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Cross-sectional area reference values for high-resolution ultrasonography of the lower extremity nerves in healthy Korean adults

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Abstract

The cross-sectional area (CSA) reference values of the lower extremity nerves in Asians have been rarely reported. For this study, 107 sex- and age-matched, healthy subjects with a mean age of 46 years (range, 24–75 years) were recruited. All subjects underwent standardized nerve conduction studies of the upper and lower extremities. The CSA was measured unilaterally at 12 sites in the lower extremity nerves, including the femoral, lateral femoral cutaneous, sciatic, common peroneal, superficial peroneal, deep peroneal, tibial, and sural nerves. The CSA significantly correlated with height, weight, and body mass index. The CSA was significantly larger in males than females at most nerves except for the lateral femoral cutaneous, common peroneal (fibular head), and superficial peroneal nerves (distal calf). There was no statistically significant difference between the age groups except for the tibial nerve (ankle). The results of this study provide CSA reference values for the lower extremity nerves including small branches and the values can be useful in the ultrasonographic investigation of various peripheral neuropathies in East Asian populations.

Abbreviations: ASIS = anterior superior iliac spine, BMI = body mass index, CSA = cross-sectional area, FH = fibular head, HRUS = high-resolution ultrasonography, LFCN = lateral femoral cutaneous nerve, NCS = nerve conduction study, PF = popliteal fossa, SD = standard deviation.

Keywords: cross-sectional area, lower extremity, peripheral nerves, reference values, ultrasonography

1. Introduction

Since Fornage[1] presented the first report on peripheral nerves using ultrasonography in 1988, ultrasound technology has developed rapidly, including the availability of high-frequency transducers. When used in association with electrodiagnostic testing, high-resolution ultrasonography (HRUS) has allowed physicians to increase the yield of clinical diagnoses of peripheral nerve disorders.[2] Pathology of the peripheral nervous system typically results in a nerve enlargement, which can be imaged with ultrasound to increase the cross-sectional area (CSA), and CSA is the most valuable and reliable ultrasonographic parameter.[3–5] HRUS provides a reliable diagnosis for entrapment neuropathies, traumatic peripheral nerve injuries, and tumors of the peripheral nerves.[6–10] As the utility of HRUS is further expanding to various peripheral neuropathies such as hereditary or acquired polyneuropathies,[11–15] the importance of the reference value of CSA, which is critical to the identification of nerve pathology and proper diagnosis, is increasing.[4,5] CSA reference values for the lower extremity nerves were reported in several studies.[4,5,16–23] However, investigations of CSA reference values for the lower extremity nerves in Asians remain more insufficient than those of the upper extremity nerves.[5,16–18]

Therefore, the aim of this study was to establish normal CSA reference values for multiple nerves in the lower extremities, including pure sensory branches, in healthy Korean adults, and to analyze the correlation between demographic characteristics and our CSA reference values.

2. Methods

Participants: The study protocol was approved by our Institutional Review Board, and all participants signed informed consent. Based on history-taking, physical examinations, and nerve conduction studies (NCSs), the subjects with a history of any neurological disorders or symptoms or signs associated with peripheral nerve disease were excluded from the study. NCSs were unilaterally performed on the median, ulnar, tibial, peroneal, and sural nerves by an experienced technician blinded to the results of the clinical evaluation. Between December 2018 and August 2019, 107 healthy subjects, including physicians, clinical assistants, nurses, and persons who accompanied

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The authors have no conflicts of interest to disclose.

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patients during their clinic visit were evaluated using HRUS. In all subjects, the following information was collected: age, gender, height, weight, and body mass index (BMI).

Ultrasonographic Examination: Ultrasound scanning of the lower extremity nerves was performed unilaterally (right side) using a linear array transducer with a bandwidth of 6 to 18 MHz (ACUSON S2000, Siemens Medical Solutions, Mountain View, CA). All studies were performed by a single neurologist with 4 years of experience in diagnostic neuromuscular ultrasound. The CSA was measured at the following locations: the lateral femoral cutaneous nerve, the intermuscular space between the tensor fasciae latae, and the sartorius muscle just below the anterior superior iliac spine; the femoral nerve, inguinal ligament (the level of the "lacuna musculorum" near the femoral vessels); the sciatic nerve, just proximal before the bifurcation of the popliteal fossa; the common peroneal nerve, popliteal crease, and fibular head before the fibular tunnel; the superficial peroneal nerve, distal calf (in the fascial plane between the peroneus longus muscle and the extensor digitorum longus); the deep peroneal nerve, the ventral fold of the ankle (lateral next to the anterior tibial artery); the tibial nerve, popliteal crease, 7cm proximal to the medial malleolus and the ankle; the sural nerve, distal calf (next to the small saphenous vein between the 2 heads of the gastrocnemius muscle), and the ankle (next to the small saphenous vein posterior to the lateral malleolus). These locations were chosen based on several factors, including anatomical landmarks and clinically important points. The subjects were supine during the HRUS of the lateral femoral cutaneous nerve, femoral nerve, deep peroneal nerve at the ankle, superficial peroneal nerve at the distal calf, and prone to sciatic, tibial, common peroneal, and sural nerves. During scanning of the nerves, the angle of the transducer was adjusted until it was perpendicular to the nerve, and the pressure of the transducer on the skin was minimized to avoid the artifactual deformation of the underlying structures. The CSA measurements were performed at the inner border of the hyperechoic epineural rim using the continuous tracing technique and the average values were calculated after serially measuring twice. The color Doppler mode was used to differentiate nerves from blood vessels.

2.1. Statistical analysis

Statistical analysis was conducted using SAS version 9.4 (SAS Institute, Cary, NC). The Shapiro–Wilk test was used to examine the normality of the measured variables. The reference range was then determined as the mean ± standard deviation for the normally distributed data and from the 2.5th–97.5th percentile for the nonnormally distributed data. One-way analysis of variance or Kruskal–Wallis test was used for data analysis based on age group, and 2-sample t test or the Wilcoxon rank-sum test was used to compare data between the 2 groups based on gender. The correlations between the CSA of the nerves, height, weight, and BMI were evaluated using Spearman correlation analysis. A P value of <.05 was considered statistically significant.

3. Results

Our study included 107 healthy adults with a mean age of 46.29 ± 14.19 years (range, 24–75). All subjects were Korean. The subjects were divided into 3 life stages depending on their age: the younger group (20–39 years, n = 40), the middle group (40–59 years, n = 40), and the older group (60–80 years, n = 27). The mean height was 165 ± 8.64 cm (range, 148–183), the mean weight was 64.4 ± 11.39 kg (range, 43–92), and the mean BMI was 23.3 ± 2.73 (range, 17.4–30). Of the subjects, 56 (52%) were females. The nerve CSA values were not normally distributed at all sites. The mean CSA and reference range for each nerve are listed in Table 1. Males had significantly larger values than females in the lower extremity nerves except for the lateral femoral cutaneous, peroneal (popliteal fossa), and superficial peroneal nerves (distal calf; Table 2). There was no statistically significant difference between the age groups except for the tibial nerve at the ankle (Table 2). Height, weight, and BMI correlated significantly with the nerve CSA values (Table 3).

4. Discussion

The CSA values in our study are comparable to the values published in a few studies for Asians, but the values differed depending upon the nerve measurement site in those studies. Compared to the study by Seok et al,[5] our results were similar for the peroneal nerve at the popliteal fossa, the tibial nerve at the popliteal fossa and calf, and the sural nerve at the distal calf; slight differences were noted in the peroneal nerve at the fibular head, and there were some differences in the sciatic nerve at the popliteal fossa. As for the study of Kim et al,[17] our results showed similar results for the peroneal nerve at the popliteal fossa, and slight differences for the peroneal nerve at the fibular head and the sciatic nerve. Compared to normal CSA values of the sciatic nerve in a Chinese population reported BY Chen et al,[18] some differences were observed for the sciatic nerve at the popliteal fossa. In a comparison of demographic factors, our results were very similar to the studies of Seok et al[5] and Kim et al[17] regarding height, weight, and BMI, and slightly different from the study of Chen et al[18] regarding weight. Compared to the values obtained from 69 healthy, middle East Asians, reported by Bedewi et al,[16] slight differences were observed for the peroneal nerve and tibial nerve at the ankle, and similar results were noted for the sural nerve. Some differences were observed for the tibial nerve at

Table 1

HRUS CSA of the lower extremity nerves in healthy Asian adults.

	Site	Mean	SD	Minimum	Maximum	Reference range
Femoral	Inguinal	29.26	8.76	11	54	14–29
LFCN	ASIS	3.01	0.87	1	5	2–5
Peroneal	FH	12.45	3.45	6	22	6–21
	PF	11.35	3.67	5	22	6–21
Superficial peroneal	Distal calf	2.6	0.93	1	6	1–4
Deep peroneal	Ankle	2.09	0.95	1	6	1–4
Tibial	Ankle	15.55	3.80	9	27	9–24
	Distal calf	12.97	3.71	8	26	8–22
	PF	24.73	6.03	13	42	16–38
Sciatic	Distal thigh	51.94	14.43	27	96	29–83
Sural	Ankle	3.77	1.15	1	7	2–7
	Distal calf	3.29	1.01	2	6	2–6

All values are in mm². The reference range is determined as the mean ± 2 SD for normally distributed data and from the 97.5th percentile for nonnormally distributed data.

ASIS = anterior superior iliac spine, CSA = cross-sectional area, FH = fibular head, HRUS = high-resolution ultrasonography, LFCN = lateral femoral cutaneous nerve, PF = popliteal fossa, SD = standard deviation.

Table 2

Overview of CSA reference values of nerves based on age and gender.

		Age				Gender		
		<40 yr (n = 40)	40–59 yr (n = 40)	≥60 yr (n = 27)		Male (n = 51)	Female (n = 56)	
Nerve	Site	Mean ± SD	Mean ± SD	Mean ± SD	*P* value	Mean ± SD	Mean ± SD	*P* value
		30.93 ± 9.34	29.1 ± 9.12	27.04 ± 6.91	.162	32.37 ± 7.74	26.43 ± 8.73	<.001
LFCN	ASIS	2.93 ± 0.97	2.98 ± 0.86	3.19 ± 0.74	.296	3.00 ± 1.00	3.02 ± 0.75	.775
Peroneal	FH	11.63 ± 2.99	13.03 ± 3.26	12.81 ± 4.16	.157*	13.16 ± 3.49	11.80 ± 3.31	.042†
	PF	11.25 ± 3.95	11.55 ± 3.55	11.19 ± 3.53	.784	10.88 ± 3.57	11.77 ± 3.74	.21
Superficial peroneal	Distal calf	2.73 ± 1.13	2.58 ± 0.87	2.44 ± 0.64	.53	2.80 ± 1.02	2.41 ± 0.80	.051
Deep peroneal	Ankle	2.13 ± 1.09	2.18 ± 0.90	1.93 ± 0.78	.52	2.49 ± 1.07	1.73 ± 0.65	<.001
Tibial	Ankle	14.35 ± 3.53	16.65 ± 3.79	15.70 ± 3.82	.011	16.78 ± 3.64	14.43 ± 3.62	.001
	Distal calf	12.15 ± 3.22	14.13 ± 4.37	12.48 ± 2.91	.113	14.27 ± 4.03	11.79 ± 2.96	.001
	PF	24.53 ± 6.06	24.63 ± 6.38	25.19 ± 5.64	.901*	27.39 ± 5.60	22.30 ± 5.39	<.001
Sciatic	Distal thigh	51.59 ± 16.64	53.73 ± 13.65	49.73 ± 12.03	.373	57.20 ± 15.03	47.34 ± 12.26	.001
Sural	Ankle	3.68 ± 1.29	4.05 ± 1.22	3.48 ± 0.70	.158	4.20 ± 1.33	3.38 ± 0.80	.001
	Distal calf	3.33 ± 1.12	3.48 ± 0.99	2.96 ± 0.81	.108	3.67 ± 1.13	2.95 ± 0.75	.001

All values are in mm^2. Bold values are considered statistically significant ($P < .05$).

ASIS = anterior superior iliac spine, CSA = cross-sectional area, FH = fibular head, LFCN = lateral femoral cutaneous nerve, n = number of subjects, PF = popliteal fossa, SD = standard deviation.

**P* values calculated using ANOVA test.

†*P* values calculated using *t* test.

Table 3

Correlation between CSA and height, weight, and BMI.

		Correlation coefficient (*P* value)		
Nerve	Site	Height	Weight	BMI
Femoral	Inguinal	0.286 (.003)	0.269 (.005)	0.201 (.038)
LFCN	ASIS	–0.102 (.296)	0.018 (.851)	0.139 (.153)
Peroneal	FH	0.156 (.109)	0.312 (.001)	0.346 (<.001)
	PF	–0.098 (.317)	–0.002 (.981)	0.107 (.275)
Superficial peroneal	Distal calf	0.247 (.010)	0.387 (<.001)	0.351 (<.001)
Deep peroneal	Ankle	0.373 (<.001)	0.407 (<.001)	0.293 (.002)
Tibial	Ankle	0.223 (.021)	0.291 (.002)	0.238 (.014)
	Distal calf	0.337 (<.001)	0.504 (<.001)	0.466 (<.001)
	PF	0.428 (<.001)	0.437 (<.001)	0.309 (.002)
Sciatic	Distal thigh	0.352 (<.001)	0.336 (.001)	0.219 (.025)
Sural	Ankle	0.248 (.010)	0.294 (.002)	0.249 (.010)
	Distal calf	0.283 (.003)	0.379 (<.001)	0.354 (<.001)

Bold values are considered statistically significant ($P < .05$).

ASIS = anterior superior iliac spine, BMI = body mass index, CSA = cross-sectional area, FH = fibular head, LFCN = lateral femoral cutaneous nerve, PF = popliteal fossa.

the popliteal fossa. The mean BMI of this study was higher than ours. Comparing our values with those reported for non-Asians in other studies, the results were different depending upon the study. The CSA values reported by Kerasnoudis et al,[19] Boehm et al,[20] and Visser et al[21] were smaller than those of our study at the peroneal, tibial, and sural nerves. Similar results to those reported by Qrimli et al[22] were observed for the peroneal and superficial peroneal nerve and slight differences were noted for the tibial nerve at the ankle and sural nerve at the distal calf. Compared to the study by Cartwright et al,[4] similar results were observed for the peroneal, sciatic, and tibial nerve at the ankle. However, the CSA values for the tibial nerve at the popliteal fossa and ankle were larger than those of our study. Several studies reported that the reference values for the peripheral nerve CSA varied among different countries and continents, and the nerve CSA values in Americans and Europeans were greater than those in Asians.[24,25] However, depending upon the nerve or site of the CSA measurement, the CSA values in our study were similar to those in studies of non-Asians. Thus, it can be difficult to attribute the variability in the reported reference values simply to ethnic differences. The discrepancy between reference values in different study groups suggests that there is still a need for every ultrasound lab to define their own reference values.

The correlation between nerve size and demographic factors, such as age, gender, height, weight, and BMI, have been addressed in several studies. However, a consensus is still lacking. Boehm et al[20] found no correlation between the CSA values of the lower extremity nerves and age, but Seok et al[5] and Qrimli et al[22] reported a consistent correlation between the CSA of all nerves at all sites and age. In our study, a significant difference with regard to age group was observed only in the tibial nerve at the ankle, which is similar to the results reported in the study by Kerasnoudis et al.[19] The CSA values of the upper extremity nerves in males were significantly greater than those in females in many previous studies.[19,20,22,25–31] However, Bedewi et al[16] and Qrimli et al[22] reported that there was no correlation between the CSA values of the lower extremity nerves and gender. But several studies noted significant differences in some nerves, such as the peroneal nerve (fibular head), sciatic nerve, and sural nerve.[18–20] Our study found significant differences with regard to gender in 9 out of 12 sites. Previous studies also reported inconsistent results on the correlation between the CSA values of the lower extremity nerves and height, weight, and BMI. Kerasnoudis et al[19] noted no correlations between CSA and height and weight. However, Cartwright et al[4] showed that a few nerve sites were correlated with these factors. In our study, similar to the studies of

Seok et al[5] and Tagliafico et al,[23] height correlated in 9 out of 12 sites and weight and BMI showed higher correlations in 10 out of 12 sites. Therefore, consideration of these demographic factors is important when assessing the CSA results.

In clinical practice, when examining patients with unilateral mononeuropathy by ultrasound, the healthy contralateral side is often used as an internal control. Recently, previous studies described diffuse or multifocal enlargement of certain peripheral nerves in some hereditary and acquired demyelinating polyneuropathies, such as Charcot-Marie-Tooth type 1, hereditary neuropathy with liability to pressure palsies, chronic inflammatory demyelinating polyneuropathy, Guillain–Barré syndrome, multifocal motor neuropathy, and multifocal acquired demyelinating sensory and motor neuropathy.[11,12,15,32–37] Scheidl et al[37] reported significant differences in the CSA of upper and lower extremity nerves, except the sural nerve, in acquired diffuse sensorimotor demyelinating and axonal polyneuropathy, and the mean CSA value was the smallest in healthy control and was the largest in demyelinating polyneuropathy. The sural nerve could be examined in only a limited number of patients due to obesity. However, diagnosis may be difficult in the early stages of some immune-mediated polyneuropathies, resulting in long-term disability. The reference value of peripheral nerves, including pure sensory nerves, could help early diagnosis by differentiating acquired and inherited polyneuropathy from normal.

Our study had several limitations. First, despite our effort to recruit an age-matched population, the recruitment of large numbers of subjects over 60 years of age with no abnormalities in NCS, history-taking, and physical examination was difficult. Second, this study did not include intrarater reliability, and information on this topic could not be provided. Finally, because all participants were Korean and the study did not include subjects of different ethnicities, the reference values are difficult to apply across a broad population.

In conclusion, our study was a large-scale, prospective investigation of HRUS CSA of the lower extremity nerves in a healthy Korean population, recruited after excluding subjects with subclinical neuropathy in the electrophysiological study. The results of our study, which included small sensory branches, can serve as a valuable resource to clinicians performing HRUS for the evaluation of various peripheral nerve disorders in the East Asian population.

Author contributions

Conceptualization: Dae Woong Bae, Jae Young An.
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