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Measurement of the length of vertebrobasilar arteries: A three-dimensional approach

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ABSTRACT

Under the assumption that neurovascular compression can be caused by elongation or kinking of the artery, we measured the length of each section of the vertebrobasilar artery, compared the lengths between various age groups, and evaluated the involvement of the arterial sections in brain stem compression in 1000 cases. The lengths of the posterior inferior cerebellar artery (PICA)-union of both vertebral arteries (union), union-anterior inferior cerebellar artery (AICA), AICA-superior cerebellar artery (SCA), and union- superior cerebellar artery were measured using an arterial length measuring tool applied to three-dimensional images. The presence of arterial compression of the brain stem was also evaluated. The mean age of the participants was 66.8 ± 12.9 years, and 44.8% were men. Intraclass correlation coefficients for both inter-rater reliability and intra-rater reliability were high in all sections. The vessel lengths of left AICA-SCA ($P < 0.001$), left union-SCA ($P < 0.0001$), left PICA-union ($P = 0.03$), right AICA-SCA ($P = 0.002$), right union-SCA ($P < 0.0001$), and right PICA-union ($P = 0.04$) increased with age, but each R^2 was less than 0.05. Brain stem compression by PICA or vertebral artery was identified in 13.8% of cases. The proportion of the presence of brain stem compression was significantly higher in the cases with arterial elongation than in those without ($P = 0.01$). Vessel length increased with age, but age had a relatively small impact on the elongation of vertebrobasilar arteries. Brain stem compression might be caused by kinking of the artery rather than arterial elongation.

1. Introduction

Neurovascular compression (NVC) syndrome is a disease entity caused by arteries making direct contact with the brain stem and cranial nerves. The common culprit arteries are the superior cerebellar artery (SCA) in trigeminal neuralgia, and the anterior inferior cerebellar artery (AICA) or posterior inferior cerebellar artery (PICA) in facial spasm [1]. The vertebrobasilar artery or AICA can compress the abducent nerve [2], while the vertebral artery (VA) can compress the hypoglossal nerve [3], with these compressions resulting in palsy of the corresponding nerves. NVC of the optic nerve is rare; however, it can be a cause of visual impairment [4]. In such conditions, surgical decompression might be considered, and it has shown great efficacy [5,6].

The rostral ventrolateral medulla (RVLM) is a major topic regarding NVC of the medulla oblongata, because the RVLM plays a role in the regulation of blood pressure. Jannetta et al. first reported that most patients with cranial neuralgia and hypertension with NVC of the RVLM who underwent microvascular decompression (MVD) of the RVLM showed prominent blood pressure reduction [7]. Additionally, Levy et al. performed MVD of the RVLM in 12 patients with essential hypertension without neuralgia, and observed a reduction in blood pressure in ten of them [8]. There have since been several reports on the efficacy of MVD as a treatment for essential hypertension in patients with NVC of the RVLM [9–12]. Sendeski et al. divided NVC into categories based on MR findings as follows: 1) non-NVC: no sign of NVC, with arteries clearly away from the RVLM, 2) NVC type I: image of an artery in contact with the RVLM but not compressing it, and 3) NVC type II: evident compression of the RVLM by an artery [13]. They found NVC type I in 34% of the normotensive group and 39% of the hypertensive group, while NVC type II was found in 3% of the normotensive group and 27% of the hypertensive group, thereby showing that the closer the artery is to the RVLM, the higher the probability of hypertension. Such differences in distribution were statistically significant.

If both ends of an artery are fixed in a limited space, a possible mechanism by which it can cause nerve compression/brain stem

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compression is elongation of the artery along its long axis with kinking. Another possibility is that of pure torsion, without elongation of the artery, which can cause kinking toward cranial nerves or the medulla oblongata. In this study, we measured the route length of each section in the vertebrobasilar artery, using a dedicated code. We also compared each length in people of different ages in a relatively large number of cases, and investigated the relationship between arterial length and the frequency of brain stem compression caused by the artery.

2. Methods

2.1. Data acquisition

The subjects consisted of consecutive patients (n = 1000) over 40 years-of-age who underwent head magnetic resonance angiography (MRA) and magnetic resonance imaging (MRI) examinations for the purpose of follow up for cerebral infarction, cerebral hemorrhage, cerebral aneurysm, or the diagnosis of headache or brain dock screening (a health check for cerebral and cardiovascular diseases that is widely performed in Japan) at Kasumi clinic, a diagnostic imaging clinic located in Hiroshima city. All cases underwent brain MRI/MRA scanning on a 1.5-T scanner (Intera Achieva 1.5 T, equipped with a SENCE NV-16ch Coil; Philips, Netherlands) between 2015 and 2017. The following sequences were obtained: T1-weighted imaging (WI), (repetition time [TR]/ echo time [TE], 600/10 ms; flip angle (FA), 70°; field of view (FOV), 240 × 240 mm; slice thickness, 5 mm; intersection gap, 1 mm; matrix size, 272 × 190; voxel size, 0.88 × 1.26 mm; band width, 183.6 Hz/1.183 pixel), T2WI, (TR/TE, 5258/100 ms; FA, 90°; FOV, 240 × 240 mm; slice thickness, 5 mm; intersection gap, 1 mm; matrix size, 368 × 286; voxel size, 0.65 × 0.84 mm; band width, 238.4 Hz/0.911 pixel), fluid-attenuated inversion recovery (FLAIR) (TR/TE, 10000/100 ms; FA, 90°; FOV, 240 × 240 mm; slice thickness, 5 mm; intersection gap, 1 mm; matrix size, 304 × 196; voxel size, 0.79 × 1.22 mm; band width, 255.0 Hz/0.852 pixel), and three-dimensional (3D) time of flight (TOF) MRA (TR/TE, 20/3 ms; FA, 18°; FOV, 170 × 170 mm; slice thickness, 1 mm; intersection gap, −0.5 mm; matrix size, 336 × 171; voxel size, 0.53 × 1.04 mm; band width, 108.5 Hz/2.002 pixel).

2.2. Measurement of length of arteries

The lengths of the sections between each branching point of the PICA, AICA, and SCA were measured; namely, section lengths of the right and left PICA-union of both vertebral arteries (union), union-AICA, AICA-SCA, and union-SCA (a schematic picture is shown in Fig. 1).

An arterial length measuring tool developed by L Pixel Corporation (Tokyo, Japan) was applied to the 3D-images (Supplemental information 1). This software (the code is shown at https://github.com/yd328/arterial-length) was designed to automatically track the center of each cross-section along the long axis of the artery and calculate the traced length between manually pre-marked landmarks. To test the accuracy of the code, the route length on MRI between the two ends of a 100 mm phantom tube filled with contrast agent was measured using the code while the tube was bent to create direct linear distances between the ends of 90, 80, and 70 mm. According to the recommendation of ANSI/NCSL Z540 [14], the degree of effect was calculated using the following equation: degree of effect = $(A^2 + B^2)^{\hat{}1/2}$ / A, where A = the accuracy of the product, and B = the accuracy of the measuring device. The degree of effect is used in the industrial field as an indicator of the accuracy of measurements made using a product. The arterial segment was set manually by defining each branch point on the source TOF MRA images. Elongation was defined as a measurement located outside the 0.99 probability ellipse of a scatter plot showing the relationship between age and measured arterial length. Two observers (Y.D. and K.H.) independently measured 50 randomly extracted cases and the reliability of the measurements was confirmed using the intraclass correlation coefficient (ICC). Y.D. then performed the measurements in all participants. Statistical analysis was carried out using Student's t-test for two groups and one-way ANOVA. A P-value of 0.05 was considered statistically significant.

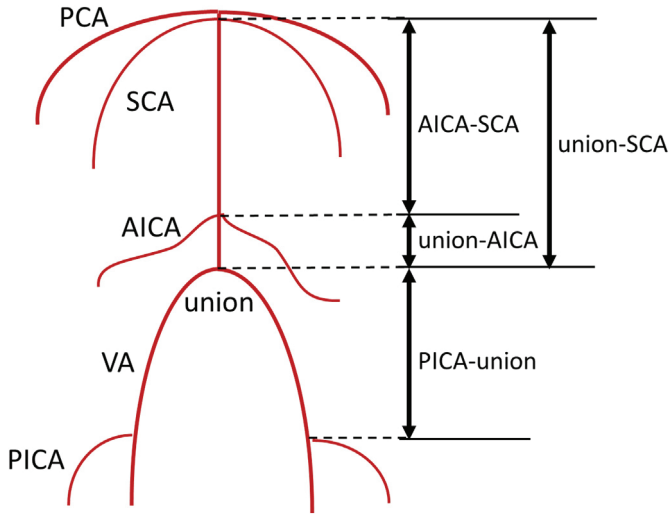

Fig. 1. Schematic picture of the arterial sections measured.
VA; Vertebral artery, PICA; Posterior inferior cerebellar artery, AICA; Anterior inferior cerebellar artery, SCA; Superior cerebellar artery, PCA; Posterior cerebral artery, union; union of both vertebral arteries.

2.3. Assessment of brain stem compression

With reference to the T1WI and TOF MRA images, the presence of arterial compression of the brain stem was determined according to the loss of symmetry of the brain stem in the axial image (Supplemental information 2), and the arteries responsible were identified by referring to maximum intensity projection MRA images [15]. The asymmetry index (right length − left length / right length + left length × 0.5) [16] was calculated to compare the differences between the left and right PICA-unions.

This research was approved by the Ethics Committee of Hiroshima University after review (E-79). None of the eligible patients opted-out of our study.

3. Results

To check the accuracy of the measuring method, we bent a phantom tube of an exact length of 100 mm to create direct linear distances between its ends of 90, 80, and 70 mm, and measured the length seven times for each trial using the developed code. The mean measured lengths of the phantom tube were 100.11 ± 0.04 mm for a direct linear distance between the ends of 100 mm, 98.32 ± 0.24 mm for 90 mm, 101.42 ± 0.04 mm for 80 mm, and 101.98 ± 0.08 mm for 70 mm (Table 1).

Of the 1000 subjects, there were 146, 152, 214, 312, and 176 participants in their 40s, 50s, 60s, 70s, and 80s respectively. The average age was 66.8 ± 12.9 years, and the proportion of men was 44.8%. There were no subjects with arterial dissection. A total of six cases with fenestration were found in this study (six in basilar artery; BA), none of which had symptoms of nerve compression. The ICC values for all the vessel lengths examined were high (inter-rater reliability, 0.92 ± 0.09; intra-rater reliability, 0.95 ± 0.04), so we judged the code to be eligible for the measurement of the section lengths.

Positive significant correlations were observed between age and vessel lengths: right PICA-union 18.9 ± 6.9 mm (range 0–36.3 mm, P = 0.04, n = 292), right AICA-SCA 20.3 ± 3.1 mm (12.0–36.1 mm,

Table 1
The measured values of the phantom tube.

Direct distance (mm)	Measured value (mm)
100	100.11
	100.11
	100.11
	100.18
	100.03
	100.11
	100.11
90	98.15
	98.15
	98.15
	98.22
	98.30
	98.86
	98.39
80	101.42
	101.42
	101.42
	101.49
	101.35
	101.42
	101.42
70	101.98
	101.98
	101.98
	101.98
	101.91
	102.17
	101.98

$P = 0.002$, $n = 454$), right union-SCA 26.4 ± 4.2 mm (10.1–48.1 mm, $P < 0.0001$, $n = 928$), left PICA-union 20.4 ± 6.8 mm (0–43.4 mm, $P = 0.03$, $n = 317$), left AICA-SCA 19.6 ± 3.0 mm (6.7–32.0 mm, $P < 0.001$, $n = 426$), and left union-SCA 26.3 ± 4.2 mm (10.1–48.1 mm, $P < 0.0001$, $n = 925$). The PICA-union was measurable on only a small number of cases because the branching point of the PICA was not shown on MRI in many cases. The data for all arterial segments measured are shown in Table 2 and Fig. 2. In particular, the left AICA-SCA tended to elongate 0.3–0.5 mm per decade of age. The R^2 values for the correlation between age and section length were less than 0.02 in all sections analyzed (Table 2).

The bilateral difference in the PICA-union section length was evaluated using Bland-Altman analysis, which showed no significant differences. Furthermore, we studied the correlation between age and asymmetry index in the PICA-union section lengths, but did not find a significant correlation ($P = 0.20$). We did not evaluate other section lengths because both sides of the SCA and AICA branched from BA at almost the same point.

We calculated the degree of effect to verify the accuracy of the code used, and found that the degree of effect was less than 0.25%, indicating that the accuracy of the measurements used in this study was satisfactory.

In our case series, no artery was found in contact with the midbrain, pons, or cranial nerves, with the arteries only making contact with the medulla oblongata. Brain stem compression caused by the PICA or VA was identified in 13.8% of patients. By percentage, the culprit vessels were 7.2% right PICA, 46.4% right VA, 37.0% left PICA, and 9.4% left VA. When classified by age, the presence of brain stem compression was 1.1%, 2.2%, 3.1%, 4.1%, and 3.3% for subjects in their 40s, 50s, 60s, 70s, and 80s respectively, with the differences not being statistically significant (Supplemental Information 3). With a definition of the outside of the 0.99 probability ellipse for the relationship between age and length as showing elongation, a total of 31 sections from 15 cases were judged as elongated sections. Among these cases, six showed brain stem compression (Table 3). The proportion of the presence of brain stem compression was significantly higher in the cases with arterial elongation than in those without ($P = 0.01$). We identified 12 cases with infarction, 13 cases with hemorrhage both in the brain stem and 12 cases with aneurysm in the vertebrobasilar artery in our series. We excluded those 37 cases, and then we performed chi-square test on compression and elongation on the remaining subject. The proportion of the presence of brain stem compression was significantly higher in cases with arterial elongation than in those without elongation even in the absence of any brain stem lesion ($P = 0.02$).

4. Discussion

As the saying goes, “a man is as old as his arteries” [17], and age is a major risk factor for cerebrovascular diseases [18,19]. The most common alterations found in the arterial walls are the enlargement of a lumen (dilatation), wall thickening/plaque formation (remodeling), and decreased elasticity [20]. For example, evaluation of arteries in the short axis by B mode ultrasonography can demonstrate an increase in intima–media thickness with age in both genders [21]. In this study, we assessed age-associated change in the length of vertebrobasilar arteries on 3D MRI images and investigated the relationship between brain stem compression and arterial elongation, finding that several sections of the investigated arteries were longer in the older subjects.

There is a 4:1 rule for the accuracy of a measuring device, which holds that the accuracy of the device should be four times more than that of the product. As documented in ANSI/NCSL Z540 [14], we defined an acceptable range for the standard deviation of the phantom measurements as being less than one-fourth of the length of the arteries measured. The ratios of the standard deviations were less than 1/15, suggesting that the employed method was sufficiently accurate for measuring the length of the arteries.

We found that segment lengths in both sides of the PICA-union, AICA-SCA, and union-SCA tended to be larger in the elderly. However, the correlations between age and section length revealed low R^2 values for all sections, indicating that age is not a critical factor for the length of all arteries. Although our study is a cross-sectional study, we believe that comparison of the arterial lengths of both sides of the PICA-union in each individual might be useful for estimating the acquired changes in length over time. If arteries undergo elongation during aging, the

Table 2
Vessel lengths and correlations between age and length.

Section	n	Length(mm) mean ± SD (range)	R^2	P	Rate of elongation/decade (mm)
Lt. PICA-union	317	20.4 ± 6.8 (0–43.4)	0.01	0.03	0.4
Lt. union-AICA	409	7.3 ± 3.1 (0–20.4)	0.0	0.8	NA
Lt. AICA-SCA	426	19.6 ± 3.0 (6.7–32.0)	0.05	< 0.001	0.5
Lt. union-SCA	925	26.3 ± 4.2 (10.1–48.1)	0.02	< 0.0001	0.5
Rt.PICA-union	292	19.0 ± 6.9 (0–36.3)	0.02	0.04	0.3
Rt. union-AICA	447	6.5 ± 2.8 (0–17.4)	0.003	0.2	NA
Rt. AICA-SCA	454	20.3 ± 3.1 (12.0–36.1)	0.02	0.002	0.3
Rt. union-SCA	928	26.4 ± 4.2 (10.1–48.1)	0.02	< 0.0001	0.4

Lt; Left, Rt; Right, PICA; posterior inferior cerebellar artery, AICA; anterior inferior cerebellar artery, SCA; superior cerebellar artery, union; union of both vertebral arteries, NA; Not Assessed.

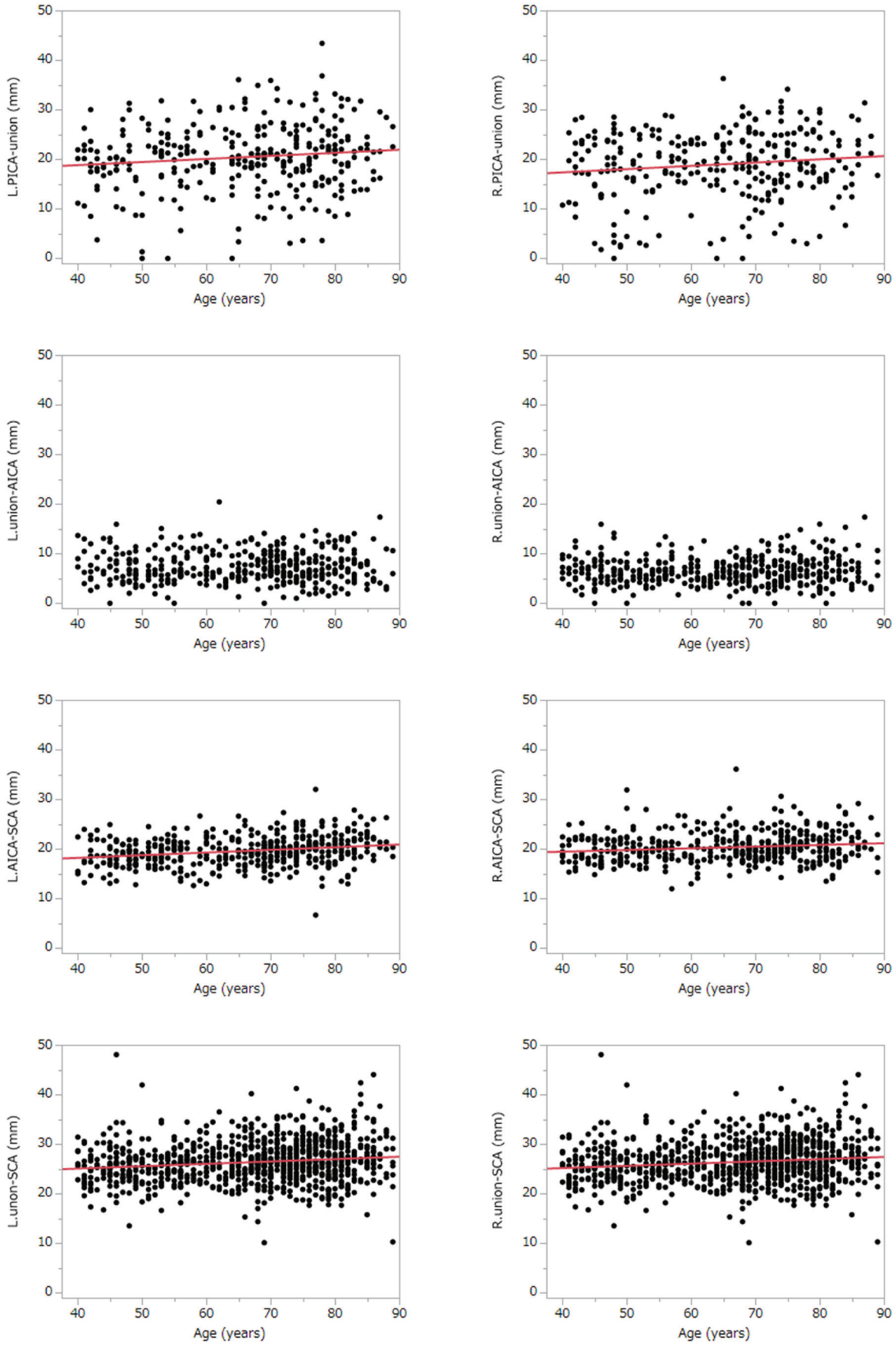

Fig. 2. Changes in vessel length with age.
The vessel lengths of left PICA-union, right PICA-union, left AICA-SCA, right AICA-SCA, left union-SCA, and right union-SCA were positively associated with age.

Table 3
The proportion of the presence of brain stem compression was significantly higher in cases with arterial elongation than in those without elongation ($P = 0.01$).

compression \ elongated	(+)	(−)	Total
(+)	6	132	138
(−)	9	853	862
Total	15	985	1000

asymmetry index of the arterial lengths in the PICA-union section would be expected to increase with age, but we found no significant correlation between age and asymmetry index, indicating that the change in the length of an artery during adulthood might be small.

A few previous studies have accessed the length of arteries [22,23]. Nishikata et al. reported a relationship between age, bending, and elongation of the BA [24] on two-dimensional (2D) MRI, and concluded that the longitudinal growth of the BA depends on aging, while bending of the BA is induced by other factors. Their study showed lengths between the top of the BA and the union of the vertebral arteries (BAL) of 24.6 ± 4.36 mm and 23.3 ± 4.01 mm for men and women respectively, with these lengths being equivalent to the union-SCA section length in our study. In comparison, the average length of the union-SCA section on 3D imaging was longer than that of BAL on 2D imaging, as expected. Regarding change in the length of arteries, Sugawara et al. showed that ascending aorta length (75 ± 20 mm) was positively associated with age (9 mm/decade) [25], but found no elongation in the carotid artery. In our study, left union-SCA length (26.3 ± 4.2 mm) was positively associated with age (0.5 mm/decade), but the ratio of the elongation rate against artery length was much lower than in the previous study, suggesting that the rate of elongation differs from site to site.

There were 138 cases showing signs of brain stem compression, but none of our cases had any symptoms caused by cranial nerve compression. We found that the frequency of brain stem compression was significantly higher in the group with arterial elongation whether or not the case has a lesion in the brain stem such as infarction, hemorrhage and vertebrobasilar aneurysm, suggesting that elongated arteries could be at least part of the cause of compression. Although the number of cases with brain stem compression tended to be higher among older adults, no significant difference was detected between the age classes. While older people tended to more frequently show brain stem compression, the differences in arterial length between age classes were small. Presumably, with regard to compression of the brain stem and cranial nerve, change in the course of the vascular route is a more critical factor than elongation of the artery.

Several limitations to our study should be noted. First, because of the retrospective nature of this study, we could not take vascular risk factors such as hypertension into account, as detailed patient backgrounds were not available. Second, this is a cross-sectional study, and a longitudinal study is necessary to confirm the changes over time. It is likely that long-term changes in the physique of the Japanese may affect the length of arteries. In Japan, the average height of women at the age of 17 in 1993 was approximately 5 cm higher than that in 1953 (see Supplemental Information 4 [26]). However, the finding of longer arterial length in older subjects with smaller stature might also indicate that arteries could elongate in middle age.

In conclusion, cerebral arteries were shown to elongate with aging, but the contribution of aging to arterial length was not high. Furthermore, arteries compressed the brain stem more frequently in the elderly. The higher frequency of arterial compression of the brain stem in older people might not be due to the elongation of the arteries themselves, but instead may be due to change in the course of a vascular route by kinking, which takes place over a period of time.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2020.116818.

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