

“Studying the cutaneous microcirculatory response during upper-limb exercise in healthy, older, sedentary people”

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Abstract. This study investigated changes incurred in cutaneous skin blood flux (SKBF) in the superficial veins of the lower limb by upper limb exercise training in the form of arm-cranking in 14 healthy participants over the age of 50 years. Changes in cutaneous microvascular function of the lower leg were assessed using laser Doppler Flowmetry (LDF) during a 30-minute exercise session undertaken over 4-exercise periods. Both SKBF and Time to reach Peak Perfusion (Tmax) were improved significantly during the 2nd (e.g. 121 (\pm 107.2) vs 280 (\pm 269.1) and 171 (\pm 34.4) vs. 247 (\pm 38.3) respectively) when compared to the first exercise period, while values approaching initial levels in the following stages. The results indicate that the thermoregulatory and vasodilation mechanisms observed during exercise in middle-aged and older healthy people are different to the one appearing in younger age groups, suggesting a more extensive effect of the age-related structural changes than it was previously thought.

Keywords: Skin blood flow, arm-cranking exercise, cutaneous microcirculation, perfusion, skin temperature

1. Introduction

The structural and functional integrity of the microcirculation is important because it is affected not only by a number of diseases and conditions (e.g. varicose veins [19], sickle cell anaemia [3], systemic sclerosis [14]), but also by age which compromises both endothelial function [9] and vasodilation [11].

Exercise can be beneficial in many ways for the microcirculation of older age-groups, improving endothelial function in both patient [4, 17] and healthy sedentary groups [18, 26]. Nevertheless, the exact acute effects of exercise on the microcirculation remain unknown although certain aspects have been clarified in a number of studies. For example, it has been suggested that exercise activates thermoregulatory mechanisms which modifies endothelium before the vascular smooth muscle cells [10, 18], affecting glabrous and non-glabrous skin sites in a different manner [20]. It is also known that skin blood flux decreases in the inactive arm at the onset of leg exercise, but increases later linearly with internal temperature [23]. However, it is largely unknown what the response of the lower limbs is during arm exercise in an older, sedentary population. It is therefore important to understand the lower limb response during arm exercise and changes in the microcirculation afterwards [18]; given that microangiopathic diseases occur more commonly in the lower limb [1], as this will give an insight as of how exercise acutely affects the microcirculation in older, exercise-inactive, populations.

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Table 1
Participant demographics (at rest)

Sex	6 female, 8 male
Age (years)	61 ± 6
Body mass (kg)	73.5 ± 15.2
Stature (cm)	171.3 ± 8.5
Body mass index (kg·m ⁻²)	25.0 ± 3.0
Systolic blood pressure (mmHg)	120 ± 7
Diastolic blood pressure (mmHg)	72 ± 5
Mean arterial pressure (mmHg)	80 ± 5
Heart rate (bpm)	74 ± 11
Peak power output (W)	63 ± 16

Therefore, the aims of this study were to examine the behaviour of the cutaneous microcirculation in the non-active limb during upper-limb exercise, to explore vascular resistance during exercise in an older population, using “time to reach maximum perfusion” (T_{max}) [16] and finally to investigate the association of those findings with skin temperature and the thermoregulatory ability of a healthy, older, sedentary population.

2. Methods

With Sheffield Hallam University Ethics Committee approval, 14 participants were recruited via posters and word-of-mouth in South Yorkshire. All participants were required to be above 50 years of age, normotensive, non-smokers, sedentary and were not taking any regular medications. Participants with past venous ulceration, lower-limb arterial disease, hypercholesterolemia, peripheral oedema or cardiac failure, and those with major skin changes in the gaiter area were excluded as well as those who take regular exercise. Female participants were studied in days 1 to 7 of their menstrual cycle to minimise the influence of cyclical changes in female hormones [2] an influence which however has been recently questioned [24]. This research was carried out in accordance with the Declaration of Helsinki of the World Medical Association and according to the ethical guidelines of “Clinical Hemorheology and Microcirculation” [6], with all volunteers providing written informed consent. Demographic data are shown in Table 1.

2.1. Procedures

2.1.1. Day 1 – arm-cranking fitness assessment

After habituation to the procedures, along with providing a brief medical history and informed consent, resting blood pressure and heart rate was recorded, while participants completed an incremental arm-cranking exercise test to define compatibility. The test was performed on a Lode Angio (Lode BV, Groningen, Netherlands) until maximal volitional exertion was reached. It comprised 2-minute bouts of constant-intensity work at a pedalling rate of 50 rev per min to maximum exercise tolerance. The initial intensity was 7 W with power output being increased by 7 W until exhaustion was reached. Heart rate (HR) was continuously monitored using a HR monitor (Sports Tester, Polar, Finland). Perceived exertion using the Borg Ratings of Perceived Exertion (RPE) 15-graded scale and the degree of pain experienced

57 using the Borg Category Ratio-10 (CR-10) scale were also recorded during the last 30 of each exercise
58 increment.

59 2.1.2. Day 2- Experimental protocols for assessment of outcome measures

60 Participants were instructed to abstain from ibuprofen, herbal supplements, food and caffeine within
61 2 h of testing and refrain from exercise for 24 h prior to assessment. All assessments were performed in
62 a temperature-controlled room (range 22-23°C).

63 The gaiter area of the left leg (chosen as such for protocol adherence purposes) was cleaned with an
64 alcohol wipe and allowed to dry before applying a single point laser probe (PF383; Perimed AB, Jarfalla,
65 Sweden), connected to a laser Doppler flowmeter (PF5001; Perimed AB), to the surface of the leg 4–8 cm
66 proximal to the medial malleolus to obtain an index of skin blood flow and assess cutaneous red cell flux.
67 It should be noted that LDF measurements are not an absolute quantification of the cutaneous blood flow
68 but are an integral over flowing red blood cells and their velocity instead, represented by the formula
69 “Red Blood Cells Concentration × RBC velocity = Blood Flux”. The laser-Doppler probe signals were
70 monitored via an online software chart recorder (PSW; Perimed AB).

71 After 5 min recording of baseline flux, while being idle, participants were exercised at 60–70% intensity
72 (defined by Day 1 results) in cycles of 5 min exercise at a rate of 50 rev/min, followed by 1 min of rest
73 (which the exception of the last exercise period which was followed by a 2 min rest) for a total exercise
74 time of 20 min in a 30 min session. Cutaneous skin blood flux measurements were recorded during the
75 whole exercise session, with the fibre optic cables of the LDF probe being secured to a solid object to
76 avoid artefacts in the LDF signal as described previously [27].

77 Skin temperature was continuously recorded using a temperature sensor. Heart rate (Sports Tester,
78 Polar, Finland) was recorded continuously. There were no adverse effects.

79 2.2. Data recording and analysis

80 Peak cutaneous flux responses recorded in conventional perfusion units (PU), were used as measures
81 of cutaneous microvascular perfusion during exercise. The time needed for each participant to reach
82 peak perfusion (Tmax) was also calculated as described in the literature [16]. Outcome measures were
83 first tested for normal distribution using the Kolmogorov-Smirnov goodness of fit test and were logarith-
84 mically transformed where necessary. Acute effects of exercise on peak cutaneous flux responses were
85 assessed using ANOVA for repeated measures, with paired-samples *t*-tests used to interpret interaction
86 effects. Mauchly’s Test was used to test the assumption of data’s sphericity. Effect sizes (Cohen’s *d*) were
87 calculated for exercise-induced changes in peak cutaneous flux responses, with 0.2, 0.5, and 0.8 repre-
88 senting small, medium, and large effects, respectively [21]. Statistical significance was set at $P \leq 0.05$.
89 Data is expressed as mean ± standard deviation.

90 3. Results

91 3.1. Skin blood flux

92 The assumption of sphericity was violated for maximum skin blood flux perfusion ($\chi^2(9) = 27.12$,
93 $p = 0.002$). Consequently, degrees of freedom were corrected using the Greenhouse-Geisser estimates
94 of sphericity ($\epsilon = 0.55$). The results show that the period in which skin blood flux measurements were

95 taken had a statistically significant effect on cutaneous skin blood flux ($p < 0.001$, $d = 0.94$). Pair-wise
 96 comparisons suggested a statistically significant difference between the baseline and all 4 exercise periods
 97 (Fig. 1) and also between the first and all consecutive exercise periods [e.g. First vs. Second vs. Third vs.
 98 Fourth; $121 (\pm 107.2)$ vs. $280 (\pm 269.1)$ vs. $228 (\pm 190)$ vs. $263 (\pm 247)$]. No significant differences were
 99 observed between any other exercise periods (Fig. 1).

100 3.2. T_{max}

101 As the assumption of sphericity was violated ($\chi^2 (5) = 21.13$, $p < 0.001$), degrees of freedom were
 102 corrected using the Greenhouse-Geisser estimates of sphericity ($\epsilon = 0.46$). Similarly to skin blood flux,
 103 exercise period appeared to play a significant role in the speed of reaching peak perfusion ($p = 0.03$,
 104 $d = 0.52$), with values being significantly decreased on the second time period but returning to initial
 105 levels at the 2 consecutive periods (e.g. Second vs. First; $171 (\pm 34.4)$ vs. $247 (\pm 38.3)$ and Second vs.
 106 Third vs. Fourth; $171 (\pm 34.4)$ vs. $228 (\pm 33.9)$ vs. $212 (\pm 58.3)$). No significant differences were observed
 107 between any other exercise periods (Fig. 2).

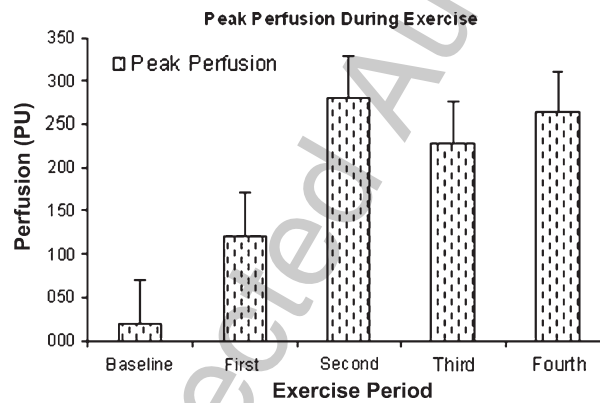


Fig. 1. Peak Perfusion variations during the exercise periods. $p < 0.001$ (ANOVA for repeated measures).

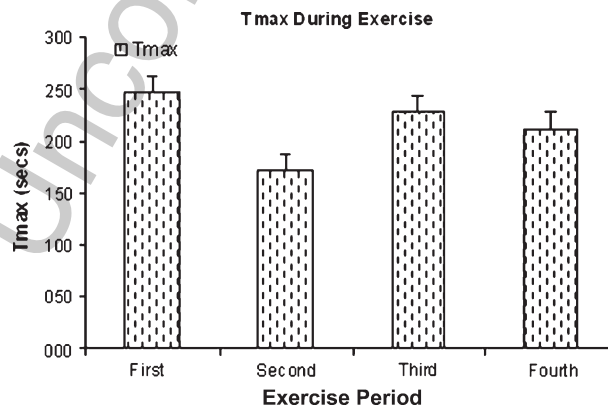


Fig. 2. Tmax variations during the exercise periods. $p = 0.03$ (ANOVA for repeated measures).

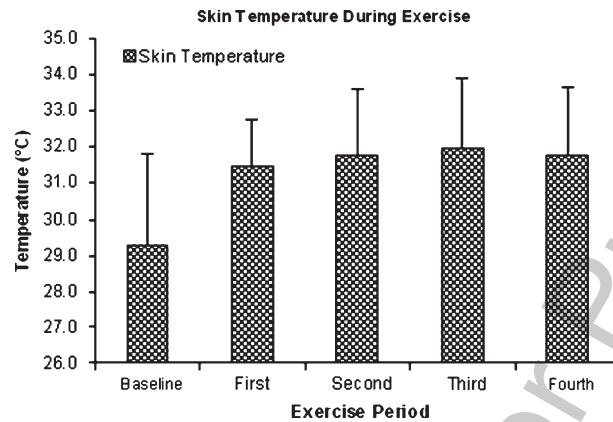


Fig. 3. Skin Temperature variations during the exercise periods. $p < 0.001$ (ANOVA for repeated measures).

3.3. Skin temperature

The Greenhouse-Geisser estimates of sphericity ($\epsilon = 0.43$) was used to correct the degrees of freedom, as the assumption of sphericity was violated here in Skin Temperature as well ($\chi^2(9) = 48.73, p < 0.001$). The ANOVA revealed a statistically-significant importance of the period in which skin temperature measurements were obtained ($p = 0.005, d = 0.42$), with values increasing from baseline in the 1st exercise period and stabilising afterwards (Fig. 3).

4. Discussion

Previous work in younger populations [12, 25] observed a progressively rising cutaneous blood flux and falling cutaneous microvascular tone, suggesting that the skin is a site of falling peripheral resistance and increasing blood volume during prolonged dynamic exercise, with Jung et al. [13] reporting an initial oxygen partial pressure (pO₂) increase, thought to be due to the recruitment of capillaries. This is because during exercise, cutaneous blood flux responds to two conflicting demands: Exercise induced vasoconstriction and temperature induced vasodilation [15]. Consequently, this leads to an integrated cutaneous blood flux after a short exercise period [27] with cutaneous vasodilation facilitating heat loss, possibly being under control of sympathetic pathways [15].

Our study however undertaken in an older population, resulted in a slightly different finding. Similarly to paraplegics [27] and in contrast to younger populations [25], we didn't observe vasoconstriction during the beginning of exercise. In contrast, we detected a continuous increase in perfusion increase until the 2nd exercise period, suggesting a passive behaviour of their lower limb vascular system, possibly due to limited innervations in the leg area, a finding that is common in patient populations [27]. Similar findings have been reported previously [25], with the only difference being that in our study perfusion values remained higher from the baseline and first exercise period levels, at all consecutive exercise periods. Additionally, and in contrast to reports from studies in younger populations [27] we observed a stabilised skin temperature (after an initial, statistically significant increase) throughout the different exercise periods. This increase reflects cutaneous thermoregulatory responses [8] and matches results

133 observed in paraplegics, suggesting an ineffective heat dissipation mechanism and a limited evaporation
134 of sweat. Further studies are required to establish the importance of this observation.

135 It has been suggested that active cutaneous vasodilation occurs after a body core temperature threshold
136 has been reached [15]. This contributes to the preservation of thermal homeostasis during exercise, by
137 dissipating heat arising in active muscles [27], with the role of exercise on blood fluidity and the NO
138 system being currently under careful consideration [8]. Hence it is possible that this threshold occurs at
139 an earlier stage in older populations, which would explain the earlier vasodilation increase. This however,
140 does not fully account for the observed plateau or small reduction reached in both speed and peak perfusion
141 during exercise. This may be explained by a skin blood shunting dysfunction, similar to those observed
142 in patient populations, where dry heat exchange in the paralyzed regions is not favoured, resulting in
143 higher thermal strain [22]. Therefore, further work is required to explain the mechanisms behind this
144 phenomenon.

145 We also observed an initial increase in T_{max} during exercise, which later returned to near-starting
146 levels. This may have been due to age-related structural changes occurring at arterial and vascular vessels
147 [7, 25], affecting vascular compliance and resistance over a medium-duration stimulus, challenging the
148 cutaneous, and “microvascular stiffness” balance even in a healthy group of participants. In order to gain
149 further insight, it would be interesting to observe what the response would be in an age-matched, trained
150 population.

151 The lack of measurement of internal (oesophageal) temperature may be considered as one of the main
152 limitations of the study. As however, conflicting interpretations exist on its effects and importance [23,
153 25], a choice was made not to include it in our measurements to avoid misinterpretation. In addition, a
154 decision was made to train our participants on single exercise intensity. Vasoconstriction in non-active
155 limbs contributes to an increase in arterial perfusion pressure and permits redistribution mediated by
156 sympathetic nerves and has been shown to be dependent in exercise intensity [25, 27]. As this has been
157 well-documented in the literature, a single, moderate-to-high intensity was chosen for our experiments.
158 Finally, a 30 minute exercise was only implemented, despite the possibility of perfusion or T_{max} values
159 returning to baseline or reducing if a longer intervention was implemented. Nevertheless, as our partic-
160 ipants belonged to an older, sedentary group, it is our belief that a different choice wouldn't have been
161 tolerated well.

162 In summary, we observed an increased and faster microvascular perfusion in the lower limb, in the
163 initial exercise periods of our intervention when compared to the baseline, accompanied by an increase
164 in skin temperature. This phenomenon appears to be less prominent at later stages of exercise, being
165 similar to what is observed in patient populations [27] and younger populations in the upper body [23],
166 suggesting that the age-related structural changes, which have been observed at both arterial and vascular
167 vessels [7, 25] have a more extensive effect than previously considered.

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