



RESEARCH ARTICLE

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Nailfold capillary microscopy for evaluating hand-arm vibration syndrome

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Abstract

Objectives: We evaluated nailfold capillary abnormalities in patients with hand-arm vibration syndrome using nailfold capillary microscopy.

Methods: Fifty workers who underwent a special health examination because of exposure to hand-arm vibration at Ulsan University Hospital in 2012 (exposed group) and a control group of 50 white-collar employees were evaluated through a questionnaire survey regarding their present tasks, types of tools used, vibration exposure duration, use of protective wear, and medical history. Then, an occupational physician performed a physical examination for any hand deformities, skin problems, or motor and sensory dysfunctions of the upper extremities. The nailfold capillary morphologies (tortuous, crossing, bushy, meandering, branching, hemorrhage, avascular area, enlarged, and giant), capillary dimensions (afferent, top, venous, total width, and length), and specific counts (crossing and branching) on both fourth fingers were determined by a rheumatologist. Thereafter, the exposed subjects were assessed according to the Stockholm workshop classification scale. In total, 8 and 6 subjects in the exposed and control groups, respectively, were excluded from the study because of poor capillary microscopic image quality. In addition, 24 subjects in the exposed group with Stockholm vascular stage 0 were excluded. Finally, capillary morphology, dimensions, and specific counting were compared between the exposed ($n = 18$) and control groups ($n = 44$).

Results: The exposed group had significantly greater crossing capillaries and abnormal capillary numbers that included crossing capillaries (crossing, branching, bushy, and meandering) but smaller branching and abnormal capillary numbers that excluded crossing capillaries (branching, bushy, and meandering) than the control group did. No significant difference in capillary dimensions was observed between the two groups. Despite the adjustment for age, smoking status, and underlying diseases, the statistical significance was unchanged. In the specific counting of the type of capillaries, the exposed group had a significantly higher total crossing count but fewer total branching count than the control group did. However, no statistical significance resulted after adjustment for age, smoking status, and underlying diseases.

Conclusions: In this study, the exposed group had significantly more crossing capillaries and a higher crossing count than the control group did.

Keywords: Hand-arm vibration syndrome, Nailfold capillary microscopy, Crossing capillary number, Crossing count

Introduction

Hand-arm vibration is defined as the transmission of vibrations produced by handheld tools to the hands and arms of the tool-wielding individual. Hand-arm vibration syndrome (HAVS) is the manifestation of one or more specific neurological, vascular, and musculoskeletal disorders that are causally associated with vibration exposures

from handheld vibrating tools. In particular, the syndrome is known to be a complex combination of disorders that insidiously and passively affect HAVS patients [1]. In England, approximately 288,000 people have HAVS. According to the Medical Research Council Survey conducted between 1997 and 1998, nearly 5 million people are exposed to hand-transmitted vibrations at work in a given week, most of whom are male, with a male-to-female ratio of approximately 8:1 among those who have developed HAVS [2]. Most of the studies associated with HAVS have

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shown a positive correlation between exposure to high levels of hand-transmitted vibrations and the presence of vascular symptoms of HAVS [2]. The risk for HAVS was shown to be highest in occupations that use pneumatic drills, grinders, and impact wrenches [3]. Moreover, the incidence of HAVS was approximately 70% among these high-risk individuals [3].

Various methods to measure and evaluate the status of vascular disorders have been used, including the measurement of the recovery time after nail compression, nailfold capillary microscopy, plethysmography, thermometry and thermography, and laser Doppler imaging and flowmetry. These tests are used to evaluate skin microcirculation and morphology of capillary. Among these tests, nailfold capillary microscopy is considered one of the established methods to diagnose and monitor collagen-vascular diseases because it can evaluate structural changes in the superficial cutaneous vasculature [4,5].

Capillary microscopy is performed most commonly to identify patients with Raynaud's phenomenon. Through this method, patients with scleroderma (systemic sclerosis) who exhibit a high prevalence of Raynaud's phenomenon can be easily differentiated from patients with primary Raynaud's phenomenon or Raynaud's phenomenon caused by other connective tissue diseases because most patients with scleroderma (systemic sclerosis) exhibit pathognomonic changes under capillary microscopy [6,7]. Similarly, capillary microscopy can also be applied to HAVS which is a type of secondary Raynaud's phenomenon.

Outside of South Korean research on HAVS diagnosis using capillary microscopy, Kaji et al. [8] retrospectively analyzed 98 HAVS patients among 294 subjects who were exposed to hand-transmitted vibrations. In their study, the capillary morphology was differentiated into three stages (stages A, B, and C) according to the Fagrell and Lundberg classification, and then the results were compared with the control group. Among the HAVS patients in their study, stage B classification (indistinct capillaries) was the most common diagnosis accounting for 42.9% of the patients. In the control group, stage A classification (dot- or comma-shaped appearance with good tonicity) was the most common diagnosis accounting for 50.0% of the subjects in the control group. However, because the capillary microscopy results of both groups were differentiated into three stages simply based on the distinctiveness of their capillary morphology, the lack of a more specific parameter was a limitation of their study. Moreover, Littleford et al. [9] compared the capillary morphology between 10 HAVS patients and 10 control group subjects. Interestingly, their study implemented a scoring system for certain measured parameters including capillary dropout, tortuosity, subpapillary venular plexus visualization, and disarrangement of capillary polarity. However, the capillary morphologies of the control group

were all found to be normal; therefore, comparison with the patient group was difficult. Moreover, their study had a relatively small study population that further limited their findings.

The diagnostic method that measures recovery time after nail compression to confirm the presence of vascular disorders in HAVS patients can yield different applied pressures and recovery times depending on the skills and experience of the examiner. The reproducibility of this diagnostic method is also unknown, thus it is not preferred [4]. Furthermore, thermometry and thermography tends to exhibit inconsistent sensitivity and specificity depending on the study [4]. In addition, a limitation of laser Doppler flowmetry is that it has low reproducibility in microcirculation studies based on physiological changes [4]. Plethysmography is expensive, complicated, and requires a skilled examiner to ensure the accuracy of the test results [4]. Owing to the problems posed by the aforementioned diagnostic methods, cold provocation test and finger angiography are commonly used. However, even these alternative methods have limitations. In particular, the cold provocation test is time intensive and subject to the influence of seasonal changes on skin temperature [10,11]. Moreover, finger angiography is invasive. However, nailfold capillary microscopy is a simple, noninvasive procedure that can quickly evaluate the status of capillary disorders. Nonetheless, the use of capillary microscopy to diagnose HAVS in South Korean patients has not been well studied. Therefore, the present study is a pilot study that attempts to test a new diagnostic approach to evaluating HAVS in South Korea.

Materials and methods

Study participants

In 2012, 50 subjects who visited Ulsan University Hospital for a special health examination after being exposed to hand-arm vibrations presented with paleness, tingling sensations, or numbness of the hands. All subjects underwent nailfold capillary microscopy. The images of eight subjects were low quality (based on whether both sides and the center of the capillary were visible) and 24 subjects were found to have a Stockholm vascular stage of zero in the cold provocation test; thus, 32 subjects were excluded. The remaining 18 subjects were selected as the exposed group. The control group was selected from a group of 50 white-collar employees who had never been exposed to localized vibrations. Of these, six subjects were excluded because their nailfold capillary microscopic images were of poor quality; therefore, a total of 44 workers were included in the control group.

Survey and physical examination

Variables associated with vibrations that were investigated included age, present task, type of vibrating tool used, the

duration of use, occupational posture, safety equipment status, and method of commute to their workplace. Furthermore, data on subject's medical history (hypertension, heart disease, diabetes mellitus, musculoskeletal disorders, trauma, etc.), alcohol consumption, and smoking history were collected because these variables may influence any current symptoms. In the physical examination, an occupational and environmental medicine specialist evaluated all subjects for nail changes, finger deformities, skin disorders of the hands, musculoskeletal disorders of the entire upper limb, tendon reflex disorder, upper extremity range of motion, and the level of pain during these motions.

Nailfold capillary microscopy and Stockholm staging

Prior to Stockholm staging, nailfold capillary microscopy was performed to prevent any adverse effects such as vasoconstriction due to the cold water used in the cold provocation test. The capillary microscope was a CM-1000 (CM, 2009, Seoul, South Korea), and the software i-Solution/Lite (iMT i-Solution Inc.) was used to analyze the images.

Capillary microscopy was performed after the subjects rested for 15 to 30 minutes at a standardized room temperature (20–23°C). The nailfolds of the fourth fingers of both hands were examined because this finger provides superior capillary visibility over all the fingers [12,13]. Two sections of the fourth finger on each hand were marked and spanned 5 mm. Then, immersion oil or liquid paraffin was applied onto the skin to maximize the transparency of the keratin layer of the epithelial cells [14]. All subjects underwent high- ($\times 200$) and low-power ($\times 100$) microscopic examinations, with the total examination time ranging from 15 to 30 minutes. However, the dimensions of all the capillaries (afferent, top, venous, total width, and length) were not measured. Thus, the three largest or most abnormal capillaries were selected and examined. In the case of the morphological parameters (tortuous, crossing, bushy, meandering, branching, hemorrhagic, avascular area, enlarged, and giant), the number of capillaries that displayed these parameters within a 2-mm area was counted. In the case of tortuous capillaries, a more complex definition of the morphology was used for any crossing, meandering, or branching capillaries. The capillary morphologies were defined as follows: crossing, containing at least 1 circle in the capillary loop; branching, having at least 1 loop bulging with the exception of the capillary top; bushy, having a more complex morphology than branching; giant, having a capillary top larger than 50 μm ; enlarged, surpassing the average capillary top size of 15 μm ; and avascular area, the absence of capillaries within twice the shortest distance between the nailfold capillaries as observed by the examiner. Furthermore, a combined count of the crossing, meandering, branching, and bushy capillary counts was computed. However, the

counts of four particular capillaries were not combined for a specific reason. Under the high- ($\times 200$) and low-power ($\times 100$) microscopic examinations, the number of hairpin-shaped capillaries within a 1-mm area was counted to compute their respective densities, and the lowest value of the measurable range was used. The average density was defined as the average between the high- and low-power densities. In addition, the number of crossing and branching abnormalities was counted by selecting three capillaries that reflected the most severe crossing and branching ones, respectively, based on the capillary microscopic findings. As standard measures of severity, the number of circles was used as the crossing count and the number of capillaries bulging outside aside from the capillary top was used as the branching count.

Statistical analysis

A *t* test was performed to compare the mean age between the exposed and control group. Chi-square tests were used to compare the smoking statuses and medical histories between the two groups. In addition, a *t* test was used to compare the morphology and dimensions (descriptive factors) of the capillary microscopic findings between the two groups. Moreover, analysis of covariance was used to determine the statistical significance of the results after adjusting for age, smoking status, and underlying diseases. However, smoking status and underlying diseases were analyzed as dummy variables because they are categorical variables. Statistical analyses were performed using SPSS ver. 21 (IBM SPSS Inc., Chicago, IL), and a $p < 0.05$ was considered statistically significant.

Results

Characteristics of the study participants

The mean age of the 18 exposed subjects was 57.1 ± 4.9 years, whereas that of the 44 subjects in the control group was 44.5 ± 11.0 years. The mean vibration-exposure duration in the exposed group was 25.6 ± 6.7 years; the most common tools being the grinder (61.1%) and rock drill (38.9%). Among the tasks, painting and fitting were 27.8% and 22.2%, respectively, mining was the most common, at a frequency of 33.3%. Current smokers comprised the majority of the exposed and control groups at 44.4% and 38.6%, respectively; however, the difference was not statistically significant. The alcohol consumption statuses in the exposed group were 57.1% and 42.9% for drinkers and non-drinkers, respectively. In addition, 72.2% of the exposed group did not have a history of disease, 11.1% had hypertension, 11.1% had other diseases, and 5.6% had finger injuries. In the control group, 93.8% did not have any history of illness and 6.3% had a history of hypertension. However, the difference between the medical histories of the two groups was not significant. Regarding the use of

protective gloves, 66.7% of the exposed group reported wearing only cotton gloves, 22.2% reported that they always wear antivibration gloves, and 11.1% reported that they do not wear any gloves. For the mode of transportation used to commute to work in the exposed group, 46.7% rode a motorcycle, 46.7% rode a bus, and 6.7% walked to work (Table 1). Moreover, the most commonly used (at 77.8%) occupational postures were raising the arms above the shoulders, bending the neck forward or backward, squatting, and bending the back. Other

common responses included only 2 or 3 of these postures (data not shown).

Capillary microscopic findings of the exposed and control groups

The imaging results of the nailfold capillary microscopy in the exposed and control groups indicated that the numbers of crossing capillaries, avascular areas, enlarged capillaries, and abnormal capillaries (crossing, meandering, branching, and bushy) were higher in the exposed group than in the control group. However, the numbers of tortuous, bushy, meandering, branching, and abnormal capillaries (meandering, branching, bushy) and the mean density were higher in the control group than in the exposed group. The numbers of capillaries that were crossing, branching, abnormal including crossing (i.e., crossing, meandering, branching, and bushy), and abnormal excluding crossing (i.e., meandering, branching, and bushy) significantly differed between the two groups. After adjusting for age, smoking status, and underlying diseases, none of the categories was significantly different between the two groups (Table 2).

The venous capillary size and total width were smaller in the exposed group than in the control group. Afferent capillary size, top capillary size, and capillary length were greater in the exposed group than in the control group, but the results were not statistically significant. The significance of the results did not change even after adjusting for age, smoking status, and underlying diseases (Table 3).

In the specific counting of the morphological findings, the exposed group exhibited a higher total crossing count, whereas the control group exhibited a higher total branching count. While the unadjusted results were statistically significant, the fully adjusted results were not (Table 4).

Discussion

The most common cause of Raynaud's phenomenon is the exaggerated response of the blood vessels due to cold or emotional stress [15]. However, the morphological changes of the capillaries in Raynaud's phenomenon are related to capillary wall damage due to long-term exposure to vibration stimulation, not to the changes in blood flow through the autonomic nervous system. Therefore, the morphological classification of capillaries is useful as a method of differential diagnosis for HAVS [16]. However, considering the wide degree of individual variations in capillary morphology even in the control group, this method is clearly limited as a diagnostic tool.

However, since Maurice Raynaud (1834–1881) presented his theory of local ischemic damage in the hands, feet, nose, and tongue, capillary microscopy has been recognized as an important tool to visualize microvascular

Table 1 Characteristics of the exposed subjects

	VWF (n = 18)	Non-VWF (n = 44)	p value
Age (years)*	57.1 ± 4.9	44.5 ± 11.0	0.001
Vibration exposure (years)	25.6 ± 6.7	-	
Smoking† (%)			
Non-smoker	33.3	29.5	0.751
Ex-smoker	22.2	31.8	
Current smoker	44.4	38.6	
Alcohol consumption (%)			
Non-drinker	42.9	-	
Drinker	57.1	-	
Past medical history† (%)			
No past disease	72.2	93.8	0.098
Hypertension	11.1	6.3	
Finger injury	5.6	-	
Other diseases	11.1	-	
Source of vibration (%)			
Grinder	61.1	-	
Rock drill	38.9	-	
Antivibration gloves (%)			
Nothing	11.1	-	
Only cotton gloves	66.7	-	
Always	22.2	-	
Tasks (%)			
Painting	27.8	-	
Fitting	22.2	-	
Welding	11.1	-	
Mining	33.3	-	
Digging	5.6	-	
Mode of transportation to work (%)			
Walking	6.7	-	
Motorcycle	46.7	-	
Bus	46.7	-	

Mean ± SD.

*t test.

†Chi-square test.

Abbreviations: VWF vibration-induced white finger, Non-VWF non-vibration-induced white finger.

Table 2 Morphological findings of the nailfold capillary microscopy test (non-VWF vs. VWF)

Microscopic findings		Non-VWF (n = 44)	VWF (n = 18)	p value*	Adjusted p value†
Morphology	Tortuous	2.11 ± 2.13	1.94 ± 2.34	0.783	0.464
	Crossing	3.61 ± 3.03	5.89 ± 3.79	0.015	0.915
	Bushy	0.14 ± 0.90	0.00 ± 0.00	0.527	-
	Meandering	0.27 ± 1.09	0.11 ± 0.32	0.539	0.953
	Branching	1.02 ± 1.49	0.28 ± 0.75	0.012	0.142
	Hemorrhage	0.00 ± 0.00	0.00 ± 0.00	-	-
	Avascular area	0.66 ± 0.96	0.72 ± 0.89	0.812	0.562
	Enlarged	1.64 ± 2.24	1.89 ± 2.05	0.682	0.714
	Giant	0.00 ± 0.00	0.00 ± 0.00	-	-
Combined count	Abnormal capillary (including crossing)	3.80 ± 2.96	6.00 ± 3.66	0.016	0.933
	Abnormal capillary (excluding crossing)	1.11 ± 1.62	0.33 ± 0.77	0.013	0.184
Average density (capillary number/mm)		6.70 ± 0.92	6.69 ± 1.06	0.970	0.764

Unit: capillary number.

*t test.

†Adjusted for age, smoking status, and diseases using analysis of covariance.

Abbreviations: Non-VWF non- vibration-induced white finger, VWF vibration-induced white finger.

dysfunction, a characteristic of Raynaud's phenomenon [6,17]. The peripheral microangiopathy of systemic sclerosis was also easily identifiable and studied through capillary microscopy. The capillary morphological abnormalities in systemic sclerosis can largely be categorized as either minor or major. Minor abnormalities are commonly found even in healthy individuals, consisting of tortuous, crossing, and enlarged capillaries. Major abnormalities that are rarely found in normal persons and considered pathological in nature are giant, bushy, meandering, and branching capillaries [14]. However, one major difference from the results of the present study compared to those of previous studies is that branching capillaries were significantly more common in the control group than the exposed group, and the minor nonpathological abnormality such as the crossing capillary was significantly more common in the exposed group than the control group. Nevertheless, it is unknown whether the pathological findings in systemic sclerosis are also pathological in cases of HAVS. Moreover, although it is normal for some control group subjects to exhibit abnormal findings for some parameters, our results may not be entirely able to display these findings. However, one of the possible interpretations for this difference can be that the pathophysiological mechanisms of systemic sclerosis and HAVS are fundamentally different. Although the primary cause of systemic sclerosis has not been sufficiently investigated, it is known to be associated with endothelial cell damage, immune system disorders, and excessive extracellular matrix synthesis [18,19]. However, the underlying physiological mechanisms of abnormal vascular reactivity, namely, the functional vasoconstriction and structural intimal proliferation and obstruction, are not yet known

[20]. In comparison, HAVS is caused when vibrations stimulate the sympathetic nerves to induce vasoconstriction, and the recurring vasoconstriction eventually leads to the thickening of the arterial wall, causing circulation problems in the hands [11]. As a result, the difference in capillary microscopic findings can be understood as a difference in the pathophysiological mechanism between the two diseases. However, more studies must be conducted to precisely investigate the difference in capillary microscopic findings. Furthermore, through such studies, the pathological parameters in the capillary microscopic findings of HAVS should be determined.

In primary Raynaud's phenomenon, the pattern of the nailfold capillaries remains normal, whereas in systemic sclerosis, a secondary Raynaud's phenomenon, a characteristic pattern of nailfold capillaries is exhibited. Such characteristic patterns include a decrease in capillary density, avascularity, a giant capillary, and hemorrhages [4,12]. However, characteristic nailfold capillary microscopic patterns associated with HAVS have not yet been identified. Sakaguchi et al. [16] have classified the capillary loop in HAVS patients according to the number of crossings (Kusumoto's classification system). Compared with the control group, the HAVS group has been shown to exhibit a greater number of crossings in the capillary loop. The present study is meaningful in that the application of the capillary microscopic parameters confirmed the number of crossing capillaries and crossing count, which were greater in the exposed group than in the control group significantly. In addition, although capillary microscopy cannot yet be used alone as a diagnostic tool for HAVS, the characteristic capillary morphological pattern (crossing capillary number and crossing count) described in the study can distinguish patients with HAVS from individuals

Table 3 Descriptive factors of the observed capillaries (non-VWF vs. VWF)

Microscopic findings		Non-VWF (n = 44)	VWF (n = 18)	p value*	Adjusted p value [†]
Afferent	Afferent 1	15.14 ± 3.70	15.61 ± 4.02	0.663	0.591
	Afferent 2	14.59 ± 3.59	14.39 ± 4.01	0.847	0.819
	Afferent 3	13.65 ± 3.99	13.67 ± 2.75	0.990	0.625
	Afferent mean	14.46 ± 3.09	14.55 ± 3.00	0.915	0.952
	Afferent maximum	16.77 ± 3.80	16.80 ± 4.12	0.977	0.973
Top	Top 1	17.41 ± 4.86	19.60 ± 5.14	0.119	0.891
	Top 2	17.42 ± 4.28	17.58 ± 3.31	0.888	0.992
	Top 3	16.25 ± 4.76	16.36 ± 4.71	0.934	0.909
	Top mean	17.03 ± 3.75	17.85 ± 3.32	0.424	0.982
	Top maximum	19.71 ± 5.07	21.00 ± 4.84	0.363	0.875
Venous	Venous 1	20.43 ± 6.73	19.63 ± 4.94	0.650	0.478
	Venous 2	18.14 ± 3.95	17.40 ± 5.21	0.545	0.505
	Venous 3	17.65 ± 5.67	17.51 ± 4.16	0.924	0.383
	Venous mean	18.74 ± 4.60	18.18 ± 4.29	0.659	0.379
	Venous maximum	21.81 ± 6.42	20.59 ± 4.85	0.471	0.293
Total width	Total width 1	52.48 ± 13.26	50.41 ± 12.02	0.569	0.623
	Total width 2	48.11 ± 9.64	49.89 ± 13.67	0.621	0.308
	Total width 3	47.65 ± 13.42	45.39 ± 8.09	0.419	0.356
	Total width mean	49.41 ± 10.37	48.56 ± 9.46	0.764	0.345
	Total width maximum	56.28 ± 13.21	55.69 ± 12.36	0.872	0.355
Length	Length 1	341.32 ± 122.35	392.45 ± 149.93	0.167	0.996
	Length 2	321.50 ± 129.00	384.07 ± 176.19	0.126	0.256
	Length 3	334.75 ± 129.55	343.87 ± 173.84	0.821	0.116
	Length mean	332.52 ± 112.75	373.46 ± 152.51	0.248	0.848
	Length maximum	389.61 ± 138.84	445.69 ± 151.15	0.164	0.587

Unit: μm .

*t test.

[†]Adjusted for age, smoking status, and diseases using analysis of covariance.Abbreviations: *Non-VWF* non- vibration-induced white finger, *VWF* vibration-induced white finger.**Table 4 Specific counts of morphological findings (non-VWF vs. VWF)**

Microscopic findings		Non-VWF (n = 44)	VWF (n = 18)	p value*	Adjusted p value [†]
Crossing count	Crossing 1	1.66 ± 0.94	2.33 ± 0.69	0.008	0.058
	Crossing 2	1.14 ± 0.88	2.00 ± 0.84	0.001	0.376
	Crossing 3	0.77 ± 0.80	1.44 ± 0.78	0.004	0.378
	Total crossing	3.57 ± 2.35	5.78 ± 2.02	0.001	0.169
Branching count	Branching 1	0.59 ± 0.69	0.22 ± 0.55	0.032	0.280
	Branching 2	0.23 ± 0.42	0.06 ± 0.24	0.048	0.187
	Branching 3	0.16 ± 0.37	0.00 ± 0.00	0.007	0.168
	Total branching	0.98 ± 1.34	0.28 ± 0.75	0.012	0.162

Unit: number.

*t test.

[†]Adjusted for age, smoking status, and diseases using analysis of covariance.Abbreviations: *Non-VWF* non- vibration-induced white finger, *VWF* vibration-induced white finger.

without HAVS. Therefore, capillary microscopy has the potential as a diagnostic indicator of HAVS. Through such discoveries, meaningful data for differential diagnosis of Raynaud's phenomenon can also be provided.

The present study is distinct from the previous studies because we included new parameters that were previously not studied, in particular nailfold capillary microscopy for HAVS. Based on the qualitative factor of capillary morphology and the quantitative factor of capillary dimensions, the respective parameters were quantitatively compared contingent to the presence of HAVS.

However, the present study had several limitations. First, we could not match the ages of the exposed group with those of the control group, and the exposed group was significantly older than the control group. Although age has been shown to only slightly influence blood flow compared with vibration stimulation [16], the influence of age on vibration stimulation cannot be ignored. Second, both the exposed and control groups were comprised primarily of current smokers. Considering the decrease in cutaneous microcirculation due to smoking [21], not excluding subjects with a history of smoking is another limitation of the study. Third, only one examiner performed the nailfold capillary microscopic measurements; therefore, errors in the capillary morphological and dimensional measurements may have occurred, resulting in problems with the reliability of our study. Fourth, the diagnosis of HAVS was only dependent on the Stockholm Workshop Scale, which might have led to errors in diagnosis. The Stockholm stages are difficult to clearly differentiate; therefore, the use of a non-objective diagnostic tool as a stand-alone diagnostic method may also be a limitation. Fifth, the diagnostic utility of capillary microscopy should be evaluated in terms of its sensitivity and specificity and in comparison with those of conventional diagnostic methods. Last, the number of study subjects, especially in the exposed group, was small, thus restricting the power of the analysis to determine a correlation between the capillary microscopic parameters and HAVS.

Conclusions

In conclusion, HAVS research using capillary microscopy has not been thoroughly studied in South Korea; thus, large-scale studies are needed to confirm the effectiveness of capillary microscopy as a diagnostic tool. In particular, the present study only confirmed the presence of abnormal findings in the exposed and control groups through capillary microscopy. However, the ratio of normal to abnormal capillaries may be helpful and the differences between normal and abnormal capillaries should be compared. Moreover, serological testing using the serum markers soluble thrombomodulin (sTM) or soluble intercellular adhesion molecule-1 (sICAM-1) [2,22,23] as well as prospective studies on a 3- or 6-month cycle can aid in

research efforts [6]. Furthermore, capillary microscopic findings differentiated by the Stockholm vascular stage should be analyzed to investigate changes in capillary microscopic parameters with increased stage. However, capillary morphology, dimensions, and specific counting (crossing and branching) did not show a consistent trend according to the increase in Stockholm vascular stage (stages 0–3), and there were no significant differences among stages 0–3 (data not shown). However, the quantitative and qualitative parametric changes due to stage increases should be analyzed in a future, large-scale study.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CBL: The first author of this article. He designed the study, collected and interpreted the data, and drafted the manuscript. JHS: He suggested the study design, interpreted the data, and revised the manuscript. CSS: He interpreted the data, revised the manuscript. JHP: He collected the data. CIY: He interpreted the data, revised the manuscript. JSO: He suggested the study design, interpreted the data. HL: He suggested the study design, interpreted the data, and revised the manuscript. All authors read and approved the final manuscript.

Acknowledgments

This work was supported by Ulsan University Hospital Education & Research Assistant Manager.

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Received: 24 December 2013 Accepted: 27 June 2014

Published online: 10 October 2014

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