Journal of Exercise Science & Fitness 22 (2024) 375–382

Contents lists available at ScienceDirect

Journal of Exercise Science & Fitness

journal homepage: www.elsevier.com/locate/jesf

Gut microbiome related to metabolic diseases after moderate-to-vigorous intensity exercise

Somi Yun [1], Yongsuk Seo [1], Yunbin Lee, Dae Taek Lee [*]

Exercise Physiology Laboratory, Kookmin University, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Metabolic disease
Exercise intensity
Microbiome
Intestinal environment

ABSTRACT

Background objectives: The purpose of this study is to investigate changes in gut microbiota related to metabolic diseases after moderate and high-intensity exercise. A total of 24 participants were divided into three groups: Non-Exercise Group (NEG, n = 8, 28.6 ± 5.3 years, 176.0 ± 7.8 cm, 81.3 ± 14.6 kg), Moderate Intensity Exercise Group (MIEG, n = 8, 26.5 ± 3.3 years, 176.9 ± 5.0 cm, 75.4 ± 9.5 kg), and Vigorous Intensity Exercise Group (VIEG, n = 8, 30.6 ± 5.9 years, 174.2 ± 3.5 cm, 77.8 ± 12.2 kg).

Methods: The participants were selected by assessing physical activity, gut health status, presence of diseases, recent disease diagnoses, and dietary disorders. Those who reported any presence disease or recent disease diagnosis were excluded from the current study. Stool samples were collected after a 10-h fast for gut microbiome analysis. MIEG participants trained at 40–59 % heart rate reserve (HRR) for at least 150 min per week, while VIEG participants trained at ≥ 60 % HRR for at least 90 min per week. After 4 weeks, all participants provided stool samples for gut microbiome analysis.

Data analysis was conducted using the Wilcoxon test, with statistical significance set at ≤ 0.05.

Results: The results indicated an increase in Prevotella in MIEG, while Veillonella, Dorea_formicigenerans, and Dorea_longicatena exhibited a decrease ($p < 0.05$). In VIEG, there was an increase in Bacteroides, Butyricimonas, Odoribacter, and Alistipes ($p < 0.05$).

Conclusion: These modified microbial groups were associated with factors related to metabolic diseases, including inflammatory bowel disease, obesity, colorectal cancer, diabetes, hypertension, metabolic liver diseases, and ischemic heart diseases. Additional research is essential to delve into the relationship between exercise and these alterations in the microbiome.

1. Introduction

The gut microbiota is associated with metabolic disorders. Disruption of the balance of gut microbial communities can lead to physiological changes[1] and increase the risk of metabolic disorders such as obesity, diabetes, cardiovascular disease, liver disease, as well as conditions related to gut health such as colorectal cancer and irritable bowel syndrome.[2,3] Patients with inflammatory bowel disease (IBD),[4] obesity,[5] colorectal cancer (CRC),[6] and diabetes[7] have been reported to exhibit decreased levels of specific microbes or reduced diversity compared to healthy individuals.

One of the key factors that can help improve metabolic disorders is exercise, which is utilized as an effective method for prevention and intervention to provide health benefits.[8] Exercise is effective in lowering blood sugar levels in diabetic patients[9] and can improve and prevent obesity and metabolic syndrome.[10] Additionally, it has been reported to alleviate symptoms in patients with colorectal cancer, irritable bowel syndrome (IBS), and IBD.[11–13] To improve and prevent metabolic disorders through regular exercise, the American College of Sports Medicine (ACSM) recommends moderate-intensity aerobic exercise for at least 30 min a day, five days a week, or a total of 150 min per week, or vigorous-intensity aerobic exercise for at least 20 min a day, three days a week.[14]

Exercise influences the composition and changes of gut microbiota. Analysis of habitual exercise levels has shown that groups with higher weekly exercise volumes had higher levels of Prevotella,[15] athletes exhibited higher diversity of gut microbiota with significantly higher proportions of Akkermansia, and individuals with better aerobic

* Corresponding author.
E-mail address: dtlee@kookmin.ac.kr (D.T. Lee).
[1] Somi Yun and Yongsuk Seo contributed equally to this work.

https://doi.org/10.1016/j.jesf.2024.07.003
Received 2 March 2024; Received in revised form 17 July 2024; Accepted 23 July 2024
Available online 25 July 2024

capacity had higher levels of bacteria such as Clostridiales, Roseburia, Lachnospiraceae, and Erysipelotrichaceae, which contribute to butyrate production.[16,17] After six weeks of exercise, butyrate-producing bacteria such as Clostridiales spp., Lachnospira spp., Roseburia spp., Lachnospiraceae unclass, and Faecalibacterium spp. Increased, but decreased after returning to sedentary behavior.[18] A group that performed aerobic and resistance exercise of moderate to high intensity for 12 weeks showed an increase in Bacteroides and a decrease in Clostridium cluster IX in the aerobic exercise group.[19] High-intensity competitive training altered various species of microbes, particularly those producing butyrate, such as Dorea longicatena, Bacteroides vulgatus, Faecalibacterium prausnitzii, Bacteroides uniformis, Prevotella copri, and Eubacterium rectale.[20,21]

Previous research suggests that the microbiota can be altered through exercise habits or interventions. Specifically, it is proposed that exercise promotes the proliferation of microbiota clusters responsible for producing butyrate and short-chain fatty acids (SCFAs) [21,22] This, in turn, activates essential regulators of energy metabolism within muscle cells, establishing a link between muscle-microbiota communication. This connection holds potential for preventing or improving metabolic disorders through various metabolic pathways. Additionally, both low-intensity exercise, below 40 % of maximal oxygen uptake, and high-intensity exercise exceeding 60 % activate the hypothalamic-pituitary-adrenal (HPA) axis, inducing physiological and psychological stress as well as homeostatic changes. Exercise intensity is thus proposed as a crucial factor in altering gut microbiota composition.[21,23–26]

However, due to the diverse range of subjects and varied lifestyles in previous studies, findings on the alterations in gut microbiota resulting from interventions based on exercise intensity are insufficient. Furthermore, there is a scarcity of studies specifically investigating whether the changes in gut microbiota induced by exercise are correlated with metabolic disorders. Therefore, purpose of the current study is to examine the alterations in gut microbiota linked with moderate and vigorous-intensity exercise. It seeks to understand whether exercise affects microbiota composition in a manner relevant to metabolic health. It is hypothesized that moderate to vigorous intensity exercise may influence microbiota composition.

2. Methods

1) Participants

Twenty-four healthy men participated in this study. Participants were recruited through public recruitment notices and online platforms. They were given the option to choose their desired group from the following: Non-Exercise Group (NEG), Moderate Intensity Exercise Group (MIEG), and Vigorous Intensity Exercise Group (VIEG). To minimize variables affecting changes in gut microbiota other than exercise, the selection process included assessing physical activity, gut health status, the presence of diseases, recent disease diagnoses, and dietary habits (Table 1).

This study, conducted on human subjects, received ethical approval from the Institutional Review Board of Kookmin University to consider the ethical situations of researchers and participants, in accordance with the Helsinki Declaration (KMU-202001-HR-227). Before participating in the experiment, potential participants were screened to minimize external environmental factors that could influence changes in their gut microbiota. Only individuals meeting all the following conditions were included in the study: Absence of chronic illnesses, no history of surgical procedures within the last 3 months, responded 'NO' to all 7 items in the Physical Activity Readiness Questionnaire (PAR-Q), engaged in only moderate physical activity or less over the past week, according to the International Physical Activity Questionnaire (IPAQ), no self-diagnosis of irritable bowel syndrome (Rome III Process) and no abnormalities in bowel symptoms severity, as per the Bowel Symptom Severity Scale (BSSS), no medication intake within the last week, no regular aerobic exercise in the last 3 months, and absence of any eating disorders.

Table 1
Physical characteristics of the subject.

	NEG (n = 8)	MIEG (n = 8)	VIEG (n = 8)	*p*
Age (yrs)	28.6 ± 5.3	26.5 ± 3.3	30.6 ± 5.9	0.272
Height (cm)	176.0 ± 7.8	176.9 ± 5.0	174.2 ± 3.5	0.620
Weight (kg)	81.3 ± 14.6	75.4 ± 9.5	77.8 ± 12.2	0.633
BMI (kg/m^2)	26.1 ± 3.3	24.0 ± 2.5	25.6 ± 3.5	0.403
IPAQ (METs/week)	401.4 ± 100.5	397.5 ± 96.3	408.7 ± 104.8	0.975
BSSS (score)	2.7 ± 2.5	1.6 ± 2.0	1.7 ± 2.7	0.604

NEG: Non-Exercise Group, MIEG: Moderate Intensity Exercise Group, VIEG: Vigorous Intensity Exercise group, BMI: Body Mass Index, IPAQ: International Physical Activity Questionnaires, BSSS: Bowel Symptom Severity Scale.

2) Procedure

2.1. Preliminary examination

The experimental procedure is presented in Fig. 1.

Before the commencement of the experiment, the height and weight of the participants were measured, and resting heart rate was assessed to determine exercise intensity.

Participants were instructed to maintain their usual dietary routines. The nutritional analysis software Canpro 5.0 (Korean Nutrition Society, Korea) was utilized to evaluate their dietary intake based on three-day records, documented twice on weekdays and once on weekends. These records comprehensively detailed the quantities of food consumed, including water, supplements, and others. It was emphasized that participants maintain their regular diets as short-term dietary interventions have been shown to quickly alter microbiota diversity in humans.[27]

Additionally, prior to commencing a 4 weeks exercise program, participants were provided with individualized heart rate reserve (HRR) ranges. Throughout the 4 weeks period, participants engaged in exercise within their prescribed HRR ranges, either in a laboratory setting or outdoors. Participants reported the start and end times of exercise sessions. Each participant's exercise volume was calculated in MET-min/week using Kaminsky's formular.[28–30]

For gut microbiome analysis, a fecal sample kit (green biome, GC Green Cross Genome, Korea) was utilized. One day before fecal collection, participants limited food intake, maintaining a 10 h fasting period until the next day's stool collection, excluding water. The collected kit was stored in a location not exceeding 20 °C and shielded from sunlight, and it was submitted to the analysis facility within 10 days.

2.2. Training

Participants in the exercise groups followed the exercise intensity guidelines of theACSM for 4 weeks. The MIEG engaged in exercise intensity corresponding to 40–59 % (HRR for at least 150 min per week. The VIEG performed high-intensity aerobic exercise at an intensity of ≥ 60 % HRR, including a 5 min warm-up, at least three times a week, for more than 30 min per session, totaling at least 90 min per week.

MIEG performed walking and cycling, while VIEG performed in running and cycling for a duration of 4 weeks. The initial and final exercise sessions was conducted in the laboratory, while the remaining 4 weeks of exercises performed in both laboratory and outdoor. In the laboratory, participants wore heart rate monitors (M400, Polar, Oulu, Finland), while during outdoor activities, personal wearable devices (such as the Apple Watch, Apple, USA, or Galaxy Watch, Samsung, Korea) was utilized to keep heart rate ranges.

Fig. 1. Research procedures.

2.3. Post-examination

After 4 weeks, a post-examination was conducted using the same methods as the preliminary examination.

2.4. DNA preparation and sequencing

Stool suspension (600–800 μl) was used for DNA extractions. DNA was extracted from all samples at GC Genome, corp. Using chemagic DNA Stool Kit (PerkinElmer Inc., USAs) according to the manufacturer's recommendations with modified pretreatment bead-beating step. DNA concentration was determined fluorometrically on the Qubit® 3.0 Fluorometer (Thermo Fisher Scientific, USA) using the QubitTM dsDNA HS Assay Kit. Based on these values the DNA was diluted with nuclease free water. These prepared DNA samples were used for 16 S library construction using the NEXTflex 16 S V4 Amplicon-Seq (BioO Scientific, USA). The prepared library was checked with a 4200 Tape Station System (Agilent Technologies; USA). The library was diluted to an equimolar concentration and samples with different barcode sequences were pooled together. Paired-end sequencing was performed with the Miseq reagent kit v2 nano using a MiSeq. 2000 instrument according to the manufacturer's instructions (Illumina, USA). For measuring the overall quality of Illumina MiSeq paired-end (PE, 2 × 250 nt) sequencing runs 12 % of PhiX DNA (Illumina, USA) was used.

2.5. Bioinformatic analysis

Primer trimming of paired-end data was performed by cutadapt and the fastq files were imported into a QIIME2 data artifact ending in. Qza. Quality trimming, paired-end sequence merging and removal of chimera sequence were performed by using the DADA2 software and we truncated the forward and reverse reads at 200, 160 nucleotides respectively. For quality control of filtered data, samples less than 20,000 reads or bases scoring q30 less than 85 % were retested. For created output feature table, features with fewer than 10 reads in a batch were removed. Alpha diversity tests was performed in the QIIME2 pipeline and Shannon's index was calculated. For sample normalization a 20,000 read depth was set. For taxonomy classification, filtered features were combined and classified with same taxonomy using Naïve Bayesian classifier trained with the Refseq reference databases.

3) Data analysis

All experimental data were analyzed using statistical Package for Social Sciences software (IBM Corp, Released 2019, IBM SPSS Statistics for Window, Version 26.0. Armonk, NY: IBM Corp). Graphics were produced using Microsoft Excel and OriginPro 2023.

The Wilcoxon test was used to analyze the changes in gut microbiota within groups before and after the intervention based on exercise intensity. Data are presented as mean ± SD throughout and the statistical significance level was set at $\alpha \leq 0.05$.

3. Results

Table 2 presents the exercise volume and dietary intake among group over 4 weeks.

Measurements of the exercise frequency, average HR, exercise intensity by % HRR, and metabolic scope by METs showed significant differences between groups ($p \leq 0.05$). However, exercise volume, energy expenditure, total calorie intake and the proportions of carbohydrate, protein, and fat were not significantly different between groups ($p \geq 0.05$).

The change in gut microbiota clusters before and after the moderate and high-intensity exercise are presented in Fig. 2.

In this study, the major microbial clusters collected were analyzed to identify factors related to chronic diseases in MIEG and VIEG, as presented in Fig. 3.

In MIEG, Prevotella increased (pre: 12.8 ± 19.6 %, post: 16.2 ± 20.6 %, $z = -2.380$, $p = 0.017$), while Veillonella (pre: 0.8 ± 1.3 %, post: 0.1 ± 0.2 %, $z = -1.960$, $p = 0.049$), Dorea_formicigenerans (pre: 0.06 ± 0.06 %, post: 0.03 ± 0.05 %, $z = -2.023$, $p = 0.043$), and Dorea_longicatena (pre: 0.14 ± 0.14 %, post: 0.03 ± 0.04 %, $z = -2.023$, $p = 0.043$) decreased.

In VIEG, Bacteroides (pre: 18.7 ± 12.7 %, post: 27.3 ± 16.1 %, $z = -2.521$, $p = 0.012$), Butyricimonas (pre: 0.02 ± 0.03 %, post: 0.14 ± 0.16 %, $z = -2.521$, $p = 0.012$), Odoribacter (pre: 0.1 ± 0.1 %, post: 0.3 ± 0.3 %, $z = -1.992$, $p = 0.046$), and Alistipes (pre: 0.3 ± 0.4 %, post: 0.8 ± 0.6 %, $z = -2.521$, $p = 0.012$) increased.

Table 2
Exercise volume and dietary intake among group over 4 weeks.

	NEG (n = 8)	MIEG (n = 8)	VIEG (n = 8)	p
Exercise Frequency (per week)	–	5.0 ± 0.5	3.5 ± 0.3	<0.001
Average HR (bpm)	–	135.4 ± 6.5	153.0 ± 3.2	<0.001
Average Intensity (% HRR)	–	52.1 ± 2.9	70.3 ± 3.5	<0.001
Average Metabolic Scope (METs)	–	6.0 ± 0.8	9.5 ± 1.5	<0.001
Exercise Volume (MET-min/week)	–	932.1 ± 132.4	915.1 ± 140.2	0.806
Energy Expenditure (kcal/week)	–	1214.7 ± 125.3	1230.8 ± 180.0	0.839
Average Caloric Intake (kcal/day)	2240.9 ± 179.1	2192.7 ± 164.1	2347.9 ± 262.3	0.325
Average Carbohydrate Intake (g/day)	293.3 ± 29.5	265.6 ± 29.8	287.8 ± 27.0	0.150
Average Protein Intake (g/day)	86.1 ± 12.1	91.3 ± 11.7	82.7 ± 11.3	0.358
Average Fat Intake (g/day)	76.5 ± 11.8	74.6 ± 18.8	81.5 ± 20.9	0.721

NEG: Non-Exercise Group, MIEG: Moderate Intensity Exercise Group, VIEG: Vigorous Intensity Exercise Group.

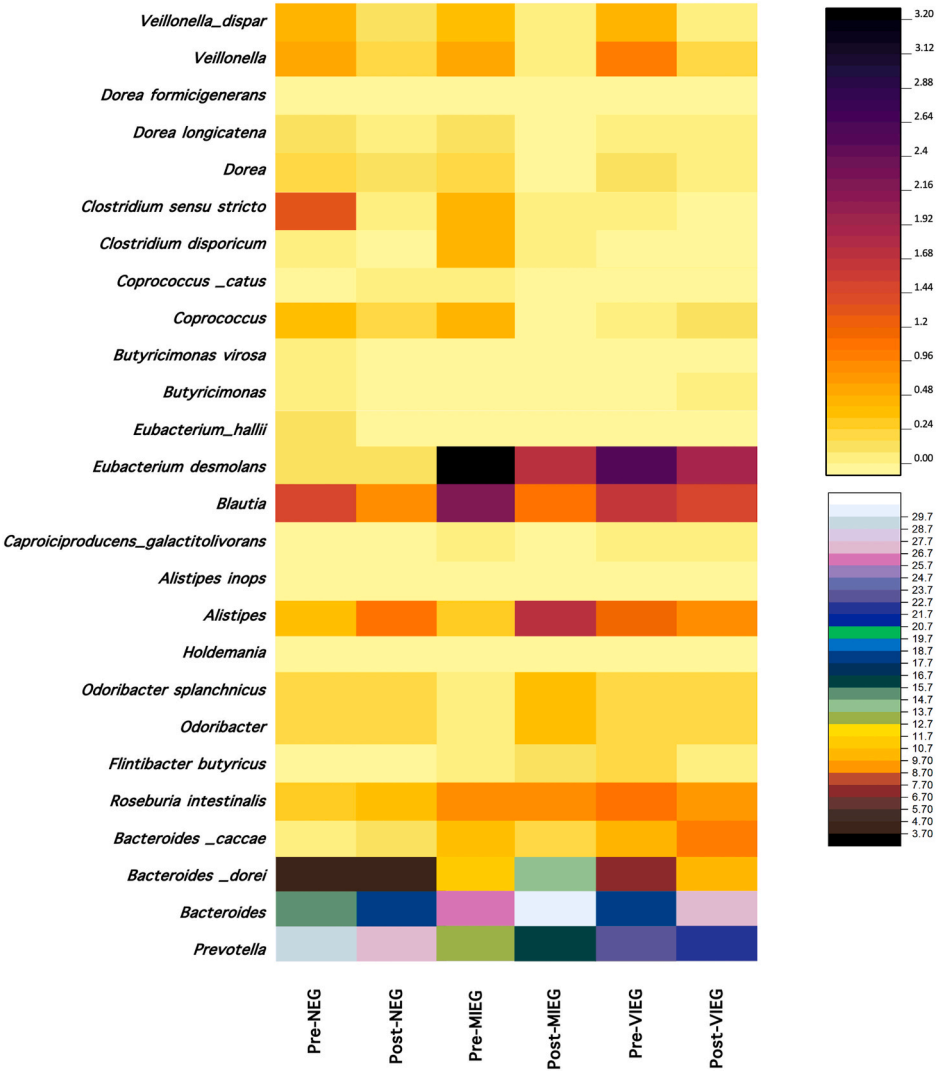

Fig. 2. The key components of three groups before and after exercise.

4. Discussion

This study investigated the changes in gut microbial clusters after moderate and high-intensity exercise and the metabolic disease-related factors. Increased Prevotella in the MIEG ($p < 0.05$) is known as a major bacterium determining gut type, producing thiamine, and exerting a significant influence on SCFAs production.[31,32] Prevotella has been associated with gut health, as higher levels are linked to better prognosis in CRC patients,[33] while lower levels are associated with higher recurrence rates in IBD patients.[31] Moreover, Prevotella has been reported to be lower in individuals with atherosclerotic cardiovascular disease (ACVD) and obesity.[34,35]

In the present study, Prevotella significantly increased after 4 weeks of continuous moderate-intensity exercise, consistent with previous research suggesting a correlation between higher Prevotella levels and regular exercise, as well as its association with exercise volume.[8,11,36] However, it is premature to assign significance solely based on this study's results because Prevotella relies on dietary fiber-rich foods or vegetarian diets and is associated with inflammatory diseases,[8,33,36] future studies are needed to explore various intervention variables such as exercise duration, type, and diet.

Veillonella, Dorea_formicigenerans, and Dorea_longicatena significantly decreased in the MIEG ($p < 0.05$). Veillonella has been shown to increase or have a higher distribution in ischemic heart disease (IHD) patients.[34,37] Dorea_formicigenerans and Dorea_longicatena are more prevalent in obese individuals and considered as obesity biomarkers.[38] Regular physical activity and organized exercise are essential for patients with IHD and obesity, recommending moderate-intensity regular physical activity unless contraindicated.[39] Although the current results from MIEG alone may be insufficient, diseases where exercise is essential such as IHD and obesity may expect correlation through additional research on changes in gut microbiota.

In the VIEG, Bacteroides, Butyricimonas, Odoribacter, and Alistipes significantly increased ($p < 0.05$). Bacteroides, a major determinant of gut type, provides nutrients and vitamins to hosts and other gut microbes through carbohydrate metabolism, contributing to health improvement. Additionally, it plays a role in assisting other microbes as providers or symbionts near hosts.[40] Previous studies have shown a decrease or low distribution of Bacteroides in patients with ACVD, obesity, IBD, hypertension, and diabetes.[34,41–47] Butyricimonas is known as a butyrate-producing microorganism, promoting immune cell response, immune function, anticancer, and anti-inflammatory effects, preventing bacterial proliferation or pathogen formation, and contributing to carbohydrate metabolism, insulin stability, and insulin sensitivity to regulate blood sugar. It also contributes to lowering systolic blood pressure, crucial for maintaining gut microbial balance. Indeed, compared to healthy individuals, Butyricimonas has been reported to decrease or have a low distribution in patients with hypertension and

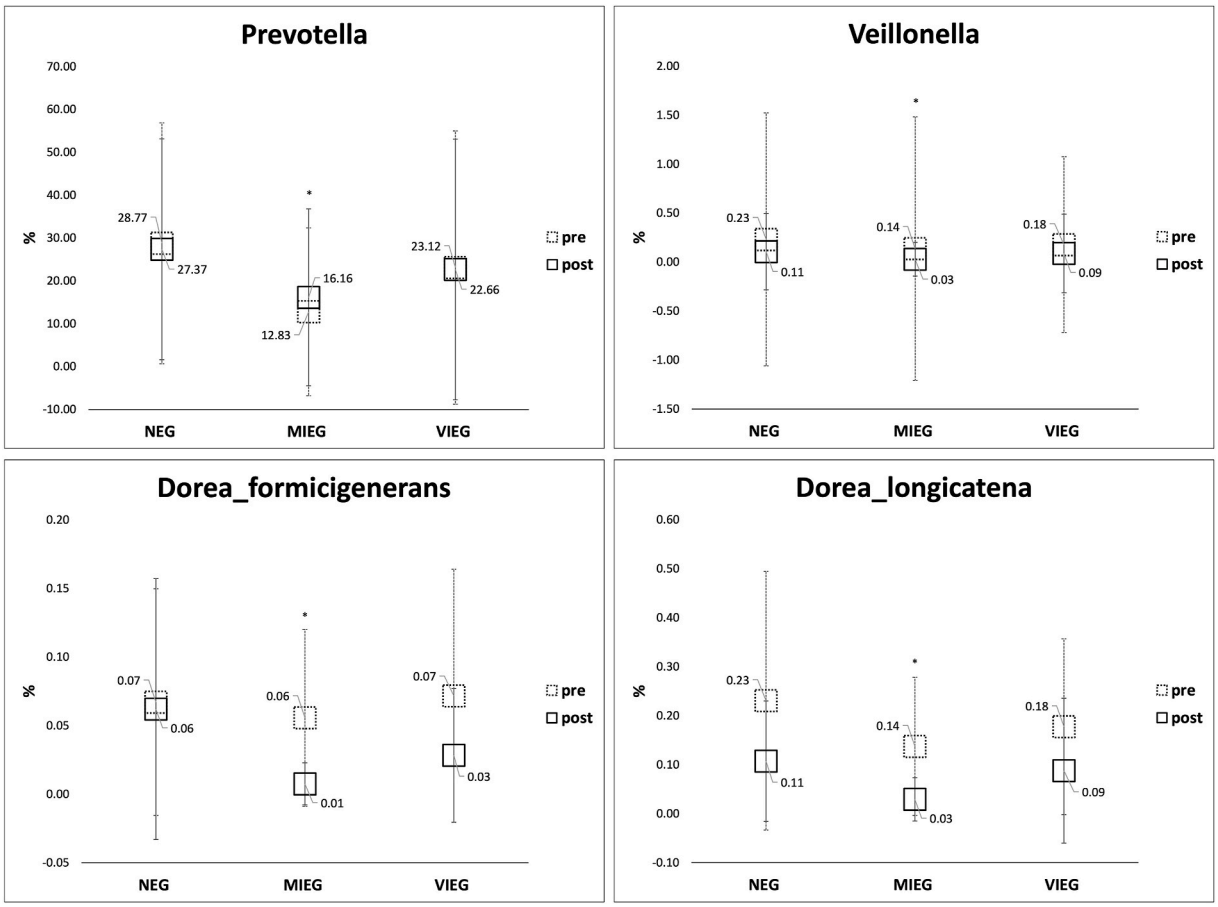

Fig. 3. Changes in factors related to metabolic disorders before and after exercise (a) Change in microbiota of MIEG (b) Change in microbiota of VIEG.

diabetes.[44,48–50] Increased Odoribacter, another part of the healthy and balanced gut microbiota, produces SCFAs. It protects the gut barrier against pathogens, activates anti-inflammatory and immune regulation, maintaining homeostasis for health promotion. Odoribacter has been reported to decrease or show low distribution in patients with metabolic liver disease and IBD.[51–53] Alistipes, commonly found in healthy intestines, acts as a producer of SCFAs, preventing inflammation and colonization of harmful bacteria, aiding in nutrient absorption and energy generation from carbohydrates. It has been shown to have an inverse correlation with metabolic liver disease, ACVD, CRC, and IBD in previous studies.[51,54]

The increased microbial clusters observed after moderate and high-intensity exercise in this study are closely related to SCFAs. SCFAs are considered the major metabolites of gut microbiota, regulating host carbohydrate metabolism, energy balance, and local as well as systemic immune function. Previous studies have reported relationships between SCFAs and exercise. The SCFAs promote immune function in athletes, aiding exercise recovery through anti-inflammatory activity, and providing the energy for exercise, particularly enhancing metabolic efficiency during endurance exercise.[55,56]

In the present study, participants in the MIEG trained at 40–59 % of HRR for at least 150 min per week, while those in the VIEG trained at ≥60 % of HRR for at least 90 min per week over 4 weeks without supervision. These exercise protocols influenced changes in the gut microbiome. These results are consistent with previous studies indicating that 6 weeks of moderate to vigorous aerobic exercise training (60–75 % of HRR) altered the gut microbiota and increased microbial-derived SCFAs in previously sedentary lean and obese adults, without changes to dietary patterns.[18] This study also linked exercise-induced changes in the gut microbiota and SCFAs to alterations in body composition in lean individuals and oxygen uptake in obese individuals, suggesting the role of the gut microbiota in regulating physiological adaptations to exercise.[18] Another previous study reported that after 5 weeks of moderate-intensity aerobic exercise, acetate, propionate, and butyrate levels increased.[57]

The possible explanation for the difference in gut microbial diversity and composition between exercise intensities are due to several connected factors. Higher exercise intensities increase endogenous metabolic inputs, such as lactate, which gut bacteria can utilize.[18,58] Exercise also enhances intestinal contents mixing, promoting better bacterial fermentation of dietary fibers. Additionally, exercise changes colonic oxygen saturation and pH levels, assisting anaerobic fermentation.[18,58] This leads to reduced intestinal utilization and uptake of SCFAs, resulting in higher fecal SCFAs levels. Moreover, exercise increases the activity of key genes involved in SCFAs production, such as BCoAT and methylmalonyl-CoA decarboxylase, which enhance the microbiota's ability to ferment dietary fibers and produce butyrate and propionate.[18,58,59] These factors could collectively contribute to the observed differences in gut microbial diversity and SCFAs production between exercise intensities.

A previous study has shown increased gut microbial richness in professional rugby players compared to sedentary individuals matched for BMI. However, the impact of physical fitness could not be isolated from dietary influences due to significant dietary differences.[16] Some studies suggest significant differences in the microbiomes of athletes competing in different types of sports, such as resistance and endurance-based sports (weightlifting vs. long-distance running).[60] Microbiome composition has been shown to predict exercise gains in

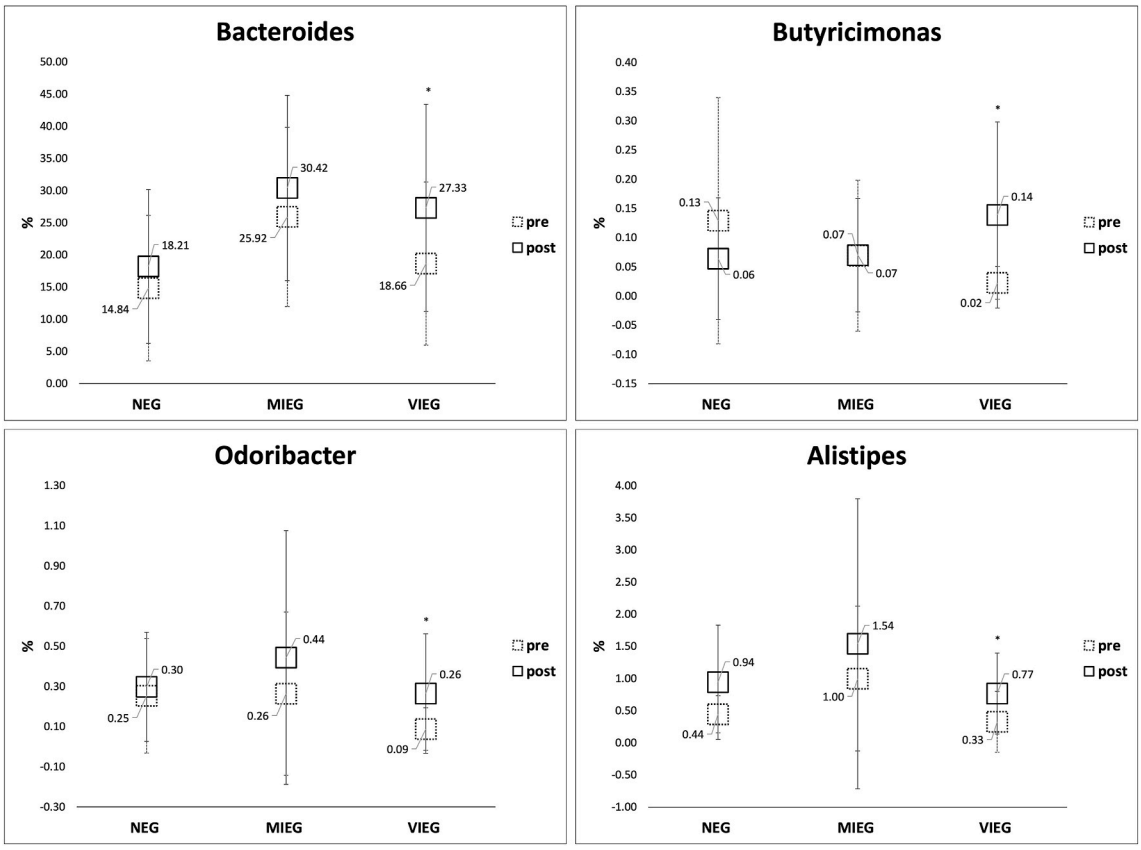

Fig. 3. (*continued*).

both resistance and cardiovascular exercise, with different taxa being significant for each exercise modality. Cardiovascular exercise has a minor and transient effect on microbiome composition.[61] A study by Scheiman et al. reported that the species Veillonella atypica was highly enriched in the fecal samples of marathon runners.[62] This finding is consistent with another study that observed a dramatic increase in the genera Veillonella and Streptococcus in the guts of ultra-marathon runners post-race.[63] Fontana et al. revealed a correlation between gut microbial profiles and athletes' categories through taxonomical profiling. This correlation is evidenced by a recurrent microbial pattern primarily defined by SCFAs producers, including Faecalibacterium, Eubacterium, Blautia, and Ruminococcus species, which are statistically associated with athletes' samples. The enzymatic functional clusters (EFCs) related to athletes were positively linked to 752 enzymes (Enzyme Commission nomenclature, EC numbers) and 73 high biological impact synthases (HIBS), a subset of manually identified biosynthetic reactions. In contrast, the EFCs related to sedentary individuals were positively linked to only 105 EC numbers and 14 HIBS, highlighting the reduced ability of sedentary individuals' gut microbiota to affect host health through the production of secondary metabolites.[64]

Several limitations to this study exist and should be considered for generalization and interpretation to those with metabolic disorders. First, the study design employed only healthy individuals, which limited the external validity of the results to metabolic disorders. Future research should include participants with diverse metabolic conditions to better understand how exercise-induced changes in the gut microbiota in population with metabolic disorders. Second, we did not control the participants' diet or modify their usual dietary habits, nor did we control other lifestyle habits or factors besides exercise. Therefore, it is insufficient to confirm the correlation with metabolic disorders through the effects of 4 weeks of moderate and high-intensity aerobic exercise. However, an animal model study also showed that increased species richness is robust only under high-fat diets after voluntary wheel running.[65] Therefore, it is challenging to determine the characteristics of altered gut microbiota clusters according to moderate and high-intensity aerobic exercise. Future studies should delve into specific and comprehensive changes in exercise and microbial communities to determine the most suitable exercise parameters based on individual conditions.

While increased microbial clusters generally contribute positively, they can potentially become opportunistic pathogens and cause infections when the gut environment changes, underscoring challenges in definitively correlating these changes with metabolic disorders.[40] Despite these limitations, investigating exercise's effects on microbial groups could yield positive outcomes in mitigating risks associated with metabolic disorders. Although numerous studies have explored effects of exercise on altering the gut microbiome profile, definitive conclusions on the optimal exercise type, intensity, and duration remain elusive.[66] Future examinations of this topic would benefit from focusing on the effect of exercise on changes in microbial communities and composition.[67] Based on the present data, additional investigations into the gut microbiome should explore its potential effects on patients with chronic diseases such as metabolic disorders, diabetes, and hypertension. The current results suggest that further research is needed to examine the applicability of these findings to metabolic disorders.

5. Conclusion

The findings reveal distinct changes in gut microbiota induced by moderate and high-intensity exercises. Moderate exercise resulted in increased Prevotella but decreased Veillonella, Dorea_formicigenerans, and Dorea_longicatena, while high-intensity exercise led to elevated levels of Bacteroides, Butyricimonas, Odoribacter, and Alistipes. Notably, both exercise intensities augmented microbial groups associated with SCFAs production and metabolic processes, suggesting

potential roles in anti-inflammatory responses, immune functions, and metabolic regulation. However, the duration of these changes and their actual impact on metabolic disease remain uncertain, future studies are needed for further comprehensive investigations.

Declaration of interest statement

The author(s) have no conflicts of interest relevant to this article.

Ethical statement

This study was approved by the Institutional Review Board of Kookmin University (KMU-202001-HR-227), and in accordance with the World Medical Association and Helsinki Declaration.

Funding statement

This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF–2021R1A6A3A01086909).

References

1. Wang PX, Deng XR, Zhang CH, Yuan HJ. Gut microbiota and metabolic syndrome. *Chin Med J*. 2020;133:808–816.
2. Sharon I, Quijada NM, Pasolli E, et al. The core human microbiome: does it exist and how can we find it? A critical Review of the concept. *Nutrients*. 2022;14:2872.
3. Fan Y, Pedersen O. Gut microbiota in human metabolic health and disease. *Nat Rev Microbiol*. 2021;19:55–71.
4. Willing BP, Dicksved J, Halfvarson J, et al. A pyrosequencing study in twins shows that gastrointestinal microbial profiles vary with inflammatory bowel disease phenotypes. *Gastroenterology*. 2010;139:1844. U1105.
5. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature*. 2006;444:1022–1023.
6. Ahn J, Sinha R, Pei Z, et al. Human gut microbiome and risk for colorectal cancer. *J Natl Cancer Inst*. 2013;105:1907–1911.
7. Kootte RS, Vrieze A, Holleman F, et al. The therapeutic potential of manipulating gut microbiota in obesity and type 2 diabetes mellitus. *Diabetes Obes Metabol*. 2012;14:112–120.
8. Bonomini-Gnutzmann R, Plaza-Diaz J, Jorquera-Aguilera C, Rodriguez-Rodriguez A, Rodriguez-Rodriguez F. Effect of intensity and duration of exercise on gut microbiota in humans: a systematic Review. *Int J Environ Res Publ Health*. 2022;19.
9. Boule NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. *Diabetologia*. 2003;46:1071–1081.
10. de Mello MT, de Piano A, Carnier J, et al. Long-term effects of aerobic plus resistance training on the metabolic syndrome and adiponectinemia in obese adolescents. *J Clin Hypertens*. 2011;13:343–350.
11. Johannesson E, Simren M, Strid H, Bajor A, Sadik R. Physical activity improves symptoms in irritable bowel syndrome: a randomized controlled trial. *Am J Gastroenterol*. 2011;106:915–922.
12. Lin KY, Shun SC, Lai YH, Liang JT, Tsauo JY. Comparison of the effects of a supervised exercise program and usual care in patients with colorectal cancer undergoing chemotherapy. *Cancer Nurs*. 2014;37:E21–E29.
13. Lund K, Knudsen T, Kjeldsen J, Nielsen RG, Juhl CB, Norgard BM. The IBD-FITT study - moderate-intensity exercise for patients with inflammatory bowel disease with moderate disease activity: an open-label randomized controlled trial. *Trials*. 2023;24:742.
14. American College of Sports Medicine. *ACSM's Guidelines for Exercise Testing and Prescription*. eleventh ed. Wolters Kluwer; 2021.
15. Petersen LM, Bautista EJ, Nguyen H, et al. Community characteristics of the gut microbiomes of competitive cyclists. *Microbiome*. 2017;5:98.
16. Clarke SF, Murphy EF, O'Sullivan O, et al. Exercise and associated dietary extremes impact on gut microbial diversity. *Gut*. 2014;63:1913–1920.
17. Estaki M, Pither J, Baumeister P, et al. Cardiorespiratory fitness as a predictor of intestinal microbial diversity and distinct metagenomic functions. *Microbiome*. 2016;4:42.
18. Allen JM, Mailing LJ, Niemiro GM, et al. Exercise alters gut microbiota composition and function in lean and obese humans. *Med Sci Sports Exerc*. 2018;50:747–757.
19. Morita E, Yokoyama H, Imai D, et al. Aerobic exercise training with brisk walking increases intestinal Bacteroides in healthy elderly women. *Nutrients*. 2019;11:868.
20. Keohane DM, Woods T, O'Connor P, et al. Four men in a boat: ultra-endurance exercise alters the gut microbiome. *J Sci Med Sport*. 2019;22:1059–1064.
21. Wegierska AE, Charitos IA, Topi S, Potenza MA, Montagnani M, Santacroce L. The connection between physical exercise and gut microbiota: implications for competitive sports athletes. *Sports Med*. 2022;52:2355–2369.
22. Lustgarten MS. The role of the gut microbiome on skeletal muscle mass and physical function: 2019 update. *Front Physiol*. 2019;10:1435.
23. Helgerud J, Høydal K, Wang E, et al. Aerobic high-intensity intervals improve VO2max more than moderate training. *Med Sci Sports Exerc*. 2007;39:665–671.
24. Dalton A, Mermier C, Zuhl M. Exercise influence on the microbiome-gut-brain axis. *Gut Microb*. 2019;10:555–568.
25. Leal LG, Lopes MA, Batista Jr ML. Physical exercise-induced myokines and muscle-adipose tissue crosstalk: a Review of current knowledge and the implications for health and metabolic diseases. *Front Physiol*. 2018;9:1307.
26. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. *Compr Physiol*. 2012;2:1143–1211.
27. David LA, Materna AC, Friedman J, et al. Host lifestyle affects human microbiota on daily timescales. *Genome Biol*. 2014;15, R89.
28. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43:1334–1359.
29. Ainsworth BE, Haskell WL, Herrmann SD, et al. Compendium of Physical Activities: a second update of codes and MET values. *Med Sci Sports Exerc*. 2011;43:1575–1581, 2011.
30. Kokkinos P, Myers J, Faselis C, et al. Exercise capacity and mortality in older men A 20-year follow-up study. *Circulation*. 2010;122:790–797.
31. Heo M, Park YS, Yoon H, et al. Potential of gut microbe-derived extracellular vesicles to differentiate inflammatory bowel disease patients from healthy controls. *Gut Liver*. 2023;17:108–118.
32. Wan Z, Zheng J, Zhu Z, et al. Intermediate role of gut microbiota in vitamin B nutrition and its influences on human health. *Front Nutr*. 2022;9, 1031502.
33. Huh JW, Kim MJ, Kim J, et al. Enterotypical Prevotella and three novel bacterial biomarkers in preoperative stool predict the clinical outcome of colorectal cancer. *Microbiome*. 2022;10:203.
34. Fan Y, Ying J, Ma H, Cui H. Microbiota-related metabolites fueling the understanding of ischemic heart disease. *iMeta*. 2023;2, e94.
35. Zsálig D, Berta A, Tóth V, et al. A Review of the relationship between gut microbiome and obesity. *Appl Sci-Basel*. 2023;13:610.
36. Soltys K, Lendvorsky L, Hric I, et al. Strenuous physical training, physical fitness, body composition and Bacteroides to Prevotella ratio in the gut of elderly athletes. *Front Physiol*. 2021;12, 670989.
37. Liu H, Chen X, Hu X, et al. Alterations in the gut microbiome and metabolism with coronary artery disease severity. *Microbiome*. 2019;7:68.
38. Companys J, Gosalbes MJ, Pla-Pagà L, et al. Gut microbiota profile and its association with clinical variables and dietary intake in overweight/obese and lean subjects: a cross-sectional study. *Nutrients*. 2021;13:2032.
39. Boden WE, Franklin B, Berra K, et al. Exercise as a therapeutic intervention in patients with stable ischemic heart disease: an underfilled prescription. *Am J Med*. 2014;127:905–911.
40. Zafar H, Saier Jr MH. Gut Bacteroides species in health and disease. *Gut Microb*. 2021;13:1–20.
41. Castaner O, Goday A, Park YM, et al. The gut microbiome profile in obesity: a systematic Review. *Internet J Endocrinol*. 2018;2018, 4095789.
42. Hu HJ, Park SG, Jang HB, et al. Obesity alters the microbial community profile in Korean adolescents. *PLoS One*. 2015;10, e0134333.
43. Nomura K, Ishikawa D, Okahara K, et al. Bacteroidetes species are correlated with disease activity in ulcerative colitis. *J Clin Med*. 2021;10:1749.
44. Dong S, Liu Q, Zhou X, et al. Effects of losartan, atorvastatin, and aspirin on blood pressure and gut microbiota in spontaneously hypertensive rats. *Molecules*. 2023;28:612.
45. Guo Y, Li XS, Wang ZJ, Yu B. Gut microbiota dysbiosis in human hypertension: a systematic Review of observational studies. *Front Cardiovasc Med*. 2021;8, 650227.
46. Larsen N, Vogensen FK, van den Berg FW, et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. *PLoS One*. 2010;5, e9085.
47. Zhao X, Zhang Y, Guo R, et al. The alteration in composition and function of gut microbiome in patients with type 2 diabetes. *J Diabetes Res*. 2020;2020, 8842651.
48. Cui J, Ramesh G, Wu M, et al. Butyrate-producing bacteria and insulin homeostasis: the microbiome and insulin longitudinal evaluation study (MILES). *Diabetes*. 2022;71:2438–2446.
49. Li Y, Fu R, Li R, et al. Causality of gut microbiome and hypertension: a bidirectional mendelian randomization study. *Front Cardiovasc Med*. 2023;10, 1167346.
50. Zhang X, Wang H, Xie C, et al. Shenqi compound ameliorates type-2 diabetes mellitus by modulating the gut microbiota and metabolites. *J Chromatogr, B: Anal Technol Biomed Life Sci*. 2022;1194, 123189.
51. Albhaisi SAM, Bajaj JS, Sanyal AJ. Role of gut microbiota in liver disease. *Am J Physiol-Gastr L*. 2020;318:G84–G98.
52. Hiippala K, Barreto G, Burrello C, et al. Novel odoribacter splanchnicus strain and its outer membrane vesicles exert immunoregulatory effects in vitro. *Front Microbiol*. 2020;11, 575455.
53. Osawa M, Handa O, Fukushima S, et al. Reduced abundance of butyric acid-producing bacteria in the ileal mucosa-associated microbiota of ulcerative colitis patients. *J Clin Biochem Nutr*. 2023;73:77–83.
54. Parker BJ, Wearsch PA, Veloo ACM, Rodriguez-Palacios A. The genus Alistipes: gut bacteria with emerging implications to inflammation, cancer, and mental health. *Front Immunol*. 2020;11:906.
55. Bongiovanni T, Yin MOL, Heaney LM. The athlete and gut microbiome: short-chain fatty acids as potential ergogenic aids for exercise and training. *Int J Sports Med*. 2021;42:1143–1158.
56. Carey RA, Montag D. Exploring the relationship between gut microbiota and exercise: short-chain fatty acids and their role in metabolism. *BMJ Open Sport Exerc Med*. 2021;7, e000930.

57. Meliala A, Narwidina P, Nirwati H, et al. The impact of moderate-and high-intensity exercise on microbiota population and short-chain fatty acid production in the cecum of rats. *J Appl Pharmaceut Sci*. 2021;11:90–97.
58. Louis P, McCrae SI, Charrier C, Flint HJ. Organization of butyrate synthetic genes in human colonic bacteria: phylogenetic conservation and horizontal gene transfer. *FEMS Microbiol Lett*. 2007;269:240–247.
59. Hippe B, Zwielehner J, Liszt K, Lassl C, Unger F, Haslberger AG. Quantification of butyryl CoA:acetate CoA-transferase genes reveals different butyrate production capacity in individuals according to diet and age. *FEMS Microbiol Lett*. 2011;316:130–135.
60. O'Donovan CM, Madigan SM, Garcia-Perez I, Rankin A, O OS, Cotter PD. Distinct microbiome composition and metabolome exists across subgroups of elite Irish athletes. *J Sci Med Sport*. 2020;23:63–68.
61. Bycura D, Santos AC, Shiffer A, et al. Impact of different exercise modalities on the human gut microbiome. *Sports. (Basel)*. 2021;9.
62. Scheiman J, Luber JM, Chavkin TA, et al. Meta-omics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism. *Nat Med*. 2019;25:1104–1109.
63. Grosicki GJ, Durk RP, Bagley JR. Rapid gut microbiome changes in a world-class ultramarathon runner. *Phys Rep*. 2019;7, e14313.
64. Fontana F, Longhi G, Tarracchini C, et al. The human gut microbiome of athletes: metagenomic and metabolic insights. *Microbiome*. 2023;11:27.
65. Evans CC, LePard KJ, Kwak JW, et al. Exercise prevents weight gain and alters the gut microbiota in a mouse model of high fat diet-induced obesity. *PLoS One*. 2014;9, e92193.
66. Suryani D, Subhan Alfaqih M, Gunadi JW, et al. Type, intensity, and duration of exercise as regulator of gut microbiome profile. *Curr Sports Med Rep*. 2022;21:84–91.
67. Boytar AN, Skinner TL, Wallen RE, Jenkins DG, Dekker Nitert M. The effect of exercise prescription on the human gut microbiota and comparison between clinical and apparently healthy populations: a systematic Review. *Nutrients*. 2023;15.