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Original

Association of Total and Differential White Blood Cell Counts with Physical Energy Expenditure

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Objective: To assess the association between physical energy expenditure and the total and differential white blood cell (WBC) counts which reflect systemic inflammation.

Methods: This study included 953 and 277 apparently healthy middle-aged men and women who were employed and had participated in a general health examination in 2006-2007. They completed a questionnaire regarding their usual patterns of activity during the previous month. Such behaviors included occupational, locomotive, household, leisure, and exercise activities, as well as sleep and sedentary time.

Results: In men, the total WBC count decreased with increasing levels of exercise energy expenditure, after adjusting for confounders. A similar result was observed for neutrophil counts in both genders. A multivariate logistic regression model showed that exercise energy expenditure had significant negative linear relationships with the elevated WBC and neutrophil counts in men ($p = 0.019$ and 0.026, respectively). As compared to men who didn't exercise regularly the odds ratios of the elevated total WBC and neutrophil counts decreased significantly in the third tertile by 50 % and 51 %, respectively. However, no similar association was observed in women.

Conclusion: Exercise energy expenditure is inversely and independently associated with the WBC and neutrophil counts among healthy Japanese male workers.

Key Words: white blood cell count, physical activity, energy expenditure

Introduction

Low levels of physical activity are associated with increased risk of coronary heart disease (CHD)[1], type 2 diabetes mellitus (DM)[2], and cardiovascular disease (CVD)-caused mortality[3], although the precise mechanisms remain unclear. Recently, evidence has shown that chronic inflammation is an important factor associated with the progression of atherosclerosis[4] and insulin resistance[5]. Low-grade systemic chronic inflammation is reflected by increased levels of markers such as white blood cell (WBC) count, C-reactive protein (CRP), fibrinogen, and some cytokines. WBC count is an inexpensive to measure, widely available, simple, and well-standardized biological marker of acute infection, tissue damage, and other systemic inflammatory

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conditions. Several studies have shown that increased total WBC count is associated with the risk of developing type 2 DM[6], CHD, and all-cause mortality[7][8]. Regarding WBC subtypes, recent studies suggest that elevated neutrophil or granulocyte counts may be the strongest predictor of carotid arteriosclerosis, CHD, and CVD-caused mortality[9]~[11]. Thus, the total and differential WBC counts are powerful predictors of several atherosclerotic diseases.

Previous studies have reported that higher levels of physical activity are associated with lower levels of inflammatory markers[12]~[14]. These studies used questionnaires regarding leisure-time physical activities. However, the Japan National Health and Nutrition Survey conducted by the Japanese Ministry of Health, Labour and Welfare[15] reported that the 25-30 % of the Japanese population (including both genders) exercise regularly, while ＜60 % attempt physical activity during their leisure time. The association between WBC count and habitual energy expenditure due to occupational, household, exercise, and leisure activities, as well as sleep and sedentary time, is unknown. Moreover, little is known about the association between differential WBC counts and physical activity levels[16], especially in Japanese. Thus, the purpose of this study was to assess the cross-sectional relationships between the total and differential WBC counts and daily physical activities in Japanese men and women.

Materials and Methods

Study subjects

From October 2006 to September 2007, Saitama-ken Saiseikai Kurihashi (SSK) Hospital conducted a health check-up program, in which 1,481 workers aged 25-69 years had participated, and they were followed up in the Kurihashi Lifestyle Cohort Study. Subjects were excluded if they had known DM, CVD, cancer, asthma, or certain infectious diseases, or if they were under pharmacological treatment for hypertension or dyslipidemia. Moreover, 251 subjects with abnormal WBC counts (≥10,000/μL or ＜4,000/μL), indicative of an infectious disease or the pathological state of leucopenia, were later excluded. The remaining 1,230 subjects (953 men and 277 women) were considered for this study.

Measurement of variables

The general health check-up procedure at SSK Hospital included biochemical laboratory tests and a self-administered questionnaire regarding smoking status, medical history, alcohol habits, and in women, menopausal status. Smoking status was classified into 3 categories (never smoked, past smoker, and current smoker). Alcohol habits were divided into 3 categories (never, occasionally, and regularly). The height, weight, blood pressure, and waist circumference (Wc) of all subjects were measured. Body height was measured to the nearest 0.1 cm with the subject standing without wearing shoes. The subjects were requested to wear light indoor clothes and the body weight was measured to the nearest 0.1 kg. Blood pressure was measured in a sitting position after 5 min of rest by using an automatic sphygmomanometer. Wc was measured to the nearest 0.1 cm at the level of the navel at the end of the expiration of a normal breath, with the subject in a standing position. Body mass index (BMI) was calculated as the body weight (in kg) divided by the body height squared (in meters). Blood samples were collected in the morning after a 10-h-long fast. The levels of fasting plasma glucose (glucose oxidase method), triglycerides (enzymatic method), and high-density lipoprotein cholesterol (direct method), and WBC counts (Kinetic WBC optical count, CELL-DYN; Abbott Japan, Tokyo) were measured at the hospital laboratory. Insulin concentrations were measured by an immunoradiometric assay at a commercial laboratory.

Physical activities

The participants completed the Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire (JALSPAQ)[17][18] regarding their usual patterns of physical activity during the previous month. The questionnaire comprises 14 questions on sleep time, occupation, locomotion, housework, leisure-time physical activities (e.g., gardening, home carpentry, car washing), and exercise. Questionnaire data were converted using the intensity of each physical activity expressed in metabolic equivalents (METs), according to the Compendium by Ainsworth et al[19], and summarized as METs・h/day and energy expenditure. In this questionnaire, occupational physical activity was assessed by recording the duration of sitting (1.5 METs), standing (2.0 METs), and walking (3.0 METs). Similarly, locomotional physical activity was assessed by walking (3.0 METs) and cycling (4.0 METs); housework physical activity was assessed by cooking (2.3 METs), washing (2.0 METs), cleaning (3.5 METs), and nursing or providing child care (3.0 METs). Leisure-time and exercise physical activities were calculated by each selected physical activity value (METs) multiplied by activity duration. The JALSPAQ values were validated against the "gold standard" doubly labeled water (DLW) method by using the data from 226 Japanese men and women aged 20-83 years[20]. JALSPAQ slightly underestimated total energy expenditure: the difference in the mean and standard error was -1.15 ± 1.92 kcal・kg^{-1}・day^{-1}. The total energy expenditure values obtained using JALSPAQ and DLW were moderately correlated (Spearman's correlation coefficient = 0.742, $p < 0.001$; intraclass correlation coefficient = 0.648, $p < 0.001$), and the 95 % limit of agreement was 4.99 to 2.69 kcal/kg. The energy expenditure of each physical activity (kcal・kg^{-1}・day^{-1}) in JALSPAQ was validated by the 24-hour weighed physical activity record among 122 Japanese participants (average age, 55.8 years). Spearman's correlation coefficients were as follows: 0.75 for occupational physical activity, 0.13 for locomotional physical activity, 0.59 for housework physical activity, 0.60 for exercise physical activity, and 0.41 for leisure-time physical activity[17].

Statistical analysis

Statistical analyses were performed and reported separately for men and women. The chi-square test was used to compare proportions and the student's t-test was used to compare the mean values between genders. Because of the skewed distribution of triglyceride, we used log-transformed values in the analyses and showed the medians and interquartile ranges. The Mann-Whitney's U test was used to compare the values of each energy expenditure. Spearman's correlation coefficients were used to examine the correlation between the total and differential WBC counts and each of the daily energy expenditures. Participants were categorized into 4 groups of energy expenditure in selected physical activities that showed significant correlation between the total and differential WBC counts (total energy expenditure in both genders [Quartile: <31.3, 31.4-33.0, 33.1-36.7, ≥36.8 kcal・kg^{-1}・day^{-1} in men; <32.3, 32.4-33.8, 33.9-37.2, ≥37.3 kcal・kg^{-1}・day^{-1} in women] and exercise in both genders [0 and tertile: 0, <0.69, 0.70-1.48, ≥1.49 kcal・kg^{-1}・day^{-1} in men; 0, <0.54, 0.55-1.38, ≥1.39 kcal・kg^{-1}・day^{-1} in women]). Sleep energy expenditure was not selected given its discrete distribution related to questionnaire framing. The general linear model was used to test the equality of means of total WBC and differential counts across the 4 groups of energy expenditure. The crude and multivariate adjusted odds ratios (ORs) and their 95 % confidence intervals (CIs) associated with the highest quartile of total WBC and neutrophil counts were calculated for each category of total or selected physical activity by using logistic regression models. In the multivariate model, age (continuous), BMI (continuous), Wc (continuous), alcohol habits (categorical), smoking status (categorical), fasting insulin concentrations, and menopause status (in women only; categorical) were included as confounding factors. To confirm the causal impact of physical activity levels on WBC counts in this cross-sectional study, the equality of means of physical activities across quartiles of WBC counts were examined.

The Statistical Package for Social Sciences (SPSS) for Windows (version 21.0, Chicago, IL, USA) was used for all statistical analyses. All reported *p* values are two-tailed, and $p < 0.05$ was considered statistically significant. The study was approved by the Institutional Review Board of SSK Hospital, and informed consent was obtained from the study participants.

Results

Characteristics of study subjects

Overall, the male subjects were more obese, had worse CVD risk profiles, and had a higher preva-

Table 1 Characteristics of study subjects

	Men (n = 953)	Women (n = 277)	p value
Age (years)	49 ± 8	49 ± 8	0.837
Body mass index (kg/m²)	23.7 ± 3.2	22.8 ± 3.2	<0.001
Waist circumference (cm)	85.4 ± 8.3	81.5 ± 8.6	<0.001
Systolic blood pressure (mmHg)	124 ± 15	120 ± 16	<0.001
Diastolic blood pressure (mmHg)	80 ± 12	72 ± 12	<0.001
High-density lipoprotein cholesterol (mmol/L)	1.40 ± 0.36	1.68 ± 0.39	<0.001
Triglyceride (mmol/L)	1.16 (0.87, 1.60)	0.89 (0.64, 1.22)	<0.001
Fasting plasma glucose (mmol/L)	5.3 ± 0.7	5.1 ± 0.8	<0.001
Fasting insulin (μU/mL)	6.9 ± 5.9	6.1 ± 3.4	0.008
Alcohol intake regularly (%)	40.6	11.1	0.799
Current smoker (%)	65.6	15.9	<0.001
Menopause (%)	–	49.2	
Total white blood cell count (/μL)	5,798 ± 1,203	5,320 ± 1,013	<0.001
Energy expenditure (kcal·kg⁻¹·day⁻¹)			
Total	33.6 (31.5, 37.3)	35.2 (32.6, 38.6)	<0.001
During Sleep	6.8 (6.0, 7.1)	6.4 (6.0, 7.1)	<0.001
Occupation	10.7 (8.6, 16.4)	8.5 (5.0, 13.5)	<0.001
Locomotion	1.5 (0.5, 3.0)	1.2 (0.5, 2.5)	<0.001
Household	0.2 (0.0, 0.8)	4.9 (3.0, 6.8)	0.032
Exercise	0.3 (0.0, 1.2)	0.1 (0.0, 0.8)	<0.001
Leisure-time	0.2 (0.0, 0.7)	0.2 (0.0, 0.9)	0.006
Sedentary	11.6 (9.1, 13.6)	12.1 (9.5, 14.6)	0.223

Variables are the mean ± standard deviation or median and interquartile range for continuous variables and percentages of subjects for categorical variables.

Table 2 Spearman's correlation coefficients (γ) between total white blood cell count and each type of energy expenditure

	Men		Women	
	γ	p value	γ	p value
Total WBC count				
Energy expenditure (kcal·kg⁻¹·day⁻¹)				
Total	0.010	0.766	−0.060	0.323
During sleep	−0.071	0.029	0.021	0.730
Occupational	0.028	0.385	0.035	0.567
Locomotion	−0.044	0.174	0.020	0.741
Household	0.048	0.136	−0.077	0.200
Exercise	−0.072	0.026	−0.159	0.008
Leisure-time	−0.006	0.846	−0.002	0.972
Sedentary	0.008	0.809	−0.050	0.404
Neutrophil count				
Energy expenditure (kcal·kg⁻¹·day⁻¹)				
Total	−0.028	0.496	−0.028	0.704
During sleep	−0.068	0.091	−0.030	0.684
Occupational	0.035	0.392	0.084	0.260
Locomotion	−0.018	0.096	−0.006	0.939
Household	−0.048	0.238	−0.133	0.073
Exercise	−0.085	0.035	−0.007	0.928
Leisure-time	−0.001	0.759	0.040	0.593
Sedentary	0.012	0.759	−0.055	0.465

WBC, white blood cell.

lence of current smokers compared to the female subjects. With respect to energy expenditure, men, when compared to women, were physically more active in occupational, locomotion, and exercise activities, while physically less active in household activities and in all activities taken together (Table 1).

Table 3 Adjusted means of total and differential white blood cell counts in the four groups of each of physical energy expenditure

	Group 1	Group 2	Group 3	Group 4	p for linear trend
Men					
Total	240	240	237	236	
Energy expenditure (kcal·kg^{-1}·day^{-1})	<31.3	31.4–33.0	33.1–36.7	≥36.8	
Total WBC (/μL)	5,857±1,187	5,807±1,252	5,738±1,160	5,792±1,216	0.759
Exercise					
Number	428	172	177	176	
Energy expenditure (kcal·kg^{-1}·day^{-1})	0	<0.69	0.70–1.48	≥1.49	
Total WBC (/μL)	5,932±1,257	5,748±1,117	5,653±1,111*	5,628±1,088*	0.012
Neutrophil (/μL)	3,430±905	3,256±790	3,251±810	3,176±630*	0.033
Lymphocyte (/μL)	1,974±604	1,961±626	1,902±550	1,819±515	0.122
Monocyte (/μL)	341±105	318±90	326±88	316±91	0.061
Eosinophil (/μL)	207±141	207±122	190±145	206±131	0.648
Basophil (/μL)	31±19	32±20	28±17	28±15	0.241
Women					
Total	70	70	68	69	
Energy expenditure (kcal·kg^{-1}·day^{-1})	<32.3	32.4–33.8	33.9–37.2	≥37.3	
Total WBC (/μL)	5,383±1,036	5,441±1,183	5,213±792	5,241±1,000	0.487
Exercise					
Number	157	40	41	39	
Energy expenditure (kcal·kg^{-1}·day^{-1})	0	<0.54	0.55–1.38	≥1.39	
Total WBC (/μL)	5,290±1,094	5,520±1,141	5,239±770	4,968±627	0.253
Neutrophil (/μL)	2,957±722	3,405±818	2,941±728	2,667±575	0.032
Lymphocyte (/μL)	1,793±522	1,624±506	1,737±410	1,676±340	0.342
Monocyte (/μL)	271±90	287±93	247±118	223±120	0.066
Eosinophil (/μL)	179±133	175±138	125±115	158±154	0.135
Basophil (/μL)	28±20	31±18	22±18	27±30	0.261

WBC, white blood cell. Variables are the mean±standard error.
Adjusted for age, body mass index, waist circumference, smoking status, alcohol habits, fasting insulin concentrations in both men and women, and only in women, menopausal status.
*$p<0.05$ vs group 1.
Four groups: Total energy expenditure in both genders [Quartile: <31.3, 31.4–33.0, 33.1–36.7, ≥36.8, kcal·kg^{-1}·day^{-1} in men; <32.3, 32.4–33.8, 3.9–37.2, ≥37.3 kcal·kg^{-1}·day^{-1} in women] and exercise in both genders [0 and tertile: 0, <0.69, 0.70–1.48, ≥ 1.49 kcal·kg^{-1}·day^{-1} in men; 0, <0.54, 0.55–1.38, ≥1.39 kcal·kg^{-1}·day^{-1} in women].

Correlation between energy expenditure and WBC count

Table 2 shows that energy expenditure during sleep time negatively correlated with the total WBC count in men, and exercise energy expenditure negatively correlated with the total WBC counts in both genders. The exercise energy expenditure was inversely correlated with the neutrophil count in men. No significant correlation was found between other differential WBC counts and each form of energy expenditure in either gender.

Total and differential WBC counts and physical energy expenditure

No significant relationships were found in the total WBC counts across quartiles of total energy expenditure in either gender. There were also no significant associations between the total WBC counts and the 4 groups of energy expenditure during sleep time. The total WBC count decreased with increasing levels of exercise energy expenditure, after adjusting for confounding factors in men. Similar results appeared for neutrophil counts in both genders (Table 3).

The multivariate logistic regression model

Table 4 Odds ratios and their 95% confidence intervals for the total and exercise energy expenditure associated with the highest quartile of total WBC and neutrophil counts

	Total energy expenditure				p for linear trend
	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	
Men					
Number	240	240	237	236	
Energy expenditure (kcal·kg^{-1}·day^{-1})	<31.3	31.4–33.0	33.1–36.7	≥36.8	
WBC					
Crude OR (95%CI)	1.00 (ref)	0.82 (0.55–1.25)	0.86 (0.57–1.29)	0.89 (0.60–1.35)	0.234
Multivariate OR (95%CI)	1.00 (ref)	0.75 (0.48–1.17)	0.88 (0.57–1.36)	0.82 (0.53–1.28)	0.634
Women					
Number	70	70	68	69	
Energy expenditure (kcal·kg^{-1}·day^{-1})	<32.3	32.4–33.8	33.9–37.2	≥37.3	
WBC					
Crude OR (95%CI)	1.00 (ref)	2.07 (0.93–4.63)	1.74 (0.76–3.96)	1.71 (0.75–3.88)	0.247
Multivariate OR (95%CI)	1.00 (ref)	3.10 (0.93–10.29)	2.02 (0.65–6.30)	2.94 (0.91–9.54)	0.910
	Exercise energy expenditure				p for linear trend
	Group 1	Group 2	Group 3	Group 4	
Men					
Number	428	172	177	176	
Energy expenditure (kcal·kg^{-1}·day^{-1})	0	<0.69	0.70–1.48	≥1.49	
WBC					
Crude OR (95%CI)	1.00 (ref)	0.75 (0.50–1.11)	0.60 (0.39–0.91)	0.48 (0.30–0.75)	0.004
Multivariate OR (95%CI)	1.00 (ref)	0.87 (0.53–1.41)	0.68 (0.42–1.12)	0.50 (0.27–0.91)	0.019
Neutrophil					
Crude OR (95%CI)	1.00 (ref)	0.75 (0.45–1.25)	0.66 (0.35–1.22)	0.42 (0.19–0.93)	0.015
Multivariate OR (95%CI)	1.00 (ref)	0.87 (0.48–1.55)	0.68 (0.31–1.22)	0.49 (0.26–0.82)	0.026
Women					
Number	157	40	41	39	
Energy expenditure (kcal·kg^{-1}·day^{-1})	0	<0.54	0.55–1.38	≥1.39	
WBC					
Crude OR (95%CI)	1.00 (ref)	1.01 (0.46–2.19)	0.97 (0.45–2.11)	0.30 (0.10–0.90)	0.193
Multivariate OR (95%CI)	1.00 (ref)	1.68 (0.63–4.43)	1.27 (0.45–3.61)	0.34 (0.07–1.66)	0.318
Neutrophil					
Crude OR (95%CI)	1.00 (ref)	2.44 (0.66–9.08)	0.98 (0.30–3.26)	0.61 (0.12–3.15)	0.115
Multivariate OR (95%CI)	1.00 (ref)	1.22 (0.40–3.75)	0.98 (0.33–2.91)	0.62 (0.20–1.96)	0.506

WBC, white blood cell; OR, odds ratio; CI, confidence interval.
Adjusted for age, body mass index, waist circumference, smoking status, alcohol habits, fasting insulin concentrations in both men and women, and menopausal status only in women.
Four groups: Total energy expenditure [Quartile: <31.3, 31.4–33.0, 33.1–36.7, ≥36.8 kcal·kg^{-1}·day^{-1} in men; <32.3, 32.4 kcal·kg^{-1}·day^{-1} 33.8, 33.9–37.2, ≥37.3 kcal·kg^{-1}·day^{-1} in women] and exercise [0 and tertile: 0, <0.69, 0.70–1.48, ≥1.49 kcal·kg^{-1}·day^{-1} in men; 0, <0.54, 0.55–1.38 ≥1.39 kcal·kg^{-1}·day^{-1} in women].

showed that exercise energy expenditure had statistically significant linear negative relationships with the WBC and neutrophil counts in men (p = 0.019 and 0.026, respectively, for the linear trends) (Table 4). The adjusted OR related to the highest quartiles of the total WBC and neutrophil counts decreased significantly in group 4 (3rd tertile) of exercise energy expenditure (≥1.49 kcal・kg^{-1}・

day^{-1}) when compared to group 1 (no habitual exercise) of exercise energy expenditure by 50 % and 51 %, respectively (Table 4). In contrast, no significant association was found between exercise energy expenditure and the highest quartiles of the WBC and neutrophil counts in women.

In contrast, the WBC counts did not predict the physical activity levels in either gender (data not shown).

Discussion

The current study has shown that the total WBC and neutrophil counts, which reflect chronic inflammatory conditions, decreased with increasing levels of exercise energy expenditure in men, after adjusting for confounding factors. In women, only the neutrophil count decreased with increasing levels of exercise energy expenditure. In Japan, few people exercise regularly[15], and physical activity (including non-exercise activity) thermogenesis was examined in this study. However, no association was found between daily physical activity excluding exercise and total WBC and its differential counts. Thus, our results indicated a dose-responsive negative association between exercise and total WBC and neutrophil counts among healthy Japanese male workers.

Previous cross-sectional studies have shown an association between the total WBC count and physical activity. Geffken et al[12] reported that persons in the highest quartile of leisure-time physical activity (≥2,270 kcal/week) had 6 % lower concentrations of total WBCs compared with those in the lowest quartile (< 367.5 kcal/week) in a healthy elderly population. Wannamethee et al[13] showed a significant and inverse dose-response relationship between physical activity (walking, cycling, recreational activity, and sports) and total WBC count in elderly men. Abramson and Vaccarino[14] have reported that a higher frequency of physical activity was independently associated with lower ORs for elevated total WBC count among healthy adults. These reports were consistent with our findings.

Recent studies have shown that elevated neutrophil counts may be the strongest predictor of CVD, CHD, and death[11][21]. Johannsen et al[16] reported that higher levels of cardiorespiratory fitness were associated with lower counts of total WBC, neutrophils, lymphocytes, and basophils. In contrast, another study that assessed the association between maximal oxygen uptake and the subtypes of WBC showed that monocyte count, not neutrophil count, was related to aerobic capacity[22]. Our results show that higher levels of exercise energy expenditure may decrease the neutrophil count, leading to reduced risk of CVD.

Despite evidence for an association between the total and differential WBC counts and physical activity, the underlying biological mechanisms remain unclear. Proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-6, which are secreted from the adipose tissue, are known to increase WBC counts[23]. TNF-α is a potent stimulator of IL-6 production, and IL-6 directly stimulates neutrophils[24]. Several studies have demonstrated that habitual exercise was inversely related to both TNF-α and IL-6 levels[25][26]. In animal model, it has shown that IL-6 derived from skeletal muscle by acute exercise mediate the increase of leptin and insulin sensitivity in hypothalamus[27]. These findings indicated that exercise could have appetite-suppressive actions via hypothalamus and might lead decreasing adipocyte which was associated with chronic inflammation. Moreover, exercise intervention reduced the levels of IL-8, a neutrophil chemokine derived from the adipose tissue[28], which subsequently contributed to the migration of granulocytes and decreased the levels of granulocyte colony-stimulating factor, monocyte chemoattractant protein-1 (MCP-1)[29]. Recently, it has known that one of the effects of exercise on muscle is mediated by the transcriptional coactivator peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α). PGC-1α expression in muscle stimulates secretion of new hormone, irisin. It is shown that irisin drives browning of white fat and thermogenesis[30]. These changes of adipose tissue may reduce circulating leptin which has been shown to activate neutrophils[31]. Thus, exercise may be important to suppress chronic systemic inflammation, which leads to CVD, among Japanese male workers, who rarely exercise regularly. It has been examined that exercise influenced the immunological parameters through alteration of autonomic nervous system, however, the association between WBC counts and autonomic nerve activity is unknown.

There is a gender-based difference in the progression of DM and CVD[32]. A similar gender bias has been reported in the total and differential WBC counts[33]. In the current study, we were unable to find a significant association between exercise energy expenditure and the elevated WBC and neutrophil counts in women. The reasons for this are unclear. The number of women in our study was less than one-third the number of men, thus our findings in women might be weakened by the smaller sample size. There may also be environmental gender-based differences in lifestyle such as smoking status. In our study, the male subjects included a higher proportion of smokers than the female subjects. In addition, a female sex hormone, estrogen, may protect against atherosclerosis by decreasing inflammatory cell adhesion[34]. The menstrual cycle also affects WBC counts. It is known that granulocyte counts are higher in the luteal phase compared to the follicular phase[35]. Gender-based differences are also noted in the subcutaneous and visceral fat distribution. It was reported that visceral adipose tissue produced more MCP-1 than did subcutaneous adipose tissue[36]. Therefore, visceral fat is a more important inducer of low-grade inflammation than subcutaneous fat. As women are known to have more subcutaneous fat and less visceral fat than men, these differences might influence our results.

There were several limitations in our study. First, this study had a cross-sectional design, precluding the establishment of temporal relationships between the total and differential WBC counts and activity energy expenditure. Further prospective data analysis is needed to confirm our findings. Second, the results of the questionnaire-based survey for alcohol consumption and smoking status were self-reported and not validated. Third, the JALSPAQ has been validated in prior studies[17][20]; however, participants of these validation studies were limited to middle-aged adults, and the degree of correlation between estimated energy expenditure in JALSPAQ and DLW or 24-hour record was moderate. Validation studies utilizing a combination of accelerometry and 24-hour record study spanning various ages are necessary for accurate estimation of physical activity level. Fourth, high-sensitivity C-reactive protein (hs-CRP) is known as a sensitive marker for the inflammatory component of metabolic syndrome and CVD[37][38]. However, acquiring CRP data was cost-prohibitive, whereas WBC count is a stable, well-standardized, and inexpensive marker of routine health care data. Further research is needed to examine the relationships between a more sensitive inflammatory marker and physical activity. In addition to its limitations, our study has some major advantages. First, we excluded subjects whose WBC counts exceeded 10,000/μL or were <4,000/μL, limiting our subjects to individuals whose WBC counts were within the normal range. Second, to avoid systematic bias, we were extremely careful in data collection. We excluded subjects who had a medical history of diseases associated with low-grade inflammation.

Conclusion

The exercise energy expenditure is inversely and independently associated with the WBC and neutrophil counts among healthy Japanese male workers. Further prospective data analysis is needed to confirm our findings.

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身体消費エネルギー量と総白血球数，白血球分画の関係

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〔背景〕総白血球数（WBCC）上昇は心血管疾患（CVD）予測の簡便な炎症マーカーである．身体活動量の増加によりCVD発症予防が期待されるが，身体活動量とWBCCとその分画の関連についての報告は少ない．

〔目的〕各種身体活動の1日の体重当たり消費エネルギー量（EE）とWBCC，白血球分画との関連を横断的に検討する．

〔方法〕対象は，就業中の25-69歳の非糖尿病，高血圧や脂質異常症の薬物療法を受けていないドック受診者1,230名（男性953名，平均年齢49±8歳，平均BMI 23.5±3.3 kg/m^2）である．身体活動質問票を用いて過去1か月間の身体活動内容を調査し，男女別に睡眠，仕事，運動，非活動，合計のEEを算出した．EEとWBCCの間で相関を認めた活動ごとに，WBCCか白血球分画高値（4分割の最上位）を目的変数，活動のEEを説明変数としたロジスティック回帰モデルを用いて，活動のEE（G1-4に4分割）の独立した関連性を分析した．

〔結果〕合計EEはWBCCと一定の傾向を示さなかったが，男女ともに運動EEとWBCCは負の相関，男性でのみ睡眠EEとWBCCに負の相関を認めた．睡眠EEの4分位でWBCC，白血球分画には一定の傾向は見られなかったが，運動EEの4分割（運動なし：G1，する者で3分位：G2-4）では，仕事EE，睡眠EE，年齢，BMI，臍周囲径，飲酒，喫煙，インスリン濃度，女性ではさらに閉経で調整後も，男性ではWBCCと好中球数が，女性では好中球数が，活動量の増加にともなって低下した．男性で，運動EEのWBCC高値に対するオッズ比は，G1と比較しG2→G4に向け，0.87, 0.68, 0.50（Trend p＝0.019），好中球高値に対するオッズ比は0.87, 0.68, 0.49（Trend p＝0.026）であった．同様の解析を女性で行ったが有意な傾向はなかった．男性では運動EEが1.49 kcal/kg/day（＝G4）以上でWBCC，好中球数高値のリスクが有意に上昇していた．

〔総括〕男性では運動EEと白血球数，特に好中球数との負の関連性が認められた．