

## PATHOLOGICAL CHANGES OF FINGER AND TOE IN PATIENTS WITH VIBRATION SYNDROME

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### ABSTRACT

Pathological findings of the fingers and toes were studied in finger and toe skin specimens from 21 male patients with vibration syndrome and 13 referent male cadavers. Thickening of the medial muscle layer of small arteries or arterioles, and increase of collagen fibers in the connective tissues, especially in perivascular regions, were noted in not only the finger but also the toe in patients with vibration syndrome. The ratio of the media/external diameter in the finger and toe was significantly greater in the patients than in the referents, even in the patients who had operated chain saws, bush cutters or grinders and had not been exposed to vibration of the foot directly. And the ratio in the finger was approximately parallel with that in the toe in the same subject. The present findings pathohistologically confirmed the existence of circulatory disturbances in the feet as well as the hands. The medial thickening of arteries and perivascular fibrosis in the toe can result from not only direct vibration exposure of the foot, but also long-term repeated vasoconstriction and circulatory disturbances in the foot through the activation of the sympathetic nerve system caused by hand-arm vibration.

Key Words: Vibration syndrome, Finger, Toe, Pathological change, Medial muscle layer, Perivascular fibrosis

### INTRODUCTION

Vibration syndrome is generally known as peripheral circulatory disturbances, peripheral nervous disturbances and musculoskeletal disturbances in the hand-arms. Pathologically, thickening of the medial muscle layer of small arteries, demyelinating changes in the peripheral nerves and increase of collagen in the connective tissues are demonstrated to be characteristic in the fingers of patients with vibration syndrome.<sup>1-4)</sup>

On the other hand, some studies have indicated the existence of circulatory disturbances in the foot in vibration syndrome. There are some reports on patients with Raynaud's phenomenon of the toe,<sup>5-10)</sup> and it has been shown that patients with more frequent attacks of Raynaud's phenomenon in the fingers had a higher prevalence of coldness felt in the feet.<sup>11)</sup> Moreover, the dermal blood flow and skin temperature of patients with vibration syndrome was lower in both the arm and leg than those of the referents.<sup>12,13)</sup> However, there is only one pathological study on the foot.<sup>2)</sup>

The purpose of the present study was to investigate the pathological changes in skin specimens of the toe as well as the finger of patients with vibration syndrome.

## SUBJECTS AND METHODS

Both finger and toe skin specimens were obtained from 21 patients with vibration syndrome and 13 referents. All the patients were males aged 51–68 years, mean 59 (SD 5) years, under medical treatment, who were selected from cases without complications such as collagen disease, hypertension, heart disease, diabetes mellitus, cerebral vascular disease, and liver dysfunction. The referents were all male cadavers aged 48–99 years, mean 71 (SD 14) years. The causes of their death were respiratory failures, heart failures, carcinomas and the like, but did not include collagen disease and cerebrovascular disease.

Among the patients, fourteen had operated rock drills (RD). The other seven had used chain saws, grinders or bush cutters (non-RD). The RD operators had been directly exposed to vibration of the foot used to press a drill, while the non-RD operators had not been exposed to vibration of the foot directly. The RD patients had operated rock drills for 16.0 years and the non-RD patients had operated vibrating tools like chain saws for 20.3 years. Eleven of all patients had Raynaud's phenomenon of the finger, four had Raynaud's phenomenon of both the finger and toe, and six had no Raynaud's phenomenon.

The patients were informed of the nature of the present study. All of them gave informed consent in writing to biopsies of the finger and toe.

Biopsy skin specimens were obtained from the middle phalanx of the left fourth finger and left giant toe of each patient. After the finger or toe was fully anesthetized with lidocaine, biopsy specimens were obtained from the skin without the effect of the local anesthesia. Each tissue slice removed was about 1 cm wide and 0.25 cm long, including the skin and the subcutaneous connective tissue bed. Autopsy skin specimens were also obtained from the middle phalanx of the left fourth finger and left giant toe of cadavers. All the biopsy and autopsy specimens obtained were fixed in 10% neutral formalin. Usual cut sections from paraffin-embedded blocks were stained with hematoxylin-eosin, Elastica-van Gieson and Azan trichrome.

In the analysis, to evaluate the thickening of medial muscle layer of arteries, we selected one available specimen containing a small artery or an arteriole in the shape of a circle with the external diameter of about 100–150 microns for each subject and measured the thickness of media and the external diameter across the short axis of the artery. Then, the ratios of media (M) to external diameter (E),  $M/E$ , were calculated to neglect the difference of artery size.

The comparison between the patients and the referents was statistically evaluated using Student's *t*-test or chi-square test.

## RESULTS

Fig. 1 and 2 shows light-microscopic pathological changes in skin specimens of the finger and toe of a patient with vibration syndrome and a referent. The patient was a 60-year-old male, and the referent was a 61-year-old male. In comparison to the referent, the thickening of the medial muscle layer of the small artery, and an increase of collagen fibers in the connective tissues, especially in perivascular regions, were noted in both the finger and toe of the patient with vibration syndrome.

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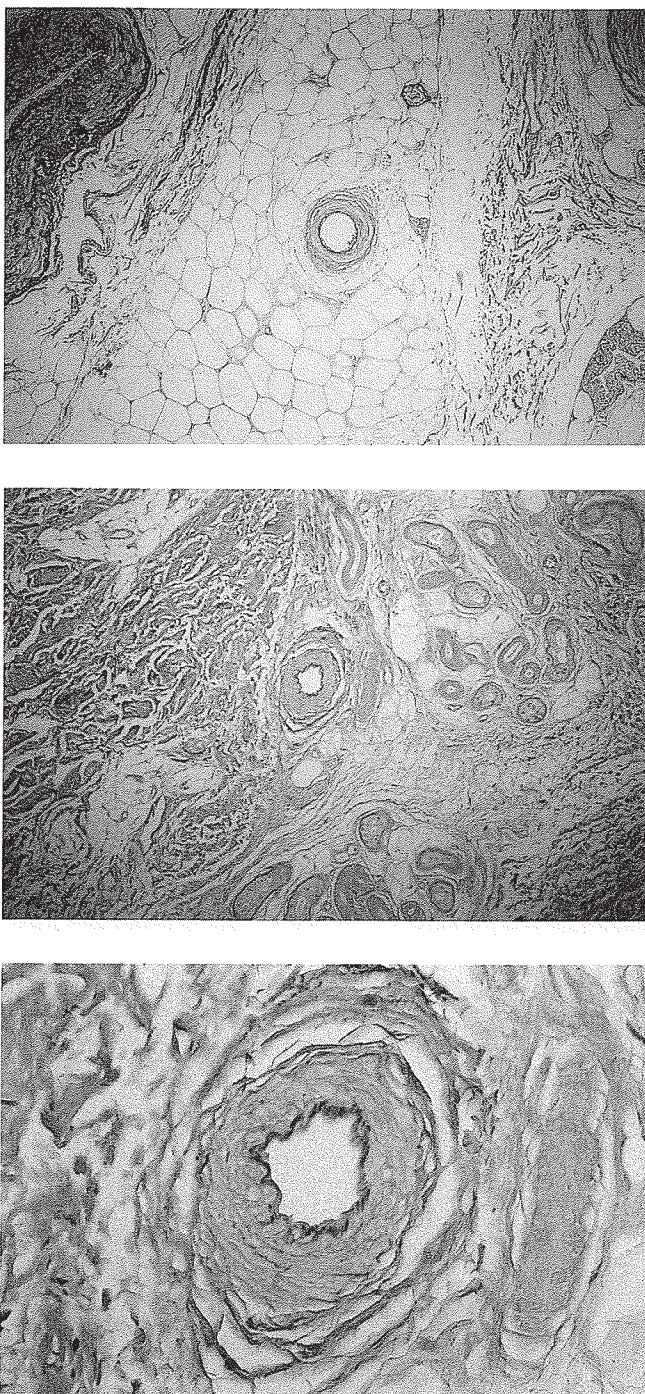


Fig. 1. Thickening of the medial muscle layer and an increase of collagen fiber in the connective tissue, especially the perivascular region in the finger of a patient with vibration syndrome (top, 61-year-old referent, 25  $\times$ ; middle, 60-year-old male patient, 25  $\times$ ; bottom, 60-year-old patient, 100  $\times$ ; Elastica-van Gieson stain).

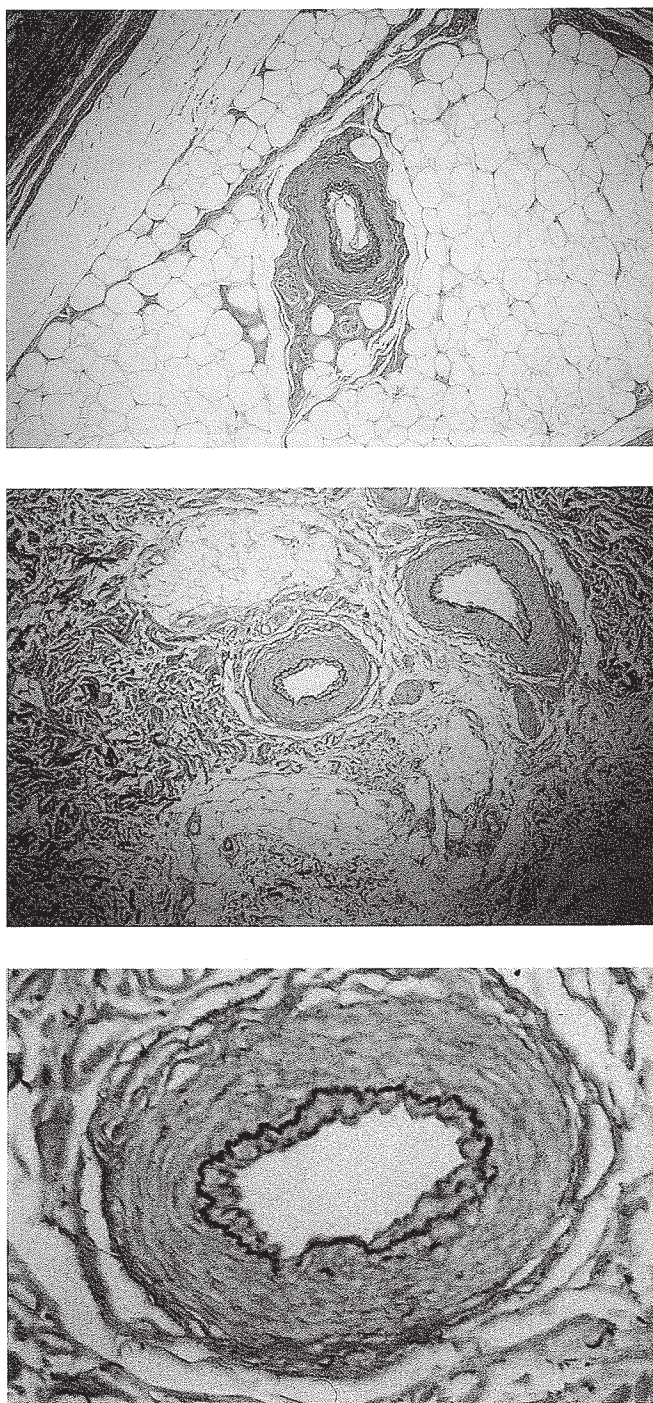


Fig. 2. Thickening of the medial muscle layer, mild intimal fibrosis and an increase of collagen fiber in the connective tissue, especially the perivascular region in the toe of a patient with vibration syndrome. (top, 61-year-old referent, 25  $\times$ ; middle, 60-year-old male patient, 25  $\times$ ; bottom, 60-year-old patient, 100  $\times$ ; Elastica-van Gieson stain).

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Table 1 shows the mean and standard deviation of M/E. The mean M/E in both the fingers and toes was significantly much more increased in the patients than in the referents ( $p < 0.001$ ). The M/E in the fingers and toes was greatest in the RD operators, somewhat smaller in the non-RD operators, and smallest in the referents (Fig. 3). The M/E in the fingers and toes was significantly greater in the non-RD operators as well as the RD operators than in the referents ( $p < 0.001$ ).

Prevalence of the thickening of medial muscle layer and perivascular fibrosis in both fingers and toes was significantly higher in the patients than in the referents ( $p < 0.001$  or  $P < 0.01$ , Table 2). The thickening of medial muscle layer was evaluated as positive when the M/E was greater than the mean  $+1.5$  SD of M/E of the referents (0.24 in the finger, 0.23 in the toe). Prevalence of intimal fibrosis was not significantly different between the patients and the referents (Table 2). The M/E between the finger and the toe showed a statistically positive correlation ( $r=0.657$ ,  $p < 0.001$ ).

Table 1. Mean  $\pm$  standard deviation of the thickness of medial muscle layer of arteries in the finger and toe, represented as the ratio of media to external diameter of the artery in the finger and toe.

\*\*\*  $p < 0.001$ , differences statistically significant from the referent values according to Student's t-test

	Patients (n=21)	Referents (n=13)
Finger	$0.27 \pm 0.04^{***}$	$0.16 \pm 0.05$
Toe	$0.26 \pm 0.05^{***}$	$0.17 \pm 0.04$

Table 2. Prevalence of pathohistological changes in the finger and toe.

\*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , differences statistically significant from the referent values according to chi-square test

	Patients (n=21)	Referents (n=13)
Thickness of media		
Finger	18 (85.7%)***	1 ( 7.7%)
Toe	17 (81.0%)***	2 (15.4%)
Increase of collagen in perivascular region		
Finger	17 (81.0%)***	0 ( 0.0%)
Toe	16 (76.2%)**	3 (23.1%)
Intimal fibrosis		
Finger	5 (23.8%)	3 (23.1%)
Toe	5 (23.8%)	4 (30.8%)

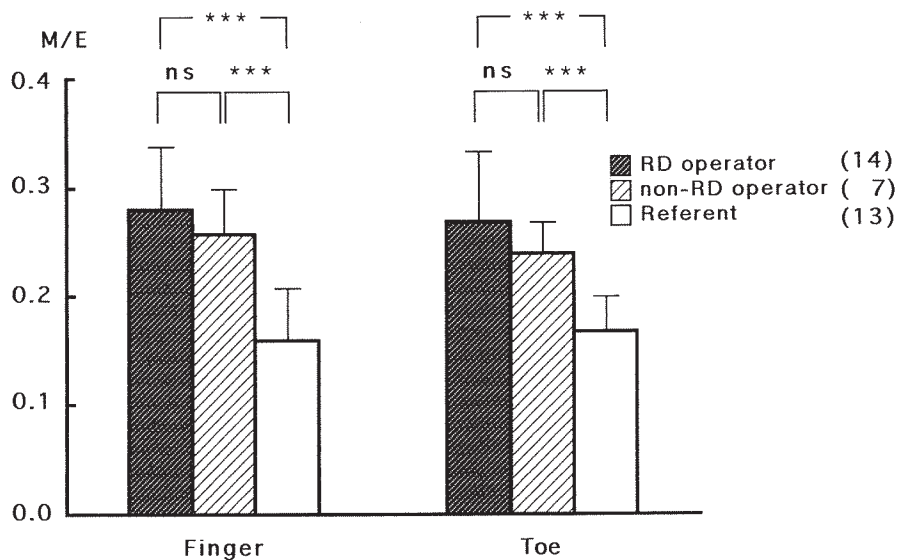


Fig. 3. Changes in the thickness of medial muscle layer (presented as M/E) of the arteries in the finger and toe. M: media; E: external diameter; (n): number of subjects  
 \*\*\*  $p < 0.001$ , differences statistically significant from the referent values according to Student's *t*-test

## DISCUSSION

In the present study, thickening of the medial muscle layer of small arteries or arterioles, and increase of collagen fibers in the connective tissues, especially in the perivascular regions, were often observed in the finger of patients with vibration syndrome in comparison with the referents. Though there was a difference in age between patients and referents (59 years vs. 71 years), the effect of aging on medial thickening has been undefined so far and the age did not seem to affect the findings so much. The thickening of the medial muscle layer and perivascular fibrosis with abundant collagen in the finger are considered to be a typical pathological changes in vibration syndrome.<sup>1-4)</sup> The present results were in accordance with the previous findings. Prevalence of intimal sclerosis was not different between the patients and referents, as indicated by Takeuchi *et al.*,<sup>4)</sup> although some studies indicated that intimal thickening was observed to correlate with the clinical severity such as a gangrene of the fingertip<sup>2,3)</sup> and was found in an experiment of animals exposed to vibration.<sup>14)</sup>

The Medial thickening of small arteries or arterioles and perivascular fibrosis were also frequently encountered in the toe of patients with vibration syndrome. Ashe and Williams<sup>2)</sup> reported medial muscular hypertrophy in the pedal arteries of all five jack-drill operators they examined, a finding confirmed in the present observations. Moreover, the present study demonstrated medial thickening of toe arteries, not only in the RD patients who had been exposed to vibration of the foot, but also in the non-RD patients who had not been exposed to direct vibration of the foot. The medial thickening, however, tended to be somewhat greater in the RD operators than the non-RD operators.

Medial thickening of arteries can result in stenosis of the arteries and then circulatory disturbances. It has been indicated that patients with vibration syndrome, particularly with Raynaud's phenomenon of the finger, have circulatory disturbances in both the upper and lower ex-

tremities: the patients are likely to complain of coldness felt in both the hands and feet,<sup>11)</sup> and have lower skin temperature and dermal blood flow of the finger and toe,<sup>12,13)</sup> and some patients have Raynaud's phenomenon of toe.<sup>5-10)</sup> The present pathological findings observed in the toe histologically confirmed the existence of circulatory disturbances of the foot, even in the patients who have not been exposed to vibration of the foot directly.

In addition, the medial thickening of arteries was shown to correlate in the finger and toe. The present result was consistent with the indication by Ashe and Williams<sup>2)</sup> that the wall/lumen ratio of the pedal arteries was roughly parallel to that seen in the finger arteries in the same patient. This suggests that patients with more severe circulatory disturbances of the hand are likely to have circulatory disturbances of the foot as well, which may explain the finding that patients with more frequent attacks of Raynaud's phenomenon in the finger are likely to complain of coldness in the feet.<sup>11)</sup>

It is known that vibration exposure of the hand evokes skin sympathetic nerve activity and leads to vasoconstriction in the contralateral finger and also in the toe.<sup>15-19)</sup> A previous experiment demonstrated that operation of a chain saw lowered the blood flow in both finger and foot.<sup>20)</sup> These pathophysiological findings indicate that hand-arm vibration can induce vasoconstriction of the foot through the activation of the sympathetic nerve system. Pathological changes in the finger such as medial muscle hypertrophy and perivascular fibrosis are considered to result from long-term repeated vasoconstriction and edema due to circulatory disturbances in the hand. It is, therefore, considered that, as in the finger, the medial thickening of arteries and perivascular fibrosis in the toe can be brought about by long-term repeated vasoconstriction and circulatory disturbances in the foot. These are induced by hand-arm vibration through the activation of the sympathetic nerve system.

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