Background and Objectives: Intracranial aneurysmal rupture is the major cause of subarachnoid hemorrhage (SAH). Misdiagnosis of the ruptured sites may result in postoperative rebleeding and the patients may eventually die. The variation of circle of Willis (CW) patterns could increase wall shear stress, leading to aneurysm formation. Therefore, this study aimed to investigate the sites of aneurysms inside the CW in aneurysmal SAH patients and the association between the CW patterns and ruptured aneurysm sites.

Methods: This retrospective study was performed on the digital subtraction angiography (DSA) and three dimensional rotational angiography (3DRA) of patients with aneurysmal subarachnoid hemorrhage. The sites of aneurysms in the CW were assessed and the internal diameters of the component arteries were measured to classify the patterns of CW as the typical and the atypical patterns. Atypical patterns were divided into 3 subtypes: 1) atypical CW with transitional artery but without hypoplastic artery 2) atypical CW with hypoplastic artery and 3) atypical CW with aplastic artery.

Results: All 90 aneurysmal SAH patients enrolled in this study were 30% (27/90) males and 70% (63/90) females with the mean age of 55.93 ± 12.87 years. Atypical CW...
Introduction

Subarachnoid hemorrhage (SAH) refers to extravasation of blood into the subarachnoid space. There are many causes of SAH such as trauma, hemorrhage from arteriovenous abnormality, hematologic disorders, and cerebral aneurysm ruptures. More than 80% of SAH are due to rupture of a cerebral aneurysm.1 Cerebral aneurysm occurs in many areas of cerebral vasculature. The incidence of aneurysmal SAH has been reported in Thai patients by digital subtraction angiography (DSA).2 The cerebral aneurysm have a close relationship to the angle of branching and anastomosis in the circle of Willis (CW).3 About 85% of aneurysms occurring in the CW is berry aneurysm which is the most common cause of SAH.4,5 There are many risk factors of cerebral rupture such as female sex,6,7 size and site of cerebral aneurysms,8,9 hypertension,9,10 smoking,9,11 and elderly patients.9,12 Previous studies reported that the aneurysm forming and rupture were associated with CW variations.13,14 The CW anomalies can change blood flow.15,16 In a recent year, Nam and his partners analyzed wall shear stresses related to aneurysm formation in CW variation by microfluidic system. They suggested that the variation of CW morphology increased wall shear stress and could lead to aneurysm formation.17 The CW variations produce hemodynamic changes.18,19 The force from these changes acts on the vessel wall in collateral sites leading to aneurysm formation and rupture.18,19 Emergency aneurysmal SAH and multiple cerebral aneurysms challenge the interventional radiologists and neurosurgeons. The physicians must determine which one is ruptured because it is impossible to treat all aneurysms in single craniotomy. Misdiagnosis of ruptured site may result in rebleeding and the patient will eventually die because the true rupture site is untreated.20 Accurate localization of aneurysm ruptures in patient with multiple cerebral aneurysms is still a problem in clinical practice. Additionally, the CW anomalies in Thai SAH patients associated with aneurysmal rupture has not been reported by three dimensional rotational angiography (3DRA) which can assess very small arteries. Therefore, this study aimed to investigate the sites of aneurysm on the CW in aneurysmal SAH patients and the association between the aberrant CW patterns and ruptured aneurysm sites based on DSA and 3DRA.

Materials and Methods

1. Sample collection: The DSA and 3DRA of aneurysmal SAH patients were retrospective studied.
The patients underwent four vessels angiography at Interventional Radiology unit, Department of Radiology, Faculty of Medicine, Khon Kaen University since January 2015 to March 2016. The age, gender and sites of aneurysm were recorded. This study has been performed under the Khon Kaen University Ethics Committee in human research.

2. **Image technique:** The SAH angiography was conducted on a biplane system with 2 projections per vessel. Angiography was performed on a biplane neuroangiographic unit (Siemens Artis Zee Biplane). The DSA was conducted with a 1024 x 1024 matrix with a 17- to 20-cm field of view (FOV) and injection of 16 ml contrast material in the internal carotid and vertebral arteries in 2 projections. After processing, relevant images were sent to the picture archiving and communication system (PACS). A complete cerebral 3DRA is carried out on biplane system with 2 projections per vessel with an 8-second 180° rotational run, with acquisition of 200 images and injection of 3-4 milliliters contrast material per second in the internal carotid or vertebral arteries.

3. **Measurement and classification of CW patterns:** The internal diameters of component vessels of CW including supraclinoid part of internal carotid arteries (ICA), A1 segment of anterior cerebral arteries, posterior communicating arteries (PCoA), P1 segment of posterior cerebral arteries, basilar artery (BA), and anterior communicating artery (ACoA) were measured at the proximal and distal parts to calculate the average diameters. The internal diameters of anterior and posterior communicating arteries can be detected and measured at only proximal part. Measurement was performed to classify the types of arteries as normal, hypoplastic and aplastic. The CW arteries with the internal diameter larger than 1 millimeter were classified as normal arteries. Any arteries with the diameter less than 1 millimeter were previously described as hypoplastic artery and the vessels invisible on angiogram were classified as an aplastic artery. The term “transitional vessel” is used to describe PCoA with the diameter equal or larger than P1, but P1 was not hypoplastic.

According to the internal diameter of CW arteries described above, types of CW were classified into 2 groups: typical and atypical groups. Typical group possesses normal diameter of all components of CW. Atypical group comprised of the anomalies of some component arteries in CW. Atypical group was classified into 3 subtypes including; 1) atypical CW with transitional artery but without hypoplastic artery, 2) atypical CW with hypoplastic artery, and 3) atypical CW with aplastic artery. (Figure 1)

![Figure 1](image_url) The example of CW pattern A; Typical CW pattern, B-D; atypical CW pattern (B; with transitional artery but without hypoplastic artery, C; with hypoplastic artery and D; with aplastic artery)
Results
Among SAH patients enrolled in this study, there were 90 aneurysmal subjects with males in 30% (27/90) and females in 70% (63/90). The mean age of all aneurysmal subjects was 55.93 ± 12.87 years (range 1-70). Of the 90 aneurysmal SAH patients, 60% (54/90) had aneurysms inside the CW and 40% (36/90) outside. (Table 1)

Table 1 The distribution of intracranial aneurysmal subjects relating with the CW

<table>
<thead>
<tr>
<th>Pattern of CW</th>
<th>Aneurysmal subjects</th>
<th>Aneurysms inside CW</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inside CW</td>
<td>Outside CW</td>
<td>total</td>
</tr>
<tr>
<td>Typical 4 (4.44%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without hypoplastic or aplastic artery</td>
<td>4</td>
<td>0</td>
<td>4 (4.44%)</td>
</tr>
<tr>
<td>Atypical 86 (95.56%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With transitional artery but without hypoplastic artery</td>
<td>2</td>
<td>1</td>
<td>3 (3.33%)</td>
</tr>
<tr>
<td>With hypoplastic artery</td>
<td>27</td>
<td>22</td>
<td>49 (54.44%)</td>
</tr>
<tr>
<td>With aplastic artery</td>
<td>21</td>
<td>13</td>
<td>34 (37.78%)</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>36</td>
<td>90 (100%)</td>
</tr>
</tbody>
</table>

The typical CW pattern was found in 4.44% among 90 aneurysmal patients, whereas that of atypical pattern was 95.96% as shown in Table 1. The atypical pattern of CW with hypoplastic vessels was the subtype outnumbered with 54.44% of aneurysmal group. The lowest incidence (3.33%) was found in the subtype of atypical pattern with transitional artery but without hypoplastic artery.

Table 2 The association between the CW patterns and the ruptured aneurysm sites

<table>
<thead>
<tr>
<th>Patterns of CW</th>
<th>Anterior circulation</th>
<th>Posterior circulation</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rt ICA</td>
<td>Lt ICA</td>
<td>Rt A1</td>
</tr>
<tr>
<td>Typical 4 (4.44%)</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Without hypoplastic / aplastic artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atypical 86 (95.56%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With transitional artery but without hypoplastic artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With hypoplastic artery</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>With aplastic artery</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

(1.85%) | (1.85%) | (18.53%) | (25.93%) | (38.89%) | (38.89%) | (1.85%) | (1.85%) | 6 (11.11%) |
The association between the CW patterns and ruptured aneurysm sites was shown in Table 2. There were 88.88% of patients with aneurysms at the anterior circulation and 11.11% at the posterior circulation. The aneurysmal rupture were found at ACoA in 38.89%, the right PCoA in 25.93% and the left PCoA in 18.53%. Of 54 patients with aneurysms inside the CW, hypoplastic vessels and aplastic vessels subtypes appeared most frequently with 50% and 38.89%, respectively. ACoA was the ruptured aneurysm site with the highest incidence in all subtypes of atypical pattern: with transitional artery but without hypoplastic artery in 50% (1/2) with hypoplastic vessels in 33.33% (9/27) and with aplastic vessels in 47.62% (10/21).

Discussion

The mean age of aneurysmal SAH patients in the present study was similar to that of a previous work. In the present study, the prevalence of atypical pattern was as high as 95.96% of the aneurysmal SAH patients. These variations were previously reported by Kapoor and partners in 40% investigated in the Indian population. They proposed that usual causes for such anomalies were the persistence of some embryonic vessel that normally disappear, disappearance of vessels that would normally persist or sprouting of new vessels due to hemodynamic and genetic factors. Most aneurysms in this study occurred within the CW. This is supported that the aneurysms frequently develop at the sites of arterial branching which was mostly found on CW. Predominant aneurysm site was ACoA, corresponding to a previous study. Kasuya and coworkers described that ACoA site had smaller A1-A2 junction, leading to higher hemodynamic stress and aneurysm formation. The efficacy of ACoA vasodilatation was also limited, comparing to the rest of intracranial arteries, because it is the only cerebral artery developing from the plexiform blood vessels. ACoA and PCoA aneurysms with CW irregularities were associated with rupture because both sites seemed most relevant to hemodynamic changes due to CW anomalies. Ruptured aneurysms occurred more frequently in patients with atypical pattern of CW because the CW anomalies altered blood flow in the circle. The CW variations generated hemodynamic changes with the force acting on the vessel wall in collateral sites, leading to aneurysm formation and rupture.

In conclusions, most non-traumatic aneurysmal rupture in this study occurred within the CW and ACoA was the predominant aneurysm site. The prevalence of atypical pattern was very high among the aneurysmal SAH patients and ACoA was the predominated ruptured aneurysm site in all atypical subtypes, showing the association between the aberrant CW patterns and ruptured aneurysm sites. These findings should be imperative for the diagnosis and the surgical approaches of the intracranial aneurysm.

Acknowledgements

This study was supported by the Department of Anatomy and the Department of Radiology, Faculty of Medicine, Khon Kaen University.

References