusion: a study of 500 circles†

Vassil Papantchev*, Vesela Stoïnova, Alexander Aleksandrovs, Daniela Todorova-Papantcheva, Stanislav Hristovs, Dimitar Petkovs, Gencho Nachevas and Wladimir Ovtscharoffs

* Department of Cardiac Surgery, ‘St Ekaterina’, University Hospital, Sofia, Bulgaria
† Section of Diagnostic Imaging, ‘St Ekaterina’, University Hospital, Sofia, Bulgaria
‡ Department of Forensic Medicine, Medical University, Sofia, Bulgaria
§ Department of General, Experimental and Genetic Psychology, Sofia University, Sofia, Bulgaria
¶ Department of Anatomy and Histology, Medical University, Sofia, Bulgaria

† Corresponding author. Department of Cardiac Surgery, University Hospital ‘St Ekaterina’, Medical University, 1431 Sofia, Bulgaria. Tel: +359-889-700343; e-mail: vassil.papanchev@yahoo.com (V. Papantchev).

Received 14 September 2012; received in revised form 5 January 2013; accepted 15 January 2013

Abstract

OBJECTIVES: During unilateral selective cerebral perfusion (uSCP), with right axillary artery or brachiocephalic trunk cannulation, the brain receives blood only via the right common carotid artery and right vertebral artery (VA). The left hemisphere is perfused mainly through the circle of Willis (CW). However, at least 50% of individuals have some variation in the CW. The aim of the present work was to study the variations in CW and VA that could have an impact on haemodynamics during uSCP.

METHODS: From May 2005 to March 2012, a total number of 250 circles obtained via routine dissection for medico-legal reasons were examined. The external diameters of all CW segments and both VAs were measured. From January 2008 to March 2012, a total number of 250 patients subjected to computed tomographic angiography of the CW were also examined.

RESULTS: Nine evident configurations of the CW that could cause hypoperfusion during uSCP were observed. They were subdivided in seven types, according to location and the number of major vessels at risk of hypoperfusion. Type IA: hypo/aplasia of left posterior communicating artery (PComA), found in 35.6% of cases; Type IB: hypo/aplasia of anterior communicating artery (ACoMA), found in 2% of cases; Type IIA: hypo/aplasia of both left PComA and ACoMA, found in 4.8% of cases; Type IIB: hypo/aplasia of precommunicating (P1) segment of left posterior cerebral artery or right VA, found in 9.2% of cases; Type IIIA: hypo/aplasia of precommunicating (A1) segment of right anterior cerebral artery, found in 6% of cases; Type IIIB: hypo/aplasia of both right VA and ACoMA, found in 0.2% of cases; Type IV: hypo/aplasia of both right A1 and right VA or both right A1 and left P1, found in 0.8% of cases. All types were present in 58.6% of all examined CWs.

CONCLUSIONS: Our results show that CW variations are present in a significant number of patients. Our data support the need for extensive preoperative examination and meticulous intraoperative monitoring of cerebral perfusion during uSCP. Finally, our data support the superiority of bilateral SCP over uSCP, because most of the variations reported do not have haemodynamic significance during bilateral SCP.

Keywords: Cerebral protection • Willis circle • Variations • Aortic surgery • Stroke

INTRODUCTION

Neurological injuries, stroke and paraplegia are the most devastating complications of aortic surgery [1, 2]. For this reason, cerebral protection is a key issue [1–3]. Its major goal is to guarantee the optimal ratio between the blood supply and the metabolic demands of the brain [1–3]. There are three methods of cerebral protection that are in clinical use: selective cerebral perfusion (SCP), introduced by DeBakey et al. [4], deep hypothermic circulatory arrest, introduced by Griepp et al. [5] and retrograde cerebral perfusion, introduced by Ueda et al. [6]. Each of these methods suffers from limitations, some of which could be termed ‘major’ [1, 2]. While deep hypothermic circulatory arrest is still a gold standard for cerebral protection, the question of its safe duration still remains open [1, 2, 7]. It is well known that metabolic activity decreases with temperature by ~7% per 1°C. Nevertheless, many works have shown that at 20°C cerebral activity is still around 25% [2, 7]. In this respect, arrest durations up to 20 min are considered safe, under these circumstances [2, 7]. This period, however, is too short for some complex arch reconstructions. The major problems with retrograde cerebral perfusion are cerebral oedema and whether the brain is really perfused.
with oxygenated blood or it is shunted [1]. On first sight, SCP offers unlimited duration, with physiological blood flow to the brain [1, 2, 7]. However, one of the major questions is how much epiaortic vessels must be perfused in order to ensure adequate cerebral perfusion. Several modifications are used in surgical practice [1–3, 8–10]. SCP could be performed as unilateral, with cannulation of right axillary artery or brachiocephalic trunk, or bilateral, with additional cannulation of left common carotid artery [2, 7, 9]. Some centres add a third cannula in the left subclavian artery [3], while other centres perform cerebral perfusion only via the common carotid artery [10].

Our current interest is directed towards unilateral SCP (uSCP). Looking anatomically, during uSCP, with cannulation of the right axillary artery or brachiocephalic trunk, the brain receives blood only via the right common carotid artery and right vertebral artery (VA). The assumption of the protective effect of uSCP is based on the understanding that collateral circulation, mainly through the arterial circle of Willis (CW), is sufficient to maintain adequate perfusion of the contralateral (left) hemisphere (Fig. 1).

According to the literary data, some variations of the circle exist in at least 50% of the people [9, 11–20]. Furthermore, it was shown that these variations usually affect more than one segment of the circle [9, 11–20]. Unfortunately, most studies of the Willis’ circle examine its segments separately, but not the circle as a whole [21, 22]. The number of works, examining the entire circle is low and the results are contradictory [8–20]. In this respect, the aim of present work was to study the variations in the CW and vertebral arteries that could have an impact on haemodynamics during uSCP. This study was approved by the Ethical Committee for Scientific Studies, Medical University, Sofia.

MATERIALS AND METHODS

A total number of 500 circles of Willis were collected. The average age of the subjects was 60 years (between 18 and 91). Two-hundred and one were female, while 299 were male. Circles were collected as follows:

From May 2005 to March 2012, a total number of 286 circles were examined prospectively in the Department of Forensic Medicine of Medical University, Sofia. All circles were obtained from cadavers via routine dissection. All subjects had died natural or violent deaths and were candidates for autopsy for medicolegal reasons. In the course of the study, 36 circles were excluded because their morphology was distorted by decay, cranial trauma, cerebral haemorrhage, cerebral neoplasm, aneurysm or headshot. All other 250 circles were included. The circles were carefully dissected and the external diameters of the following vessels were measured with a calliper-gauge: internal carotid artery, precommunicating (A1) segment of anterior cerebral artery, middle cerebral artery, precommunicating (P1) segment of posterior cerebral artery, AComA, PComA and intracranial segment of both vertebral arteries (Fig. 1A). All data were collected in a database. A digital photo of each circle was taken for further analysis.

From January 2008 to March 2012, a total number of 272 consecutive patients underwent computed tomography (CT)-angiography of the CW in the Section of Diagnostic Imaging, ‘St Ekaterina’ University Hospital, Sofia. In the course of enrolment, 22 circles were excluded, because their morphology was affected by...
Table 1: Classification of the variations of the CW, significant during uSCP

<table>
<thead>
<tr>
<th>Type</th>
<th>Variation</th>
<th>Zone at risk of hypoperfusion</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type IA</td>
<td>Left PComA</td>
<td>Left middle cerebral artery</td>
<td>35.6% (178/500)</td>
</tr>
<tr>
<td>Type IB</td>
<td>AComA</td>
<td>Left anterior cerebral artery</td>
<td>2% (10/500)</td>
</tr>
<tr>
<td>Type IIA</td>
<td>Left PComA + AComA</td>
<td>Left anterior cerebral artery + left middle cerebral artery</td>
<td>4.8% (24/500)</td>
</tr>
<tr>
<td>Type IIIB</td>
<td>Left P1 or right VA</td>
<td>Left middle cerebral artery + left posterior cerebral artery</td>
<td>9.2% (46/500)</td>
</tr>
<tr>
<td>Type IIIA</td>
<td>Right A1</td>
<td>Right anterior cerebral artery + left anterior cerebral artery + left middle cerebral artery</td>
<td>6% (30/500)</td>
</tr>
<tr>
<td>Type IIIB</td>
<td>AComA + right VA</td>
<td>Left anterior cerebral artery + left posterior cerebral artery</td>
<td>0.2% (1/500)</td>
</tr>
<tr>
<td>Type IV</td>
<td>Right A1 + right VA or right A1 + left P1</td>
<td>Right anterior cerebral artery + left middle cerebral artery + left posterior cerebral artery</td>
<td>0.8% (4/500)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>58.6% (293/500)</td>
</tr>
</tbody>
</table>

Showing affected vessels, vessel basins at risk of hypoperfusion and frequency of each variations type for this study. PComA: posterior communicating artery; AComA: anterior communicating artery; VA: vertebral artery; uSCP: unilateral selective cerebral perfusion.

aneurysm, cerebral haemorrhage, cerebral neoplasm or arteriovenous malformation. All other 250 circles were included. In 145 patients, the examination was done on a detector Toshiba Aquilion one™ (Toshiba, Japan), while in others, it was done on 105 GE Light Speed™ 16-slice CT (General Electric, USA). All examinations were performed in the arterial phase, after IV administration of 60 ml iodine-based contrast medium (Iomeron® 400 mg/ml; Patheon Italia S.p.A.; Italy) with an injection speed of 4 ml/s. The slice thickness was either 0.5 or 1.25 mm, respectively. The results were analysed by two different experienced radiologists (V.S. and V.G.) who divided the circles into variant and normal. All circles classified as variant were then examined by one of the authors (V.P.) and finally classified.

In both groups, a vessel diameter of 1 mm was used as the threshold for hypoplasia [9]. The threshold of 1 mm was chosen in order to be consistent with other major morphological studies of the CW reported in the literature [9,12–15,18–20].

Explanation marks were added to all pictures, using Adobe Photoshop CS 3.0 (Adobe, USA).

RESULTS

Four segments of CW, namely right A1, AComA, left PComA and left P1 and right VA were defined as critical during uSCP (Fig. 1C), considering the specificity of haemodynamics during uSCP (Fig. 1B) and the Poiseuille/Hagen law:

$$R = 8L \eta/\pi r^4,$$

where $R$ is resistance, $L$ is length of the pipe (vessel), $\eta$ is viscosity of the fluid (blood) and $r$ is the radius of the pipe (vessel).

Thus, nine distinct circle configurations, which could cause hypoperfusion during uSCP, were identified. They were subdivided into seven types, according to the number of major vessels at risk of hypoperfusion during uSCP (Table 1, Figs. 2–4):

Type IA includes all circles with hypo- or aplasia of left PComA (Table 1, Figs. 2–4). If this circle type is present, the territories supplied by the left middle cerebral artery are at risk of hypoperfusion during uSCP (Table 1, Figs. 2–4). This was the most common variation. It was found in 35.6% of all cases.

Type IB includes all circles with hypo- or aplasia of AComA (Table 1, Figs. 2–4). If this circle type is present, the territories supplied by the left anterior cerebral artery are at risk of hypoperfusion during uSCP (Table 1, Figs. 2–4). This variation was found in 2% of all cases.

Type IIA includes all circles with hypo- or aplasia of left P1 (Table 1, Figs. 2–4) or right VA (Table 1, Figs. 2–4). If this circle type is present, the territories supplied by both left anterior cerebral artery and left middle cerebral artery are simultaneously at risk of hypoperfusion during uSCP (Table 1, Figs. 2–4). This variation was found in 4.8% of all cases.

Type IIIB includes all circles with hypo- or aplasia of both left PComA and AComA (Table 1, Figs. 2–4). If this circle type is present, the territories supplied by both left anterior cerebral artery and left middle cerebral artery are simultaneously at risk of hypoperfusion during uSCP (Table 1, Figs. 2–4). This variation was found in 9.2% of all cases.

Type IIIB includes all circles with hypo- or aplasia of right A1 (Table 1, Figs. 2–4). If this circle type is present, the territories supplied by the three major vessels are simultaneously at risk of hypoperfusion during uSCP, namely right anterior cerebral artery, left anterior cerebral artery and left middle cerebral artery (Table 1, Figs. 2–4). This variation was found in 6% of all cases.

Type IIIA includes all circles with hypo- or aplasia of both right A1 and right VA (Table 1, Figs. 2–4). If this circle type is present, the entire left hemisphere is at risk of hypoperfusion during uSCP (Table 1, Figs. 2–4). This was the rarest variation. It was found in only 0.2% of all cases (1 patient).

Type IV includes all circles with hypo- or aplasia of both right A1 and right VA (Table 1, Figs. 2–4) or both right A1 and left P1 (Table 1, Figs. 2–4). This was the most severe variation. If this circle type is present, territories supplied by the four major vessels are simultaneously at risk of hypoperfusion during uSCP, namely right anterior cerebral artery, left anterior cerebral artery, left middle cerebral artery and left posterior cerebral artery (Table 1, Figs. 2–4). This circle type was found in 0.8% of all cases.
All types were present in 58.6% of all examined circles (Table 1, Figs. 2–4).

**DISCUSSION**

Our results reported here require profound discussion. The first major question is: are the data obtained with two different scanners compatible? In our work in press (Papancthev et al., in preparation), we compared 105 Willis’ circles, examined with GE Light Speed® (General Electric) and 105 Willis’ circles, examined with Toshiba Aquilion one® (Toshiba) with no difference in demographic data between the groups (Table 2). We discovered that there is no statistically significant difference either between the overall frequency of the circle’s variations, or between the frequency of each of the seven circle types (Table 2). We, however, observed a statistically significant difference in the frequency of hypoplastic and aplastic vessels, but this does not affect our classification of Willis’ circle variations (Table 2).
Figure 3: Willis circle variations, observed during CT angiography. (A) Example of circle Type IA with aplasia of left PComA (white arrow). (B) Example of circle Type IB with hypoplasia of AComA (white arrow). (C) Example of circle Type IIA with hypoplasia of both AComA (white arrow) and left PComA (black arrow). (D) Example of circle Type IIB with hypoplasia of precommunicating (P1) segment of left posterior cerebral artery (white arrow). (E) Example of circle Type IIB with hypoplasia of right VA (white arrow). (F) Example of circle Type IIIA with hypoplasia of precommunicating (A1) segment of right anterior cerebral artery (white arrow). (G) Example of circle Type IIIB with hypoplasia of AComA (white arrow) and right VA, showing only the Willis’ circle. (H) Same examination from plane (G). Showing the hypoplasia of right VA (black arrow). (I) Example of circle Type IV with hypoplasia of both A1 segment of right anterior cerebral artery (white arrow) and P1 segment of left posterior cerebral artery (black arrow). (J) Same examination from plane (I). Showing better view of hypoplastic P1 segment of left posterior cerebral artery (black arrow). (K) Example of circle Type IV with hypoplasia of both A1 segment of right anterior cerebral artery (white arrow) and right VA, showing only the Willis’ circle. (L) Same examination from plane (K). Showing hypoplasia of right VA (black arrow).
The second major question is: are the data obtained with CT angio (examining internal vessel diameter) and autopsy (examining external vessel diameter) compatible? In our work in press (Papantchev et al., in preparation), we compared 120 Willis’ circles examined with CT angio and 120 Willis’ circles examined with routine dissection, with no difference in demographic data between the groups (Table 3). We discovered that there is no statistically significant difference either between the overall frequency of the circle’s variations, or between the frequency of each of the seven circle types (Table 3). Results from these two works showed that the data obtained with modern scanners and autopsy are compatible and could be collected in a single database.

It is well known that the CW is a highly variable structure. A PubMed search performed in September 2012, with keywords ‘Willis Circle’, revealed over 2500 publications. Most of the works, however, studied the variations of each segment of the circle separately [21, 22]. According to the best of our knowledge, only 13 publications studied the variations of the CW as a whole—Riggs and Rupp [11], Fisher [12], Lazorthes et al. [13], El Khamlichi et al. [14], Eftekhar et al. [15], Papantchev et al. [16], Merkkola et al. [8], Papantchev et al. [9], Urbanski et al. [10], Dadmehr et al. [17], Papantchev et al. [18], De Silva et al. [19] and Ansari et al. [20]. Unfortunately, the data reported here could not be compared with most of those studies for several reasons:

First, eight of those studies, namely Riggs and Rupp [11], Fisher [12], Lazorthes et al. [13], El Khamlichi et al. [14], Eftekhar et al. [15], Urbanski et al. [10], De Silva et al. [19] and Ansari et al. [20] classify the variations without paying attention to their lateralization. These authors consider it irrelevant whether the variation is on the right or the left side of the circle [10-15, 19, 20]. Since the haemodynamics during uSCP is unique, the left-right lateralization is of crucial importance [9].

Secondly, in nine of the studies, namely Riggs and Rupp [11], Fisher [12], Lazorthes et al. [13], El Khamlichi et al. [14], Eftekhar et al. [15], Urbanski et al. [10], De Silva et al. [19] and Ansari et al. [20], there are no data concerning variations

Figure 4: Schematic drawing of all circle types and vessel territories at risk during uSCP, where hypo/aplastic vessels are present as missing segment, vessels at risk of hypoperfusion during uSCP are presented in black and cerebral territories at risk are present hatched. (A) Circle Type IA with hypo/aplasia of left PComA. (B) Territories supplied by left middle cerebral artery are at risk of hypoperfusion during uSCP, if circle Type IA is present. (C) Circle Type IB with hypoplasia of AComA. (D) Territories supplied by left anterior cerebral artery are at risk of hypoperfusion during uSCP, if circle Type IB is present. (E) Circle Type IIA with hypoplasia of both left PComA and AComA. (F) Territories supplied by both left anterior cerebral artery and left middle cerebral artery are at risk of hypoperfusion during uSCP, if circle Type IIA is present. (G) Circle Type IIB with hypoplasia of precommunicating (P1) segment of left posterior cerebral artery. (H) Circle Type IIB with hypoplasia of right VA. (I) Territories supplied by both left middle cerebral artery and left posterior cerebral artery are at risk of hypoperfusion during uSCP, if circle Type IIB is present. (J) Circle Type IIIA with hypoplasia of precommunicating (A1) segment of right anterior cerebral artery. (K) Territories supplied by right anterior cerebral artery, left anterior cerebral artery and left middle cerebral artery and left posterior cerebral artery are at risk of hypoperfusion during uSCP, if circle Type IIIA is present. (L) Circle Type IIIB with hypo/aplasia of AComA and right VA. (M) Territories supplied by left anterior cerebral artery, left middle cerebral artery and left posterior cerebral artery are at risk of hypoperfusion during uSCP, if circle Type IIIB is present. (N) Circle Type IV with hypo/aplasia of both A1 segment of right anterior cerebral artery and P1 segment of left posterior cerebral artery. (O) Circle Type IV with hypo/aplasia of both A1 segment of right anterior cerebral artery and right VA. (P) Territories supplied by right anterior cerebral artery, left anterior cerebral artery, left middle cerebral artery and left posterior cerebral artery are at risk of hypoperfusion during uSCP, if circle Type IV is present.
of vertebral arteries. This fact is not a surprise, since vertebral arteries are not a part of the Willis circle ‘per se’, but variations in those arteries could have a crucial importance during uSCP [9].

Thirdly, De Silva et al. [19] used 10% formaldehyde-fixed brains, while most of other major studies examined unfixed specimens. Because of their low molecular weight, all formaldehyde solutions are hypertonic and thus 9, 6 and even 3% formaldehyde solutions cause dehydration and consecutive tissue shrinkage [23]. In this respect, the results reported by De Silva et al. could not be compared with other morphological studies, which used unfixed specimens.

Fourthly, the study of Dadmehr et al. [17] is written in Arabic and could not be used for comparison.

And finally, different authors used different classifications of the circle’s variations and also different definitions for hypoplastic vessels. Most authors, namely Fisher [12], Lazorthes et al. [13], Elkhamlich et al. [14], Eftekhar et al. [15], De Silva et al. [19], Papantchev et al. [9, 16, 18], Ansari et al. [20] accept as hypoplastic all arteries with a diameter under 1 mm. On the other hand, Merkkola et al. [8] accept as hypoplastic all arteries with a diameter under 0.5 mm. Rigg’s and Rupp [11] and Urbanski et al. [10] do not give any size for defining the hypoplastic artery.

Nevertheless, two of these works require further discussion [8, 10]. The work of Merkkola et al. [8] is one of the major works on variations in the Willis circle and their role during SCP. The authors study the variations in the circle, using a permanent silicon cast with added plumb oxide [8]. Authors also used a perplex X-ray-based method for the visualization of cerebral arteries [8]. They classified the vessels according to particular threshold diameter, which is either 0.5 or 1 mm. We could not compare our current results with this work for several reasons: First, the authors used silicon casts and it is not clear whether the results obtained with casts are similar to those obtained with other investigation modalities. Secondly, silicone casting has its own possible artefacts, the most important of which is that very small vessels could not be visualized, because of the possible lack of silicone mixture in them. In this respect, we must stress that there was a very high percent of aplastic vessels reported by authors—50 of all 51 variant circles had ‘missing’ vessels [8]. On the contrary, in our current series, aplastic vessels were observed in only 33.45% (98 of all 293 circles with variations). Thirdly, the perplex roentgenograms-based method for the visualization of the circle after casting, called ‘angiography’ is incomparable with any other studies. Fourthly, the sample of Merkkola et al. is only 87 circles, which may be the reason why some very rare variations were not present. Last, but not least—the authors give their attention only to two segments of the circle—left PComA and AComA. No information is available for other segments of the circle, important during uSCP, namely right A1, left P1 and right VA. Nevertheless, we were able to reclassify the variations described by Merkkola et al., according to our classification (Table 4).

Another work that requires particular attention is that of Urbanski et al. [10]. The authors study 99 patients in the period 2004–06 in whom aortic surgery was performed with SCP via common carotid artery cannulation. All patients regained consciousness. Focal neurological deficit was found in 1% of patients, while temporary neurological dysfunctions were observed in 7% (7 patients, 5 of which with normal circle). In general, the authors deny the role of the Willis circle as a collateral pathway during uSCP [10].

We can neither compare our results with this work, nor reclassify the variations reported for several reasons. Information about the diameter at which the vessels were classified as ‘hypoplastic’ is absent. No information on vertebral arteries, the type of CT scanner or on section thickness is given. The classification proposed by authors is without any lateralization of variations.

The good results that were reported (8% neurological complications) could have several explanations. It is obvious that the authors have a perfect surgical technique. This, in combination with the major procedure performed (in 74 patients it was Ascending Aorta Replacement with open distal), explained the very short duration of SCP—average 18 ± 10 min with only 41 patients requiring SCP over 20 min. The authors used Thiopenthal and obtained 0-line or burst suppression at electroencephalogram, both signs of optimal reduction of oxygen consumption. The moderate hypothermia 29.8 ± 1.9°C and aortic

Table 2: Summarizing the data obtained by comparison between GE Light Speed® 16 Slice and Toshiba Aquilion one®

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (GE Light Speed® 16 Slice) 105 patients</th>
<th>Group 2 (Toshiba Aquilion one®) 105 patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>53</td>
<td>46</td>
<td>0.333</td>
</tr>
<tr>
<td>Age (average)</td>
<td>61.91</td>
<td>60.59</td>
<td>0.442</td>
</tr>
<tr>
<td>Willis circle variation type (%)</td>
<td>Type IA 44</td>
<td>48</td>
<td>0.793</td>
</tr>
<tr>
<td></td>
<td>Type IB 2</td>
<td>3</td>
<td>0.750</td>
</tr>
<tr>
<td></td>
<td>Type IIA 7</td>
<td>7</td>
<td>0.812</td>
</tr>
<tr>
<td></td>
<td>Type IIb 7</td>
<td>11</td>
<td>0.463</td>
</tr>
<tr>
<td></td>
<td>Type III 9</td>
<td>7</td>
<td>0.432</td>
</tr>
<tr>
<td></td>
<td>Type III 0</td>
<td>1</td>
<td>0.345</td>
</tr>
<tr>
<td></td>
<td>Type IV 1</td>
<td>2</td>
<td>0.632</td>
</tr>
<tr>
<td></td>
<td>Total 70</td>
<td>79</td>
<td>0.171</td>
</tr>
<tr>
<td>Type of vessel variation</td>
<td>Hypoplasia 20</td>
<td>43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Aplasia 50</td>
<td>36</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CNS: central nervous system.
<table>
<thead>
<tr>
<th>Type</th>
<th>Variation</th>
<th>Papantchev et al. [16]</th>
<th>Papantchev et al. [9]</th>
<th>Papantchev et al. [18]</th>
<th>Merkkola et al. [8] (threshold 0.5 mm)</th>
<th>Merkkola et al. [8] (threshold 1 mm)</th>
<th>Present study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type IA</td>
<td>Left PComA</td>
<td>26.6% (22/83)</td>
<td>27.3% (27/99)</td>
<td>41.9% (44/105)</td>
<td>35% (30/87) Classified as 'good group' with aplasia of left PComA</td>
<td>32% (28/87) Classified as 'good group' with aplasia of left PComA</td>
<td>35.6% (178/500)</td>
</tr>
<tr>
<td>Type IB</td>
<td>AComA</td>
<td>2.4% (2/83)</td>
<td>0% (0/99)</td>
<td>1.9% (2/105)</td>
<td>10% (9/87) 8% classified as 'good group' with aplasia of AComA</td>
<td>16% (14/87) 8% classified as 'good group' with aplasia of AComA</td>
<td>2% (10/500)</td>
</tr>
<tr>
<td>Type IIA</td>
<td>Left PComA + AComA</td>
<td>3.6% (3/83)</td>
<td>3% (3/99)</td>
<td>6.67% (7/105)</td>
<td>14% (12/87) 12% classified as 'bad group' with aplasia of both AComA and left PComA</td>
<td>17% (14/87) 3% classified as 'compromised group' with one aplastic and one hypoplastic vessel</td>
<td>4.8% (24/500)</td>
</tr>
<tr>
<td>Type IIB</td>
<td>Left P1 or right VA</td>
<td>7.2% (6/83)</td>
<td>9.1% (9/99)</td>
<td>6.67% (7/105)</td>
<td>Not mentioned No information on left P1</td>
<td>Not mentioned No information on left P1</td>
<td>9.2% (46/500)</td>
</tr>
<tr>
<td>Type III</td>
<td>Right A1</td>
<td>7.2% (6/83)</td>
<td>3% (3/99)</td>
<td>8.57% (9/105)</td>
<td>Not mentioned No information on right VA</td>
<td>Not mentioned No information on right VA</td>
<td>6% (30/500)</td>
</tr>
<tr>
<td>Type III</td>
<td>AComA + right VA</td>
<td>0% (0/83)</td>
<td>0% (0/99)</td>
<td>0% (0/95)</td>
<td>Not mentioned No information on right A1</td>
<td>Not mentioned No information on right A1</td>
<td>0.2% (1/500)</td>
</tr>
<tr>
<td>Type IV</td>
<td>Right A1 + right VA</td>
<td>1.2% (1/83)</td>
<td>0% (0/99)</td>
<td>0.95% (1/105)</td>
<td>Not mentioned No information on right VA</td>
<td>Not mentioned No information on right VA</td>
<td>0.8% (4/500)</td>
</tr>
<tr>
<td></td>
<td>or right A1 + left P1</td>
<td>1.2% (1/83)</td>
<td>0% (0/99)</td>
<td>0.95% (1/105)</td>
<td>Not mentioned No information on left P1</td>
<td>Not mentioned No information on right VA</td>
<td>0% (0/500)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>48.2% (40/83)</td>
<td>42.4% (42/99)</td>
<td>66.67% (70/105)</td>
<td>59% (51/87) 65% (57/87)</td>
<td>58.6% (293/500)</td>
<td></td>
</tr>
</tbody>
</table>

PComA: posterior communicating artery; AComA: anterior communicating artery; VA: vertebral artery; uSCP: unilateral selective cerebral perfusion.
graft with side branches also must be mentioned. In this respect, the good results are more likely due to the excellent surgical technique, optimal pharmacological cerebral protection and hypothermia rather than SCP itself. Furthermore, the patient population consists mainly of patients with degenerative or atherosclerotic aneurysms. Since atherosclerosis is a generalized disease, we could speculate that in this particular patients cohort, there is a possibility for pathological expansion of secondary collaterals (leptomeningeal, ophthalmic artery, etc.), which could also explain the good results. We can also speculate, by looking at the period during which the investigation was performed (2004–06), that the CT scanner used is an older-generation one with low spatial resolution, and thus vessels with a diameter over 1 mm were most probably misclassified as aplastic or hypoplastic.

For all the mentioned reasons, this work could not be used as a landmark for denying the role of the variations of the CW. Furthermore, in the light of all the data reported here, we think that proclaiming the (left) carotid artery perfusion as an alternative to right auxiliary artery or brachiocephalic trunk perfusion has neither an anatomical, nor physiological background.

We can compare our current results with our previous three publications [9, 16, 18] and partially with Merkkola et al. [8].

Looking chronologically, our first study was theoretical and was done using illustrations, so its results must be interpreted with caution [16]. The second study uses autopsy material [9], the third is available only as an abstract and reports briefly the results from 105 patients examined with CT angio [18]. Our current data and the four mentioned studies are in good agreement on some points and seriously discrepant in others (Table 4). In all studies, the most frequent variation is Type IA, which is not a surprise, because PCOMa is the most variable part of the circle [24]. The frequency of Type IA in the current study was 35.6%, which is 10% higher than the frequency reported in 2006 [16] and 2007 [9] and 5% lower than the frequency reported in 2011 [18]. This frequency is similar to the one reported by Merkkola et al. [8] regardless of threshold diameter (Table 4). In the work of Merkkola et al. [8], circle Type IB was found in 9% of all circles, if the threshold was 0.5 and in 16%, if the threshold was 1 mm. In our experience, circle Type IB is a rare variation and is observed with a frequency of 2% (Table 4). A possible explanation of this discrepancy could be simply an example of a casting-induced artefact. Literary data also support our current findings. Thus, Ansari et al. [20] find aplastic ACoMA in 1% of examined circles, Alpers et al. report the incidence of aplasia of ACoMA in 2% and hypoplasia in 3% of examined brains [9], Fawcett and Blachford report aplasia of ACoMA in 0.14% of examined cases [21], Windle find aplastic ACoMA in 1.5% of studied cases [22] and finally, Adachi do not find any aplastic ACoMA [9]. The same is true for circle Type IIA (Table 4). All other circle types were found with similar frequency (Table 4). The overall frequency of variations in the current study is 58.6%, which is similar to the 59% frequency reported by Merkkola et al. [8] for a threshold of 0.5 mm, and it is even lower compared with the 65% frequency reported by the same team for a diameter of 1 mm (Table 4). It is worth to mentioning that the overall frequency reported in this study is 8% lower than that reported by us in 2011 (Table 4). This difference has an explanation— the vast majority of the patients included in the 2011 study had a neurological deficiency [18]. Similar results were reported also by Riggs and Rupp [11] who studied the Willis’ circles in 994 patients with previous history of neurological dysfunction and found abnormal circles in 79% of them. And finally in our work in press (Papancthev et al., in preparation), we found that among 131 patients with variant circles, 63.33% had a history of neurological dysfunction (P < 0.001).

An important question is, how do we have such high percentage of circle variations without a corresponding increase in the percentage of neuronal injury? There are several possible explanations. The first is how we define ‘neuronal injury’. Often, only gross injuries, like focal neurological deficit, plegia, choreoathetosis, coma and death, are classified as neuronal injuries. Other clinical manifestations like delirium, cognitive deficiency, mental problems, personality changes, small vision-field defects, are overlooked and do not classify as neurological injuries [2, 9, 25]. A second possible explanation is that a lot of patients requiring arch surgery are operated on an emergency basis, when profound preoperative neurological examination is either impossible or not appropriate, so some neurological injuries could be termed ‘pre-existing’. In the third place, since the infarction zone of watershed infarctions caused by hypoperfusion is usually not specific and their clinical manifestation is quite variable (from dense plegia to lack of any symptoms), many cerebral infarctions without clinical manifestation are overlooked [9, 24]. A short summary of the possible ischaemia-induced clinical signs and symptoms is given in our previous work [9].

Many authors have shown the role of intraoperative monitoring of regional cerebral oxygenation with near-infrared spectroscopy (NIRS). It allows fast and non-invasive on-line neuromonitoring of brain perfusion and the early detection of malperfusion [25]. It was shown that a decrease of cerebral oxygen saturation below 55% for more than 5 min and/or total oxygen index below 15–20% of baseline results in neuronal injury. In their work, Harrer et al. [25] used NIRS in 13 patients subject to bilateral SCP. According to their protocol, in all patients SCP was started as unilateral and switched to bilateral with the second cannula inserted in the left common carotid artery after the arch was opened. In 12 of 13 patients (92%), the authors observed a drop of cerebral oxygen saturation of the left hemisphere to 44 ± 7.9% after 2 min of uSCP. Decreases in the total oxygen index of 15% in 11 patients and 20% in one were also observed. After a switch to bilateral SCP, a statistically significant increase in cerebral oxygen saturation of the left hemisphere to 63 ± 5% was noted [25]. We can speculate that in the series of Harrer et al., the drop in the cerebral oxygen saturation and total oxygen index during the period of uSCP was the result of hypoperfusion of the left hemisphere, because some of the variations in the CW reported here were present. Since most circle variations, important during uSCP, have no role during bilateral SCP, switching to bilateral SCP led to restoration of perfusion in the left hemisphere.

Another important question is whether the classification proposed by us is a complicated one. We believe that this classification is straightforward and simple. It is based on the number of vessel basins at risk of hypoperfusion during uSCP—one in Type I circles, two in Type II, etc. (Table 1). It divides a large number of complex variations into only seven types, which is a very low number compared with other classifications. For example, the classification of Lazorthes et al. [13], which is widely used, divides the variations of the circle into 23 types, without including the vertebral arteries. Merkkola et al. [8] divided the variations of the circle into four groups, but they used only two segments of the circle, without including the vertebral arteries,
and the proposed groups are descriptive and perplex—hypoplasia and aplasia of the same segment are considered different and classified into different groups (Table 4). The classification proposed by Urbanski et al. [10] is quite bewildering. It does not include the vertebral arteries and divides the variations of the circle into only three groups, without any lateralization. For example, all circles with one hypo/aplastic segment, no matter of its localization, were united in one group. If we apply this classification to our results, it means that circles Type I A, Type IB, Type II B and Type III A are identical (Figs. 2–4). We think that this classification is too mechanistic and does not pay enough attention to haemodynamics during uSCP.

The present study has the following limitations: the diameter of the ‘hypoplastic’ vessels may increase with time and exceed 1 mm. Since autopsy specimens were not controlled with angiography, we could never be sure that measured diameters were similar with those in living subjects. Some vessels with borderline diameter could be misclassified, using CT angio. Finally, not all subjects that were examined were candidates for aortic arch surgery. This last limitation is related to the fact that in some patients with arch aneurysms there is a possibility for the expansion of secondary collaterals, because of concomitant stenoses/occlusions of segments of the CW, carotid and/or vertebral arteries. Since the aim of our present work was to study systemically the variations of the Willis’ circle, only hypo/aplastic vessels were classified. No specific attention was directed to vessels with stenosis or occlusion, notwithstanding, such were also observed during the study (Fig. 2 A). We believe that additional studies unifying both vessels variations and vessels stenoses are required in order to clarify the role of secondary collaterals during uSCP. The present work cannot provide any sound data on this issue.

In a conclusion, we can say that cerebral protection is a complicated inter-disciplinary problem. This entails combining the efforts of specialists from different areas: cardiac surgeons, anaesthesiologist, roentgenologists, morphologists, neurologists, neurosurgeons, etc. Awareness of the variations in the cerebral vessels is a requisite for the choice of the most appropriate method for cerebral protection. In the present work, we report seven distinct types of variations in the Willis’ circle which, if present, could vitiate the protective effect of the uSCP and even cause stroke. These variations are present in a significant number of patients (58.6%). The presence of such variations could explain the unfavourable postoperative psychical, sensorial and/or motor outcome after uSCP that occurs in some patients. This study supports the need for extensive preoperative examination (including CT angio, particularly in patients with preoperative neurological symptoms) and meticulous intraoperative monitoring of cerebral perfusion during uSCP (NIRS, etc.). Finally, our data support the superiority of bilateral SCP over uSCP, because most of variations showed in the present work do not have haemodynamic significance during bilateral SCP.

ACKNOWLEDGEMENTS

The authors would like to express their gratitude to Adrian Paloff and Dimka Hinova-Palova for their constant support since the very beginning of this project. Authors are also grateful to Violeta Groudeva for her efforts concerning the CT angiographic part of the study and to Metodi Goshev and Dimitar Nikolov for their efforts concerning the legal-medical part of the study.

Funding

This work was supported by Medical University, Sofia [2011 Grand program, Contract No 19/Project 20].

Conflict of interest: none declared.

REFERENCES

APPENDIX. CONFERENCE DISCUSSION

Dr T. Siors (Tampere, Finland): You have material from autopsies performed for medicolegal reasons and this may not represent the general population because of certain, shall we say, lifestyle differences in the people who end up with medicolegal autopsies, meaning smoking habits and head trauma and so on. And so this might be a little different from the general population. Also, you had a look at the external diameter of the vessels, as opposed to some other studies, such as the Finnish one, where a blood-like latex solution with low viscosity was infused into the brain vessels under 120–180 mmHg pressure and added with a catalyst making it hard only about 4–5 hours after infusion. So some differences.

I definitely agree with all your conclusions bringing forth the need to pay attention to transient neurological deficits, not only the strokes, because even the transient ones will cause problems later on. The bilateral technique was reviewed very nicely by the Hannover group presenting a variation of the Bachet technique for bilateral selective perfusion. And even so, there were 13% temporary and 9.6% permanent problems. So the issue, unfortunately, depends on other things.

Now, I have a couple of questions. You had a tremendous number of patients, and the question came into my mind from a patient with Loeys-Dietz, who had bilateral posterior communicating artery aplasia and also, unfortunately, aplasia of the right vertebral artery. So it was quite a situation we were able to resolve. Now, what do you think about the left subclavian? Is there any anatomy in your series which would really justify specifically the need for perfusion of the left subclavian artery to make the procedure even safer for the brain and the spinal cord?

And the second question is, there is talk of a steal phenomenon when you perfuse the right trunk and the left carotid and you have blood leaking out of the left subclavian. Is there an anatomy that might, perhaps, actually protect people from such a problem, preventing the steal phenomenon?

Dr Papantchev: First, I would like to make a comment. Autopsies in Bulgaria are performed, as a rule, for everyone who died at home or died in an accident, so I believe that the 250 cases are quite representative of the general population. They are not only performed on homeless people who died on the street.

Second, about your question, we usually occlude the left subclavian artery in order to avoid the steal phenomenon, so I believe that occlusion of the left subclavian artery is enough to reduce the steal phenomenon. And about the variations, I cannot answer this question at this moment because I don’t have the material in front of me. We don’t pay particular attention to the left side vessels, other than those which were classified as critical.

Dr P. Urbanski (Bad Neustadt, Germany): I think we have the largest experience with unilateral cerebral perfusion worldwide and for this reason I have to make some comments because I don’t agree with your conclusion. You said that bilateral perfusion is better than unilateral perfusion. You cannot make this claim, because you didn’t present any clinical data; your examination is strictly anatomical. We exactly know that about 50% of people have incompleteness of the circle of Willis. It is well-known and you yourself presented this five years ago to this Association. Now there is no new insight in this aspect.

We went even a step further and did operate on the patients with incomplete circles of Willis. In this patient group we performed unilateral cerebral perfusion and we didn’t see any increased neurological adverse outcome. For this reason it would be more interesting also for your further work to find out the reason why the incompleteness of the circle of Willis doesn’t translate to neurological outcome. Maybe the vessels, which apparently are hypoplastic, open widely during unilateral cerebral perfusion. Maybe the role of extracranial circulation is underestimated.

The clinic shows completely other results. We have recently performed a multicentre study and matched the patients with unilateral cerebral perfusion and bilateral perfusion. We are going to present this data in the upcoming AATS meeting showing that unilateral cerebral perfusion is neurologically slightly better than bilateral perfusion.

Dr Papantchev: So to the first part of your question, I said that bilateral cerebral perfusion is better compared to the unilateral according to these anatomical results, not based on our clinical results, because I don’t report clinical results in this study.

According to the second part of the question, it is the most logical question because I show variation of more than 50% of examined circles and the neurological complications that are reported are very low. So I believe that there are several possible answers. The first answer is what we actually call neurological injury because, in general, only strokes, plegia, choreoathetosis, coma or death are classified as neurological injury. Usually the minor neurological injuries like cognitive changes, personality disorders, visual field defects, all this stuff, are usually overlooked. So I think that we just underestimate the overall percentage of neurological injury.

And the other thing that you mentioned, the extracranial anastomosis: it’s well-known that in acute settings or acute changes of the flow, for example, occlusion of one carotid artery, the answer from the organism is just to reverse the flow through the Willis circles. For the secondary collaterals, usually a longer period is required, or a chronic disease, in order for the secondary collaterals to develop.

And what we saw from our experience, because in the patients with aneurysm who were operated on schedule, we performed a CT angiography of the head and we saw that there is expansion of secondary collaterals in this particular subset of patients. So this could explain why unilateral selective cerebral perfusion in these patients doesn’t have adverse outcome — because of these secondary collaterals which expand because of the disease itself. So this is what I think on this question.

Dr J. Bacht (Abu Dhabi, United Arab Emirates): You know that I can’t make very quick comments! But this is very important. We can speak hours, years, about unilateral or bilateral perfusion.

Dr Urbanski, I disagree a little with what you said. You use systematically unilateral perfusion and you say it is better. But in your works (I’m thinking of the last one alluded to by Dr Jakob), the mean duration of your circulatory arrest was 17 minutes. So this is very short. Are you sure that unilateral perfusion and you say it is better. But in your works (I’m thinking of the last one alluded to by Dr Jakob), the mean duration of your circulatory arrest was 17 minutes. So this is very short. Are you sure that unilateral perfusion in patients with a cerebral perfusion of 60 minutes, for instance, would be exactly the same? I’m not sure at all.

Secondly, according to what Dr Papantchev said, we have to systematically assess the circle of Willis before surgery. I disagree also. In many patients it is not very easy to do a CT scan of the circle of Willis, in particular during emergency. But there is a very simple thing to do, which is common sense-based medicine: it takes 30 seconds or 1 minute, to put a cannula into the origin of the left carotid artery. You open the arch, you place the cannula and you perfuse bilaterally. And then, whether the circle of Willis is normal or abnormal, the patient is perfused completely. So why should we put the patients at undue risk just for surgical fancy?