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ORIGINAL ARTICLE

Wall-to-lumen ratio of intracranial arteries measured by indocyanine green angiography

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ABSTRACT

Background: The wall-to-lumen ratio (WLR) is an important parameter in vascular medicine because it indicates the character of vascular wall as well as the degree of stenosis. Despite the advances in medical imaging technologies, it is still difficult to measure the thin-walled normal intracranial arteries, and the reports on the WLR of normal intracranial artery are limited. It might be possible to calculate the WLR using the indocyanine green (ICG) angiography, which is used to observe intracranial vessels during microsurgery.

Purpose: To evaluate the WLR of normal intracranial arteries using ICG angiography.

Materials and Methods: From the three cases in which ICG angiography was recorded with a ruler during microsurgery, 20 measurement points were chosen for the analysis. The ICG was injected intravenously with a dose of 0.2 mg/kg, and the vessels were inspected at high magnification using an operating microscope equipped with near-infrared illumination system. The vessel outer diameter and the luminal diameter were measured using the images before and after the ICG arrival based on the pixel ratio method using a ruler as reference, respectively. The WLR was calculated as 0.5 × (vessel outer diameter − vessel luminal diameter).

Results: The WLR (mean ± standard deviation) of normal intracranial arteries was 0.086 ± 0.022. The WLR tended to be high in small arteries.

Conclusion: The WLR of normal intracranial arteries calculated using ICG angiography was consistent with the WLR reported in the previous reports based on human autopsy.

Key words: *In vivo*, indocyanine green angiography, intracranial artery, normal, vascular wall, wall-to-lumen ratio

Introduction

The wall-to-lumen ratio (WLR) is the ratio of vascular wall thickness to luminal diameter, which is one of the important parameters in the field of vascular medicine because it indicates the character of vascular wall as well as the degree of vascular stenosis.[1] For example, the WLR is useful to narrow the differential diagnosis of intracranial vascular stenosis.[2] In the case of the arteriosclerotic stenosis, the WLR is reported to increase reflecting the increased wall thickness due to the atheromatous lipid deposition.[3] In contrast, in the case of moyamoya disease, intracranial arteries are reported to constrict without increase or decrease of the WLR.[4]

To calculate the WLR, the thickness of the vessel wall should be obtained. The development of magnetic resonance imaging made it possible to measure the thickened wall of atheromatous

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intracranial arteries.[5-9] However, it is still difficult to measure the thickness of normal thin-walled intracranial arteries. This is the reason why the existing reports on the WLR of normal intracranial arteries are limited to those based on the measurements from autopsies of rats and humans.[10-14]

During the microsurgery of various intracranial diseases, we can inspect intracranial arteries closely, and the outer diameter of intracranial arteries can be measured. In addition, we can also inspect the inner lumen of intracranial arteries at high magnification using indocyanine green (ICG) angiography, which is now widely applied to assess the flow dynamic changes during microsurgery.[15-18] Thus, the WLR of intracranial arteries could be obtained from the archived video recording of ICG angiography during microsurgery.

The aim of the present study is to evaluate the WLR value of the normal intracranial arteries without atheromatous changes using ICG angiography during microsurgery.

Materials and Methods

Subjects

This study was approved by the Ethics Committee of our institute (No. 2231-2, approved on 9/30/2013). The patients in this study provided written informed consent.

Between January 2014 and August 2014, there were 27 cases with ICG angiography during microsurgery. Reviewing the archived video recordings of these cases, we found three cases in which a ruler, which was necessary as a reference to calculate the diameters of arteries, was recorded simultaneously during ICG angiography. All three cases, with a mean age of 64.3 years old, were operated on unruptured cerebral artery aneurysms. They had no particular previous disease and no predisposing factors of atherosclerosis.

Indocyanine green angiography

ICG angiography uses intravenously administered ICG as a dye and observes cerebral vessels at high magnification under the operating microscope equipped with near-infrared illumination system. ICG angiography was done at least twice in each case before and after the surgical clips were applied to the aneurysms. ICG was injected intravenously with a dose of 0.2 mg/kg. All operations were performed using an operating microscope equipped with a near-infrared illumination system (OME-9000; Olympus, Tokyo, Japan). During ICG angiography, the operating microscope was not moved. ICG angiography was recorded continuously using a high-definition recording system (AG-MDC10G; Panasonic, Japan).

Measuring vessel outer diameter and vessel luminal diameter

The images with a ruler on the same plane as the measurement point appearing in the surgical fields were selected from the videos, and they were exported to an image editing software (Photoshop®; Adobe Systems Incorporated, San Jose CA, USA). Healthy-looking segments of the arteries without visible atheromatous plaques were chosen as the measurement points of the vessel diameters. Six or seven measurement points were chosen from each case. The images before the ICG arrival with sufficient light illuminations were used to measure the vessel outer diameter, and the images after the ICG arrival with sufficient fluorescence under the near-infrared light were used to measure the vessel luminal diameter based on the pixel ratio method [Figure 1a and b]. Three neurosurgeons (D.N., M.S., and S.N.) confirmed that the vessels were healthy (e.g., the absence of arteriosclerosis). Measurement segments were supposed to be identical between the images before and after the ICG arrival since the operating microscope was not moved during the ICG angiography.

Calculating wall-to-lumen ratio

The WLR is the ratio of vascular wall thickness to luminal diameter. Thus, the WLR was calculated according to the equation below, based on the vascular outer diameter, and the vascular luminal diameter measured as described above.

$$\mathrm{WLR} = \frac{1}{2} \times \frac{vessel\ outer\ diameter - vessel\ luminal\ diameter}{vessel\ luminal\ diameter}$$

Statistical analysis

Statistical analysis and graphic display of data were performed by using GraphPad software (version 5.00 for Windows; GraphPad Software, San Diego, CA). All values are reported as mean ± standard error (standard deviation [SD]). Analysis of variance with multiple comparison Tukey test was used to compare the variables affecting the WLR.

Results

The outer diameter and the luminal diameter were measured, and the WLR was calculated at 20 points in the three cases [Table 1]. The measurement points included 16 middle cerebral artery (MCA) branches lying on insula, two anterior temporal arteries, and two lenticulostriate arteries. The vascular outer diameters ranged from 0.76 mm to 4.04 mm, with an average of 2.52 mm, and the vascular luminal diameters

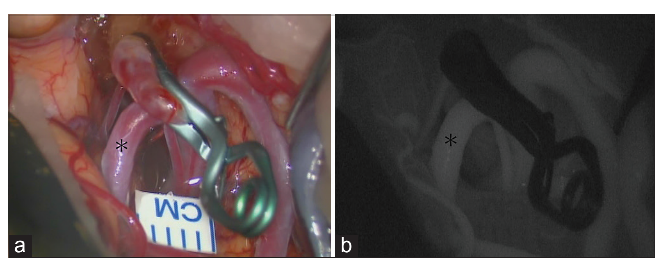

Figure 1: (a) Measurement of the vascular outer diameter using an intraoperative image. *The measurement point for vascular outer diameter. (b) Measurement of the vascular luminal diameter using indocyanine green angiography in the same scale as that in Figure 1a. *The measurement point for vascular luminal diameter

Table 1: Vessel diameter and wall-to-lumen ratio

Measurement point	Outer diameter (mm)	Luminal diameter (mm)	WLR
M2	2.18	1.86	0.087
M2	3.01	2.52	0.099
LSA	0.76	0.64	0.096
M2	3.47	3.00	0.079
M2	3.04	2.53	0.099
ATA	1.00	0.81	0.118
M2	2.99	2.63	0.070
M2	3.04	2.50	0.109
M2	2.23	1.93	0.076
M2	2.89	2.56	0.065
LSA	0.77	0.64	0.099
M2	3.45	2.93	0.088
M2	2.23	1.93	0.077
M2	3.51	3.02	0.081
ATA	1.01	0.77	0.154
M2	4.04	3.55	0.069
M2	2.77	2.45	0.064
M2	3.00	2.59	0.079
M2	2.08	1.89	0.050
M2	2.95	2.59	0.071

M2 – Middle cerebral artery branches lying on the insula; LSA – Lenticulostriate artery; ATA – Anterior temporal artery; WLR – Wall-to-lumen ratio

measured using the ICG angiography ranged from 0.64 mm to 3.55 mm, with an average of 2.17 mm. The WLR (mean ± SD) was 0.086 ± 0.022. The WLR of the MCA branch lying on insula was 0.093 ± 0.011, that of the anterior temporal artery was 0.136 ± 0.0011, and that of the lenticulostriate artery was 0.079 ± 0.004. According to the Levene's test, a distribution of the widths of the WLR by artery has a normal distribution ($P = 0.12$). The WLR of the anterior temporal artery was slightly larger than the other two ($P < 0.001$) [Figure 2a]. The WLR of the small artery (<2 mm in diameter) was 0.116 ± 0.023, that of the medium-sized artery (2–3 mm) was 0.070 ± 0.010, and that of the large artery (more than 3 mm) was 0.088 ± 0.012. According to the Levene's test, a distribution of the widths of the WLR by arterial size has a normal distribution ($P = 0.19$). The WLR of the small artery was slightly larger than the other two ($P < 0.001$). The small artery group included two anterior temporal arteries and two lenticulostriate arteries [Figure 2b]. The systolic and diastolic blood pressures at the time of ICG angiography were 95–105 mmHg (99 mmHg in average) and 50–58 mmHg (54 mmHg in average), respectively.

Discussion

In the present study, the WLR of the healthy-looking intracranial artery was measured by using ICG angiography during microsurgical clipping of unruptured cerebral aneurysms. The WLR of healthy-looking that is, normal intracranial artery was 0.086 ± 0.022. Several studies demonstrated that lumen

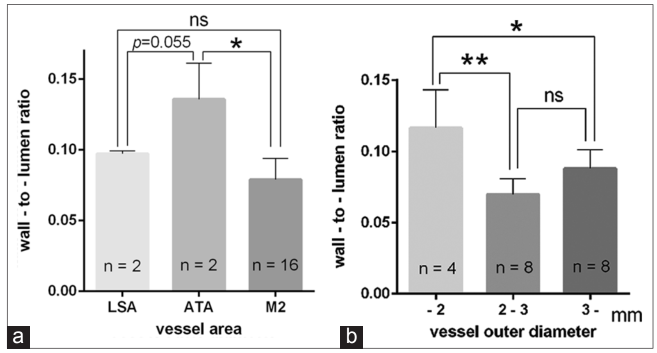

Figure 2: (a) Bar graph of normal wall-to-lumen ratio by vessel area. Analysis of variance with multiple comparison Tukey test was used to compare the variables of vessel area. $*P < 0.05$, ns: Not significant. (b) Bar graph of normal wall-to-lumen ratio by vessel size. Analysis of variance with multiple comparison Tukey test was used to compare the variables of vessel size. $*P < 0.05$, $**P < 0.001$, ns: Not significant. LSA: Lentriculostriate artery, ATA: Anterior temporal artery, M2: Branches of middle cerebral artery lying on insula

diameter of intracranial arteries can be measured precisely by using ICG. This is the first report that ICG is used to measure WLR.

The existing reports on the WLR of normal intracranial arteries are broadly classified into two groups. In one group, the studies were based on rats;[10-13] whereas in the other group, the studies were based on human autopsies.[11,14] The WLR was calculated based on the measurements of cross-sectional arteries mounted on histological slides in these studies. Currently, many articles refer these studies as to the WLR of normal intracranial arteries.[19-21] According to the study based on rat,[10] the WLR of normal intracranial artery is 0.08, whereas the WLR of hypertensive intracranial artery is increased up to 0.14. According to the study based on human autopsy, the WLR of normal intracranial vessels ranges between 0.05 and 0.12.

The vessels subjected to our study had approximately 0.7–4.0 mm of outer diameter, which covers the general diameter of major intracranial arteries. The small arteries (<2 mm in diameter) tend to have slightly larger WLR in our study. Similar findings are described in one of the previous papers reporting the WLR tends to be high when the vessel diameter is small.[11] Our results could be well-applied to medium-sized or large intracranial arteries. This method may help neurovascular surgeon to choose the correct treatment area for aneurysms clipping or graft anastomosis.

The present study has several limitations to be discussed. At first, our results are based on low number of cases. The correlation between the vascular diameter and the WLR would presumably be clearer with a larger number of cases. The second limitation is that the measurements are based on the images exported from the video recordings. The vessel diameters are determined with the pixel ratio method using a ruler in the operative field as reference. The differences in depth between the ruler and the measured arteries might have influenced the measurements of the vessel diameter. Thus, we chose the measurement points in the vicinity of the rulers. It should also be mentioned about the limitation of the ICG angiography, the limited observation angle, and the inability to observe the lumens of vessels with arteriosclerosis-related calcification.[22] As anticipated, the operative field in measurements of the vascular diameters was narrow, and the vascular observation angle was available only in one direction in the present study. However, there were no patients whose vascular luminal diameters were not visualized by ICG video angiography because of calcification because we chose healthy subject vessels. In spite of these limitations, the WLR calculated in the present study was consistent with the previous reports that adopt different measuring methods. This might indicate that the WLR calculation using the ICG angiography had a sufficient precision to visualize the lumens of intracranial arteries.

Conclusion

The WLR of normal intracranial arteries calculated using ICG angiography was 0.086 ± 0.022, which was consistent with the previously reported WLR based on the human autopsy.

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Conflicts of interest
There are no conflicts of interest.

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