Cerebral cross-perfusion and the circle of Willis: does physiology trump anatomy?

Introduction: Cerebral cross-perfusion is essential for ipsilateral brain viability during unilateral insult. Aortic arch and great vessel procedures depend on its function for safe practice, unless adjuncts like shunts are used. This paper assesses the contribution of cerebrovascular anatomy against physiology in determining requisite hemispheric perfusion during carotid endarterectomy (CEA).

Materials and methods: A review of shunting requirements for CEAs under locoregional anesthesia (LA) at the John Radcliffe Hospital during 1999–2013 was performed. A PubMed search for “Circle of Willis” was screened for all original articles defining cerebrovascular anatomy by postmortem or angiography.

Results: Over 14 years, 1137 CEAs were performed under cervical plexus block; during this period, the departmental standard of practice evolved from exclusively general anesthesia to predominantly LA. CEAs performed under LA during the early phase (1999–2003) had a shunt rate of 15.1%, compared to 20% as predicted by stump pressures alone. However, shunting decreased as higher perioperative systolic pressures were routinely practiced; shunt rates were 8.0% during the intermediate (2004–2007) and 6.4% during the later (2008–2013) phase. By comparison, 25 articles characterizing 6414 brains report an intact circle of Willis in 33–35% of people, with a complete hemi-circle anteriorly (77%) seen more commonly than posteriorly (42%), and 11–16% deficient in both hemi-circles with no cross-flow.

Conclusion: Cerebral cross-perfusion is fundamental for safe CEA. Anatomy of the circle of Willis alone does not itself determine adequacy. Physiological mechanisms are important in overriding apparent deficiencies, and these can be manipulated perioperatively. Consequently, only 1 out of 15 patients requires shunting during CEA.

Keywords: Circle of Willis, cerebral, cross-perfusion, carotid, shunt, anatomical variation

Introduction

Cerebral function is of utmost importance to survival, and unsurprisingly, there are multiple overlapping anatomical and physiological mechanisms by which adequate cerebral perfusion is maintained. Cerebral vascular anatomy consequently features many large- and small-scale, seemingly redundant, arterial networks to allow cross-perfusion should any single major vessel occlude, including the well-characterized circle of Willis (Figure 1). However, various anatomical studies, including postmortem dissections and imaging series, indicate that the circle of Willis manifests in complete configuration in less than half the population. Physiological mechanisms appear to have a significant role in maintaining cerebral perfusion, not only by phenomena such as cerebral autoregulation, which allows for...
constant flow over a broad range of systemic mean arterial
drances, but also cerebral cross-perfusion. Logically, the
fate of the ipsilateral cerebral cortex during unilateral vas-
cular deficiency depends on the ability of the individual to
activate these cerebral cross-perfusion pathways.
Aortic arch and great vessel interventions depend on cere-
bral anatomical and physiological homeostatic mechanisms
for safety, unless adjuncts like shunts can be used. However,
preoperative imaging and perioperative monitoring are noto-
riously poor predictors of patient response during intraopera-
tive manipulation, including carotid cross-clamping during
carotid surgery or selective antegrade cerebral perfusion
during aortic arch surgery.5,6

This study examines the relative contribution of cerebro-
vascular anatomy and physiology in maintaining adequate
hemispheric perfusion, specifically by quantifying the popula-
tion at risk of poor cerebral cross-perfusion due to anatomical
circle of Willis deficiencies, and comparing it to the population
that required shunting during carotid cross-clamping.

A secondary outcome of the study is to assess overall
shunt rates during carotid endarterectomy (CEA), and in
light of this, any consequent implications on surgical training.

Materials and methods

Anatomical data

A PubMed search using the keyword “Circle of Willis”
was performed. All articles were screened for original research
pieces quantifying human variations of the circle of Willis.
For each original paper, mode of assessment, ethnicity of
the population and proportions of circle of Willis variants
were recorded; specifically, patient populations were strati-
fied according to completeness and deficiencies in both the
anterior and posterior hemi-circles.

Physiological data

An audit of consecutive CEs performed under locoregional
anesthesia (LA) at the John Radcliffe Hospital during 1999–
2013 was compiled. Superficial cervical plexus block was
applied, and hemodynamic monitoring was by radial arterial
line. Carotid bifurcation exposure and endarterectomy were
performed by techniques of choice of the consultant vascular
surgeon; these included eversion or standard endarterectomy,
with or without vein or prosthetic patch anastomotic repair.
Unilateral carotid occlusion tolerance was monitored by regu-
lar gross neurological assessment, which included patients’
recall of their own full name, date of birth and residential
address, in addition to contralateral handgrip and ankle plan-
tar flexion power, as well as general agitation. The necessity
for shunting was determined perioperatively at the discretion
of the consultant vascular surgeon, and typically occurred if
clamp intolerance manifested early during the routine 5-min
internal carotid artery (ICA) test clamp (prior to arteriotomy),
or during the endarterectomy or anastomotic repair.

Over the 14-year period described, there were 3 distinct
the learning curve for surgeons and anesthetists following
the introduction of local anesthetic. Shunts were used for
all patients who had neurological defect during test clamp-
ing. In Era 2 (2004–2007), any neurological deficit during
test clamping was initially dealt with by raising the systolic
pressure and repeating a trial clamp. Only if a residual neu-
rological deficit was present would shunting proceed. In Era
3 (2008–2013), any neurological deficit during trial clamping
was responded to with both a raise of systolic pressure and
increased arterial oxygenation.

Results

Anatomical data

The PubMed search utilizing the keyword “Circle of Willis”
yielded 2675 publically available articles; however, only 34
papers described a distinct human population case series that
could be assessed. The total publications finally analyzed
were reduced to 25 that contained comparable numerical
anatomical descriptions, which together reported a total of
6414 individual cerebrovascular anatomies of diverse ethnic
backgrounds.
Of 14 postmortem dissection reports, assessing 4393 individual brains, a complete circle of Willis was seen in 35% of cadaveric specimens. It was noted that the complete anterior portion was more common (77%) than a complete posterior portion (42%) (Table 1). Of 11 angiographic studies (computed tomography, magnetic resonance or digital subtraction modalities) examining 2021 vasculatures, a complete circle of Willis was seen in 33% of all scans. Again, a complete anterior portion was observed more commonly (77%) than a complete posterior portion (42%) (Table 2). Overall, the anatomical data indicated that 11% (radiological) to 16% (cadaveric) of the population had deficiencies in both anterior and posterior hemi-circles.

Physiological data

The John Radcliffe Hospital Department of Vascular Surgery evolved its CEA practice from exclusively general anesthesia (GA) to predominantly LA circa 1999. Over the 14-year study period since LA uptake, 1137 CEAs were performed under cervical plexus block (Table 3). Initial rates of shunting in our unit showed a mean of 15.1% during 1999–2003, following a similar trend to the anatomy data. However, during 2004–2007, a shunt rate of 8.0% was observed, and this further decreased to 6.4% during 2008–2013.

International experience with CEA under LA demonstrates a reported average shunt rate of 15%; however, only a Korean group has managed to reduce it to 4% (Table 4).7

Discussion

Cerebral cross-perfusion is essential in preserving ipsilateral brain survival and function during unilateral vascular interruption. Various mechanisms have been described including anatomical collaterals4–11 and physiological alterations, but neither preoperative scanning nor perioperative surrogate physiological cerebral monitoring has been a good predictor of postoperative outcomes.

Anatomical explanations for cross-perfusion have relied on a series of collateral pathways that are deemed essential. First described by Dr Thomas Willis in 1664, the eponymous intracranial circle, loop or polygon as it is variously referred to, has been the benchmark respected by generations of physicians and anatomists. However, despite the perceived importance of this intracranial network, multiple human variations exist, including hypoplastic and aplastic communicating vessels that frequently result in incomplete hemi-circles, with no apparent disadvantages. Perhaps due to the “higher” end organ significance or due to the less individual elements, the anterior circulation tends to be complete in a greater proportion of the population than the posterior circulation.12–14 Interestingly, 11–16% of the population have no evidence of classic anatomical pathways allowing for cross-brain perfusion.1,13,15

Alternative intracranial pathways include the leptomeningeal anastomoses of Heubner and micronetworks of Schmidt and Pfeiffer, which collateralize the ipsilateral anterior circulation only.16 Supplementary extracranial collateral pathways that can develop include external to internal carotid anastomoses, via the superficial temporal and middle maxillary arteries, to supraorbital and dorsal nasal branches of the ophthalmic artery, respectively. These certainly become important sources of alternate blood flow if hemodynamically significant lesions develop at the ICA origin, as typically

Table 1

<table>
<thead>
<tr>
<th>Report</th>
<th>Year</th>
<th>Ethnicity</th>
<th>Total</th>
<th>Complete (%)</th>
<th>Anterior (%)</th>
<th>Posterior (%)</th>
<th>Deficient (%)</th>
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<tbody>
<tr>
<td>Papantchev et al22</td>
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<td>250</td>
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<td>86</td>
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<td>Iqbal12</td>
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<td>Indian</td>
<td>50</td>
<td>60</td>
<td>92</td>
<td>68</td>
<td>0</td>
</tr>
<tr>
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<td>2013</td>
<td>Iranian</td>
<td>200</td>
<td>46</td>
<td>82</td>
<td>53</td>
<td>12</td>
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<td>Siddiqi et al23</td>
<td>2013</td>
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<td>51</td>
<td>41</td>
<td>84</td>
<td>41</td>
<td>16</td>
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<tr>
<td>De Silva et al24</td>
<td>2011</td>
<td>Sri Lankan</td>
<td>220</td>
<td>15</td>
<td>52</td>
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<tr>
<td>Manninen et al25</td>
<td>2009</td>
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<td>76</td>
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<td>Kapoor et al17</td>
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<td>1000</td>
<td>66</td>
<td>94</td>
<td>72</td>
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<tr>
<td>Eftekhari et al16</td>
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<td>88</td>
<td>33</td>
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<tr>
<td>el Khamlichi et al9</td>
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<td>Moroccan</td>
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<td>18</td>
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<td>Lazorthes and Gouazé24</td>
<td>1979</td>
<td>French</td>
<td>200</td>
<td>15</td>
<td>58</td>
<td>21</td>
<td>37</td>
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<tr>
<td>Fisher et al27</td>
<td>1965</td>
<td>USA</td>
<td>414</td>
<td>5</td>
<td>58</td>
<td>6</td>
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<td>Riggs and Rupp28</td>
<td>1963</td>
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<td>UK</td>
<td>700</td>
<td>73</td>
<td>100</td>
<td>73</td>
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<td>35</td>
<td>77</td>
<td>42</td>
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</table>

Notes: The circle of Willis configurations were designated as “complete” (if no segments were aplastic or hypoplastic), “anterior” (if no segments were aplastic or hypoplastic in the anterior portion only), “posterior” (if no segments were aplastic or hypoplastic in the posterior portion only) or “deficient” (if segments were aplastic or hypoplastic in both).
occurs due to atherosclerotic disease, although they may not be able to compensate during acute occlusion.

Perioperative proxy cerebral physiological monitoring during GA has been notoriously hampered by interpretation inaccuracies. Stump pressure assessment is performed following clamping the common carotid and external carotid arteries by needling the ICA connected to an arterial transducer; arbitrarily, pressures above 50 mmHg are deemed to be adequate. Using this technique, shunt rates are around 20%; however, false positives are 1.45%, and negatives are 70.4%.5 Transcranial Doppler is performed by setting the probe to monitor the flow in the ipsilateral middle cerebral artery and monitoring for changes in peak systolic velocity. Using this technique, shunt rates are 11%; however, false positives are 2%, and negatives are 29%.6 Electroencephalography with somatosensory evoked potential monitoring requires up to 16 leads to monitor changes in background brain electrical activity. Using this technique, shunt rates are around 6%; however, false positives are approximately 1%, and negatives are up to 40.6%.5 Due to the complexities and inaccuracies of these techniques, when performing CEA under GA, the surgical community is divided into the majority routine-shunters and minority selective-shunters, the latter of which may use any of the above techniques with a clinical assessment of strong pulsatile backbleeding.

The gold standard for cerebral hemispheric tolerance of unilateral carotid occlusion is a neurological assessment.17 This can easily be performed if the procedure is done under LA and with the application of a hemostatic clamp or an occlusive balloon at the ICA origin. Certainly, the initial John Radcliffe Hospital experience with shunt rates of 15.1% on average seemed to appropriately reflect the anatomical data of doubly deficient circle of Willis variants at 11–16%. However, with physiological manipulation, the shunt rates have progressively decreased to 6.4% despite the population group remaining the same. This is mostly attributed to the deliberate increase in mean arterial pressures during cross-clamping; many patients will reflexively increase their own systemic blood pressure through the process of autoregulation; however, some require additional support, typically with addition of boluses of metaraminol.

The latest Vascular Society Quality Improvement Program (VSQIP) report 2015 shows that the John Radcliffe Hospital has performed 260 CEAs over a 3-year period, with an overall

### Table 2 Anatomical data based on radiological studies across various mono- and multiethnic groups

<table>
<thead>
<tr>
<th>Report</th>
<th>Year</th>
<th>Ethnicity</th>
<th>Total</th>
<th>Complete (%)</th>
<th>Anterior (%)</th>
<th>Posterior (%)</th>
<th>Deficient (%)</th>
<th>Mode</th>
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<td>Papantchev et al22</td>
<td>2013</td>
<td>Bulgarian</td>
<td>250</td>
<td>41</td>
<td>86</td>
<td>49</td>
<td>6</td>
<td>CTA</td>
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<tr>
<td>Pennekamp et al22</td>
<td>2013</td>
<td>Dutch</td>
<td>140</td>
<td>9</td>
<td>80</td>
<td>15</td>
<td>14</td>
<td>CTA</td>
</tr>
<tr>
<td>Pennekamp et al23</td>
<td>2013</td>
<td>Dutch</td>
<td>284</td>
<td>9</td>
<td>83</td>
<td>32</td>
<td>0</td>
<td>MRA</td>
</tr>
<tr>
<td>Cho et al8</td>
<td>2013</td>
<td>Korean</td>
<td>45</td>
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<td>60</td>
<td>60</td>
<td>9</td>
<td>CTA</td>
</tr>
<tr>
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<td>2013</td>
<td>Polish</td>
<td>250</td>
<td>17</td>
<td>47</td>
<td>27</td>
<td>43</td>
<td>CTA</td>
</tr>
<tr>
<td>Chiang et al20</td>
<td>2013</td>
<td>Taiwanese</td>
<td>64</td>
<td>33</td>
<td>81</td>
<td>52</td>
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<td>CTA</td>
</tr>
<tr>
<td>Li et al11</td>
<td>2011</td>
<td>Chinese</td>
<td>160</td>
<td>27</td>
<td>79</td>
<td>31</td>
<td>17</td>
<td>CTA</td>
</tr>
<tr>
<td>Cavestro et al8</td>
<td>2011</td>
<td>Italian</td>
<td>429</td>
<td>67</td>
<td>88</td>
<td>75</td>
<td>4</td>
<td>MRA</td>
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<tr>
<td>Urbanski et al12</td>
<td>2008</td>
<td>German</td>
<td>99</td>
<td>60</td>
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<td>N/A</td>
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<tr>
<td>Waaijer et al13</td>
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<td>CTA</td>
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<tr>
<td>Macchi et al30</td>
<td>2002</td>
<td>Italian</td>
<td>118</td>
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<td>MRA</td>
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<tr>
<td>Total</td>
<td>1137</td>
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<td>33</td>
<td>77</td>
<td>42</td>
<td>11</td>
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</tbody>
</table>

Notes: These include CTA, MRA and digital subtraction angiography. The circle of Willis configurations were designated as “complete” (if no segments were aplastic or hypoplastic), “anterior” (if no segments were aplastic or hypoplastic in the anterior portion only), “posterior” (if no segments were aplastic or hypoplastic in the posterior portion only) or “deficient” (if segments were aplastic or hypoplastic in both).

Abbreviations: CTA, computed tomography angiography; MRA, magnetic resonance angiography; N/A, not available.

### Table 3 Physiological data based on the John Radcliffe Hospital experience of carotid endarterectomy under locoregional anesthesia over specific time periods

<table>
<thead>
<tr>
<th>Year</th>
<th>Ethnicity</th>
<th>Total (n)</th>
<th>Shunt (n)</th>
<th>Shunt (%)</th>
</tr>
</thead>
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<tr>
<td>1999–2003</td>
<td>Mixed UK residents</td>
<td>199</td>
<td>30</td>
<td>15.1</td>
</tr>
<tr>
<td>2004–2007</td>
<td>Mixed UK residents</td>
<td>363</td>
<td>29</td>
<td>8.0</td>
</tr>
<tr>
<td>2008–2013</td>
<td>Mixed UK residents</td>
<td>575</td>
<td>37</td>
<td>6.4</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1137</td>
<td></td>
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### Table 4 Physiological data based on the perioperative experience of carotid endarterectomy under locoregional anesthesia across various vascular surgical units and ethnic groups

<table>
<thead>
<tr>
<th>Report</th>
<th>Year</th>
<th>Ethnicity</th>
<th>Total (n)</th>
<th>Shunt (n)</th>
<th>Shunt (%)</th>
</tr>
</thead>
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<tr>
<td>Pennekamp et al22</td>
<td>2013</td>
<td>Dutch</td>
<td>431</td>
<td>65</td>
<td>15</td>
</tr>
<tr>
<td>Cho et al22</td>
<td>2013</td>
<td>Korean</td>
<td>45</td>
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<td>4</td>
</tr>
<tr>
<td>Lee et al22</td>
<td>2004</td>
<td>Korean</td>
<td>117</td>
<td>23</td>
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</tr>
<tr>
<td>Kim et al22</td>
<td>2002</td>
<td>Korean</td>
<td>67</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td></td>
<td>660</td>
<td></td>
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</tr>
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<td>Mean</td>
<td>26</td>
<td></td>
<td>15</td>
<td></td>
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</tr>
</tbody>
</table>
stroke and death rate of 2.1%, despite a 6.4% shunt rate. This is well within the top decile of outcomes in the UK.\textsuperscript{18}

The experience and physiological data, with respect to CEA under LA, have also been published by other units with various results. The Korean experience appears to be similar, with initial publications reporting shunt rates of 21% in 67 patients\textsuperscript{19} and 20% in 117 patients,\textsuperscript{20} while more contemporary articles report shunt rates as low as 4% in 45 patients.\textsuperscript{7} However, the Dutch experience remains more conservative, with shunt rates remaining at 15% in 431 patients.\textsuperscript{21}

Cerebral cross-perfusion is fundamental for safe completion of CEA. Anatomy of the circle of Willis alone does not itself determine adequacy. Physiological mechanisms are important in overriding apparent deficiencies, and these can be manipulated peroperatively. With such measures, only 1 in every 15 patients may require shunting during CEA, and this could have implications for the training of future vascular surgeons.

Acknowledgments
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Disclosure
The authors report no conflicts of interest in this work.

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\begin{enumerate}
\item Kim GE, Cho YP, Lim SM. The anatomy of the circle of Willis as a predictive factor for intra-operative cerebral ischemia (shunt need) during carotid endarterectomy. Neurol Res. 2002;24(3):237–240.
\end{enumerate}

