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Effect Of Meal Frequency On Insulin Response And Total Insulin Secretion In Physically Active People

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Abstract

Aims: To investigate the impact of meal frequency on insulin response and total insulin secretion in physically active people.
Methods: The research was conducted as a carefully designed experimental cross-over study at the Department of Biochemistry and Department of Physiology, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, after ethical approval. Using non-probability convenience sampling, the study took place from June 2023 to November 2023, adhering to a prior study's sample size calculations and clear inclusion and exclusion criteria.
Results: The results indicated that while there were slight variations in the mean insulin area under the curve between one-day and two-day meal patterns, these differences lacked statistical significance ($p = 0.853$). However, initial measurements at specific time intervals showed noticeable correlations, suggesting changing insulin response patterns in the early stages of the study. Additionally, significant associations were found between meal frequency, age, body composition, waist circumference, and insulin response.
Conclusion: This research suggests that meal frequency may influence insulin response patterns in physically active adults, with significant associations at certain time intervals and correlations with specific body composition characteristics, contributing to our understanding of how meal frequency impacts insulin regulation in this demographic.

Keywords: insulin, meal frequency, active individuals, meal timing, body composition

Introduction

Insulin, a pivotal hormone for maintaining metabolic function in the human body, is instrumental in several fundamental processes. One of its primary roles is to facilitate the uptake of essential molecules, especially glucose, by cells, predominantly in muscle and adipose tissues.1 This action helps regulate blood glucose levels and also influences amino acid absorption, DNA replication, and protein synthesis, which contribute to cellular growth and overall metabolic balance.2 Insulin decreases the liver's production of glucose from non-carbohydrate sources. When insulin levels decrease, the liver produces more glucose from various substrates, highlighting the significance of insulin in preventing excessive glucose production.3

Insulin's influence extends to various physiological processes. It reduces protein breakdown (proteolysis) and inhibits autophagy, a process involved in organelle degradation.4 After a meal, insulin levels can completely halt autophagy. It also enhances amino acid uptake by cells, encouraging them to absorb circulating amino acids. Conversely, when insulin levels drop, this absorption is inhibited. Insulin has effects on arterial muscle tone, promoting relaxation in arterial muscles and increased blood flow, particularly in micro-arteries. A decrease in insulin levels can lead to muscle contraction, reducing blood flow.5 Moreover, insulin influences the secretion of hydrochloric acid by parietal cells in the gastrointestinal tract and promotes potassium absorption, aiding in nutrient uptake. Without insulin, the absorption of nutrients is impaired, potentially reducing potassium levels in blood plasma due to its role in potassium uptake by skeletal muscle cells.

The customary practice of consuming three or more meals a day may lead to a prolonged anabolic state throughout the day. The metabolic response to a meal typically involves an initial peak in blood sugar levels during the first hour, followed by a gradual decline over the next two hours.6 Correspondingly, insulin secretion rises during the first hour and then declines over the next four hours. Plasma triglyceride (TAG) levels tend to increase progressively, peaking after 3 to 5 hours. Even after 6 hours, TAG levels remain approximately 50% higher than the initial baseline.7

Research indicates that plasma TAG levels remain elevated for up to 12 hours even with only two meals per day.8 The addition of a third meal accentuates this pattern. The relationship between meal frequency and the circulating profiles of insulin, TAG, and glucose throughout the day demonstrates that TAG levels, insulin, and glucose concentrations remain elevated until late hours.9 Extended periods of post-meal states favour fat synthesis and storage, reducing the opportunity for net fat breakdown.

Traditional diet and exercise strategies focus on reducing post-meal fluctuations in order to stimulate the release and utilization of internal lipid stores. While intermittent fasting may help minimize post-meal oscillations by introducing meal gaps, it establishes a more balanced relationship between fasting and eating times. Extending the intervals between meals has demonstrated metabolic advantages that go beyond just managing energy balance. Prolonged fasting periods can induce beneficial metabolic shifts, promoting the utilization of lipid-derived substances, enhancing body composition, and reducing insulin resistance. Recent research also suggests that having fewer meals might offer health benefits, particularly in terms of metabolic health and cardiovascular risk factors.10, 11 Consuming four or more meals a day has been linked to lower cholesterol levels, and regular meal scheduling can contribute to better health outcomes,12 highlighting the importance of meal timing within the context of overall dietary patterns.

The time-restricted eating patterns with a limited daily food intake window of 6 to 8 hours have shown various health benefits, independent of calorie intake.13 Such patterns are associated with improved metabolic health, reduced disease risk factors, and a range of health-related advantages. Physical activity plays a vital role in overall health and well-being, alongside diet, sleep, and recovery. Exercise and insulin have intricate interactions, with exercise promoting insulin sensitivity, especially in physically active individuals.14 Exercise positively influences glucose management, glycogen synthesis, and insulin sensitivity in muscles, improving metabolic health and reducing the risk of insulin resistance. It's crucial for athletes to adjust insulin and food intake based on their exercise volume and duration to optimize glucose management. Exercise, whether aerobic, resistance, or a combination, offers considerable benefits for metabolic health, including reduced risk factors for metabolic syndrome. These advantages can be attributed to exercise's effects on insulin resistance, adipose tissue metabolism, inflammation, and epigenetic factors.

The study's rationale is based on the relationship between meal frequency and insulin release; more frequent meals result in more insulin releases, while one meal a day (OMAD) only triggers insulin release once. The objective is to compare the impact of meal frequency on total insulin secretion in physically active individuals, defined as those engaging in exercise or sports at least 4-5 days a week for the past 6 months. The study aims to determine how various meal frequencies affect insulin response, with a hypothesis that suggests that having a single daily meal or intermittent fasting may be beneficial for physically active individuals.

Materials and Methods

The study investigated meal frequency's influence on insulin response in physically active 17 participants from 5 gyms and 2 sports complexes, employing an experimental cross-over design conducted at Khyber Medical University, Institute of Basic Medical Sciences, Peshawar. The research employed a non-probability convenience sampling technique, and the study took place from June 2023 to November 2023.

Participants were selected based on specific inclusion criteria, which included being physically active, aged 18 to 25, having a BMI between 18 and 24 kg/m², and meeting various health criteria. Exclusion criteria involved the presence of any diseases, smoking, recent surgery, or medication use. Participants were recruited through various methods, and the study protocol was carefully explained to them. They were informed of the confidentiality of their results and the voluntary nature of their participation.

The study involved two days of dietary intervention. On the first day, participants consumed 800 kcal meal, while on the second day, the same meal was divided into two equal halves of 400 kcal, one in the morning and one in the evening (table 1). The table 1 provides a breakdown of the nutritional content, including carbohydrates, proteins, fats, and total calories, for day 1 and day 2 meals. The meals are categorized as DAY-1 (MEAL), DAY-2 (MORNING), and DAY-2 (EVENING). The percentage of macronutrients is also included for easy comparison. The meals were standardized to reduce variation.

Table 1: Nutritional Composition of Daily Meals

MEAL	INGREDIENTS	QUANTITY	CHOs (g)	Proteins (g)	Fats (g)	CALORIES
DAY-1 (MEAL)	Grilled Chicken	220g	0g	58g	22.5g	435
	Boiled Egg	1	1g	5.5g	6g	80
	Mixed Vegetables	1 cup	7.5g	2.5g	0.5g	45
	Skimmed Milk	250ml	12g	10g	0g	90
	Roti	1	32.5g	5g	0g	150
Total Calories			53g (26.5%)	81g (40.5%)	29g (33%)	800 kcal
DAY-2 (MORNING)	Grilled Chicken	110g	0g	14.5g	11.25g	217.5
	Boiled Egg	01-Feb	0.5g	2.75g	3g	40
	Mixed Vegetables	1/2 cup	3.75g	1.25g	0.25g	22.5
	Skimmed Milk	125ml	6g	5g	0g	45
	Roti	01-Feb	16.25g	2.5g	0g	70
Total Calories			26.5g (26.5%)	40.5g (40.5%)	14.5g (33%)	400 kcal

DAY-2 (EVENING)	Grilled Chicken	110g	0g	14.5g	11.25g	217.5
	Boiled Egg	01-Feb	0.5g	2.75g	3g	40
	Mixed Vegetables	1/2 cup	3.75g	1.25g	0.25g	22.5
	Skimmed Milk	125ml	6g	5g	0g	45
	Roti	01-Feb	16.25g	2.5g	0g	70
Total Calories			26.5g (26.5%)	40.5g (40.5%)	14.5g (33%)	400 kcal

Blood samples were collected on both days at specific time intervals to measure insulin levels. The samples were processed and stored at -80°C for further analysis. The study used calbiotech ELISA kit to quantify insulin levels in serum. This kit employed a solid-phase sandwich ELISA method and was based on the principle of forming a sandwich complex to measure insulin concentration.

Data analysis involved checking for normality using statistical tests, calculating the area under the curve (AUC) of insulin secretion, and performing statistical tests, such as independent sample t-tests and Pearson correlation, to examine relationships between variables.

Ethical approval was taken from Research Ethical Committee of Khyber Medical University Peshawar (KMU/IBMS/IRBE/7th meeting/2023/1209) and Advanced Study and Research Board (ASRB002172/EM/IBMS).

Results

Out of the total 73 participants, 42 individuals were recruited from the gym, constituting 57.53% of the total, while 31 participants, making up 42.47%, were selected from the sports complex based on the inclusion criteria (table 2). However, 17 participants from the gym (40.48%) and 15 from the sports complex (48.39%) declined to participate. Subsequently, 25 gym participants (59.52%) and 16 from the sports complex (51.61%) were approached for consent. A total of nine participants from the gym (36%) and eight from the sports complex (50%) withdraw from the study without providing specific reasons. Finally, 14 participants from the gym (33.33%) and 8 from the sports complex (50%) were successfully recruited. Unfortunately, three participants from the gym (21.43%) and two from the sports complex (25%) dropped out during the course of the study. The final data analysis was conducted on 11 participants from the gym (78.57%) and 6 participants from the sports complex (75%).

Table 2: Participant Recruitment and Inclusion Percentages

Participant Recruitment Location	Initially approached	Declined (to Participate)	Successfully Recruited	Drop outs	Total Participants
Gym	42	17	14	3	11
Sports Complex	31	15	8	2	6
Total	73	32	22	5	17

Following the recruitment of physically active participants, baseline descriptive statistics were conducted to assess their characteristics (table 3). The participants exhibited the following characteristics: an average age of 21.76 years (±1.68 years), a mean weight of 72.18 kilograms (±3.70 kg), an average height of 1.91 meters (±0.27 meters), a body mass index (BMI) of 21.17 (±2.32), a mean muscle mass of 29.59 kilograms (±2.06 kg), a muscle mass percentage of 40.47% (±2.35%), and a waist circumference of 39.41 inches (±1.42 inches).

Table 3: Baseline descriptive statistics to assess their characteristics

Baseline Characteristics	Mean ± Std. Deviation
Age (Years)	21.76 ± 1.68
Weight in kilogram (kg)	72.18 ± 3.70
Height in Meters (m)	1.91 ± 0.27
BMI kg/m^2	21.17 ± 2.32
Muscle Mass in kilogram (kg)	29.59 ± 2.06
Muscle Mass Percentage (%)	40.47 ± 2.35
Waist Circumference (In Inches)	39.41 ± 1.42

Table 4 provides a comprehensive comparison of insulin levels between one-meal (Day 1) and two-meal patterns, specifically focusing on morning and evening meals at various time intervals. This investigation targets physically active individuals and aims to understand how meal frequency impacts insulin response and total insulin secretion. Each time interval is accompanied by the mean insulin level (MEAN±SD). Significant associations were identified at specific time intervals. For instance, at the 15-minute mark, the one-meal group exhibited a higher mean insulin level of 25.43 mIU/L, compared to the two-meal group 19.63 mIU/L, with a significant p-value of 0.035. Similarly, at the 30-minute mark, the one-meal group maintained a higher mean insulin level of 23.88 mIU/L compared to the two-meal group's 17.43 mIU/L, with a p-value of 0.038. Furthermore, at the 60-minute mark, the one-meal group showed a higher mean insulin level than the two-meal group, with a p-value of 0.034, all of which signify significant differences. However, no statistically significant differences in insulin responses were observed at various other time points. These findings emphasize the potential impact of meal frequency and timing on insulin responses among physically active individuals and call for further exploration in this field.

Table 4: Comparison of insulin levels on different days

	DAY 1	**DAY 2 1ST MEAL**	**DAY 2 2ND MEAL**	
Baseline	Insulin levels(mIU/L) MEAN ± SD	Insulin levels(mIU/L) MEAN± SD	Insulin levels(mIU/L) MEAN± SD	P value
0	4.15 ±2 .46	3.61 ± 2.45		0.502
15	25.43 ± 13.04	19.63 ± 21.87	15.25 ± 8.36	**0.035**
30	23.88 ± 14.44	17.43 ± 16.39	13.28 ± 7.45	**0.038**
60	15.86 ± 12.89	11.15 ± 8.48	7.32 ± 6.50	**0.034**
90	8.11 ± 6.26	11.69 ± 9.65	6.29 ± 5.81	0.060
120	6.92 ± 5.50	6.74 ± 4.50	4.61 ± 1.60	0.433
150	5.78 ± 4.45	7.41 ± 5.60	4.57 ± 1.81	0.312
180	5.27 ± 3.33	5.52 ± 4.99	3.81 ± 2.08	0.504
240	4.78 ± 3.24	5.75 ± 4.82	3.39 ± 1.74	0.268
300	5.04 ± 3.74	5.41 ± 6.20	3.82 ± 2.17	0.666
360	4.78 ± 2.99	6.03 ± 3.07	3.93 ± 2.37	0.088
420	3.86 ± 2.73			
480	4.13 ± 3.82			
540	4.48 ± 3.12			
600	4.74 ± 3.70			
660	4.94 ± 2.77			
720	4.26 ± 2.58			

The study compared insulin levels on two different days to analysis the association between meal frequency, timing, and insulin dynamics in physically active individuals. (figure 1). At the baseline, insulin levels were slightly lower on Day 2 (3.61) compared to Day 1 (4.15). However, after meal consumption, insulin levels surged on Day 1 (25.43 at 15 minutes) compared to Day 2 (19.63 at 15 minutes). This suggests a more pronounced insulin response on Day 1. Throughout the subsequent time intervals, insulin levels fluctuated between the two days. Interestingly, on Day 2, insulin levels spiked at the 420-minute mark (15.25), suggesting a unique response pattern. Additionally, on Day 2, there was a secondary peak in insulin levels at the 90-minute mark (11.69), followed by another peak at the 150-minute mark (7.41). These peaks suggest a significant insulin response to the meals consumed at those times.

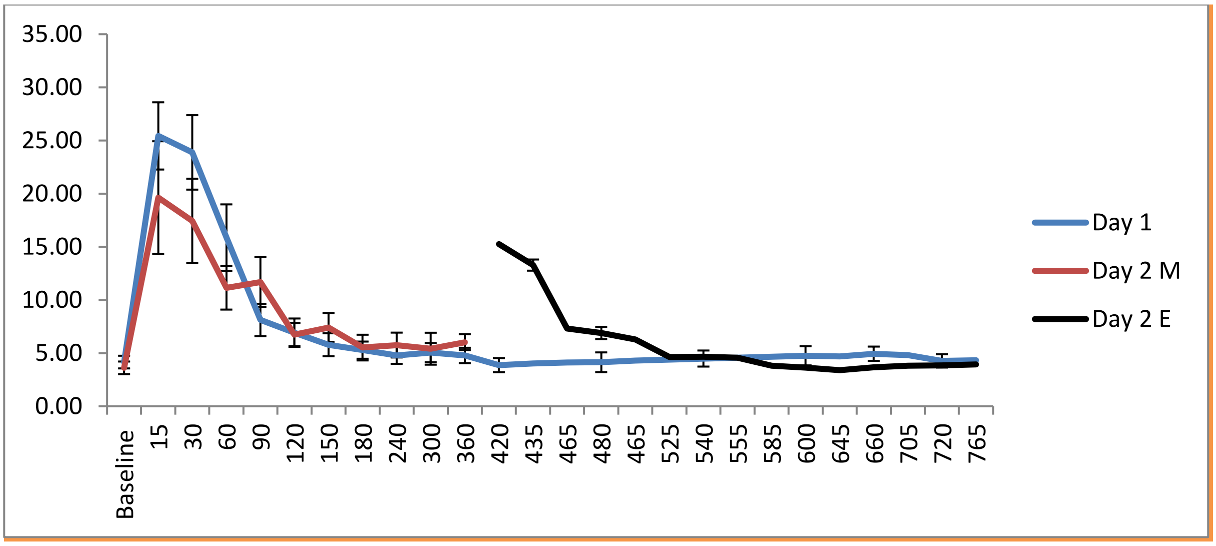

Figure 1: Comparison of insulin levels a different time points on different days

By comparing the insulin response and total insulin secretion in physically active individuals (table 5), the area under the insulin response curve was higher in the "One Day Meal" group (mean = 4601.51, SD = 1665.77) compared to the "Two Meals a Day" group (mean = 4504.38, SD = 2519.84). However, statistical analysis revealed that the two meal trials within the "Two Meals a Day" group were not significantly different from each other, suggesting that meal frequency may influence insulin response, but the specific number of meals within a day might not be the sole determinant. These findings highlight the complex interplay of meal timing and frequency on insulin dynamics in physically active individuals.

Table 5: Comparison of area under curve (AUC)

	Mean	SD	Std. Error Mean
Insulin AUC Day 1	4601.55	1665.77	439.77
Insulin AUC Day 2 Combined	4504.38	2519.84	611.15

A correlation analysis was performed to investigate the relationships among age, body composition, waist circumference, and insulin response in physically active individuals. The results, presented in Table 7 revealed several significant correlations ($p < 0.05$), shedding light on the interplay between these variables. Age and waist circumference exhibited a negative correlation ($r = -0.462$, $p = 0.062$), suggesting that waist circumference tends to decrease as individuals age. Weight and muscle mass displayed a positive correlation ($r = 0.641$, $p = 0.006$), highlighting the connection between weight and muscle development. BMI and muscle percentage displayed a negative correlation ($r = -0.950$, $p < 0.001$), indicating that individuals with higher BMI values tend to have a lower proportion of muscle mass relative to their body composition. Muscle mass and muscle percentage exhibited a positive correlation ($r = 0.649$, $p = 0.005$), emphasizing the strong link between overall muscle mass and the proportion of muscle in the body. Waist circumference and AUC 1 combine showed a positive correlation ($r = 0.405$, $p = 0.107$), implying a potential connection between abdominal adiposity and insulin response. AUC 1 combine and AUC 2 combine were positively correlated ($r = 0.551$, $p = 0.022$), suggesting some consistency or similarity in insulin response patterns between these two variables.

Table 6: Correlation Analysis of Variables in Physically Active Individuals

		Age (Years)	**Weight in kg**	**Height in Meters**	**BMI**	**Muscle Mass in kg**	**Muscle Mass Percentage**	**Waist Circumference in inches**	**AUC Day 1 combine**	**AUC Day 2 combine**
Age (Years)	r	1	-0.053	0.195	-0.006	-0.427	-0.462	-0.036	0.285	**.565***
	p		0.839	0.453	0.983	0.088	0.062	0.892	0.267	**0.018**
Weight in kilogram	r	-0.053	1	0.182	0.112	.641**	-0.161	0.033	-0.063	-0.242
	p	0.839		0.485	0.670	0.006	0.536	0.900	0.809	0.349
Height in meters	r	0.195	0.182	1	0.098	0.015	-0.176	-0.038	-0.122	-0.203
	p	0.453	0.485		0.710	0.954	0.500	0.883	0.641	0.435
Body Mass Index BMI kg/m^{2}	r	-0.006	0.112	0.098	1	0.043	-0.047	.950**	0.331	0.111
	p	0.983	0.670	0.710		0.870	0.857	0.000	0.194	0.672
Muscle Mass in kilogram	r	-0.427	.641**	0.015	0.043	1	.649**	0.126	-0.089	-0.262
	p	0.088	0.006	0.954	0.870		0.005	0.631	0.733	0.310
Muscle Mass Percentage %	r	-0.462	-0.161	-0.176	-0.047	.649**	1	0.126	-0.056	-0.085
	p	0.062	0.536	0.500	0.857	0.005		0.630	0.831	0.745
Waist Circumference in inches	r	-0.036	0.033	-0.038	.950**	0.126	0.126	1	0.405	0.195
	p	0.892	0.900	0.883	0.000	0.631	0.630		0.107	0.453
AUC Day 1 combine	r	0.285	-0.063	-0.122	0.331	-0.089	-0.056	0.405	1	**.551***
	p	0.267	0.809	0.641	0.194	0.733	0.831	0.107		**0.022**
AUC Day 2 combine	R	.565*	-0.242	-0.203	0.111	-0.262	-0.085	0.195	.551*	1
	P	0.018	0.349	0.435	0.672	0.310	0.745	0.453	0.022	

**. Correlation is significant at the 0.05 level (2-tailed).*

***. Correlation is significant at the 0.01 level (2-tailed).*

Discussion

This study investigated the effect of meal frequency on total insulin secretion in physically active individuals. The study was an experimental crossover study with non-probability convenience sampling. The participants were male physically active individuals with an age of 18 to 25 years, BMI between 18 and 24 kg/m2, and fat mass of 12% to 22%. Each participant underwent the study protocol for 2 non-consecutive days. On the first day, the participants were given an iso-caloric meal (800 kcal) only at one time, and blood was collected for 12 hours. On the second day, the meal was distributed in 2 meals (400 kcal for every 6 hours) on the same day. The findings of the study revealed no significant differences in insulin response between the two meal frequency patterns. However, the pattern of response for insulin levels showed a significant association between day 1 meal and day 2 meal at the baseline (t=15, 30 and 60 min), likely due to the high glucose load.
There was no significant association between day 1 meal and day 2 meal at the baseline (t= 0, 90, 120, 150,180,240, 300, 360, 420, 480, 540, 600, 660 and 720 minutes). Additionally, the area under the insulin response curve showed no significant

association between one day meal and two meals a day, indicating that the total insulin response was not dramatically different between the two study days. Smith et al [15] reported that higher protein intake with frequent meal consumption decreases both the insulin and glucose response as compared to a meal higher in CHO, they concluded in healthy individuals, glucose levels remained elevated throughout the day with frequent CHO meals compared to CHO meals, without any differences in the insulin levels. Increasing the protein content of frequent meals attenuated both the glucose and insulin response. Another study by Carlson et al [16] noted no changes in fasting levels of insulin, leptin, and ghrelin with alterations in meal frequency (1 meal/day vs. 3 meals/day).

The current study also investigated the relationship between meal frequency and other variables, such as age, weight, height, muscle mass, and BMI. The findings revealed a significant association between age and day 1 with other parameters, while there was no significant association between weights, height, muscle mass, BMI, and day 2 meal frequencies. The findings of this study suggest that meal frequency may not have a significant impact on total insulin secretion or insulin response in physically active individuals. However, more research is needed to confirm these findings, particularly in larger and more diverse populations.

Additionally, the study highlighted the importance of nutrient timing for athletes. It is noted that a well-balanced diet is essential for growing athletes to maintain proper growth and optimize performance in athletic endeavors. An ideal diet for athletes comprises 45% to 65% carbohydrates, 10% to 30% protein, and 25% to 35% fat. Fluids are also very important for maintaining hydration, and should be consumed before, during, and after athletic events to prevent dehydration. The timing of food consumption is also important to optimize performance. Meals should be eaten at least 3 hours before exercise, and snacks should be eaten 1 to 2 hours before activity. Recovery foods should be consumed within 30 minutes of exercise and again within 1 hour to 2 hours of activity to allow muscles to rebuild and ensure proper recovery. Understanding that optimal nutrient composition is important for athletes and coaches because of the impact diet can play on nutrient utilization during exercise as well as in the recovery of exercise as mentioned by Dhiman & Kapri.17

Solomon and colleagues18 reported that there were no differences in the 8 h insulin AUC between the iso-caloric ingestion of 2 meals compared to 12 meals. Meta-analysis also showed a lower insulin response in the day compared to during the night (SMD = −0.35; 95% CI, −0.63 to −0.06; p = .016). They suggest poor glucose tolerance at night compared to the day. This may be a contributing factor to the increased risk of metabolic diseases observed in those who habitually eat during the night, such as shift workers.19 The current findings provide valuable insights into the complex relationships between age, body composition, waist circumference, and insulin response in physically active individuals. They underscore the importance of considering these factors when investigating the influence of meal frequency on insulin regulation. For example, the negative correlation between age and waist circumference suggests that waist circumference may be a useful marker of age-related changes in body composition. The positive correlation between weight and muscle mass highlights the importance of muscle mass in weight management. The negative correlation between BMI and muscle percentage indicates that BMI may not be the most accurate measure of body composition in physically active individuals, as it does not account for muscle mass. The positive correlations between muscle mass and muscle percentage, and between waist circumference and AUC_1_combine, suggest that muscle mass and abdominal adiposity may play important roles in insulin regulation. Lastly, the positive correlation between AUC_1_combine and AUC_2_combine suggests that insulin response patterns may be relatively consistent over time.

Limitations

The sample size was relatively small, which may limit the generalizability of the findings. The limited time available may have restricted the scope of the study and the rigor of the data collection and analysis. Financial constraints may have limited the ability to use more sophisticated methods or to recruit a larger and more diverse sample.

Conclusion

This study aimed to explore the influence of meal frequency on insulin response and total insulin secretion in physically active individuals. The findings indicate that meal frequency does not significantly affect total insulin levels, regardless of whether participants follow a one-day or two-day meal pattern. However, the substitution of dietary protein for dietary carbohydrate among this group led to a reduced insulin response, suggesting that individuals, especially those encouraged to consume more frequent meals, should consider increasing their dietary protein intake if they are interested in managing glucose levels effectively. While the mean insulin AUC showed a minor difference between the two meal patterns, this variation did not reach statistical significance (p = 0.853). Nevertheless, significant correlations emerged at specific early time points (t=15, t=30, and t=60 minutes), signifying variations in insulin response patterns. The AUC was slightly higher in the one-day meal group, but this difference lacked statistical significance. Despite these findings, the research highlights the importance of assessing insulin response at specific time intervals and underscores associations between age, body composition, waist circumference, and insulin response.

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Conflicts of Interest

No conflicts of interest to disclose.

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