INTRODUCTION

Wallenberg syndrome (WS) is caused by dorsal lateral medullary infarction (LMI) that results from occlusion of the vertebral artery or posterior inferior cerebellar artery (PICA). Clinical symptoms of WS include hoarseness, dysphagia, sensory disturbance, vertigo, ataxia, and Horner’s syndrome. Recently, the lateral difference in body surface temperature (BST) has been reported as a symptom of WS, resulting from disturbances of the sympathetic nerve pathway. We have previously reported the laterality of skin temperature depending on sensory symptoms in patients with WS. Our study showed that patients with sensory dysfunction in WS had lateral BST differences, which were detected by infrared thermography. We presumed that the laterality of BST and sensory dysfunction in patients with WS may be associated with the disturb
Min et al. Laterality of Skin Temperature in Wallenberg Syndrome

SUBJECTS AND METHODS

The methods of this study have been published in a previous study. In brief, patients were eligible if they were ≥20 years old and had their first LMI within 7 days of symptom onset. Patients with recurrent cerebral infarction, ankle-bracing index <0.9, or abnormal autonomic function tests were excluded from this study.

The patients’ accompanying vascular risk factors, laboratory tests, BST, and brain MRI were assessed at admission. BST was measured using an infrared thermal camera (SMART T-1000; MESH Co, Wonju, Korea) at 7±3 days and 90±30 days after the onset of symptoms (Fig. 1). The BST in this study was not a true skin surface temperature but a noncontact temperature for lateral comparison. BST was analyzed at four locations (the nasolabial fold on the face, 5 cm above the umbilicus, and anterior forearm and shin) bilaterally. Laterality was defined as significant when the BST was macroscopically different, and the discrepancy was more than 0.5°C between the right and left sides. An experienced researcher performed all BST measurements, and throughout the trial, the researcher was blinded to the clinical symptoms of the patients.

Three neurologists blinded to the thermography results classified the patients’ MRI findings according to the well-known LMI classification system (Fig. 2). Briefly, the lesions were categorized as rostral, middle, and caudal medulla rostrocaudally and typical, ventral, large, dorsal, and lateral type horizontally. In the case of disagreement in classifying a medullary lesion by the raters, a category that was agreed upon by two of the three raters was considered as the final classification for the analyses.

1. Statistical analyses

Descriptive data are expressed as numbers (%) or means±standard deviations. Categorical data between groups were compared using chi-square and Fisher exact tests. The Mann-Whitney U test was used to compare non-normally distributed data, and Student’s
t-test was used to compare normally distributed data. Two-sided null hypotheses of no difference were rejected if p-values were lower than 0.05. Statistical analyses were performed using SPSS version 25.0 for Windows (IBM Co., Armonk, NY, USA).

RESULTS

A total of 1,005 patients who had experienced first-ever ischemic stroke between June 2018 and November 2020 were screened. During the trial, 16 patients had WS, of which four refused to participate in the study. The final analyses included 12 patients with WS (10 patients with pure LMI and two patients with concomitant PICA territorial cerebellar infarction). The baseline characteristics of the patients are as follows. There were 10 males and two females, aged 43 to 81 (mean 59.9±11.9) years. Fifty percent of the patients had a history of hypertension, 42.0% had diabetes, 33.0% had dyslipidemia, 8.0% had coronary artery disease, and 23.0% were current cigarette smokers. There were no differences in age or sex in the presence of lateral BST differences. The most frequent stroke subtype was a stroke of undetermined etiology, negative workup (41.6%), followed by cardioembolism (16.7%), lacunes (16.7%), vertebral artery dissections (16.7%), and large artery atherosclerosis (8.3%).

Tables 1, 2 show the results of the infrared thermography. The median time from symptom onset to conducting thermographic scanning was 8 days (5-10 days) and 93 days (63-115 days), respectively. In the 7-day study, the laterality of BST was not detected in patients without sensory symptoms. In contrast, all patients with sensory symptoms showed laterality of BST (three patients with right side lesion in Table 1, five patients with left side lesion in Table 2). Of these, six patients showed lateralized BST at multiple sites (face, body, upper limb, or lower limb) and warmer ipsilateral to the infarction. Laterality was more common in the upper limb (88.0%), lower limb (63.0%), body (63.0%), and face (13.0%). Two patients showed laterality of BST only in the upper or lower limb only. Follow-up thermography at 90 days was performed in eight patients. Five patients had residual sensory symptoms and lateralized BST. Laterality was also common in the upper or lower limb (60.0%) and body (40.0%), and warmer ipsilateral to the infarction. Lateralized BST was not observed in three patients with no sensory symptoms, suggesting that residual sensory symptoms were related to the laterality of BST.

Brain MRI and diffusion-weighted imaging were performed in all patients. MRI revealed that the medullary lesions were on the right in five patients and on the left in seven patients. In this study, the lesions were categorized rostrocaudally and horizontally according to the LMI classification system. In the right LMI group, one patient with no lateralized BST (Fig. 3A), had a small caudal medullar infarction (caudal medulla-lateral type) and patients with lateralized BST had a larger middle medullary infarction (middle medulla-typical in Fig. 3B-D and large type in Fig. 3E). In the left LMI group, two patients with no lateralized BST showed a caudal medulla-lateral type (Fig. 4A) or a middle medulla-dorsal type (Fig. 4B) infarction. Four patients with lateralized BST showed middle medulla-typical (Fig. 4C) or...
### Table 1. Patients’ thermography results in patients with right side lesion

<table>
<thead>
<tr>
<th>No.</th>
<th>Sensory Sx.</th>
<th>7 days (°C)</th>
<th>90 days (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Face</td>
<td>Body</td>
</tr>
<tr>
<td>1</td>
<td>-</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Lt. numbness</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>Lt. burning</td>
<td>27.1</td>
<td>26.9</td>
</tr>
<tr>
<td>4</td>
<td>Lt. burning</td>
<td>28.2</td>
<td>27.8</td>
</tr>
<tr>
<td>5</td>
<td>Lt. cold</td>
<td>27.5</td>
<td>27.2</td>
</tr>
</tbody>
</table>

**Sx.**: symptom, **Rt.**: right, **Lt.**: left, **N/A**: not available.

*It shows the presence of lateral differences (>0.5°C) and the warmer side of body surface temperature.*

### Table 2. Patients’ thermography results in patients with left side lesion

<table>
<thead>
<tr>
<th>No.</th>
<th>Sensory Sx.</th>
<th>7 days (°C)</th>
<th>90 days (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Face</td>
<td>Body</td>
</tr>
<tr>
<td>1</td>
<td>-</td>
<td>26.1</td>
<td>25.8</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>27.7</td>
<td>27.3</td>
</tr>
<tr>
<td>3</td>
<td>Lt. numbness</td>
<td>26.5</td>
<td>26.3</td>
</tr>
<tr>
<td>4</td>
<td>Rt. heaviness</td>
<td>29.4</td>
<td>29.6</td>
</tr>
<tr>
<td>5</td>
<td>Rt. cold</td>
<td>26.6</td>
<td>26.9</td>
</tr>
<tr>
<td>6</td>
<td>Rt. cold</td>
<td>26.9</td>
<td>26.6</td>
</tr>
<tr>
<td>7</td>
<td>Rt. cold</td>
<td>24.6</td>
<td>25.3</td>
</tr>
</tbody>
</table>

**Sx.**: symptom, **Rt.**: right, **Lt.**: left, **N/A**: not available.

*It shows the presence of lateral differences (>0.5°C) and the warmer side of body surface temperature.*
FIG. 3. Brain magnetic resonance imaging findings of the right lateral medullary infarction (LMI). (A) One patient with no lateralized body surface temperature (BST) shows a small caudal medullar infarction (caudal medulla-lateral type) and patients with lateralized BST have a larger middle medullary infarction (middle medulla-typical in [B-D] and large type in [E]).
FIG. 4. Brain magnetic resonance imaging findings of the left lateral medullary infarction. Two patients with no lateralized body surface temperature (BST) show (A) a caudal medulla-lateral type or (B) a middle medulla-dorsal type infarction. Four patients with lateralized BST have (C) middle medulla-typical or (D–F) large type infarction. One patient with lateralized BST reveals (G) a rostral medullary infarction.
large type (Fig. 4D-F) infarction. One patient with lateralli-
zed BST showed a rostral medullary infarction (Fig.
4G). Taken together, two patients without lateralized
BST had a lateral caudal medullary infarction, and one
patient had a dorsal middle medullary infarction. One
patient with lateralized BST had a rostral medullary
infarction and the other had a typical or large middle
medulla infarction.

DISCUSSION

This study explored the relationship between the
laterality of BST and brain MRI findings in 12 patients
with WS. Our study showed that while patients without
lateralized BST had caudal medulla-lateral type or mid-
dle medulla-dorsal type LMI, all patients with lateral-
ized BST had a middle medulla-typical or large type, or
rostral medullary infarction.

The hypothalamus, which receives information from
cutaneous and internal thermoreceptors and sends
efferent signals to thermoregulatory effector organs,
plays a key role in controlling body temperature.8 In the
brain stem medulla, the medullary raphe and RVLM
are important structures in controlling cutaneous vaso-
motor activity for thermoregulation.9,10 The medullary
raphe contains a narrow sheet of cells in the midline
of the medulla that extends caudally from a level to
the rostral pole of the facial nucleus to the level of the
pyramidal decussation.11 It has sympathetic premotor
neurons that connect to the central neural pathway
intermediate thermoregulatory signals to sympathetic
preganglionic neurons controlling cutaneous sympa-
thetic vasoconstrictor nerves.9,10 The RVLM has sympa-
thetic premotor neurons for influencing the thermo-
regulatory control of cutaneous vasomotor activity and
the blood pressure.9 Based on anatomical knowledge,
the most plausible explanation for lateralized BST in
patients with WS may be the disturbance of the sympa-
thetic nervous system pathway descending from the
RVLM. Deficits in sweating and skin blood flow may
cause BST laterality.

The strengths of this study were that it prospectively
recruited consecutive patients with WS. Unlike tradi-
tional retrospective studies, this method can eliminate
selection bias. Thermographic scan was performed at
the same time points in all patients. As the laterality
of BST decreased with residual sensory symptoms and
time,5,12 this study could provide more clinically im-
portant information.

Our study had several limitations. Although our study
demonstrated that all patients with sensory symptoms
showed lateralized BST, we were unable to conclude
whether the BST decreased contralateral to the LMI or
increased ipsilateral to the LMI. It has been known that
vasomotor autonomic dysregulation is associated with
asymmetric BST in stroke patients; however, the results
of previous studies are conflicting, with some reporting
increased and others decreased BST in contralateral
to the infarction.8,13,14 It may be related that most of
these studies are performed in a small population, and
no prospective investigations were conducted. Recent
studies have consistently shown a marked decreased
in BST contralateral to cerebral infarction.8 This phe-
nomenon is related to the paretic limbs in hemispheric
infarction and to the presence of the LMI in brain stem
infarction. However, one study suggests that the cause
of lateralized BST in patients with WS is a disruption
of the connecting pathway of sweating and skin blood
flow descending from the lateral brainstem, including
the ventrolateral medulla.5 Disrupted sweating and va-
soconstrictive function are likely to increase the BST
in the ipsilateral to the infarction in patients with WS.
Another study showed that lateralized BST in patients
with WS is probably caused by damage to the medullary
vasomotor centers.5 They reported that the ipsilateral
side of the face is warmer and hypohidrosis compared
with the other side in patients with LMI and Horn-
er’s syndrome. Considering the pathway and function
of the sympathetic nervous system in the brainstem
medullar, our study suggests that BST may be increased
ipsilateral to the infarction, especially in patients with
WS. Further studies are warranted to determine wheth-
er the lesion side BST decreased or increased with
cerebral hemispheric and brainstem infarction. Due to
the rarity of LMI, only a small number of patients were
recruited during the study period. We were unable to
evaluate the clinical factors associated with lateralized
BST. These limitations should be considered when in-
terpreting the data.

In conclusion, this study showed that lateralized BST
in patients with WS may be associated with disturban-

http://www.j-nn.org 53
J Neurosonol Neuroimag 2021;13(2):47-54
es in the sympathetic nervous pathway that descends from the RVLM. These results support the assumption that autonomic dysfunction may be related to abnormal sensory symptoms in patients with WS.

**Ethics Statement**
Written informed consent was obtained from all participants before enrollment in the study. This study was approved by the Clinical Trial Review Committee of Inje University Sanggye Paik Hospital (Approval No. SGPAIK 2018-01-002) and conducted in accordance with the Good Clinical Practice guidelines and the Declaration of Helsinki.

**Availability of Data and Material**
The data that support the findings of this study are available from HJY but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of HJY.

**Acknowledgments**
None.

**Sources of Funding**
None.

**Conflicts of Interest**
No potential conflicts of interest relevant to this article were reported.

**REFERENCES**


