Kallikrein 7 and metabolic responses after acute aerobic exercise in inactive young adults

Calicreína 7 y respuestas metabólicas tras el ejercicio aeróbico agudo en adultos jóvenes inactivos

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Abstract

Introduction: Kallikrein 7 (KLK7) is a protease linked to adipose inflammation, lipid metabolism, and insulin sensitivity in obesity-related low-grade inflammation. Its acute response to exercise in humans remains unclear.
Objective: To examine the immediate effects of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) on circulating KLK7 and its association with metabolic responses in physically inactive young adults.
Methods: This exploratory pooled analysis included two quasi-experimental studies (MICT, n = 16; HIIT, n = 20) in adults aged 18–28 years. MICT involved 30 min at 60% heart rate reserve (HRR), while HIIT consisted of five 3-min bouts at 80% HRR interspersed with 3 min at 20% HRR. Blood samples were collected pre- and post-exercise. KLK7 was assessed by Western blot, and changes (Δ) were analyzed using correlations, multivariable regression, and principal component analysis (PCA).
Results: KLK7 levels did not change significantly after either protocol ($p > 0.05$). Most metabolic markers were unchanged, except for a reduction in insulin after MICT ($p < 0.05$). ΔTriglycerides, ΔHDL-cholesterol, and Δglycemia explained 36.6% of ΔKLK7 variance ($p = 0.002$). PCA suggested clustering between ΔKLK7 and metabolic variables, though with limited robustness.
Conclusion: Acute aerobic exercise did not significantly modify circulating KLK7, but its association with metabolic responses suggests a potential regulatory role. Further longitudinal studies are needed.

Keywords

Aerobic exercise; interval training; kallikrein 7; low-grade inflammation; metabolism.

Resumen

Introducción: La calicreína 7 (KLK7) es una proteasa vinculada con la inflamación del tejido adiposo, el metabolismo lipídico y la sensibilidad a la insulina en la inflamación crónica de bajo grado asociada a la obesidad. Sin embargo, su respuesta aguda al ejercicio en humanos sigue siendo poco clara.
Objetivo: Examinar los efectos inmediatos del entrenamiento continuo de intensidad moderada (MICT) y del entrenamiento interválico de alta intensidad (HIIT) sobre la KLK7 circulante y su asociación con las respuestas metabólicas en adultos jóvenes físicamente inactivos.
Métodos: Este análisis exploratorio agrupado incluyó dos estudios cuasiexperimentales (MICT, n = 16; HIIT, n = 20) en adultos de 18 a 28 años. El MICT consistió en 30 min al 60% de la reserva de frecuencia cardíaca (RFC), mientras que el HIIT consistió en cinco intervalos de 3 min al 80% de la RFC, intercalados con 3 min al 20% de la RFC. Se recolectaron muestras de sangre antes y después del ejercicio. La KLK7 se evaluó mediante Western blot, y los cambios (Δ) se analizaron mediante correlaciones, regresión multivariable y análisis de componentes principales (ACP).
Resultados: Los niveles de KLK7 no cambiaron significativamente después de ninguno de los protocolos ($p > 0,05$). La mayoría de los marcadores metabólicos no se modificaron, excepto por una reducción de la insulina después del MICT ($p < 0,05$). ΔTriglicéridos, Δcolesterol HDL y Δglicemia explicaron el 36,6% de la varianza de ΔKLK7 ($p = 0,002$). El ACP sugirió una agrupación entre ΔKLK7 y las variables metabólicas, aunque con una robustez limitada.
Conclusión: El ejercicio aeróbico agudo no modificó significativamente la KLK7 circulante, pero su asociación con las respuestas metabólicas sugiere un posible papel regulador. Se requieren estudios longitudinales adicionales.

Palabras clave

Calicreína 7; ejercicio aeróbico; entrenamiento interválico; inflamación de bajo grado; metabolismo.

Introduction

Physical inactivity is a major global health burden and a key contributor to obesity, metabolic syndrome, and cardiometabolic diseases (Pišot, 2022; Strain et al., 2024). Prolonged sedentary behavior reduces skeletal muscle contractile activity, leading to mitochondrial dysfunction, oxidative stress, and impaired glucose uptake (Pišot, 2022). In addition, physical inactivity can lead to an excessive accumulation of adipose tissue (Bourke et al., 2024; Pišot, 2022). These effects promote insulin resistance, metabolic dysfunction, and systemic low-grade inflammation (Booth et al., 2017).

Serine proteases play a relevant role in the regulation of low-grade inflammation by modulating immune signaling, the processing of inflammatory mediators, and the activation of proteolysis-sensitive receptors (Bhoola et al., 1992). Several serine proteases, including members of the kallikrein-related peptidase (KLK) family, have been implicated in conditions characterized by systemic low-grade inflammation, such as obesity, insulin resistance, and cardiometabolic diseases. In humans, dysregulation of serine proteases has been associated with persistent inflammatory profiles and alterations in adipose tissue immune–metabolic crosstalk, supporting their role as key molecular nodes linking metabolism and chronic subclinical inflammation rather than mediators of acute inflammatory responses (Ribas-Latre et al., 2025).

Within this context, kallikrein 7 (KLK7) has emerged as a metabolic mediator of interest. Although usually associated with skin physiology, recent evidence indicates that KLK7 plays a significant role in systemic low-grade inflammation and metabolic disease (Kunath et al., 2021; Zieger et al., 2018). For instance, increased KLK7 expression in adipose tissue has been linked to impaired insulin signaling and altered lipid handling, particularly in mice (Kunath et al., 2021; Zieger et al., 2018). In individuals with obesity, visceral adipose KLK7 expression associates with inflammatory pathways and serum KLK7 correlates with circulating inflammatory markers (Ribas-Latre et al., 2025). Mechanistically, KLK7 is inhibited by the adipokine vaspin, and vaspin–KLK7 complexes have been detected in human plasma (Heiker et al., 2013). Moreover, KLK7 can proteolytically activate prochemerin, connecting KLK7 activity to regulation of the adipokine chemoattractant chemerin (Schultz et al., 2013). While these findings derive mainly from obesity-related models, similar disturbances may also occur in states characterized by reduced skeletal muscle activity, such as physical inactivity and sedentary behavior (Dirks et al., 2016; Mikines et al., 1991; Thyfault & Krogh-Madsen, 2011; Trim et al., 2022). Because acute aerobic exercise rapidly modifies lipid mobilization, insulin signaling, inflammatory mediators, and adipose tissue–muscle crosstalk, it represents a relevant physiological stimulus for exploring whether circulating KLK7 is acutely responsive to metabolic perturbation.

Exercise is well known to exert beneficial effects on cardiometabolic health, with most evidence emphasizing chronic training adaptations (Adams & Niebauer, 2015; Allen et al., 2015; Leal et al., 2018; Man et al., 2020; Stroh & Stanford, 2023). However, a single session of aerobic exercise elicits a rapid and complex immunological, endocrine, and metabolic response (Dreher et al., 2023; Forsse et al., 2022). Moderate-intensity continuous training (MICT) promotes sustained oxidative metabolism, mild catecholamine release, increased blood flow, improved insulin sensitivity, and enhanced lipid utilization (Enríquez-Schmidt et al., 2024; Z. Guo et al., 2023; Hu et al., 2023; Mendes et al., 2019; Ryan et al., 2020; Song et al., 2024). In contrast, high-intensity interval training (HIIT) induces marked increases in lactate, rapid shifts in substrate use, and elevated lipolysis (Enríquez-Schmidt et al., 2024; Ryan et al., 2020; Sabag et al., 2022; Song et al., 2024). These acute stimuli may modulate the secretion of enzymes and proteases, including KLK7, although this remains unexplored.

Despite the emerging relevance of KLK7 to metabolic regulation, to the best of our knowledge there are no studies showing the acute effects of exercise on KLK7 plasma levels in humans. KLK7 expression and secretion are sensitive to inflammatory and metabolic cues, including changes in adipose tissue, lipid mobilization, and cytokine signaling (Kunath et al., 2021; Zieger et al., 2018). Therefore, understanding how one bout of distinct exercise intensities influences KLK7 secretion may provide new insights into the early metabolic signaling events triggered by aerobic training. Thus, the aim of this exploratory study was to investigate the acute effects of a single session of MICT and HIIT on plasma KLK7 levels in physically inactive young adults. We hypothesized that a single bout of aerobic exercise would modify circulating KLK7 levels and that the magnitude or direction of the response could differ between MICT and HIIT.

Method

Study design and ethical considerations

This quantitative exploratory study represents a secondary pooled analysis of two non-randomized quasi-experimental pre–post investigations designed to examine the acute metabolic effects of a single session of moderate-intensity continuous training (MICT) (Carrasco-Molina et al., 2024) or high-intensity interval training (HIIT) (Alvarado-Carrasco et al., 2025). Although conducted independently, both studies employed harmonized methodological procedures regarding participant eligibility criteria, exercise supervision, fasting conditions, blood collection timing, sample processing, and biochemical analyses, thereby supporting data pooling for exploratory analyses.

Both studies were reviewed and approved by the Ethics Committee of the Los Ríos Health Service (MICT protocol code: 484/2022; HIIT protocol code: 443/2023) and were registered at ClinicalTrials.gov (NCT07146867). All participants provided written informed consent before enrollment. Both studies were conducted according to the Declaration of Helsinki.

Participants

Both studies included physically inactive young adults aged 18–28 years with body mass index (BMI) between 18 and 30 kg/m^2. Physical inactivity was defined as engaging in less than 150 min/week of moderate physical activity and/or 75 min/week of vigorous physical activity according to World Health Organization recommendations (World Health Organization, n.d.). Participants receiving anti-inflammatory or insulin-sensitizing pharmacological treatments, those who were pregnant, those unable to complete the exercise session, and those with acute musculoskeletal injuries were excluded.

Using convenience sampling, the MICT study included 20 participants and the HIIT study included 21 participants. Baseline assessments included systolic and diastolic blood pressure, body weight, height, waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), and body composition assessed by bioelectrical impedance analysis (InBody® 270).

Five plasma samples were unavailable for KLK7 analysis due to insufficient remaining sample volume after completion of prior biochemical assays. Therefore, the final analytical sample for KLK7 analyses included 36 participants.

Exercise protocols

Participants assigned to the MICT protocol performed 30 minutes of treadmill walking at 60% of heart rate reserve (HRR), monitored using a heart rate monitor strap, corresponding to ratings of perceived exertion (RPE) between 5 and 6 on the modified Borg scale.

Participants assigned to the HIIT protocol completed a 30-minute treadmill-based session consisting of five cycles of 3 minutes at 80% HRR and RPE 8–9, interspersed with 3 minutes at 20% HRR and RPE 2–3 (Fig. 1). The protocols were selected to provide two physiologically distinct but feasible aerobic stimuli in physically inactive young adults. MICT at 60% HRR was intended to elicit sustained moderate oxidative demand, whereas HIIT alternating 80% and 20% HRR was selected to produce repeated high-intensity metabolic perturbations while maintaining tolerability and a comparable session duration. It is worth mentioning that all exercise sessions were supervised by trained research personnel.

Figure 1. Study design. Physically inactive young adults completed a single 30-minute session of either moderate-intensity continuous training (MICT; 60% of heart rate reserve [HRR]) or high-intensity interval training (HIIT; alternating bouts at 80% and 20% HRR). Heart rate and rating of perceived exertion (RPE) were continuously monitored during exercise to ensure adherence to the prescribed intensities. Venous blood samples were collected immediately before and after each exercise session to assess glycemia, insulin, lipid profile, liver transaminases, fibroblast growth factor 21 (FGF21), and kallikrein 7 (KLK7). Figure created in BioRender.com.

Source: The Authors.

Clinical and metabolic outcomes

Venous blood samples were collected from the antecubital vein immediately before and immediately after each exercise protocol following an overnight fast. Participants were instructed to maintain their habitual dietary and physical activity patterns throughout the study period and to avoid strenuous physical exercise for at least 48 h before testing sessions.

Biochemical analyses included glucose (glucose oxidase/peroxidase method), insulin (ST AIA-PACK IRI fluorometric enzymatic assay, Tosoh®, Japan), lipid profile (Colestat and TG Color kits, Wiener Lab®, Argentina), liver transaminases (ALT and AST), and fibroblast growth factor 21 (FGF21; RayBiotech®, catalog number ELHFGF21-1, USA).

Because blood samples were collected only immediately after exercise, the study design does not allow characterization of the temporal kinetics of circulating KLK7 responses beyond the immediate post-exercise period.

Western immunoblotting

Circulating KLK7 protein levels were analyzed by Western immunoblotting under standardized laboratory conditions. All plasma samples were processed using the same experimental workflow, antibody lot, imaging settings, and operator to minimize analytical variability.

Briefly, plasma samples (0.5 µL) were mixed with 2.5 µL of 6× Laemmli loading buffer and 12 µL of RIPA buffer (Abcam®, catalog number ab156034) and loaded directly onto pre-cast polyacrylamide gels (Bio-Rad®, catalog number 4568086). Proteins were separated by SDS-PAGE (80 V for 5 min followed by 120 V for 60 min) and transferred to nitrocellulose membranes (Bio-Rad®, catalog number 1704158) using the Trans-Blot® Turbo™ Transfer System (Bio-Rad®, Hercules, CA, USA) according to the manufacturer's instructions. Membranes were blocked for 1 h with 5% bovine serum albumin (BSA) in TBST (0.6% Tris-HCl w/v, 0.1% Tris-base w/v, 0.6% NaCl w/v, and 0.05% Tween-20 v/v). Membranes were washed three times for 10 min in TBST under orbital agitation (100 rpm, room temperature) and incubated overnight at 4°C with rabbit monoclonal anti-KLK7 primary antibody (1:2500 dilution; Abcam®, catalog number ab28309, lot 275443). After washing, membranes were incubated for 1 h at room temperature with HRP-conjugated anti-rabbit secondary antibody (1:2500 dilution; Cell Signaling®, catalog number 7074S). Chemiluminescent detection was performed using Clarity™ Western ECL substrate (Bio-Rad®, catalog number 1705061) and visualized using a Clinx Imaging System (Shanghai, China).

Protein loading normalization was performed using whole-membrane Ponceau S staining (Sander et al., 2019). Densitometric analyses were conducted using ImageJ software by the same blinded investigator under identical analysis settings.

Statistical analysis

Given the exploratory objective of investigating metabolic correlates of changes in circulating KLK7, data from both exercise modalities were pooled for the primary analyses. To evaluate the appropriateness of pooling, modality × time interaction effects were initially examined. As no significant interaction effects were observed, pooled analyses were subsequently performed to increase statistical power. Quantitative variables were expressed as mean ± standard deviation, whereas categorical variables were presented as absolute and relative frequencies. Distribution normality was assessed using the Kolmogorov–Smirnov test. Because most continuous variables were non-normally distributed, pre–post exercise comparisons were performed using the Wilcoxon signed-rank test. Standardized pre–post effect sizes were estimated using Hedges g_{av}, calculated by dividing the mean pre–post difference by the average standard deviation of the two measurements and applying a small-sample correction. Negative values indicate lower post-exercise values. Ninety-five percent confidence intervals were calculated. Associations between variables were evaluated using Spearman's rank correlation coefficient. Individual exercise-induced responses were calculated as delta (Δ) values and used in subsequent analyses. Exploratory multivariable linear regression analyses were conducted to identify variables independently associated with ΔKLK7. Predictor variables were selected a priori based on biological plausibility and prior literature to minimize model overfitting. Given the modest sample size, regression findings should be interpreted as exploratory and hypothesis-generating. Because this study represents a secondary exploratory analysis, a priori sample size calculation was not performed. Therefore, findings, particularly null associations, should be interpreted cautiously due to the possibility of limited statistical power to detect small physiological effects. Additionally, an exploratory principal component analysis (PCA) was performed to provide a descriptive visualization of covariation patterns among metabolic and anthropometric variables. Statistical analyses were conducted using SPSS version 22 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 8 (GraphPad Software, San Diego, CA, USA). Statistical significance was set at $p < 0.05$.

Results

A total of 36 participants were included in the final analysis (MICT = 16; HIIT = 20). Five plasma samples were unavailable for KLK7 quantification due to insufficient remaining sample volume after completion of prior biochemical analyses. Sex distribution was balanced, with women representing 47% of the sample. Mean age was 22.6 years, and mean BMI was 23.6 kg/m^2. Anthropometric and baseline clinical characteristics according to exercise modality are presented in Table 1.

Table 1. Baseline phenotypic and clinical characteristics of participants according to exercise modality

Parameter	MICT (n = 16) Mean (SD)	HIIT (n = 20) Mean (SD)	Total Mean (SD)
Sex[a] Male	9 (56)	10 (50)	19 (53)
Female	7 (44)	10 (50)	17 (47)
Age (years)	22.5 (1.0)	22.8 (1.6)	22.6 (1.3)
Weight (kg)	64.1 (8.1)	66.4 (21.2)	65.4 (16.5)
Height (cm)	166.3 (8.8)	166.1 (8.8)	166.2 (8.6)
BMI (kg/m^2)	23.1 (2.8)	23.9 (7.1)	23.6 (5.5)
Waist-to-hip ratio	0.8 (0.06)	0.7 (0.2)	0.8 (0.1)
Waist-to-height ratio	0.4 (0.04)	0.5 (0.1)	0.5 (0.08)
Muscle mass (%)	41.9 (6.5)	38.1 (7.2)	39.8 (7.1)
Fat mass (%)	20.9 (7.8)	30.0 (9.7)	26.0 (9.9)

[a]n (%)
Values are expressed as mean (SD), except sex, which is expressed as n (%).
BMI: body mass index

No statistically significant modality × time interactions were detected for KLK7 or the principal metabolic outcomes. Given the exploratory prespecified analytical approach, subsequent analyses were performed using the pooled sample. Across the pooled sample, acute exercise did not significantly modify lipid profile, liver transaminases, glycemia, or FGF21 concentrations immediately after exercise ($p > 0.05$; Table 2). A significant reduction in plasma insulin concentrations was observed only after the MICT session ($p < 0.05$; Table 2).

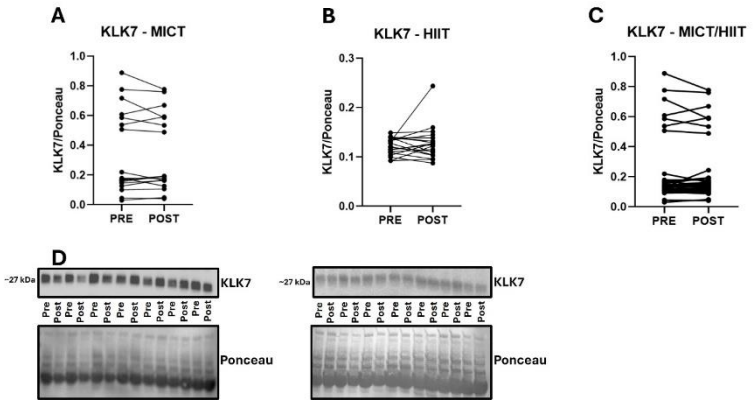
Table 2. Immediate pre–post changes and effect sizes for metabolic outcomes following MICT and HIIT

Variables	MICT (n = 16)		HIIT (n = 20)		Total (n = 36)	
	Mean (SD)	Effect size [95% CI]	Mean (SD)	Effect size [95% CI]	Mean (SD)	Effect size [95% CI]
Glycemia pre (mg/dL)	90.1 (15.6)	−0.12 [−0.58, 0.35]	91.8 (10.6)	0.32 [−0.11, 0.75]	91.1 (12.9)	0.16 [−0.17, 0.48]
post (mg/dL)	88.5 (9.8)		97.9 (23.6)		93.7 (19.1)	
Insulin pre (µU/mL)	34.4 (29.5)	−0.78 [−1.32, −0.24]	34.1 (46.9)	−0.32 [−0.75, 0.11]	34.3 (39.6)	−0.48 [−0.81, −0.14]
post (µU/mL)	16.2 (10.8)*		21.8 (22.7)		19.3 (18.4)	
TAGs pre (mg/dL)	119.1 (65.8)	0.04 [−0.43, 0.50]	137 (90.2)	−0.04 [−0.47, 0.38]	129.1 (79.7)	−0.01 [−0.33, 0.31]
post (mg/dL)	121.6 (68.8)		133.1 (78.7)		128 (73.6)	
HDL pre (mg/dL)	44.6 (19.8)	−0.64 [−1.16, −0.12]	51.1 (11.6)	0.13 [−0.29, 0.56]	48.2 (15.9)	−0.24 [−0.57, 0.08]
post (mg/dL)	31.7 (18.5)		53.2 (17.8)		43.6 (20.8)	
LDL pre (mg/dL)	89.4 (24.7)	−0.08 [−0.54, 0.39]	92.4 (22.2)	−0.27 [−0.70, 0.16]	91.1 (23.1)	−0.20 [−0.52, 0.13]
post (mg/dL)	87.3 (26.4)		84.3 (34.8)		85.6 (31)	
VLDL pre (mg/dL)	21.4 (11.3)	0.01 [−0.46, 0.47]	26 (16.2)	0.39 [−0.05, 0.83]	24 (14.2)	0.27 [−0.06, 0.59]
post (mg/dL)	21.5 (11.1)		36.5 (32.8)		29.8 (26.4)	
FGF21 pre (pg/mL)	1750.8 (3280.2)	−0.02 [−0.49, 0.44]	460.8 (588.2)	−0.05 [−0.47, 0.37]	1034.1 (2285.1)	−0.02 [−0.34, 0.30]
post (pg/mL)	1670.1 (3260.1)		432.7 (564.7)		982.6 (2262.1)	
GOT pre (U/L)	34.1 (22)	0.19 [−0.28, 0.66]	24.4 (9.1)	−0.07 [−0.49, 0.35]	28.7 (16.6)	0.09 [−0.23, 0.41]
post (U/L)	38.6 (22.9)		23.7 (10.1)		30.3 (18.3)	
GPT pre (U/L)	30.1 (25.4)	0.03 [−0.43, 0.50]	29.2 (25.5)	−0.01 [−0.43, 0.41]	29.6 (25.1)	0.01 [−0.31, 0.33]
post (U/L)	30.9 (24.6)		28.9 (25.9)		29.8 (25)	

Abbreviation list: TAGs: triglycerides; HDL: high-density lipoprotein; LDL: low-density lipoprotein; VLDL: very low-density lipoprotein; GOT: glutamic oxaloacetic transaminase; GPT: glutamic pyruvic transaminase. *p < 0.05

KLK7 was detectable in plasma samples from all participants. No statistically significant changes in circulating relative KLK7 abundance were observed immediately after either MICT or HIIT sessions (p > 0.05; Figure 2). In multivariable linear regression analyses, ΔTAGs, ΔHDL, and Δglycemia were associated with ΔKLK7, jointly explaining 36.6% of its variance (Table 3; p = 0.002).

Figure 2. Acute effects of MICT and HIIT on KLK7. (A) Individual pre- and post-exercise plasma kallikrein 7 (KLK7) levels following a single session of moderate-intensity continuous training (MICT) and (B) high-intensity interval training (HIIT). (C) Combined analysis of MICT and HIIT showing individual KLK7 responses before and after exercise. KLK7 protein abundance was quantified by Western blot and normalized to total protein loading using Ponceau S staining. Each line represents an individual participant. No significant differences in circulating KLK7 levels were observed between pre- and post-exercise conditions for either protocol (p > 0.05). (D) Representative KLK7 immunoblots and corresponding Ponceau S-stained membranes are shown.



Source: The Authors.

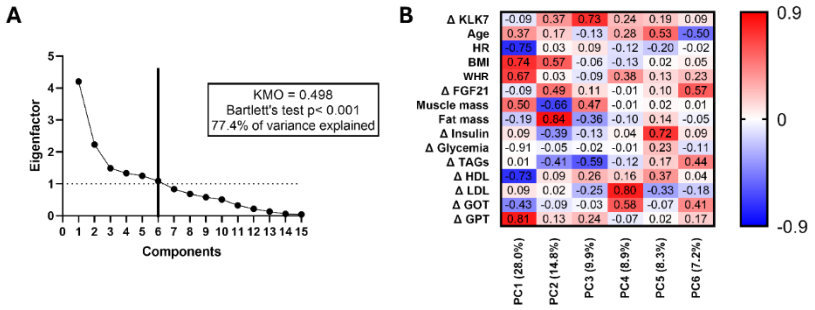
Table 3. Exploratory multivariable regression analysis of metabolic changes associated with ΔKLK7

	Δ KLK7			
Predictor	Standardized β [95% CI]	SE	t	p-value
Δ TAGs	-0.380 [−0.667, −0.093]	0.023	-2.699	0.011
Δ HDL	0.681 [0.251, 1.111]	0.034	3.223	0.003
Δ Glycemia	-0.445 [−0.875, −0.015]	0.027	-2.108	0.043
Model statistics	R^2 (95% CI) = 0.366 (0.070-0.525)	F = 6.161	p = 0.002	n = 36

Abbreviation list: TAGs: triglycerides; HDL: high-density lipoprotein; KLK7: kallikrein 7

Exploratory PCA retained six components explaining 77.4% of the total variance. However, sampling adequacy was below the conventional acceptable threshold (KMO = 0.498). Therefore, the component structure was considered potentially unstable and is presented exclusively as a descriptive visualization without inferential or biological interpretation.

Figure 3. Principal component analysis (PCA) of acute exercise–related responses. (A) Scree plot showing eigenvalues across extracted components. The horizontal dashed line indicates the Kaiser criterion (eigenvalue = 1), and the vertical line denotes the number of components retained. Sampling adequacy and factorability are shown in the inset (Kaiser-Meyer-Olkin = 0.498; Bartlett's test of sphericity $p < 0.001$), with a cumulative 77.4% of total variance explained by the retained solution. (B) Heatmap of PCA loadings for the retained principal components (PC1–PC6, variance explained shown in parentheses). Cell values represent loading coefficients; color indicates direction and magnitude (red = positive; blue = negative). Δ denotes the within-participant change (post − pre). Abbreviations: KLK7, kallikrein 7; HR, heart rate; BMI, body mass index; WHR, waist-to-hip ratio; FGF21, fibroblast growth factor 21; TAGs, triacylglycerols; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; GOT (AST), aspartate aminotransferase; GPT (ALT), alanine aminotransferase.



Source: The Authors.

Discussion

The present study aimed to investigate the acute effects of MICT and HIIT on circulating KLK7 levels and the associations between changes in KLK7 and metabolic outcomes in physically inactive young adults. To our knowledge, this is the first clinical study to examine the acute effects of aerobic exercise on circulating KLK7 levels in humans. Contrary to our initial hypothesis, neither exercise protocol elicited significant immediate changes in plasma relative KLK7 abundance.

Despite the absence of acute alterations in KLK7 levels, changes in triglycerides, HDL cholesterol, and glycemia collectively explained 36.6% of the variability in ΔKLK7. This finding suggests that inter-individual metabolic responses to exercise are associated with changes in KLK7, even in the absence of a detectable group-level effect. These results are consistent with previous evidence linking KLK7 to lipid and glucose metabolism, adipocyte function, and inflammatory signaling (Kunath et al., 2021; Zieger et al., 2018). Experimental studies have demonstrated that KLK7 deficiency improves insulin sensitivity, attenuates weight gain, and reduces adipose tissue inflammation in mice fed a high-fat diet (Kunath et al., 2021), supporting a mechanistic link between KLK7 and metabolic regulation.

The lack of acute changes in circulating KLK7 following both exercise modalities may reflect the biological nature of this protease, whose expression appears to be closely related to adipose tissue remodeling, chronic inflammatory status, and long-term metabolic adaptations rather than rapid, transient physiological responses. Therefore, it is plausible that a single bout of aerobic exercise is insufficient to elicit measurable changes in circulating KLK7, particularly in young individuals. Alternatively, KLK7 may respond preferentially to other exercise modalities, such as resistance or combined training, which induce distinct mechanical and inflammatory stimuli. These hypotheses will require designing future experiments that include several weeks of training along with consecutive sampling during the hours after the exercise protocol, in order to assess a more complete acute response.

Exploratory multivariate analyses identified clustering patterns between ΔKLK7 and selected metabolic variables. These findings align with preclinical data demonstrating that the absence of KLK7 protects against obesity-related phenotypes, including insulin resistance and impaired fatty acid metabolism

(Kunath et al., 2021; Zieger et al., 2018). Because PCA showed limited sampling adequacy, these observations should be interpreted only as hypothesis-generating and require further assessment in future clinical and preclinical studies.

Given the established role of KLK7 in adipose tissue inflammation and systemic low-grade inflammation, the relationship between aerobic exercise and KLK7 regulation warrants further investigation. Aerobic exercise is well known for its capacity to improve adipose-tissue function by promoting healthy adipogenesis, reducing extracellular-matrix accumulation and fibrotic markers, modulating cytokine secretion, and improving insulin sensitivity (Enríquez-Schmidt et al., 2024; Leal et al., 2018; Maharjan et al., 2021; Ruíz-Uribe et al., 2024; Stroh & Stanford, 2023). The absence of immediate changes does not necessarily indicate that KLK7 is unresponsive to exercise. Rather, it may reflect the temporal characteristics of KLK7 regulation, which appears to be more closely related to adipose tissue remodeling and chronic metabolic adaptation than to rapid exercise-induced signaling. Since blood samples were obtained immediately after exercise, delayed responses occurring during the recovery period cannot be excluded. Moreover, inter-individual variability in the metabolic response to exercise is well documented, and the absence of a significant group-level effect does not preclude biologically meaningful responses in specific individuals (Bouchard & Rankinen, 2001; Mann et al., 2014). Importantly, members of the kallikrein-related peptidase family have been shown to regulate adipokines and chemoattractant proteins in human tissues. Recent evidence demonstrates that kallikrein 14 (KLK14), a serine protease closely related to KLK7, proteolytically activates chemerin in human skin, thereby modulating inflammatory cell recruitment through a defined proteolytic pathway (Brzoza et al., 2026). This finding supports the concept that kallikrein-mediated proteolysis may influence adipokine and chemokine signaling in humans. Given that chemerin exhibits delayed post-exercise kinetics, these data further suggest that the absence of acute changes in circulating KLK7 immediately after exercise may reflect suboptimal sampling timing rather than a lack of biological responsiveness. Indeed, numerous exercise-responsive proteins, including cytokines and immunometabolic mediators, display delayed kinetic profiles with peak responses occurring several hours to days after exercise rather than immediately post-exercise, supporting the notion that the absence of acute changes in circulating KLK7 may reflect sampling timing rather than a lack of biological responsiveness (Nieman et al., 2005; Peake et al., 2015).

A notable strength of the study is the relatively homogeneous sample in terms of age, body mass index, and metabolic health, which reduces confounding variability. Additional strengths include the standardized exercise protocols, controlled blood collection procedures, and the inclusion of two aerobic exercise modalities with distinct physiological characteristics, allowing comparison of different acute metabolic stimuli under similar experimental conditions. However, several limitations must be acknowledged. The quasi-experimental design lacked a non-exercise control group, which limits causal inference. In addition, blood samples were collected immediately post-exercise, without extended follow-up. Given that some proteins exhibit delayed responses to exercise, later sampling time points could have revealed different KLK7 dynamics. Finally, the use of Western blotting, while adequate for protein detection, may lack sensitivity to detect subtle changes in circulating KLK7. However, this technique was used given the possible presence of post-translational modifications of this protein, which could be a confounding factor (S. Guo et al., 2014).

Conclusions

This exploratory study provides the first evidence that circulating KLK7 does not change immediately after a single session of MICT or HIIT in physically inactive young adults. Although inter-individual KLK7 changes were associated with selected metabolic responses, these findings are exploratory and require confirmation. The study establishes an initial clinical reference for investigating the temporal and training-related regulation of circulating KLK7.

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