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Article

# Acute Exercise for the Hypertensive Elderly Affects the Whole-Body Capillary: A Single-Center Pilot Trial

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**Abstract:** Objective To investigate nailfold capillary parameters in community-dwelling individuals aged over 60 years who have hypertension and do not exercise regularly. Furthermore, the study examined the correlations between capillary function and other health-related indicators. Design A single-center pilot trial Setting Faculty of Health, Tsukuba University of Technology, Japan Participants hypertensive community-dwelling elderly people Intervention Microcirculation was observed before and 1 min after arm-curl exercise by means microscopy of capillary with non-exercised limb. Additionally, we examined other health-related indicators. **Outcome measures:** Acute effects of reperfusion on nailfold density, flow, and diameters. Secondary outcomes included the correlations between microvascular parameters and other health-related indicators. We hypothesized that brief exercise could enhance microcirculation reperfusion and correlate with other health-related parameters. Results: There were 20 participants with a mean (SD) age of 67.1 (5.8) years. The capillary flow rate changed from  $2.3 \pm 6.7$  to  $2.7 \pm 0.2$  log  $\mu\text{m/s}$  ( $P < 0.01$ ), and the capillary density changed from  $0.8 \pm 0.2$  to  $0.9 \pm 0.1$  log/mm ( $P < 0.01$ ) included significant increase in the non-exercising limb. There were significant correlations were observed between the nailfold capillary diameter and body fat mass, the capillary diameter and physical activity, and the capillary density and bone mineral density. Conclusion the acute effects of exercise on high-risk elderly individuals can be safe, and even a 1-min exercise potentially improves their nonexercised of nailfold capillary function even in a brief time. The results indicate that capillaries have an impact on the function of the whole body. Thus, it may be a useful diagnostic tool for assessing nailfold capillary. (249/250 words)

**Keywords:** nailfold capillary; acute exercise; hypertensive elderly; health related parameters

## 1. Introduction

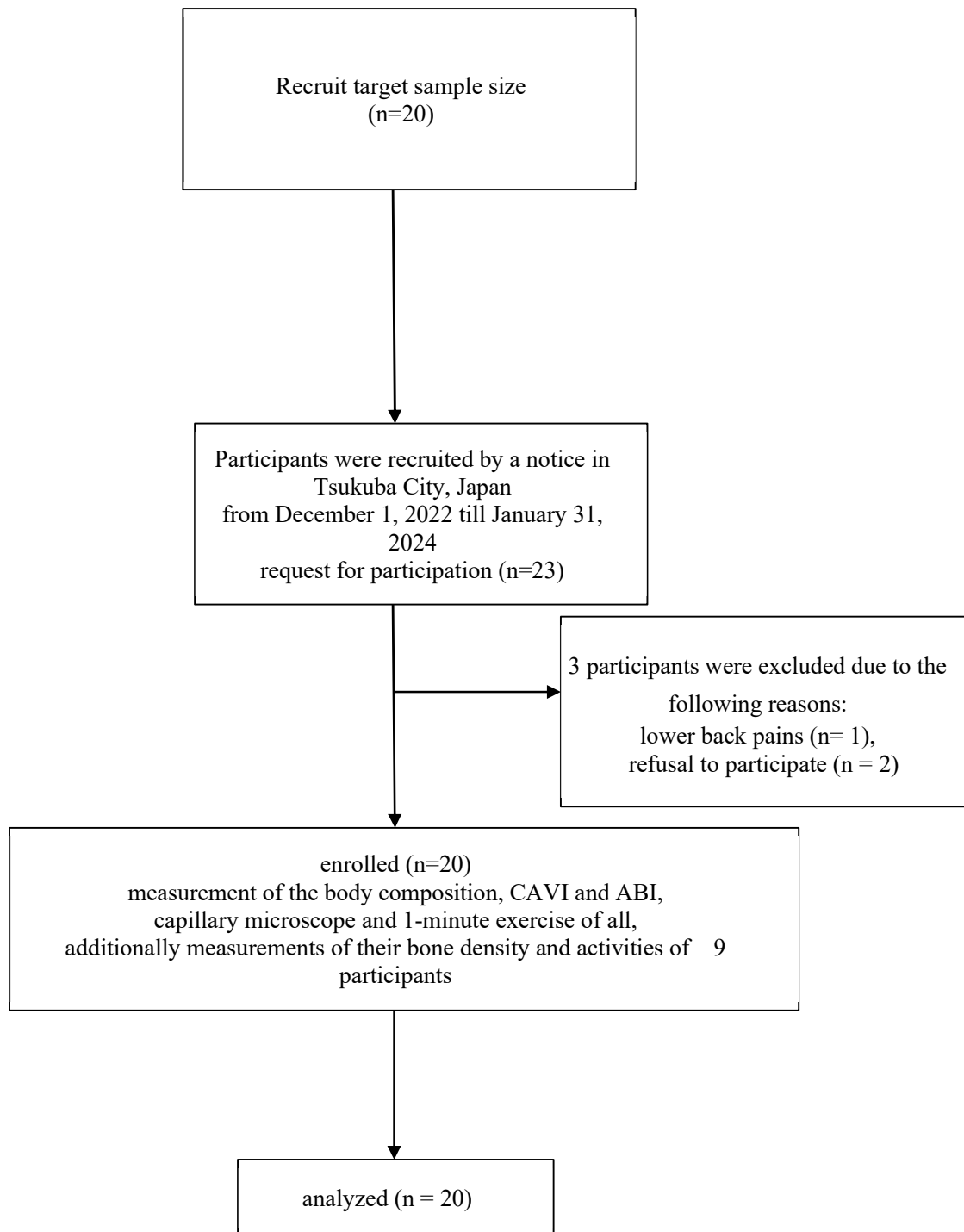
Functional and structural modifications in the microcirculation occur early in hypertension development and in aging [1–3]. Previous studies have demonstrated that a reduction in dysfunctional vessels at rest eventually leads to anatomical micro vessel loss (structural rarefaction) as well as functional impairment of capillary perfusion and recruitment [1,2] are referred to as “ghost vessels” or “dysfunctional vessels.” The microcirculation in the nailfold is considered to be a predictive and noninvasive marker of generalized microvascular and endothelial function [4]. The restoration of microvascular function can help decrease systemic blood pressure by reducing peripheral vascular resistance; this, in turn, can improve circulation in target organs and help decrease cardiovascular disease complications [5]. However, to date, the impact of local exercise on the circulation in the non-exercising limbs remains unknown. Furthermore, details of the immediate

impact of exercise on the peripheral circulation in middle-aged and elderly patients with hypertension who are at a high risk of adverse events are lacking. One of the adverse effects of exercise is the rapid activation of the sympathetic nervous system at the start of exercise, which significantly affects the peripheral circulation. Therefore, it is important to ensure the safety of exercise for high-risk individuals. For this reason, the present study aimed to investigate nailfold capillary parameters in community-dwelling individuals aged over 60 years who have hypertension and do not exercise regularly. Furthermore, the study examined the correlations between capillary function and other health-related indicators.

## **2. Materials and Methods**

### *2.1. Participants*

This study enrolled community-dwelling elderly individuals with hypertension who attended public facilities in Tsukuba City, Japan, between December 2022 and January 2024 (Figure 1). Of the 23 eligible participants, 20 provided informed consent. The baseline characteristics of the participants are shown in Table 1. Those with contraindications to these examinations, such as pacemaker use, and those with contraindications to exercise therapy as described in the American College of Sports Medicine's Guidelines for Exercise Testing and Prescription, 9th edition [6], were excluded from the study. The ethics committee of Tsukuba University of Technology approved the research protocol (approval number: 202204). Furthermore, the study was registered with the University Hospital Medical Network Clinical Trials Registry (Identifier UMIN000053790).



**Figure 1.** Flow chart showing enrollment.

**Table 1.** Baseline characteristics of the participants.

Parameter	n=20
Age (years)	67.2±6.2
Male/female	7 / 13
Diabetes	4 / 20
BMI (kg/m <sup>2</sup> )	22.1 ±3.6
Skeletal muscle mass (kg)	38.7 ± 6.2
Fat mass (kg)	22.6 ± 8.8
Systolic blood pressure (mmHg)	150.1± 17.9
Diastolic blood pressure (mmHg)	93.1± 11.7

CAVI	8.4 ± 1.0
ABI	1.1 ± 0.1
Diameter of the nailfold capillary	9.7 ± 2.6
Flow rate of the nailfold capillary	295.8 ± 172.2
Density of the nailfold capillary	7.0 ± 1.5
Bone mineral density (%)	26.3 ± 3.7 (n=9)
Physical activities (steps/day)	4714.3 ± 1277.8 (n=9)

Values represent the mean ± standard deviation of the 20 participants. BMI: body mass index, CAVI: cardio-ankle vascular index, ABI: ankle-brachial index.

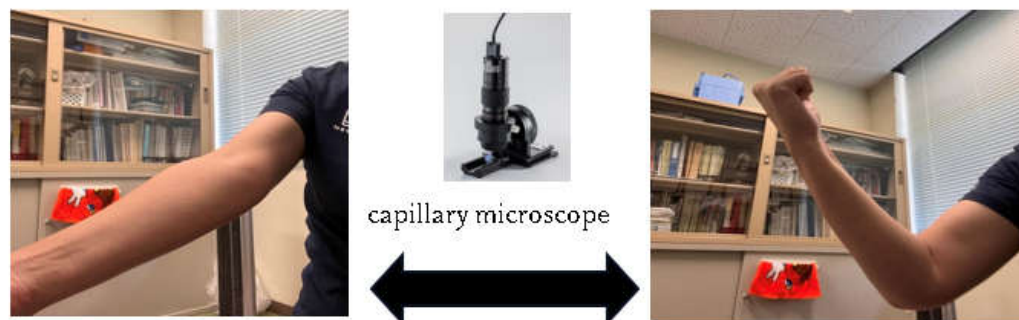
## 2.2. Study Design

The study followed a single-center pilot trial design.

The study protocol is depicted in Figure 2. The body composition and arterial stiffness of the participants were measured. Then, the participants were asked to perform elbow flexion and extension exercise in the sitting position at 13 RPE for 1 min. Before and after the exercise, the capillary diameter and the flow at the nailfold of the fourth finger for the non-exercising limb were measured with a microscope.

Fig. 2. Procedure and measurement set

The participants performed arm-curl exercise for 1 min, intensity of 13RPE. We measured an examination in pre and post of the exercise by the capillary microscope.



	Baseline	About 1 min later
Assessment period	Before exercise (n = 20)	after exercise (n = 20)
Capillary microscope	○	○
Body composition	○	×
CAVI/ ABI	○	×
Bone density	○ (n = 9)	×
Physical activities	○ (n = 9)	×

Figure 2. Procedure and measurement set.

During the session, the temperature was maintained at 23°C. All experiments were conducted simultaneously between 9 and 11 AM. The participants were prohibited from engaging in vigorous exercise, drinking caffeinated beverages, and smoking within 48 h before the experiment.

### 2.3. Sample Size

The sample size was calculated using G\*power (Heinrich-Heine-University Dusseldorf, North Rhine-Westphalia, Germany). The target number of participants was 20 ( $\alpha = 0.05$ ,  $1-\beta = 0.95$ ), which was based on a study in which capillary examination was conducted in elderly patients [7,8].

### 2.4. Measurement of Nailfold Capillary Parameters

Capillary flow was measured using a microscope (Bscan-Z, Tokuda Corporation, Japan) by filming the nailfold of the nondominant the fourth digits of the subjects [8,9]. An image analysis software (Capimetrics, KK Technology, UK) was used for the measurements. During filming, the magnification of the blood flow scope was set to 500 $\times$  (width, 0.87 mm; height, 0.65 mm; depth, 0.3 mm), and 10-s videos of the nailfold of the non-exercising limb was taken [9]; furthermore, the capillary diameter, blood flow, and density were measured from the first layer of the vessels, as shown in Figure 3-1,2.

**Figure 3-1. Measurement of the nailfold parameters**



**Figure 3-2. Nailfold capillary image of baseline and after 1-min exercise of typical subject by the microscope measurement**

74 years old, male



The magnification of the blood flow scope was set to 500 $\times$  (width, 0.87 mm; height, 0.65 mm; depth, 0.3 mm).

The capillary diameter, blood flow, and density were measured from the first layer of the vessels

### 2.5. Body Composition and Physical Activities

The participants' weight, skeletal muscle mass, and fat mass were measured by a physical therapist using a body composition analyzer (Tanita Corporation MC-780A). In addition, their height and physical activities were read from their application forms [10].

### 2.6. Measurement of the CAVI and ABI

After a 15-min rest, the Ankle Brachial Index (ABI) and Cardio Ankle Vascular Index (CAVI) of the participants were measured in the supine position in an air-conditioned room using a VS-1000 instrument (Fukuda Denshi, Tokyo, Japan) [11].

### 2.7. Bone Mineral Density

Bone mineral density (BMD) was measured at the right heel using Benus evo (Nihon Kohden Co., Japan) [12,13], which was calibrated daily according to the manufacturer's recommendation. All measurements were performed by the same operator.

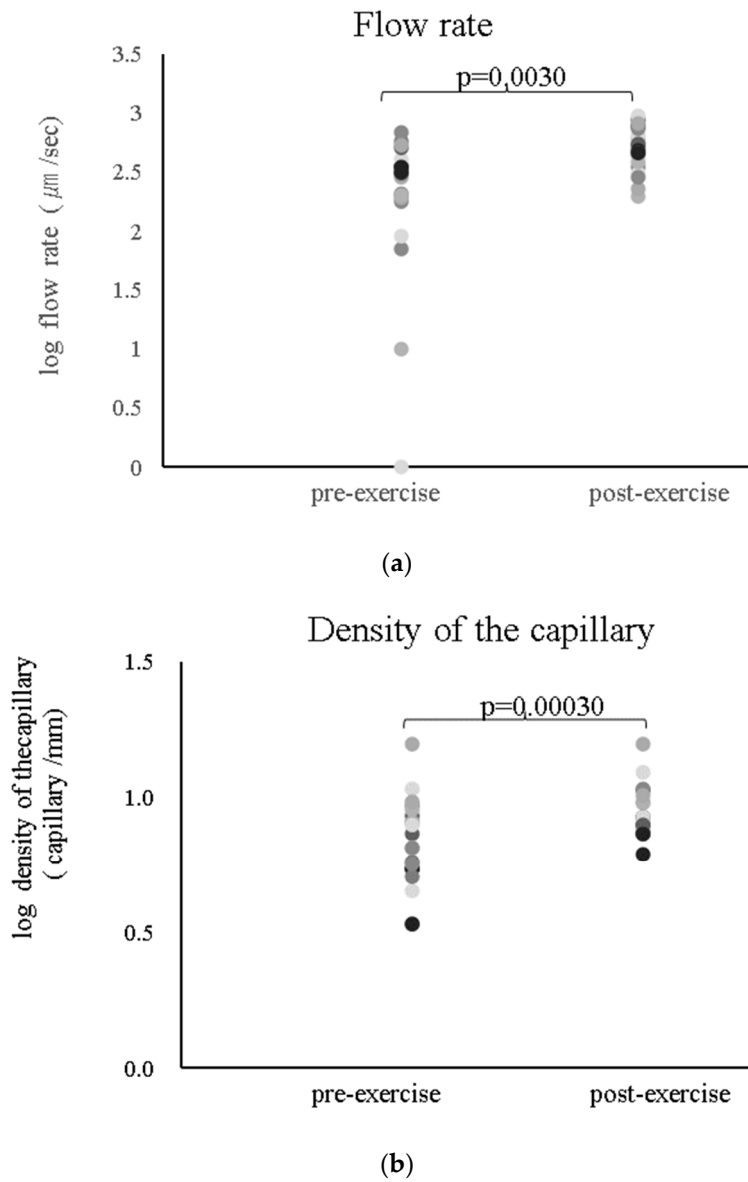
### 2.8. Statistical Analysis

The baseline characteristics were expressed as mean  $\pm$  standard deviation. All statistical analyses were conducted using the SPSS software ver. 21 (IBM Corp, Chicago, IL, USA). Student's *t*-test was employed to statistically analyze the logarithmically transformed wear data, and Pearson's product-moment correlation coefficient was used parameters of capillary and other parameters.

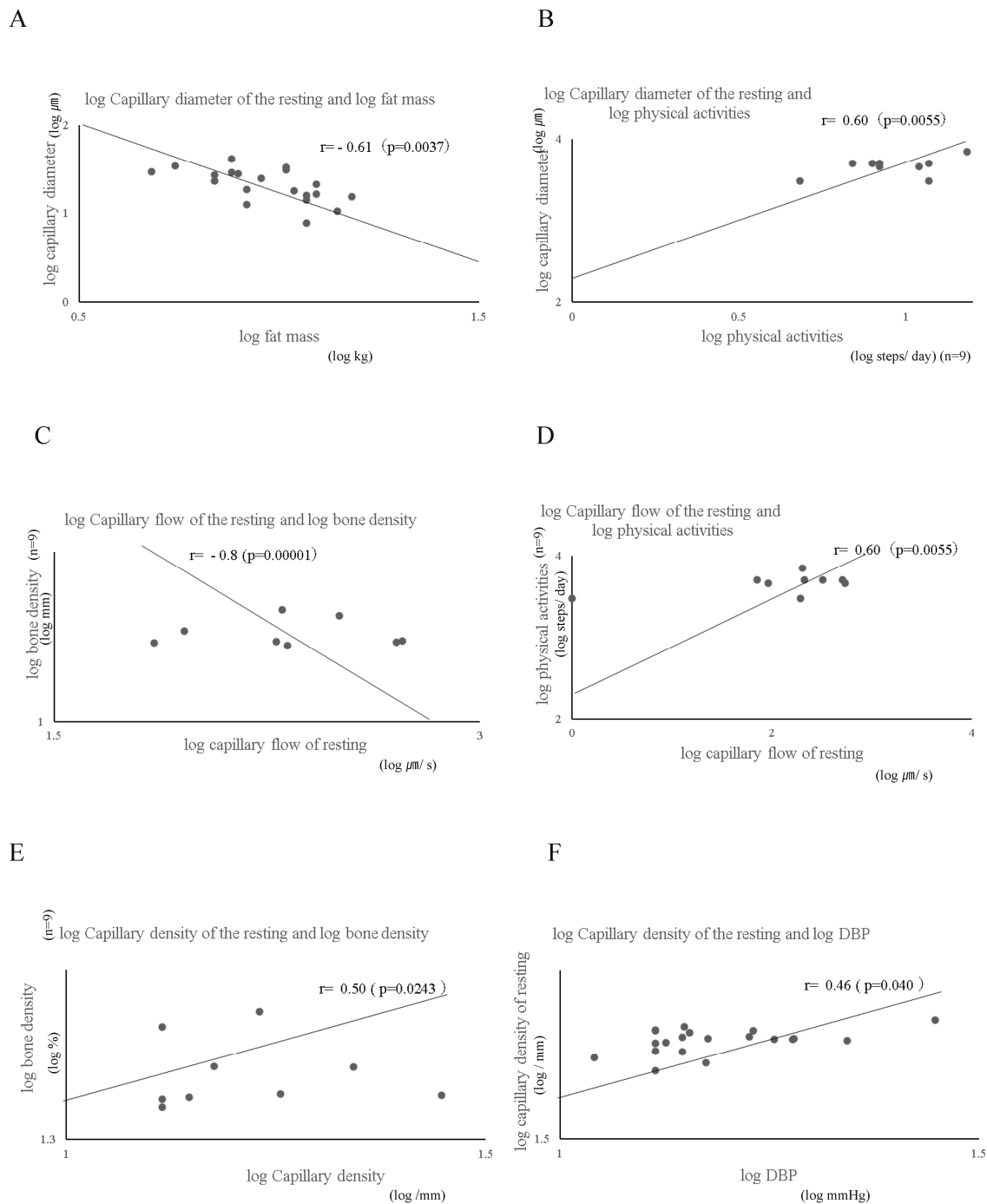
## 3. Results

All the participants completed the experiments without any difficulty or side effects. The participants' characteristics are summarized in Table 1. As shown in Figure 4-1, the capillary flow rate significantly changed from  $2.3 \pm 0.7$  to  $2.7 \pm 0.2$  log  $\mu\text{m/s}$  ( $P = 0.003$ ), and the capillary density significantly changed from  $0.8 \pm 0.2$  to  $0.9 \pm 0.1$  log/mm (0.0003). Nailfold capillary image of baseline and after 1-min exercise of typical subject by the microscope measurement in Figure 3-2. In addition, the correlation of nailfold capillary parameter at rest and other parameters is depicted in Figure 5: Figure 5A shows that the log capillary diameter at rest is negatively correlated with log fat mass ( $r = -0.61$ ;  $P = 0.0037$ ); Figure 5B shows that the log capillary diameter at rest is correlated with log physical activities ( $r = 0.60$ ;  $P = 0.0055$ ); Figure 5C shows that the log capillary flow at rest is negatively correlated with the log BMD ( $r = -0.8$ ;  $P = 0.00001$ ); Figure 5D shows that the log capillary flow at rest is correlated with the log physical activities ( $r = 0.60$ ;  $P = 0.0055$ ); Figure 5E shows that the log capillary density at rest is correlated with log BMD ( $r = 0.50$ ;  $P = 0.0243$ ); Figure 5F shows that the log capillary density is correlated with log DBP ( $r = 0.46$ ;  $P = 0.040$ ); Figure 5G shows that the log capillary density at rest is negatively correlated with log BMI ( $r = -0.49$ ;  $P = 0.0289$ ); and Figure 5H shows that the log capillary diameter at rest is correlated with log physical activities ( $r = 0.65$ ;  $P = 0.029$ ). Furthermore, the capillary diameter at rest was significantly multiple regressed with body fat mass and DBP. Moreover, In individuals who exhibited a change in the diameter of the nailfold capillary before and after exercise, a strong correlation of 0.75 was observed between the change in nailfold diameter ( $\Delta$  nailfold diameter) and body fat mass ( $p=0.012$ ). Additionally, a moderate correlation of 0.64 was observed between age and systolic blood pressure (SBP) ( $p=0.044$ ).

On the other hand, in individuals who did not show a change or exhibited a decrease in the diameter before and after exercise, a strong negative correlation of -0.71 was observed between age and the change in flow of the nailfold capillary ( $\Delta$  flow) ( $p=0.021$ ). A strong correlation of 0.95 was observed between the change in nailfold capillary flow ( $\Delta$  nailfold flow) and physical activity ( $p=0.000020$ ). Furthermore, a strong negative correlation of -0.76 was observed between body fat mass and physical activities ( $p=0.010$ ).



**Figure 4.** (a) Change in log flow rate. (b) Change in the capillary density.



**Figure 5.** Correlation of nailfold capillary parameters at rest with other health-related parameters. DBP: diastolic blood pressure, BMI: body mass index.

Correlation between the capillary parameters at rest and other health-related parameters

Graph A shows that the log capillary diameter at rest is significantly correlated with log fat mass ( $r = -0.61$ ;  $P = 0.0037$ ). Graph B shows that the log capillary diameter at rest is significantly correlated with log physical activities ( $r = 0.60$ ;  $P = 0.0055$ ). Graph C shows that the log capillary flow at rest is significantly correlated with log bone density ( $r = -0.80$ ;  $P = 0.00001$ ). Graph D shows that the log capillary flow at rest is significantly correlated with log bone density ( $r = 0.60$ ;  $P = 0.0055$ ). Graph E shows that the log capillary density at rest is significantly correlated with log bone density ( $r = 0.50$ ;  $P = 0.024$ ). Graph F shows that the log capillary density at rest is significantly correlated with log DBP ( $r = 0.46$ ;  $P = 0.040$ ). Graph G shows that the log capillary diameter at rest is significantly correlated

with log BMI ( $r = -0.49$ ;  $P = 0.029$ ). Graph H shows that log age is significantly correlated with log bone density ( $r = 0.50$ ;  $P = 0.024$ )

#### 4. Discussion

Exercise and drug therapy have been reported to be effective for dysfunctional vessels during recanalization. However, excessive response of the sympathetic nervous system to exercise may increase the risk of cardiovascular events [13]. Furthermore, whether local and acute exercises affect the capillaries remain unclear. It is crucial to explore the acute effects of exercise on high-risk elderly individuals. Therefore, this study included elderly individuals aged over 60 years who do not exercise regularly. The function of the capillaries on the non-exercising limb before and after a 1-min moderate-intensity exercise was measured. To the best of our knowledge, this is the first study to examine the immediate effects of exercise on peripheral circulation and the safety of exercise for elderly individuals with hypertension. Furthermore, it investigated the correlation between capillary function and other health-related indicators. As a result of this study, all protocols could be safely implemented. It was suggested that even a 1-min exercise could safely and effectively improve peripheral circulation, even on the non-exercising limb. The capillary examination parameters were adopted in the medical guidelines [14] and can be improved by medication and lifestyle habits. It has been demonstrated that the capillary parameters were related to other health-related indicators. In this study, a significant change was observed in the dysfunctional vessels of the non-exercising limb before and after a 1-min exercise, which could be attributed to two reasons: First, the arm-curl exercise induced systemic circulation. Although it was against the principle of specificity in the principles of exercise therapy, which was because it was not skeletal muscle but the whole body's microcirculation. Second, the capillary diameter did not significantly change. This is because the subjects were elderly individuals with hypertension, and their capillary function had declined due to aging. That was because no change was observed in the capillary diameter. Capillaries exist throughout the body and are involved in the transport of nutrients to cells, which is why a correlation with health-related indicators was observed. In recent years, it has been reported that ectopic fat decline functions in various organs of the body [15]. A recent study has demonstrated an inverse correlation between body fat mass and capillary diameter. Therefore, it is essential to reduce body fat through continuous exercise therapy. However, exercise therapy can trigger cardiovascular events in high-risk elderly individuals; thus, this therapy is difficult to implement continuously. In addition, the rapid activation of the sympathetic nervous system at the start of exercise increases the risk of cardiovascular events in this population, but results from this study, safely and effectively even for the high-risk elderly. The main reason in this study was moderate intensity. This study demonstrated not only the acute effects of exercise but also its long-term effects, such as improved capillary function, formation, and density [16]. Consequently, it is considered essential to establish regular exercise habits. The results of this study indicated that for patients with hemiplegia or plaster fixation, which causes them to be inactive, exercising healthy local limbs can positively affect the non-exercising limbs. This study has some limitations. First, the sample size was small because the study focused on a single center. Second, the participants did not exhibit long-term effects of exercise. Consequently, it is necessary to increase the sample size and extend the intervention period in future studies.

#### 5. Conclusions

In this study, community-dwelling elderly individuals with hypertension safely performed a 1-min exercise without experiencing serious adverse events and the capillary impact whole body function. Therefore, it may be a useful diagnostic tool to assess nailfold capillary.

**Author Contributions:** Conceptualization, MISA Miura; Data curation, Chie Saito and Osamu Ito; Investigation, Hisashi Sugaya, Shingo Koyama and Yasushi Matsui; Methodology, Chie Saito, Satoshi Sakai and Tohru Sakuma; Supervision, Masahiro Kohzuki, Osamu Ito and Kunihiko Yamagata; Writing – original draft, MISA Miura; Writing – review & editing, Masahiro Kohzuki, Chie Saito, Satoshi Sakai, Hisashi Sugaya and Kunihiko Yamagata.

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**Institutional Review Board Statement:** The trial was registered at Japan registry of clinical trials under 2204 and was the ethics committee (Review Board of Tsukuba University of Technology). It was conducted in accordance with the Declaration of Helsinki.

**Data Availability Statement:** The data presented in this study are available on request from the corresponding author.

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**Declaration of Conflicting Interests:** All authors declare that there are no conflicts of interest.

**Research Ethics and Patient Consent:** Informed consent was obtained from all subjects involved in the study.

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