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Sex Comparison of White-Blood-Cell Responses to Acute Vigorous-Intensity Aerobic Exercise

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Purpose: It is widely accepted that exercise alters the number and function of circulating white blood cells, and many factors are suggested to influence this phenomenon. Previous study populations have primarily been men, so this study aimed to compare mobilization of white blood cells between sexes after an acute exercise bout. ***Methods:*** The study included healthy and physically active participants, 10 men (age 26 [SD 7] y) and 10 women (age 33 [SD 8] y). Participants performed a 30-minute cycling ergometer exercise session at 70% maximal oxygen uptake, and blood samples were drawn at rest and at 3 minutes, 1 hour, and 2 hours postexercise. ***Results:*** Changes in total leukocyte, neutrophil, lymphocyte, monocyte, eosinophil, and basophil counts were analyzed and corrected for plasma volume change. Acute exercise significantly increased the number of total leukocytes and all leukocyte subpopulations excluding eosinophils in both women and men. The mobilization of all leukocyte subpopulations was similar in both sexes, but mobilization of total leukocytes, as a percentage change from baseline, was significantly greater in men (52% [SD 28%] in men, 19% [SD 23%] in women, $P = .024$, Cohen $d = 1.06$). ***Conclusions:*** These findings indicate that the sex difference in white-blood-cell mobilization in response to vigorous acute exercise is small and was only evident in total leucocyte response in the present study.

Keywords: gender, immunology, leukocyte, immune cells, mobilization, physical activity

Leukocytosis, the increase in blood leukocyte count, following acute exercise was first reported in 1893 by Schulte.[1] Since then, a variety of studies have proven that exercise induces physiological changes in the immune system.[2,3] During acute exercise white blood cells, especially neutrophils and lymphocytes, migrate from their storage organs and endothelial walls into the circulation, causing an elevation in white blood cell count.[4] The increase in white blood cell count is a transient phenomenon, as the number of all leukocyte subsets usually decreases back to resting values within minutes to 24 hours after acute exercise.[5] This exercise-induced mobilization of white blood cells is considered as part of the "fight or flight" response, where the immune system prepares the body to find infected or malignant cells and combat potential injury by redistributing cells to sites of injury or increased physical stress. The extent of the effects of immune cell mobilization is unknown, but it has been suggested that it is an important phenomenon in, for example, cancer prevention and control.[6,7]

It is well known that the intensity of exercise influences the mobilization of white blood cells.[8,9] In addition, it has been suggested that several factors, such as age, training status, nutritional status, and history of infections may alter the immune response to acute exercise, although the data have been conflicting.[10,11] The information we know today about the immune responses to exercise comes mainly from studies with male participants[2,8,9,12–15] and the data are subsequently generalized to females. To the best of our knowledge, the effect of sex on white blood cell mobilization has been studied relatively little. Some previous studies have observed sex differences in white blood cell responses to acute exercise,[16,17] but there are also studies reporting no change between sexes.[18,19] Furthermore, the observed sex differences have not been similar between the studies, as some report greater immune responses in men, and some in women.[16,17] For example, Morgado et al[16] reported greater lymphocyte response in men compared with women at any menstrual cycle phase after a maximal incremental swimming exercise, and Timmons et al[17] reported similar neutrophil, lymphocyte, and monocyte responses between men and women at any menstrual cycle phase who did not use oral contraceptives after a 90-minute cycling exercise. Furthermore, Timmons et al[17] found that immune cell responses were greater in women using oral contraceptives during luteal phase than in men.

In general, for many years, biomedical research has been conducted only with men, but recently that has been changing.[20] Inclusion of women and sex-difference studies are crucial to a deeper understanding of human health, and immunological aspects are important especially in the prevention of infections and many

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diseases. For example, it has been suggested that possible sex differences in immune system responses to exercise could partly influence exercise benefits on brain and neurodegenerative diseases through neuroinflammation.[21] Furthermore, knowing the biological sex differences in physiological responses such as exercise stimuli gives the sexes a better understanding of how their bodies adapt and recover from exercise. Consequently, the aim of the present study was to narrow the gender gap in research and to examine if the white blood cell mobilization following a single bout of acute exercise varies between sexes. Seventy percent of VO_2max was selected for exercise intensity to induce substantial physiological responses. We hypothesized that the exercise bout transiently changes individuals' white blood cell counts. Furthermore, we hypothesized that these changes may show some differences between the sexes, but we were unsure which sex would have greater immunological responses to exercise due to conflicting results in previous literature.[16–19]

Materials and Methods

This study was conducted as an investigator initiated academic study at the Turku University Hospital and Turku PET Center, Turku, Finland between November 2020, and July 2021. Informed consent was obtained from all participants and good clinical practice was followed according to the principles of the Declaration of Helsinki. The study was approved by the Ethics Committee of the Hospital District of Southwestern Finland. This study is a part of a larger trial (Clinicaltrials.gov ID NCT04255758).

Participants

A total of 20 (10 men, 10 women) healthy and physically active participants were recruited to the study. Inclusion criteria were the following: age 18–45 years, body mass index 18 to 30 kg/m^2, and resting blood pressure under 140/90 mm Hg. The exclusion criteria were the following: history of a cardiac event, medically treated diabetes, abundant use of alcohol, use of narcotics, smoking of tobacco or consuming of snuff tobacco, diagnosed depressive or bipolar disorder, abnormalities in resting ECG, pregnancy, and any chronic disease or condition that could create a hazard to the participant's safety, endanger the study procedures, or interfere with the interpretation of study results. Three of the female participants reported using hormonal contraceptives, but the type of the contraceptives were not documented. Women's menstrual cycle phase during the study was not documented and therefore not controlled for.

Study Design

During participant screening, body mass index and waist circumference were measured, and body fat percentage estimated using Durnin and Womersley[22] 4-site skinfold method. Fat-free mass was determined by subtracting fat mass from total body weight. Participants also filled out questionnaires about their use of medication and regular weekly exercise training (Table 1). Maximal rate of oxygen consumption (VO_2max) was measured with Vyntus CPX (Vyaire Medical Inc) in an incremental cycle ergometry exercise test starting at 50 W and followed by 25 W increments every 2 minutes. The criteria for VO_2max were a respiratory exchange ratio >1.1, lactate concentration over 10 mmol/L, and a heart rate ≤10 beats per minutes of the age-predicted maximal heart rate, as calculated by the Tanaka formula.[23] Within the following 2 weeks, the participants performed a personalized acute exercise bout on cycle ergometer with a total duration of 30 minutes, consisting of 5-minute warm-up at power equivalent to 50%VO_2max and 25-minute work at 70% VO_2max, intensity which would be categorized as "vigorous."[24] The chosen intensity level was designed to be challenging, promoting significant physiological responses, but not so high as to lead to exhaustion over the 30-minute period. The study was always conducted in the afternoon and participants were asked to refrain from strenuous exercise, and abstain from alcohol, as well as from food and caffeine for 24 hours prior to the study. The participants were all used to bicycling exercise. Heart rate (Palmsat 2500) and blood pressure (Apteq AE701f, Rossmax Swiss GmbH) were measured after short supine rest before and after the exercise, and during the exercise on ergometer. Before exercise, an intravenous catheter was inserted at the antecubital area of the arm for repeated blood sampling. A continuous, slow saline infusion (30 drops/min) was used to keep the catheter from clotting during the study. 10 mL of blood was collected to EDTA tubes (BD Biosciences) at 4 different time points: at rest, 3 minutes, 1 hour, and 2 hours after the exercise. The 2-hour time after the acute exercise was spent in supine rest. Lactate concentration was measured at each time point with Lactate Scout 4 (EKF Diagnostics). One participant could not finish the complete 30-minute exercise but was included in the analyses because the other measured parameters were not significantly different from the others, and he could still cycle until the 25-minute time point.

Blood-Sample Analysis

Blood samples were analyzed at the Turku University Hospital Laboratory. Total white blood cell count and the number of neutrophils, lymphocytes, monocytes, eosinophils, and basophils were analyzed using flow cytometry method (Sysmex XN analyser, Sysmex Corporation).

Change in plasma volume (PV) after exercise bout was taken into consideration and determined from hematocrit (Hct) and hemoglobin (Hb) with the following formula: $\Delta\ PV = (Hb_{pre} \times [1 - Hct_{post}])/(Hb_{post} \times [1 - Hct_{pre}]) - 1$.[25] To correct the total amount of circulating white blood cells (WBC) for plasma volume change, the following formula was used: $WBC_{corrected} = WBC_{uncorrected} \times (1 + \Delta\ PV)$.[25]

Statistical Methods

Two-tailed *t* test was used to analyze sex-differences in baseline characteristics and in baseline blood variables (results in Table 1). Repeated-measures 2-way analysis of variance was used to test the effect of exercise on white blood cells counts and on plasma volume in men and in women. The main effects were sex, time, and sex × time interaction (Results in Figures 1–3). When the main effect(s) was significant at less than $P < .05$, statistical differences were considered by Tukey post hoc test. Statistical analyses were performed with SAS (version 9.4), Graphpad prism (version 8.0), and SPSS Statistics (version 27).

Results

Baseline Characteristics

Baseline characteristics of study participants are presented in Table 1. Mean age was 26 (SD 7) years in men and 33 (SD 8) years in women, mean body mass index was 25.5 (SD 2.1) kg/m^2 in men and 24.6 (SD 2.4) kg/m^2 in women. As anticipated, men

Table 1 Baseline Characteristics of the Study Participants by Sex

	Men	Women	*P*
n	10	10	
Age, y	26 (7)	33 (8)	.064
Anthropometrics			
Height, cm	179.5 (4.5)	165.4 (6.0)	<.001
BM, kg	82.4 (10.1)	67.4 (7.3)	.002
Body fat, %	15.7 (3.7)	27.6 (3.2)	<.001
FFM, kg	69.3 (6.9)	48.7 (4.7)	<.001
BMI, kg/m^2	25.5 (2.1)	24.6 (2.4)	.393
Waist circumference, cm	84.8 (11.3)	79.7 (10.8)	.320
Health measurements			
Systolic blood pressure, mm Hg	117 (6)	112 (6)	.109
Diastolic blood pressure, mm Hg	60 (9)	67 (5)	.046
Baseline heart rate, beats/min	71 (9)	72 (5)	.931
Baseline blood analytes			
Total leukocytes, $10^9/L$	5.53 (0.79)	6.99 (2.0)	.044
Neutrophils, $10^9/L$	2.93 (0.84)	3.88 (1.87)	.162
Lymphocytes, $10^9/L$	1.88 (0.31)	2.44 (0.51)	.009
Monocytes, $10^9/L$	0.49 (0.13)	0.51 (0.13)	.716
Eosinophils, $10^9/L$	0.20 (0.16)	0.12 (0.04)	.167
Basophils, $10^9/L$	0.04 (0.02)	0.04 (0.02)	.351
Erythrocytes, $10^{12}/L$	4.70 (0.22)	4.09 (0.24)	<.001
Hemoglobin, g/L	145.1 (6.2)	124.5 (6.5)	<.001
Hematocrit, %	0.42 (0.02)	0.37 (0.02)	<.001
Mean corpuscular volume, fL	89.6 (2.1)	91.1 (2.9)	.897
Mean corpuscular hemoglobin, pg	30.8 (1.1)	30.3 (1.3)	.181
Thrombocytes, $10^9/L$	256.6 (25.7)	269.9 (48.5)	.772
Lactate, mmol/L	0.91	0.94	.825
Regular weekly exercise training			
Times/wk	4 (2)	3 (3)	.472
Hours/wk	6.3 (3.0)	4.6 (3.8)	.281
Fitness-test measurements			
VO_2max, mL/kg BM/min	45.1 (4.5)	40.1 (4.0)	.022
VO_2max, mL/kg FFM/min	53.5 (4.7)	55.4 (4.8)	.405
Maximal heart rate, beats/min	197 (9)	187 (8)	.031
Maximal lactate, mmol/L	12.8 (1.9)	12.0 (1.8)	.277
Maximal power, W	280 (41)	209 (34)	<.001
Maximal power, W/kg	3.6 (0.4)	3.3 (0.4)	.124

Abbreviations: BM, body mass; BMI, BM index; FFM, fat-free mass; VO_2max, maximal oxygen consumption. Note: Data are presented as mean (SD). Sex difference in 2-tailed *t* test.

were significantly taller and had higher body mass and fat-free mass ($P < .001$, $P = .002$, $P < .001$, respectively). Women had significantly higher body fat percentage ($P < .001$) and diastolic blood pressure ($P = .046$) at baseline compared with men. Men had higher VO_2max relative to total body mass ($P = .022$), and higher maximal heart rate and maximal pedaling power in the fitness test ($P = .031$, $P < .001$, respectively). When normalized by fat-free mass, VO_2max was similar between sexes. Moreover, the absolute number of leukocytes and lymphocytes at baseline was significantly higher in women compared with men ($P = .044$, $P = .009$, respectively). There was no sex difference in other baseline characteristics (Table 1).

Lactate and Circulatory Responses to Acute Exercise

Lactate and heart rate responses to exercise were similar in men and women. Lactate concentration at 3-minute postexercise was on average 3.8 (SD 3.1) mmol/L in men and 3.1 (SD 2.2) mmol/L in women, while the resting values were 0.9 (SD 0.4) mmol/L and 0.9 (SD 0.2) mmol/L, respectively. Heart rates during the 30-minute exercise are presented in Figure 1A. Mean heart rate was 146 (SD 12) in men and 146 (SD 13) in women. Mean heart rate percentage of maximal heart rate during the exercise was 73.0% (SD 4.3%) and 74.4% (SD 12.7%), in men and women, respectively, and at

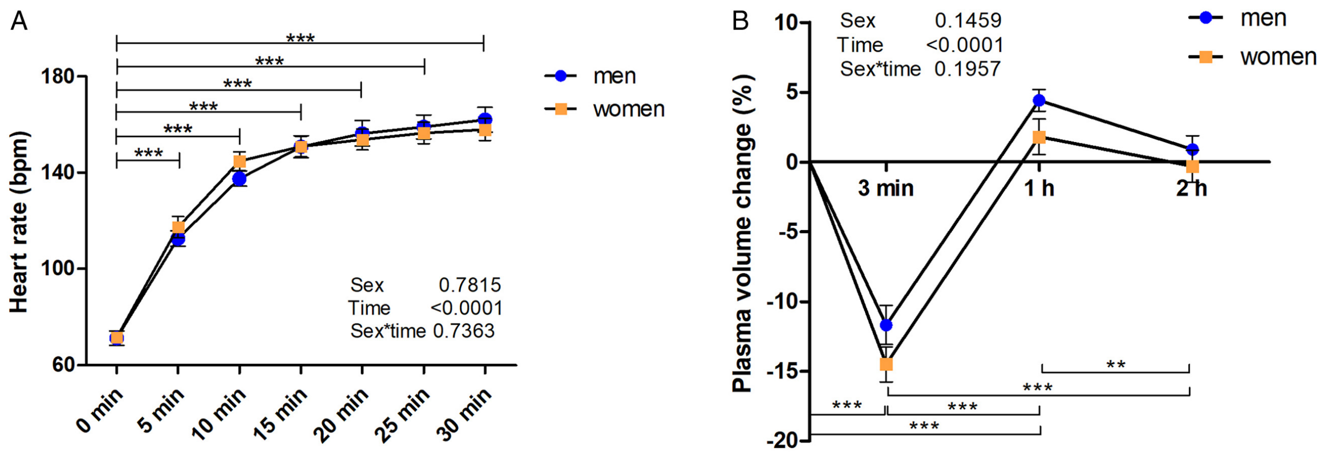

Figure 1 — (A) Heart rate during 30-minute exercise at 70% of maximal oxygen uptake and (B) mean plasma volume change after the exercise. $^{**}P < .01$. $^{***}P < .001$.

the end of the exercise, the heart rate percentage of maximal heart rate was 82.3% (SD 6.6%) and 84.3% (SD 6.0%), in men and women, respectively. The reduction in plasma volume at 3-minute postexercise compared with baseline was 11.7% (SD 4.4%) in men and 14.5% (SD 3.9%) in women ($P < .001$). The plasma volume was 4.4% (SD 2.5%) above baseline in men ($P < .001$) and 1.8% (SD 4.0%) above baseline in women at 1 hour postexercise, and at 2 hours postexercise the plasma volume was 0.9% (SD 3.1%) above baseline in men and 0.3% (SD 3.7%) below baseline in women (Figure 1B). There was no sex difference in plasma volume change.

Immune-Cell Response to Acute Exercise

Total leukocyte count increased significantly at 3 minutes postexercise ($P < .001$, Cohen $d = 0.85$) and remained elevated at 1 hour and 2 hours postexercise similarly in both sexes ($P < .05$, Cohen $d = 0.44$, $P < .001$, Cohen $d = 0.94$, respectively). There were, however, 2 peaks as the total leukocyte count decreased significantly at 1 hour postexercise compared to 3 minutes postexercise ($P < .01$, Cohen $d = 0.45$) and then again increased significantly at 2 hours postexercise compared with 1 hour postexercise in both sexes ($P < .001$, Cohen $d = 0.48$; Figure 2A). The percentage changes in total leukocytes were similar to the changes in absolute cell counts. There was significant sex × time interaction in the percentage change of total leukocytes ($P = .0237$, Cohen $d = 1.06$) as men had higher percentage increase at 2 hours postexercise from baseline compared to women (Figure 2D). However, there was no other significant sex × time interaction in any of the leukocyte subsets studied. Neutrophil count increased significantly at 3 minutes postexercise ($P < .01$, Cohen $d = 0.51$), remained elevated at 1 hour postexercise ($P < .001$, Cohen $d = 0.74$), and reached maximal values at 2 hours postexercise in both sexes ($P < .001$, Cohen $d = 1.07$; Figure 2B). Lymphocyte count increased significantly at 3 minutes postexercise compared to baseline ($P < .001$, Cohen $d = 1.11$) and decreased below baseline at 1 hour postexercise in both sexes ($P < .001$, Cohen $d = 0.87$; Figure 2C). The percentage of neutrophils of total leukocytes increased significantly at 1 hour and 2 hours compared with baseline ($P < .001$, Cohen $d = 1.07$, $P < .001$, Cohen $d = 1.14$, respectively; Figure 2E), whereas the percentage of lymphocytes decreased at 1 hour and 2 hours postexercise compared to baseline ($P < .001$, Cohen $d = 1.02$, $P < .001$, Cohen $d = 1.07$, respectively; Figure 2F).

Monocytes showed 2 increases in both sexes. First, monocyte count increased at 3 minutes postexercise compared to baseline ($P < .001$, Cohen $d = 0.76$) and after returning to baseline at 1 hour postexercise, monocyte count increased at 2 hours postexercise compared to 1 hour postexercise ($P < .01$, Cohen $d = 0.32$; Figure 3A). Eosinophil count did not change significantly at 3 minutes postexercise compared with baseline but decreased significantly at 1 hour and 2 hours postexercise compared with 3 minutes postexercise in both sexes ($P < .01$, Cohen $d = 0.25$, $P < .01$, Cohen $d = 0.27$, respectively; Figure 3B). Basophil count increased at 3 minutes postexercise ($P < .001$, Cohen $d = 0.78$) and decreased back to baseline at 1 hour postexercise ($P < .001$, Cohen $d = 0.22$; Figure 3C). Percentages of monocytes, eosinophils, and basophils of total leukocytes decreased significantly after exercise compared to baseline, and were lowest at 2 hours postexercise ($P < .001$, Cohen $d = 0.89$, $P < .05$, Cohen $d = 0.54$, $P < .01$, Cohen $d = 0.52$, respectively; Figure 3D–3F).

Figure 4 represents individual changes in immune cells between baseline and postexercise peak in men and in women. The postexercise peak represents any postexercise time point (3 min, 1 h, 2 h) in which an individual had the highest immune cell number. Both men and women had significant increases in total leukocytes ($P < .0001$ and $P = .0006$, respectively), neutrophils ($P < .0001$ and $P = .0039$, respectively), lymphocytes ($P = .0008$ and $P = .0002$, respectively), monocytes ($P = .0122$ and $P = .0040$, respectively), and basophils ($P = .0026$ and $P = .0019$, respectively; Figure 4A–4D, 4F). Moreover, eosinophil count did not change in either men or women (Figure 4E).

The percentage change of neutrophils, lymphocytes, monocytes, eosinophils, and basophils from baseline are presented in Supplementary Material (available online).

Discussion

The present study aimed to examine whether white blood cell mobilization after acute exercise differs between sexes. We found that acute exercise increased the number of all leukocyte subsets excluding eosinophils in both sexes. Moreover, the percentage of neutrophils of total leukocytes increased significantly after exercise, while the percentages of lymphocytes, monocytes, eosinophils, and basophils decreased significantly after exercise. Men had a greater increase in the percentage of total leukocytes compared to

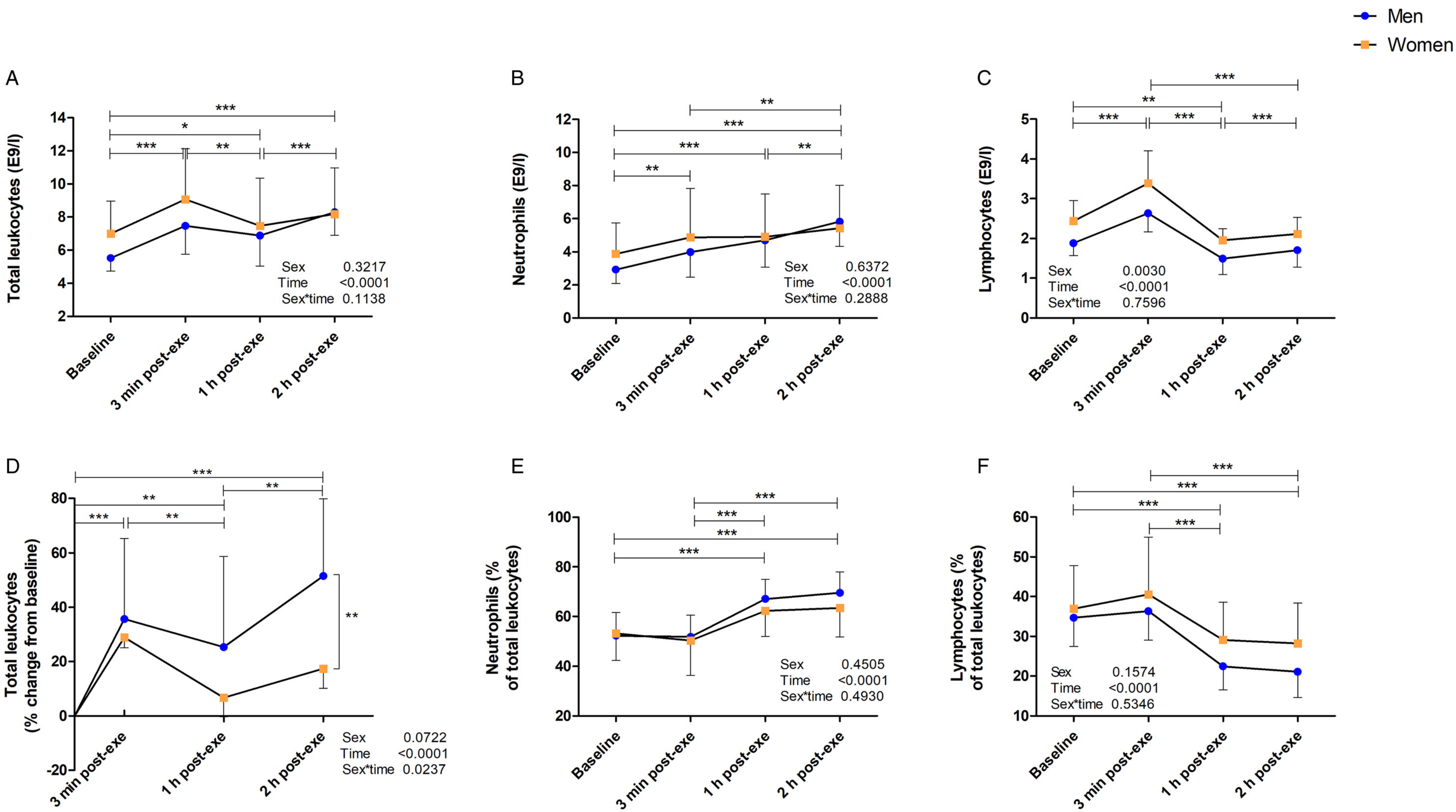

Figure 2 — Changes in the number of (A) total leukocytes, (B) neutrophils, and (C) lymphocytes; in (D) leukocyte percentage increase from baseline; and in the percentages of (E) neutrophils and (F) lymphocytes of total leukocytes. $^{*}P < .05$. $^{**}P < .01$. $^{***}P < .001$.

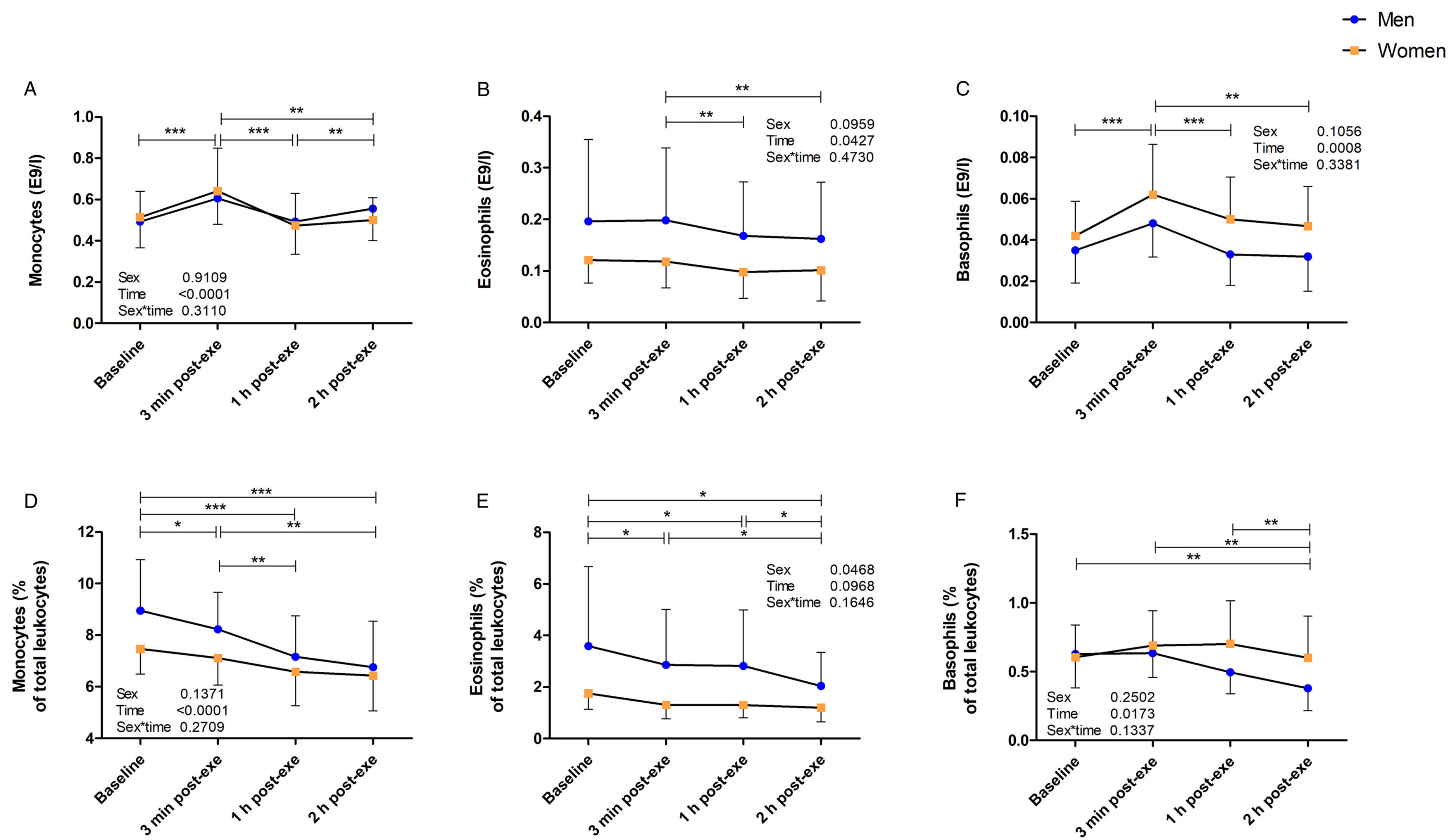

Figure 3 — Changes in the number of (A) monocytes, (B) eosinophils, and (C) basophils and in the percentages of (D) monocytes, (E) eosinophils, and (F) basophils of total leukocytes. *$P < .05$. **$P < .01$. ***$P < .001$.

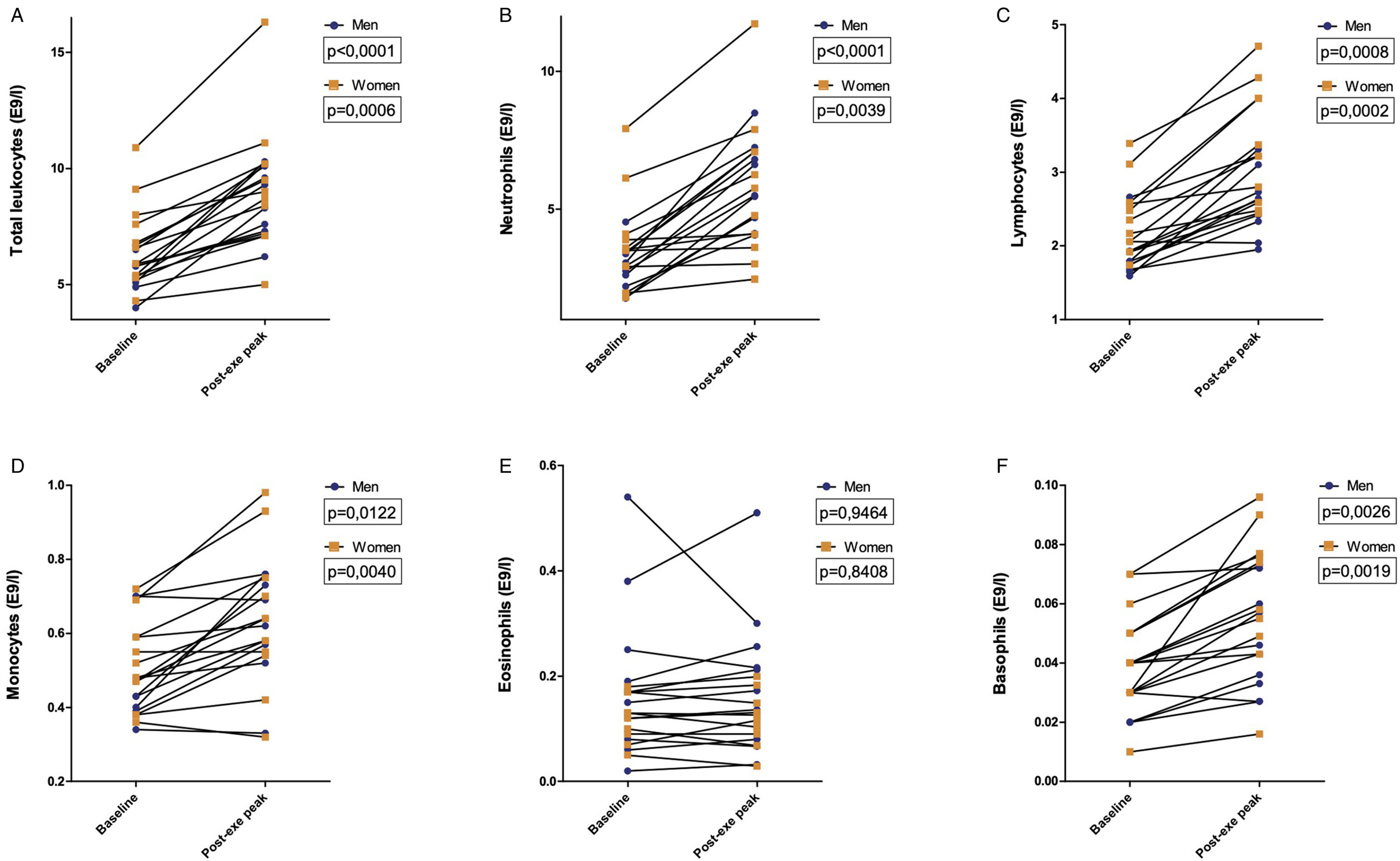

Figure 4 — Changes in the number of (A) total leukocytes, (B) neutrophils, (C) lymphocytes, (D) monocytes, (E) eosinophils, and (F) basophils from baseline to peak values postexercise.

women. However, mobilization of different leukocyte subsets was similar in both sexes.

To this date, there are relatively few studies that compare exercise-induced immune cell responses between sexes and some of the previous studies suggest there are no postexercise sex differences in immune cell count or function,[18,26] however the protocols have varied. Barriga et al[18] did not find any sex-differences in leukocyte, neutrophil, lymphocyte, or monocyte counts after 60-minute submaximal exercise at 58% of VO_2max in women and 55% of VO_2max in men. However, they did not find any significant changes in the number of immune cells after the exercise either. Furthermore, Moyna et al[27] reported that lymphocyte function, documented as mitogenic function and cytokine production, following 18-minute continuous incremental cycling exercise at 55%, 70%, and 85% of VO_2max was independent of sex. In contrast to studies reporting no differences, De Lanne et al[28] reported that acute exercise with bicycle ergometer consisting of a 30-minute pedaling at submaximal workload followed by 4-minute period at maximal workload induced leukocytosis that was greater in women compared with men. In the present study, we found that although different leukocyte subsets were affected by exercise, the response was similar in all leukocyte subsets in both sexes. A significant difference between sexes was only observed in percentage change of total leukocytes from rest to 2 hours postexercise. In men the number of leukocytes was 52% above baseline at 2 hours postexercise, whereas in women it was only 19% above baseline. However, our study did not find sex differences in absolute cell counts, which is likely due to women having higher total leukocyte count at baseline compared with men. The fact that any sex differences were not observed in absolute cell counts but were found in percentage change of total leukocytes can also be related to sex hormones and menstrual cycle discussed more below. In fact, menstrual cycle affects baseline values for leukocytes, with significantly higher concentrations observed during the luteal than during the follicular phase,[29] and therefore can contribute to women having higher leukocyte count at rest as compared with men. The current study, however, did not document the menstrual phase of the participants.

The onset of leukocytosis after an acute exercise bout is supported by several previous studies and it is recognized that different subtypes mobilize slightly differently.[30–32] Most of the previous studies, however, were conducted in only male participants.[8,9,11,12,32,33] In the present study, that included both male and females total leukocyte levels, measured as absolute cell count and as percentages increased significantly after 30-minute exercise. Furthermore, the number of neutrophils, lymphocytes, and monocytes increased significantly, having their peaks at 2 hours, 3 minutes, and 3 minutes postexercise, respectively. These results are in line with previous investigations.[30,33] The mobilization of eosinophils and basophils has been studied considerably less. Simonson and Jackson[33] did not find any changes in eosinophil or basophil levels after resistance exercise. However, Gabriel et al[31] found a 36% increase in eosinophil count after exhaustive aerobic exercise at anaerobic threshold and Harries et al[34] found elevated basophil count after interval training. In the present study, we found that basophil count increased significantly at 3 minutes postexercise in both sexes. We also found that in both sexes, eosinophil count was significantly lower at 1 hour and at 2 hours postexercise compared to 3 minutes postexercise, but not compared with baseline.

Current knowledge indicates that menstrual cycle and oral contraception may have an effect on exercise-induced immune responses,[29,35] but based on only few studies and conflicting results, no firm conclusions can yet be drawn. Timmons et al[17] examined immune cell changes controlled for menstrual phase, oral contraception, and fitness and found that neutrophil, lymphocyte, and monocyte responses to a 90-minute exercise at 65% of VO_2max were greater during luteal phase than during the follicular phase in women using oral contraceptives and also greater than responses in men. Three women in the present study reported hormonal contraceptive use, but because of the low number of the participants and because we did not record menstrual cycle phase, we did not adjust for the use of contraceptives or menstrual cycle. However, not controlling for menstrual cycle and use of contraceptives makes the findings more generalizable to everyday life. Overall, debate has been going on whether studies should control for menstrual cycle or not,[36] but the importance of sex-comparison research is widely recognized.[37] Physiological sex differences have been described previously in, for example, metabolism affecting disease vulnerability[38,39] and fitness and cardiovascular regulation,[40,41] and it appears that general physiological responses to exercise are not major and that there is little evidence that supports exercise training induced adaptations differ substantially between men and women.[42]

Moreover, we acknowledge that our study has other limitations. The number of participants is quite low which may have contributed to the results due to limited statistical power, although around 20 participants is fairly typical in similar physiological studies.[16,17,43] There was a baseline sex-difference in fitness level, which may have had an impact on leukocyte responses to exercise, as seen before.[44] However, there are also studies reporting no difference in exercise-induced leukocyte responses between trained and sedentary people.[45] The sex-difference in our study in VO_2max was only obtained when it was calculated by normalization with whole-body mass. VO_2max calculated by normalization with fat-free mass and maximal power measured as watts per kilogram was similar in both sexes, indicating that the fitness level was not actually that different between sexes, and thus, it is possible, but unlikely, that it affected leukocyte mobilization. The fitness test protocol we used led to 23- and 18-minute tests in average in men and women, respectively, which is considerably longer than recommended for VO_2max testing. This longer duration might have caused fatigue and therefore prevented some participant from reaching a true VO_2max. Furthermore, it is considered that infection history, particularly cytomegalovirus, can determine immune responses to exercise, as people with cytomegalovirus infection have greater T cell responses than those who are not infected.[11,46] To our knowledge, to date, there are no studies evaluating the effects of other infections on exercise-induced immune cell mobilization, but it has been suggested that the effects of exercise on respiratory infections may be gender-dependent.[47] We, however, did not include infection history assessment in our study protocol, which is a limitation and can contribute to the results. Last, we did not examine lymphocyte subsets, such as T cells, and NK cells[44,48–50] which could have given us further valuable information.

One strength in the present study is that we corrected the concentrations of all leukocyte subtypes for plasma volume changes to obtain more accurate results. Exercise can cause acute change in plasma volume, especially if the exercise is of high intensity and long duration.[51,52] This change is thought to result from fluid shift from the plasma into the intracellular space and from loss of fluid in the form of sweat.[53] In the present study, plasma volume decreased 11.7% in men and 14.5% in women at 3 minutes postexercise. Plasma volume was significantly above baseline at 1 hour in men and slightly above baseline in women, and at 2 hours postexercise plasma volume was close to baseline in both sexes. Participants were allowed to drink water during and after the exercise session, which may partly explain the expansion in plasma volume after exercise. Because of these changes, plasma volume affects the concentrations of blood components including white blood cell[54] and therefore ignoring the change would have led to false results.

Based on the aforementioned strengths and limitations, and current results in relation to the previous literature in the field, we suggest the following points for the future research to advance the topic further: (1) larger sample size studies with different age groups and fitness levels, (2) controlling for menstrual cycle phases and hormonal contraceptive use in female participants, (3) exploring long-term immune adaptations to regular exercise in both sexes, and (4) investigation of other immune markers (eg, cytokines) for a more comprehensive understanding of sex differences in exercise immunology.

Conclusions

In the present study, we examined sex differences in immune-cell responses to 30-minute individually standardized vigorous-intensity aerobic exercise sessions. We found that acute exercise increased the number of total leukocytes, neutrophils, lymphocytes, monocytes, and basophils in both women and men. Mobilization of all leukocyte subpopulations was similar in both sexes, but the percentage increase in total leukocytes after exercise was greater in men than in women. Our findings suggest that the role of sex in immune-cell mobilization is minor.

Practical Applications

The findings of this study indicate that the immune system of both sexes adapts and recovers from exercise similarly. The study did not control for menstrual cycle phase, which is a limitation to this study, but also increases the generalizability of the findings. If female athletes want to focus on training depending on their menstrual cycle, future research needs to investigate the effect of the menstrual phase on the exercise-induced responses of the immune system.

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