# Mechanism of medullary infarction based on arterial territory involvement

Kyoungsub Kim

Department of Medicine
The Graduate School, Yonsei University

# Mechanism of medullary infarction based on arterial territory involvement

Directed by Professor Ji Hoe Heo

The Master's Thesis submitted to the Department of Medicine the Graduate School of Yonsei University in partial fulfillment of the requirements for the degree of Master of Medical Science

Kyoungsub Kim

December 2011

# This certifies that the Master's Thesis of Kyoungsub Kim is approved.

[Signature]
Thesis Supervisor : Ji Hoe Heo
[Signature]

[Seung Min Kim: Thesis Committee Member#1)
[Signature]

[Jae Whan Lee: Thesis Committee Member#2)

# The Graduate School Yonsei University

December 2011

#### **ACKNOWLEDGEMENTS**

First of all, I am very pleased to thank Professor Ji Hoe Heo, who catches a base of study, encourages kindly and supports me from a research planning to a completion. Without his advice and help, I can't finish this thesis.

And I also thank to Professor Seung Min Kim and Professor Jae Whan Lee, who give me a professional advice and comment through the examination of a thesis.

Lastly, I thank to everyone who cares and helps me to complete a master's degree in a graduate school safely, especially my wife and my baby.

Kyoungsub Kim

## <TABLE OF CONTENTS>

ABSTRACT	1
I. INTRODUCTION	3
II. METHODS ·····	1
1. Enrolled patients	1
2. Topography of lesion	5
3. Risk factors and etiologic classification of stroke	5
4. Statistical analysis	7
III. RESULTS ······	3
1. Topography of lesion ······	3
2. Etiology of infarction	12
3. Arterial lesions	13
4. Demographic characteristics ————————————————————————————————————	13
5. Clinical features —	16
V. DISCUSSION	16
REFERENCES2	20
ABSTRACT(IN KOREAN)	23
PUBLICATION LIST	24

### LIST OF FIGURES

Figure 1. Diagrams showing the arterial territory of the
medulla oblongata ······6
Figure 2. Comparison between the groups based on
generalized estimating equation10

### LIST OF TABLES

Table 1. Topographical dif	fferences among vascular
territories involved	9
Table 2. Etiologic mechan	isms of medullary infarction14
Table 3. Demographic cha	racteristics according to arterial
territories involved	15
Table 4. Symptoms and sig	gns according to involved arterial
territories in 73 patients v	with a lesion in the single arterial
territory ·····	17

#### **ABSTRACT**

## Mechanism of medullary infarction based on arterial territory involved

#### Kyoungsub Kim

Department of Medicine The Graduate School, Yonsei University

(Directed by Professor Ji Hoe Heo)

**Background and Purpose** The blood supply to the medulla oblongata is distinct from the other areas of the brainstem. Therefore, the mechanism of medullary infarctions may be distinct. However, few studies have addressed the mechanism of medullary infarctions.

**Methods** Of 3833 stroke patients that were on the stroke registry from February 1999 until April 2008, patients with medullary infarctions that were demonstrated on diffusion-weighted MRI, were enrolled. We analyzed the topography of the lesions, arterial territories involved, and etiologic mechanisms, particularly in relation to arterial territories involved

**Results** A total of 142 patients were enrolled. Bilateral medullary infarctions were rare (2.2%). Lesions involving the anteromedial or lateral territories were common in the upper medulla oblongata, whereas lateral territorial involvements were common in the middle and lower medulla

oblongata. Significant stenosis (>50%) or occlusion of the verterbral artery was common (52.2%). Among stroke subtypes, large artery atherosclerosis was most common (34.5%), whereas lacunae and cardioembolism were rare (3.5%, 4.2%, respectively). Vertebral artery dissection was frequent. Stroke mechanisms were different among the vascular territories involved. Large artery atherosclerosis produced a lesion in the lateral, anteromedial, and posterior territories. None of the cardioembolism or other etiologies involved anteromedial or anterolateral territory, but all involved the lateral and/or posterior territories. Lacunar infarction was only found in the anteromedial and the anterolateral territory.

**Conclusions** The topography and mechanisms of infarctions involving the medulla oblongata were different among the involved arterial territories. These findings may be associated with the distinct arterial supplying pattern of the medulla oblongata.

**Key words:** Cerebral infarction, MRI, Medulla oblongata

# Mechanism of medullary infarction based on arterial territory involvement

#### Kyoungsub Kim

Department of Medicine The Graduate School, Yonsei University

(Directed by Professor Ji Hoe Heo)

#### I. INTRODUCTION

Infarctions involving the medulla oblongata are rare. Previous studies have shown characteristic clinico-lesion correlations in patients with medullary infarctions, particularly those between the medial and the lateral medullary infarction. <sup>1-5</sup> The brainstem is typically supplied by the circumferential arteries and the small direct perforating arteries from the basilar or vertebral arteries. <sup>6</sup> The blood supply of the medulla oblongata is distinct from the other areas of the brainstem. This unique arterial supply is due to the anterior and the posterior spinal arteries that supply the medulla oblongata, in addition to the perforating arteries and and the long circumferential artery. <sup>7</sup> Therefore, the mechanisms of the medullary infarctions may be distinct. However, few studies have addressed the mechanism of medullary infarctions. <sup>8</sup> We investigated the mechanisms of medullary infarctions, particularly those relative to the arterial territories

involved, in patients whose lesions were demonstrated on diffusion-weighted magnetic resonance imaging (DWI). We also investigated clinical features of medullary infarctions based on the arterial territory involved.

#### II. METHODS

#### 1. Enrolled patients

The patient pool for this study included consecutive patients with an infarction involving the medulla oblongata. They were registered to the Yonsei Stroke Registry (YSR) between February 1999 and April 2008. The YSR is a prospective hospital-based stroke registry for acute brain infarction or transient ischemic attack that occurs within 7 days after onset of symptoms. Patients were evaluated by medical history, neurologic examination, standard blood tests, brain imaging studies (CT and/or MRI), cerebral angiographic studies, and a 12-lead electrocardiogram. MRI was conducted by using a 1.5-Tesla system (Signa Horizon, GE Medical System, Milwaukee, WI or Intera or Achieva, Philips Medical System, the Netherlands) or 3.0-T system (Achieva, Philips Medical System, the Netherlands). A transesophageal echocardiography was performed except in those patients with poor cooperation due to decreased consciousness, impending brain herniation, poor systemic conditions, swallowing

difficulty, the lack of informed consent, or if the patient was intubated. 11

There were 182 patients (4.7% out of total 3833 patients with an acute stroke registered on the YSR) identified with infarctions involving the medulla oblongata during the study period. After excluding 32 patients that did not have diffusion-weighted MRI (DWI) and 8 patients that did not show the lesion on DWI, 142 patients with demonstrated lesions on DWI were enrolled in this study. Among the 142 patients, angiography was performed in 136 patients (95.8%). A digital subtraction angiography (DSA) was obtained in 54 (38.0%), while MR angiography was done in 82 (58.8%) of the patients. The degree of stenosis was measured based on the North American Symptomatic Carotid Endarterectomy Trial method, 12 or Warfarin vs. Aspirin for Symptomatic Intracranial Disease method. 13 This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System.

#### 2. Topography of lesion

The infarctions were categorized into four groups (anteromedial, anterolateral, lateral, and posterior) based on previously published templates for arterial territories (Fig. 1).<sup>6,7</sup> The lesions were further categorized into those involving the upper, middle, or lower medulla

oblongata. The upper medulla oblongata was defined as that area with massive bulging of the dorso-lateral area due to the restiform body, whereas the middle medulla oblongata was defined as that area with bulging of the lateral surface due to the inferior olive. Furthermore, the lower medulla oblongata was defined as that area characterized by a relatively round shape without bulging of the lateral surface.<sup>14</sup>

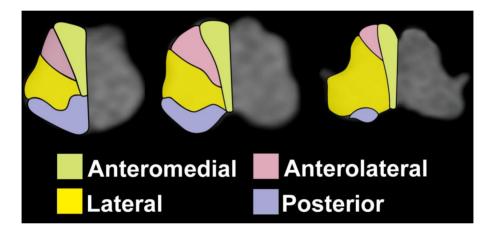


Fig. 1. Diagrams showing the arterial territory of the medulla oblongata

#### 3. Risk factors and etiologic classification of stroke

Hypertension was diagnosed, when a patient had high blood pressure recordings (systolic  $\geq$ 140 mm Hg or diastolic  $\geq$ 90 mm Hg) on repeated measurements during admission, or when the patient had been treated with any antihypertensive medication. Diabetes mellitus was diagnosed, when a patient had a high fasting plasma glucose level ( $\geq$ 7 mmol/L) or

had been treated with any oral hypoglycemic agents and/or insulin. Hypercholesterolemia was defined as a high lipid profile (fasting serum total cholesterol level ≥6.2 mmol/L or low-density lipoprotein cholesterol >4.1 mmol/L), or a history of treatment with lipid-lowering drugs after diagnosis of hypercholesterolemia. Current smokers were those who had smoked within the three months prior to admission. Etiologic mechanisms of stroke were determined by the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. <sup>15</sup> In this classification, vascular dissection, which was categorized into the subtype of stroke of other determined etiology, was determined only when typical imaging features such as 'double lumen', 'intimal flap', and 'pearl and string sign' were present. <sup>16, 17</sup>

#### 4. Statistical analysis

All statistical analyses were performed by using the Windows SPSS package (version 18.0, SPSS Inc, IL, Chicago, USA). Symptoms according to the arterial territory were compared using  $\chi^2$  test. We used the generalized estimating equation to analyze the etiologic mechanism of stroke, the difference of rostro-caudal distribution, and the difference of clinical features, because variables like the vascular territory or rostro-caudal distribution were allowed multiple checks.<sup>18</sup> The results of

the generalized estimating equation were expressed as estimated probability of event (EPE), which represents the average probability that is expected to occur corresponding to the observed responses. P-value < 0.05 was accepted as being statistically significant.

#### III. RESULTS

#### 1. Topography of lesion

The infarction in the medulla oblongata was unilateral in 139 patients and bilateral in 3 patients (two involved bilateral anteromedial territories, and the other involved bilateral anteromedial and anterolateral territories). The infarctions were isolated to the medulla oblongata in 87 patients. Co-existing infarctions outside of the medulla oblongata were present in the remaining 55 patients. There were 43 patients with concomitant lesions in the cerebellum. The involvement of the cerebellar hemisphere was seen in 42 (97.7%) patients and vermis infarction was seen in 29 (67.4%) patients. Cerebellar lesions involved the posterior inferior cerebellar artery (PICA) territory in all 43 (100%) patients. The anterior inferior cerebellar artery (AICA) territory was also involved in three (7.0%) patients, while the superior cerebellar artery (SCA) was involved in three (7.0%) patients.

Table 1. Topographical differences among vascular territories involved

	AM	AL	Lat	Post	AM + AL	Lat + Post	AL + Post	Total
Upper	14 (26.4)	1 (1.9)	22 (41.5)	1 (1.9)	15 (28.3)	0 (0.0)	0 (0.0)	53 (37.3)
Middle	4 (10.5)	0 (0.0)	24 (63.2)	2 (5.3)	2 (5.3)	5 (13.2)	1 (2.6)	38 (26.8)
Lower	2 (7.4)	0 (0.0)	17 (63.0)	6 (22.2)	0 (0.0)	2 (7.4)	0 (0.0)	27 (19.0)
Upper + Middle	2 (25.0)	0 (0.0)	5 (62.5)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	8 (5.6)
Middle + Lower	0 (0.0)	0 (0.0)	9 (69.2)	0 (0.0)	0 (0.0)	3 (23.1)	1 (7.7)	13 (9.2)
Upper + Middle + Lower	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	2 (66.7)	0 (0.0)	3 (2.1)
Total	22 (15.5)	1 (7.0)	78 (54.9)	9 (6.3)	17 (12.0)	13 (9.2)	2 (1.4)	142 (100.0)

AM: anteromedial, AL: anterolateral, Lat: lateral, Post: posterior.

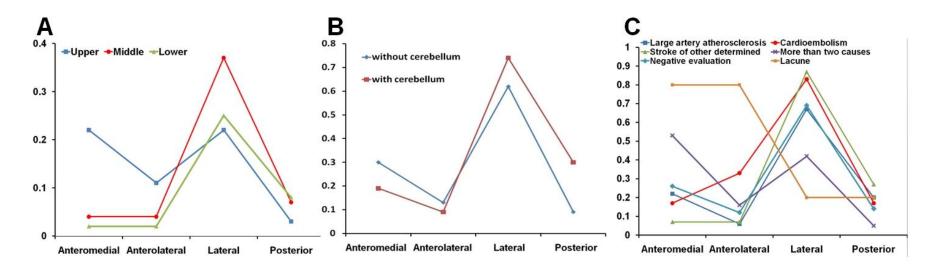
Numbers in parentheses are percentages. P-value was less than 0.001.

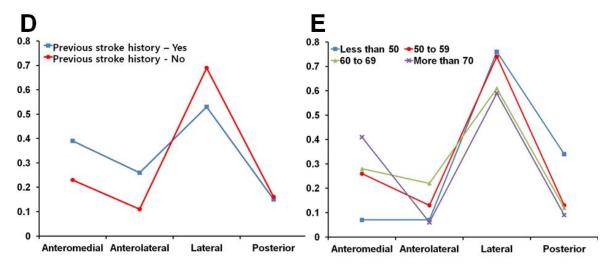
#### Fig. 2. Comparison between the groups based on generalized estimating equations analysis.

Each graph represents comparisons between the arterial territory and rostro-caudal topographical involvements (A), cerebellar involvements (B), stroke mechanisms (C), previous stroke history (D), and ages (E).

Y-axis is the estimated probability of event, which is the average predicted probability corresponding to the observed responses.

P-values were <0.001 (A), 0.043 (B), <0.001 (C), 0.003 (D), and 0.005 (E).





Among the involved vascular territories, lesions of the lateral territory were most common, followed by the anteromedial and the anteromedial plus anterolateral territories (Table 1). When we counted any vascular territory involved, involvement of the lateral territory (N=93) was most common, followed by the anteromedial (N=39), and the posterior territories (N=22). The involved vascular territories were different between the rostro-caudal topographical locations of the infarction (Table 1, p<0.001). In the upper medulla, lesions involving the anteromedial or lateral territory (EPE 0.22, each) were frequent, while those of the posterior territory (EPE 0.03) were rare. However, lesions involving the lateral territory were seen predominantly in the middle and lower medulla (EPE 0.37 and 0.25, respectively) (Fig. 2A). Those patients with co-existing cerebellar involvements showed different arterial territory involvement in the medulla oblongata. The posterior territory involvement was more common in patients with co-existing cerebellar lesions (EPE 0.30) than in those without (EPE 0.09) (Fig. 2B, p=0.043). There were 13 patients who had lesions of the posterior territory with concomitant cerebellar involvement. All of them had lesions of the cerebellum involving the PICA territory. Nine of them had vertebral artery stenosis and the remaining four had stenosis of the PICA.

#### 2. Etiology of infarction

Among stroke subtypes, large artery atherosclerosis (LAA) was most common (34.5%), whereas lacunae and cardioembolism were rare or uncommon (3.5% and 4.2%, respectively). Stroke of other determined etiologies comprised 10.6% of medullary infarctions, which included vertebral artery dissection in 13 patients (9.2%), and anti-phospholipid antibody syndrome in two patients (1.4%). The mechanism of infarction was significantly different among vascular territories (Table 2, p<0.001). LAA was common in the lateral, anteromedial, and posterior territories (EPE 0.67, 0.22 and 0.2, respectively). None of the cardioembolism or other etiologies involved anteromedial or anterolateral territory, but all involved the lateral and/or posterior territories. Lacunar infarction was only found in the anteromedial and the anterolateral territory (Table 2). The mechanism was neither different in groups categorized

according to rostro-caudal topography of the lesions (p=0.499) nor between patients with co-existing cerebellar lesions and those without (p=0.201). However, among the patients with vertebral artery dissection, only one had a lesion in the upper medulla, while the other patients had lesions in the middle or lower medulla (upper: middle: lower = 1:9:4, three of four patients with lesions of the lower medulla also had lesions of the middle medulla).

#### 3. Arterial lesions

The lesion of the vertebral artery was found in 95 patients (73.6%) of all the patients with medullary infarction. Occlusion of the vertebral artery was seen in 36 patients (25.4%), and significant stenosis (≥50%) was found in 38 patients (26.8%). Thirteen patients (10.1%) had lesions of the PICA. The frequency of the vertebral arterial lesions was not different among vascular territories (p=0.547). There were eight patients with lesions involving the anteromedial territory and they also had lesions involving the cerebellum. All of them demonstrated infarctions in the PICA territory of the cerebellum, and three of them showed additional lesions in the SCA territory. All but one patient (the remaining one patient did not undergo an angiographic study) showed atherosclerotic lesions of the vertebral artery, and the stenosis was significant in five of them, which suggests that arterial embolism might be the probable mechanism.

#### 4. Demographic characteristics

Among the 142 patients, there were 107 (75.4%) men. Median age of onset was 63 years (range 33-83). The most common risk factor was hypertension, followed by smoking, and diabetes mellitus (Table 3). Among 35 patients with a previous ischemic stroke, 14 (46.7%) had strokes in the territory of the posterior circulation. Twenty patients (14.1%) had potential cardiac sources of embolism, which included atrial fibrillation (11 patients), atrial flutter (1 patient), valvular heart disease (1 patient), and a patent foramen ovale (7 patients). When we compared demographic factors according to the vascular territories, age and previous history of stroke

**Table 2.** Etiologic mechanisms of medullary infarction

	AM	AL	Lat	Post	AM+ AL	Lat+ Post	AL+ Lat	Total
LAA	9 (18.4)	0 (0.0)	27 (55.1)	5 (10.2)	2 (4.1)	5 (10.2)	1 (2.0)	49 (34.5)
Cardioembolism	0 (0.0)	0 (0.0)	5 (83.3)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	6 (4.2)
SOD	0 (0.0)	0 (0.0)	11 (73.3)	2 (13.3)	0 (0.0)	2 (13.3)	0 (0.0)	15 (10.6)
SUD								
More than two causes	7 (38.9)	1 (5.6)	8 (44.4)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)	18 (12.7)
Negative evaluation or incomplete evaluation	6 12.2)	0 (0.0)	27 (55.1)	2 (4.1)	8 (16.3)	5 (10.2)	1 (2.0)	49 (34.5)
Lacunae	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (100.0)	0 (0.0)	0 (0.0)	5 (3.5)
Total	22 (15.5)	1 (7.0)	78 (54.9)	9 (6.3)	17 (12.0)	13 (9.2)	2 (1.4)	142 (100.0)

AM: anteromedial, AL: anterolateral, Lat: lateral, Post: posterior, LAA: large artery atherosclerosis,

SOD: stroke of other determined etiology, SUD: stroke of undetermined etiology.

Numbers in parentheses are percentages. P-value was less than 0.001.

Table 3. Demographic characteristics according to arterial territories involved

	AM	AL	Lat	Post	AM + AL	Lat + Post	AL + Lat	Total	P-value
Hypertension	18 (17.1)	0 (0.0)	58 (55.2)	4 (3.8)	14 (13.3)	9 (8.6)	2 (1.9)	105 (71.9)	0.175
Diabetes mellitus	12 (18.8)	0 (0.0)	31 (48.4)	2 (3.1)	11 (17.2)	6 (9.4)	2 (3.1)	64 (45.1)	0.469
Smoking history	13 (59.1)	0 (0.0)	42 (57.5)	3 (4.1)	5 (6.8)	8 (11.0)	2 (2.7)	73 (51.4)	0.846
Hypercholesterolemia	2 (10.0)	0 (0.0)	11 (55.0)	1 (5.0)	3 (15.0)	2 (10.0)	1 (5.0)	20 (14.1)	0.625
Previous stroke history	7 (20.0)	0 (0.0)	15 (42.9)	2 (5.7)	7 (20.0)	3 (8.6)	1 (2.9)	35 (24.7)	0.003
PCSE	4 (20.0)	0 (0.0)	12 (60.0)	0 (0.0)	4 (20.0)	0 (0.0)	0 (0.0)	20 (14.1)	0.174
Age	69.5±6.8	64.0±0.0	60.6±12.6	52.0±9.1	63.5±10.2	56.5±11.8	61.5±11.9	142 (100)	0.005

AM: anteromedial, AL: anterolateral, Lat: lateral, Post: posterior, PCSE: Potential cardiac sources of embolism.

Numbers in parentheses are percentages

were significantly different among vascular territories (Table 3). A previous history of stroke was more frequent in patients with lesions in the anteromedial or anterolateral area (Fig. 2D). Patients that had a lesion in the lateral or posterior territory were younger (EPE 0.76 and 0.34, respectively) than patients that had lesion in the anteromedial or the anterolateral territory (EPE 0.07, each) (Fig. 2E).

#### 5. Clinical features

Of the 87 patients who had infarction only involving the medulla oblongata, a single arterial territory was involved in 73 patients. None had an isolated infarction of the anterolateral territory. We accessed clinical features in those 73 patients (Table 4). Body sway, dysphagia, facial sensory change, and body sensory change were frequent in the lateral territory, and all patients with sympathetic dysfunction showed a lesion in the lateral territory. Limb weakness was frequent in the anteromedial territory. Body sway was a predominant symptom of a lesion involving the posterior territory. Tongue deviation was observed infrequently (5 patients, 6.8%; ipsilateral in 3 and contralateral in 2), and all patients had a lesion in the lateral territory. Two patients with contralateral tongue deviation had their lesions in the upper medulla oblongata.

#### IV. DISCUSSION

The present study showed several topographical characteristics of medullary infarctions. Bilateral involvement of the medulla oblongata was rare, and none of patients with infarctions in the lateral or posterior territory showed any bilateral lesions. Furthermore, concomitant involvement of the medial medulla (anteromedial and anterolateral territories) and the lateral or posterior medulla was seen in only 2 patients (anterolateral and lateral territories). These topographical characteristics may be explained by the arterial system supplying the medulla oblongata. Most parts of the medulla oblongata are supplied by paired arteries (vertebral, PICA, ASA and PSA), which may prevent bilateral infarctions. The origins of the arteries supplying the medial medulla (usually ASA) are far from those supplying in the lateral medulla (usually

**Table 4.** Symptoms and signs according to involved arterial territories in 73 patients with a lesion in the single arterial territory

	AM	AL	Lat	Post	Total	P-value
Body sway	7 (13.0)	0 (0.0)	41 (75.9)	6 (11.1)	54 (74.0)	0.037
Dysphagia	2 (7.4)	0 (0.0)	25 (92.6)	0 (0.0)	27 (37.0)	0.011
Sympathetic dysfunction	0 (0.0)	0 (0.0)	21 (100.0)	0 (0.0)	21 (28.8)	0.004
Body sensory change	5 (13.2)	0 (0.0)	33 (86.8)	0 (0.0)	38 (52.1)	0.001
Facial sensory change	2 (6.5)	0 (0.0)	28 (90.3)	1 (3.2)	31 (42.5)	0.014
Arm weakness	8 (72.7)	0 (0.0)	3 (27.3)	0 (0.0)	11 (15.1)	< 0.001
Leg weakness	7 (53.8)	0 (0.0)	6 (46.2)	0 (0.0)	13 (17.8)	0.002
Tongue deviation	0 (0.0)	0 (0.0)	5 (83.3)	0 (0.0)	5 (6.8)	0.208

AM: anteromedial, AL: anterolateral, Lat: lateral, Post: posterior.

Numbers in parentheses are percentages

#### PICA).

The involvement patterns were also different among the upper, middle, and lower medulla oblongata. The anteromedial territory involvement was predominantly seen in the upper medulla, whereas posterior territory involvement was more frequent in the middle or lower medulla. These differences may also be ascribed to the different supplying arteries between upper and middle-lower medulla. The paired anterior spinal arteries, which originate from the vertebral artery, supply the upper medulla, and then merge into a single artery, which supplies the middle-lower medulla. Therefore, occlusion of the anterior spinal artery, before the merge, may not produce infarction in the middle and lower medulla. The higher frequency of the posterior territory involvement in the middle and lower medulla may be associated with the increasing area of the posterior territory in the middle and lower medulla, when comparing with the upper medulla.

In our study, large artery atherosclerosis was the most common etiology of medullary infarctions. Cardioembolism and stroke of other determined etiology developed infarctions only in the lateral and posterior territories. The lateral territory is supplied by the PICA or the vertebral artery. The posterior territory of the medulla oblongata is usually supplied by the posterior spinal artery, which usually originates from the vertebral artery. The posterior spinal artery originates from the PICA in cases where the PICA is originated extradurally from the vertebral artery. 19 Most of the patients with stroke of other determined etiology had vertebral artery dissection. Concomitant cerebellar involvement was more frequent in patients with a lesion in the posterior territory, and most of them had atherosclerotic lesion of the proximal relevant artery. These findings suggest that emboli from the heart or the proximal arterial lesion produce infarctions more commonly in the territories supplied by the posterior spinal artery and long circumferential arteries. Lacunar infarction was an infrequent mechanism in patients with medullary infarctions, and all patients with lacunar infarctions involved the anteromedial and anterolateral territories in our study. The most common mechanism of medial medullary infarction was small vessel occlusion in a recent study, <sup>20</sup> which is consistent with our findings. Lacunae usually accounts for about 20-25% of stroke patients. 9, 21-23 Infrequent lacunae in medullary infarctions may be because of the large areas of the medulla oblongata that are supplied by the PICA, anterior spinal, and posterior spinal arteries rather than perforating arteries from the vertebral artery. Infrequent classic lacunar syndrome in lateral or posterior territory involvement, which is a prerequisite for diagnosis of a subtype of lacune in the TOAST classification, might also contribute to the low frequency of lacune in the medullary infarction.

We compared the clinical symptoms and signs according to the four vascular territories involved, while most previous clinico-topographical correlation studies were based on a dichotomized category of medial and lateral medullary infarctions. Clinical findings based on the arterial territory involved correlated well with the signs produced by dysfunction of anatomical structures in the corresponding arterial territory. Tongue deviation was rarely seen in

our patients as it was reported.<sup>8</sup> All patients with contralateral tongue paralysis had lesions in the upper medulla oblongata, which suggests involvement of the corticobulbar tract before its decussation.<sup>24</sup> However, all patients with tongue paralysis had lesions in the lateral territory. This finding was unexpected because tongue paralysis is known to be a symptom of medial medullary infarction.<sup>25, 26</sup> The typical location of the hypoglossal nucleus is in the anteromedial territory near the border between the anteromedial and lateral territory in the dorsal portion of the medulla oblongata.<sup>6</sup> Infarctions involving the anteromedial territory are usually located in the ventral portion of the medulla oblongata and they do not extend to the dorsal medulla oblongata. Therefore, the hypoglossal nucleus is seldom affected by the anteromedial territory infarctions. In addition, there are variations and overlaps between the arterial territories. These anatomical characteristics and infarct patterns in the medulla oblongata may be responsible for infrequent occurrence of tongue paralysis in the lateral territory.

Our study has several limitations. First, arterial lesions were determined based on MRA, which is prone to flow-relative artifacts, in about 60%. Second, the presence of clinical features was based on retrospective review of medical records. Therefore, their frequencies in each arterial territory may be somewhat different from those that were determined in a prospective design. Finally, although all patients with tongue paralysis in our study had a lesion in the lateral territory, the number of patients with tongue paralysis was small. Further studies on this issue may be necessary to confirm our findings.

#### REFERENCES

- 1. Sacco RL, Freddo L, Bello JA, Odel JG, Onesti ST, Mohr JP. Wallenberg's lateral medullary syndrome. Clinical-magnetic resonance imaging correlations. Arch Neurol 1993;50:609-14.
- 2. Kim JS, Lee JH, Choi CG. Patterns of lateral medullary infarction: vascular lesion-magnetic resonance imaging correlation of 34 cases. Stroke 1998;29:645-52.
- 3. Kim JS, Choi-Kwon S. Sensory sequelae of medullary infarction: differences between lateral and medial medullary syndrome. Stroke 1999;30:2697-703.
- 4. Kwon M, Lee JH, Kim JS. Dysphagia in unilateral medullary infarction: lateral vs medial lesions. Neurology 2005;65:714-8.
- 5. Kim JS. Pure lateral medullary infarction: clinical-radiological correlation of 130 acute, consecutive patients. Brain 2003;126:1864-72.
- 6. Duvernoy HM. Human brainstem vessels. Springer, 1999.
- 7. Tatu L, Moulin T, Bogousslavsky J, Duvernoy H. Arterial territories of human brain: brainstem and cerebellum. Neurology 1996;47:1125-35.
- 8. Kim JS, Han YS. Medial medullary infarction: clinical, imaging, and outcome study in 86 consecutive patients. Stroke 2009;40:3221-5.
- 9. Lee BI, Nam HS, Heo JH, Kim DI. Yonsei Stroke Registry. Analysis of 1,000 patients with acute cerebral infarctions. Cerebrovasc Dis 2001;12:145-51.
- 10. Kim YD, Choi HY, Jung YH, Nam CM, Yang JH, Cho HJ, et al. Classic risk factors for atherosclerosis are not major determinants for location of extracranial or intracranial cerebral atherosclerosis. Neuroepidemiology 2009;32:201-7.
- 11. Cho HJ, Choi HY, Kim YD, Nam HS, Han SW, Ha JW, et al. Transoesophageal echocardiography in patients with acute stroke with sinus rhythm and no cardiac disease history.
  J Neurol Neurosurg Psychiatry 2010;81:412-5.
- 12. Chaturvedi S. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1991;325:445-53.

- 13. Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Trial Investigators. Design, progress and challenges of a double-blind trial of warfarin versus aspirin for symptomatic intracranial arterial stenosis. Neuroepidemiology 2003;22:106-17.
- 14. Kim JS, Lee JH, Suh DC, Lee MC. Spectrum of lateral medullary syndrome. Correlation between clinical findings and magnetic resonance imaging in 33 subjects. Stroke 1994:25:1405-10.
- 15. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993;24:35-41.
- 16. Yonas H, Agamanolis D, Takaoka Y, White RJ. Dissecting intracranial aneurysms. Surg Neurol 1977;8:407-15.
- 17. Yamaura A, Watanabe Y, Saeki N. Dissecting aneurysms of the intracranial vertebral artery. J Neurosurg 1990;72:183-8.
- 18. Hanley JA, Negassa A, Edwardes MD, Forrester JE. Statistical analysis of correlated data using generalized estimating equations: an orientation. Am J Epidemiol 2003;157:364-75.
- 19. Seckin H, Ates O, Bauer AM, Baskaya MK. Microsurgical anatomy of the posterior spinal artery via a far-lateral transcondylar approach. J Neurosurg Spine 2009;10:228-33.
- 20. Shono Y, Koga M, Toyoda K, Matsuoka H, Yokota C, Uehara T, et al. Medial medullary infarction identified by diffusion-weighted magnetic resonance imaging. Cerebrovasc Dis 2010;30:519-24.
- 21. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoerfer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. Stroke 2001;32:2735-40.
- 22. Han SW, Kim SH, Lee JY, Chu CK, Yang JH, Shin HY, et al. A new subtype classification of ischemic stroke based on treatment and etiologic mechanism. Eur Neurol 2007;57:96-102.
- 23. Bejot Y, Caillier M, Ben Salem D, Couvreur G, Rouaud O, Osseby GV, et al. Ischaemic

stroke subtypes and associated risk factors: a French population based study. J Neurol Neurosurg Psychiatry 2008;79:1344-8.

- 24. Urban PP, Hopf HC, Connemann B, Hundemer HP, Koehler J. The course of cortico-hypoglossal projections in the human brainstem. Functional testing using transcranial magnetic stimulation. Brain 1996;119 ( Pt 3):1031-38.
- 25. Kameda W, Kawanami T, Kurita K, Daimon M, Kayama T, Hosoya T, et al. Lateral and medial medullary infarction: a comparative analysis of 214 patients. Stroke 2004;35:694-9.
- 26. Kumral E, Afsar N, Kirbas D, Balkir K, Ozdemirkiran T. Spectrum of medial medullary infarction: clinical and magnetic resonance imaging findings. J Neurol 2002;249:85-93.

#### ABSTRACT(IN KOREAN)

숨뇌경색에서 침범된 혈관의 분포영역에 따른 기전의 차이

<지도교수 허지회>

연세대학교 대학원 의학과

#### 김경섭

숨뇌의 혈액공급은 일반적으로 뇌간의 다른 부위와는 다르기 때문에, 혈액을 공급하는 동맥에 따라서 발생하는 숨뇌경색의 기전에 차이가 있을 수 있다. 하지만 이에 대한 선행연구는 거의 없는 형편이다. 이 연구에서 우리는 1999년 2월에서 2008년 4월까지 stroke registry에 등록된 뇌경색환자 3833명중에서 확산강조영상에서 숨뇌경색으로 확인된 환자들을 대상으로 하였으며, 병변의 위치, 침범된 혈관의 분포영역 및 병인론적인 기전 등에 대하여 분석하였다. 총 142명이 대상이 되었으며, 이 중 양측숨뇌경색은 드물었다 (2.2%). 전내측 혹은 가측 영역을 침범한 병변이 상부숨뇌에서 가장 흔한 반면에 중부 및 하부숨뇌에서는 가측 영역을 침범한 병변이 가장 흔했다. 뇌경색의 기전 중에는 large artery sclerosis가 가장 흔했으며 (34.5%) lacune 및 cardioembolism은 드물었다(3.5%, 4.2%). 척추동맥의 의미있는 협착증 (50%이상) 혹은 혈관폐색이 흔히 관찰되었으며 (52.2%), 척추동맥박리는 비교적 흔히 관찰되었다. 뇌경색의 기전은 침범된 혈관의 분포영역에 따라 차이가 있었는데, large artery sclerosis의 경우 주로 가측, 전내측 및 후측 영역에 병변이 관찰되는 반면, cardioembolism 및 other etiology의 경우 전내측 및 전외측에는 병변이 관찰되지 않고 모두 가측 혹은 후측 영역에만 병변이 관찰되었으며,lacune은 오로지 전내측 및 전외측 영역에서만 관찰되었다. 따라서 우리는 본 연구를 통하여 숨뇌경색의 기전 및 병변의 위치는 침범된 혈관의 분포영역에 따라 차이가 있음을 확인하였으며, 이러한 결과는 독특한 숨뇌의 혈액공급방식에 의한 것으로 판단된다.

### PUBLICATION LIST

1. Kim KS, Lee HS, Jung YH, Kim YD, Nam HS, Kim SM, Heo JH Mechanism of Medullary Infarction Based on Arterial Territory Involvement. J Clin Neurol. 2011; accepted.