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Barriers to Exercise in Type 1 Diabetes Patients and the Impact of Aerobic and Anaerobic Exercises on Blood Glucose Management: A Current Literature Review

Karina Lissak, Bianka Nowińska, Wiktoria Bińczyk, Olgierd Dróżdż, Bartłomiej Siudek, Anna Wiśniewska, Agata Konopka, Zuzanna Szczepaniak, Milena Orzeł, Bartłomiej Orzeł, Maria Myślicka, Klaudia Włodarczyk

Karina Lissak, MD
Lower Silesian Oncology Center in Wrocław,
Hirszfelda Square 12, 53-413 Wrocław, Poland
ORCID: 0009-0000-9084-4060
karina.lis2323@gmail.com

Bianka Nowińska, MD
4. Military Clinical Hospital,
Weigla Str. 5, 53-114 Wrocław, Poland
ORDID: 0000-0003-2335-3207
bianovinska@gmail.com

Wiktoria Bińczyk, MD
Wrocław Medical University, Clinical Department of Diabetology and Internal Diseases,
Borowska Str. 213, 50-566 Wrocław, Poland
ORCID: 0009-0004-6600-9259
wiktoria.binczyk98@gmail.com

Olgierd Dróżdż, MD
Wrocław Medical University, Clinical Department of Diabetology and Internal Diseases,
Borowska Str. 213, 50-556 Wrocław, Poland
ORCID: 0009-0006-6134-9101
olgierd.drozdz@gmail.com

Bartosz Siudek, MD
A. Falkiewicz Specialist Hospital,
Warszawska Str. 2, 52-114 Wrocław, Poland
ORCID: 0009-0002-4053-9724
bartosz.siudek98@gmail.com

Anna Wiśniewska, MD
A. Falkiewicz Specialist Hospital,
Warszawska Str. 2, 52-114 Wrocław, Poland
ORCID: 0009-0000-6001-2167
awis.contact@gmail.com

Agata Konopka, MD
A. Falkiewicz Specialist Hospital,
Warszawska Str. 2, 52-114 Wrocław, Poland
ORCID: 0009-0000-1004-0629
agatakonopka21@gmail.com

Zuzanna Szczepaniak, MD
Provincial Specialist Hospital in Wrocław,
H. Kamieńskiego Str. 73a, 51-124 Wrocław, Poland
ORCID: 0009-0004-8025-6037
zuzanna.a.szczepaniak@gmail.com

Milena Orzeł, MD
Wrocław Medical University,
wyb. Ludwika Pasteura 1, 50-367 Wrocław, Poland
ORCID: 0009-0005-1303-2778
milenadudek@op.pl

Bartłomiej Orzeł, MD
Wrocław Medical University,
wyb. Ludwika Pasteura 1, 50-367 Wrocław, Poland
ORCID: 0009-0003-1442-6790
bartekorzel@wp.pl

Maria Myślicka, MD
Wrocław Medical University,
wyb. Ludwika Pasteura 1, 50-367 Wrocław, Poland
ORCID: 0009-0000-6190-9128
mariamyslicka38@gmail.com

Klaudia Włodarczyk, MD
Wrocław Medical University,
wyb. Ludwika Pasteura 1, 50-367 Wrocław, Poland
ORCID: 0009-0002-0779-8564
wlodarczyk.klaudia1@gmail.com

Corresponding author: Karina Lissak, karina.lis2323@gmail.com

Abstract: Engaging in regular physical activity (PA) is crucial for managing type 1 diabetes (T1D) effectively. PA helps reduce the risk of cardiovascular disease (CVD), lower total daily insulin requirements, improve endothelial function, enhance muscular strength, and boost psychological well-being and quality of life. However, individuals with T1D tend to engage in PA less frequently than their healthy peers due to various barriers, with the fear of hypoglycemia (FOH) being a significant factor that impacts quality of life and diabetes outcomes. Understanding these barriers can increase awareness, improve comprehension, and enhance better support from non-diabetology specialists. This article aims to review the current literature on the primary limitations to regular PA, including continuous glucose management (CGM), in individuals with T1D. Additionally, we explore the impact of various types of PA on blood glucose management and overall well-being.

Keywords: physical activity, exercise, type 1 diabetes, aerobic exercise, anaerobic exercise, fear of hypoglycemia, continuous glucose monitoring system

Objectives: This article aims to review the various limitations and challenges faced by patients affected by Type 1 diabetes when attempting to engage in regular exercise, with the goal of gaining a deeper and more comprehensive understanding of their frequent avoidance of physical activity.

Methods: A literature review was conducted based on the PubMed database, using the following words "physical activity", "exercise", "type 1 diabetes", "aerobic exercise", "anaerobic exercise", "fear of hypoglycemia", "continuous glucose monitoring system".

Only articles published between 2012 and 2024 were included to endure the inclusion of recent advancements and findings.

Conclusions

・Even though regular physical activity has various beneficial impacts on overall health in patients with Type 1 Diabetes, different limitations lead to a reluctance to engage consistently, which is crucial for effective management of Type 1 Diabetes and overall health.

・While both type of exercises (aerobic and anaerobic) offer significant health benefits, they affect blood glucose levels in different ways due to their differing metabolic demands.

・Aerobic exercise typically leads to decrease in blood glucose levels in individuals with Type 1 Diabetes. This decrease occurs due to increased glucose uptake by muscles combined with potentially insufficient reduction in insulin before the exercise, in the contrary anaerobic (high-intensity) exercise has the opposite effect compared to aerobic exercise. It tends to increase blood glucose levels, particularly when performed in short bursts or sprints. This increase can help prevent hypoglycemia during and immediately after exercise.

・CGM significantly contributed to improving the quality of life for people with T1D. Nevertheless, there are certain limitations of using CGM during PA that patients and their healthcare providers should be aware of.

Introduction

Type one diabetes (T1D) is a life-long multifactorial autoimmune disorder characterized by T-cell mediated self-destruction of β-cells, leading to an absolute lack of insulin and necessitating exogenous insulin replacement therapy throughout life.

According to findings from *The Lancet Diabetes & Endocrinology*, there were approximately 8,4 million cases of T1D worldwide in 2021. This number is projected to reach roughly 17,4 million by 2040 [1, 2, 3, 4, 5].

The prevalence of T1D is highest in patients aged 10 to 14 years. Studies conducted in Sweden and Belgium revealed that the onset of the condition might be occurring earlier, although there has not been a significant rise in incidence rates. In terms of gender differences, T1D exhibits similar rates in both boys and girls under the age of 15. Other research indicates that T1D is more common among boys aged 10 to 14 years old. Generally, it has been observed that in regions with high T1D incidence, the condition tends to be more common in boys, whereas in areas with lower prevalence, it is more often observed in girls [43].

Adequate self-control is challenging but necessary to avoid acute complications and to prevent or delay long-term complications [1, 2, 3, 4].

Patients are highly recommended to engage in regular PA for a variety of health reasons. PA helps prevent heart disease and high blood pressure, reduces HbA1c by about 0,3%, decreases daily insulin requirements, and improves weight control. It also has benefits in managing dyslipidemia, osteoporosis, reducing the risk of colon and breast cancer in the general population. In patients with T1D, PA positively impacts psychological well-being and stimulates the expression of glucose transporter type 4 (GLUT-4), which increases peripheral insulin sensitivity [6, 7, 8, 9, 24, 36].

Among adults with T1D, both retinopathy and microalbuminuria are less prevalent in individuals who engage in regular PA compared to those who do not [6, 7, 8, 9, 24] .
For purpose of the paper, we divided the article in following sections:
1. Key barriers to Physical Activity in T1D
2. The Impact of Aerobic and Anaerobic Exercise on Glucose Management
3. Limitations of Using Continuous Glucose Monitoring During Physical Activity
4. New Technologies in Physical Activity Management

1. Key Barriers to Physical Activity in T1D

According to World Health Organization (WHO) physical activity refers to any body movement initiated by skeletal muscles that requires energy. PA has been proven to decrease risk of long-term health complications such as cardiovascular diseases and stroke, improve insulin sensitivity and enhance quality of life. The current WHO guidelines recommend that adults participate in 150 to 300 minutes of moderate to vigorous aerobic activity per week and engage in an average 60 minutes of moderate aerobic physical activity per day. To prevent the risk of falls, people over 65 years of age should also perform moderate PA at least three days a week [10, 11, 12].
Although the above guidelines are the same for patients with T1DM, a large percentage of them do not meet these recommendations. Moreover, they achieve lower results compared to their healthy peers [6].
The main factors contributing to the lack of regular physical exercise can be divided into two groups: diabetic-specific and non-diabetic factors.
Diabetic-specific factors include the difficult management of blood glucose, and exercise-induced fear of hypoglycemia, and hyperglycemia, complex glycemic control and exercise timing. Non-diabetic factors primarily refer to a lack of time and motivation, physical barriers and inadequate knowledge [13].

1.1 Hypoglycemia and FOH

Hypoglycemia is a major reason why patients with T1D do not engage in PA. It is the most common acute complication in which, regardless of clinical signs, plasma glucose concentration is below 70 mg/dL (3,9 mmol/L). Depending on the individual and the rate of glucose decline, symptoms may occur even glucose concentrations are higher [14]. Symptomatic hypoglycemia encompasses excessive sweating, chills, nausea, impaired vision, hunger, pallor, palpitations, dizziness, and more. If left untreated, can lead to life-threatening severe hypoglycemia, resulting in behavioral disorders, seizures, and loss of consciousness. In such case, assistance from another person is necessary to administer glucose or glucagon. Due to variations in definitions and reporting methods it is difficult to gauge the frequency of severe hypoglycemic incidents. However, up to 35% of people with T1D have reported experiencing 2-4 or even more episodes of hypoglycemia weekly [38].
People experiencing recurrent episodes of hypoglycemia are more likely to develop hypoglycemia unawareness and are at increased risk of severe hypoglycemia, where the patient is unaware of low blood glucose [15]. Excessive anxiety about emergencies may develop into abnormal fear of hypoglycemia (FOH), which is associated with reduced engagement in diabetes management and impaired diabetes outcomes.

Patients experience constant emotional stress and tend to maintain high glucose levels by consuming excessive calories, especially high-carbohydrate foods, leading to large glycemic variability and potentially preventing PA. For athletes, hypoglycemia can contribute to limited sporting success [14]. Anxious, obsessive-compulsive personality traits, female sex, frequent episodes of hypoglycemia, and impaired awareness of hypoglycemia are identified as main risk factors increasing the likelihood of FOH [16].

Currently, FOH in people with T1D can be objectively assessed using the 33-item Hypoglycemia Fear Survey-II (HFS-II). The questionnaire is designed to evaluate specific behaviors that people with diabetes engage in to avoid hypoglycemia and its negative impacts, as well as their concerns related to the risk of hypoglycemia over the past six months. The questions are divided in two sections: behavior and worry instructions. Behavior instructions refer to actions taken to prevent low blood glucose levels and their complications, while worry instructions list concerns patients with diabetes have about hypoglycemia. Each item is rated from 0 (never) to 4 (almost always). The individual item scores can highlight major concerns relates to hypoglycemia. FOH may be a strong deterrent, discouraging individuals with T1D from participating in regular PA [17, 18]. Utilization of an insulin pump and older age have been demonstrated to reduce the likelihood of severe hypoglycemia [38].

Treatment contains structured education programs and psychoeducational interventions, such as: Hypoglycemia Anticipation, Awareness, and Treatment Training (HAATT), Blood Glucose Awareness Training II (BGAT-2) and Hypoglycemia Treatment Program (HyPOS). Yeoh et al. (2015) highlight that psychotherapeutic interventions are effective in reducing severe hypoglycemia and improving glycemic control in individuals with T1D, including those with impaired awareness of hypoglycemia. The greatest results are observed in programs that include a behavioral component. Additionally, advanced technology like Continuous Subcutaneous Insulin Infusion (CSII) and CGM, especially when combined with above mentioned psychotherapeutic interventions, provide further benefits for patients with persistent awareness of hypoglycemia [39].

HAATT program developed in the United States and concentrates on educating patients about recognizing early signs of hypoglycemia, understanding the factors and focuses on learning how to treat this condition as early as possible to avoid severe hypoglycemia. [14, 39].

In BGAT-2 method, created by Cox et al., is an advanced version of the original BGAT method. Patients learn to become more aware of their blood glucose fluctuations and participate in group sessions where they learn to identify individual signs of hypoglycemia through practical examples and questions about their performance in everyday activities. Initially designed as 8 weekly sessions, BGAT-II has seen multiple revisions and has been effectively tested as an online course. This program aims to enhance existing diabetes education by providing customized strategies and has consistently led to better detection of hypoglycemia, particularly in patients with impaired awareness of hypoglycemia , and has resulted in lasting reductions in severe hypoglycemia. Even though the proven effectiveness, this approach encounters difficulties in availability and awareness, with a shortage of trained instructors and resources [39, 40, 41].

HyPOS program was adapted from BGAT and also aims to improve hypoglycemia detection, treatment, while also addressing mild, severe, and very severe hypoglycemia.

The HyPOS method demonstrated a 41% improvement in hypoglycemia detection, compared to 24% improvement with the BGAT program. It also achieved an 18% reduction im mild hypoglycemia, while BGAT achieved a 12,5% reduction [41, 42].

1.2 Hyperglycemia and Diabetic Ketoacidosis

Exercise also may lead to hyperglycemia and, in severe cases, diabetic ketoacidosis (DKA), particularly when blood glucose levels are high before starting PA. High blood glucose can occur due to stress hormones released during intense exercise. Also, insulin sensitivity can vary depending on the type and duration of the PA, making it challenging to maintain stable glucose levels. DKA is identified through various methods, but generally, it includes three key indicators: high blood sugar levels higher than 250 mg/dL, ketones in serum or urine, and acidosis, where serum bicarbonate is below 18 mEq/L and/or pH is lower than 7,30 [33]. The key elements of management of DKA are fluid and potassium replenishment, weight-adjusted fixed rate intravenous insulin infusion, and meticulous biochemical monitoring of capillary ketones, electrolytes, venous pH, and capillary glucose levels [34]. Anaerobic exercises can cause a temporary rise in blood glucose levels due to the release of counter-regulatory hormones (adrenaline and glucagon) [13].

1.3 Complex Glycemic Control and Timing of Physical Activity

Managing blood glucose levels before, during, and after exercise is complex and requires diligent monitoring and adjustments for individuals with T1D. Factors that influence blood glucose during PA are: type, intensity, and duration of exercise, as well as the timing of insulin administration and meals.

Effective pre-exercise glycemic control is crucial to prevent both hypoglycemia and hyperglycemia, which can impact the safety and efficacy of PA.

The recommended target pre-exercise blood glucose level is generally between 100-180 mg/dL (5.6-10 mmol/L). Without adequate carbohydrate ingest, blood glucose levels can plummet quickly once exercise starts, resulting in hypoglycemia [19]. Regardless of the type of PA, during the PA, the target sensor glucose levels should be maintained between 90 mg/dL and 180 mg/dL (5,0 mmoL/L and 10,0 mmoL/L) [23].

A major challenge is the risk of hypoglycemia due to insufficient carbohydrate intake before exercise. Individuals with T1D should consume an appropriate amount of carbohydrates to ensure their blood glucose levels are within a safe range before initiating PA [19].

Individual variability in response to exercise poses a significant challenge for pre-exercise glycemic control. Factors such as fitness level, duration, and intensity of exercise, and personal insulin sensitivity can all affect blood glucose levels. Therefore, personalized strategies (such as continuous glucose monitoring) are essential.

Current evidence indicates that exercising in the morning while fasting leads to an increase in blood glucose levels after exercise, compared to exercising in the afternoon after eating. Conversely, recent research shows that blood glucose decreases following afternoon exercise, which may account for the higher incidence of hypoglycemia after afternoon workouts compared to morning sessions. The underlying mechanism suggests that morning exercise (around 7:00-8:00) elevates blood glucose due to circadian increases in cortisol and growth hormone, which promotes gluconeogenesis, glucagon production and lipolysis.

In the afternoon, the levels of mentioned hormones drop, heightening the risk of hypoglycemia. Above mentioned fluctuation of glucose levels related to the circadian rhythm can also discourage individuals with T1D from engaging in regular exercise, due to the necessity of adhering to specific times of the day [13].

1.4 Motivation and Knowledge Gaps

Lack of motivation is identified as an another important barrier to exercise in patients with T1D. In the 6-week High Intensity Interval Training (HIIT) protocol by Alarcón-Gómez et al. (2021), which utilized 1:2 intervals with high-intensity intervals st 85% of Peak Power Output (PPO) and active rest at 40% PPO on a cycle ergometer three times weekly, the regimen was found to be safe. Participants completed all sessions at the required intensity without experiencing severe hypoglycemia, thereby enhancing motivation in previously sedentary individuals with T1D [37]. Lack of knowledge about the impact of aerobic and anaerobic exercise on glucose levels can contribute to frustration or helplessness regarding unexpected blood sugar fluctuations during and after the exercise, and this can potentially discourage individuals with T1D from engaging in regular PA [7].

2. The Impact of Aerobic and Anaerobic Exercise on Glucose Management

Depending on the dominant metabolism (aerobic or anaerobic) of PA, glucose levels may decrease or increase [8]. Aerobic metabolism, also known as cardio, includes activities like dancing, cycling, swimming, walking and running. These activities are moderate in intensity, rhythmic in nature, last longer, and use large muscles groups. Aerobic means "with oxygen" and relies on the aerobic energy-generating process. It can have significant effects on blood glucose levels in people with T1D [8, 9, 10].

Anaerobic exercise is higher in intensity, has short duration, and includes activities such as weightlifting, long jump, and any type of sprint (cycling, swimming, running). In contrast to aerobic activity, anaerobic activity does not depend on the exogenous delivery of oxygen [8, 9]. Based on intensity, PA can provoke a significant hormonal and metabolic response, including acid-base imbalances and alterations in microcirculation, which may potentially impact the precision of CGM [32].

2.1 Aerobic Exercise

In this type of PA, blood glucose typically decrease in individuals with T1D unless carbohydrates are ingested. This is due to the inability to reduce insulin concentrations quickly enough at the beginning of exercise, potentially resulting in a transient increase in circulating insulin because of increased blood flow to subcutaneous adipose tissue. Even when basal insulin infusion rates are reduced an hour before the exercise, free insulin levels in the bloodstream do not decrease sufficiently, and may even rise, promoting greater glucose disposal relative to hepatic glucose production and delaying lipolysis. Consequently, hypoglycemia usually develops within about 45 minutes after starting aerobic exercise [20, 31].

Aerobic training has numerous benefits, including increased mitochondrial density, insulin sensitivity, oxidative enzymes, vascular compliance and reactivity, and cardiac output.

It is linked to lower cardiovascular and overall mortality risks in both types of diabetes, whereas specially in T1D, it enhances cardiorespiratory fitness, reduces insulin resistance, and improves lipid levels and endothelial function [23, 31]. Other study has demonstrated that aerobic exercise can heighten the risk of nocturnal hypoglycemia events [37].

2.2 Anaerobic exercise

Studies have shown that high intensity (anaerobic) activities have the opposite effect on blood glucose to aerobic activities: when performed in short duration, they lead to an increase in blood glucose, and the potential for post-exercise hyperglycemia in individuals with T1D. This effect has been utilized through short sprints and intermittent high-intensity exercise protocol to prevent declines in blood glucose levels when compared to aerobic exercise alone, despite higher energy expenditure. The physiology behind blood glucose changes during various types, intensities, and timings of exercise is detailed in other reviews [20]. Incorporating short bursts of high-intensity activity, where anaerobic metabolism significantly contributes to energy supply, can help prevent hypoglycemia during and up to two hours after exercise in individuals with T1D. However two studies utilizing CGM systems indicated an elevated risk of nocturnal hypoglycemia following such exercise sessions, potentially even more than after moderate aerobic exercise. The impact of resistance training (which is an another form of anaerobic exercise) on immediate glycemia in T1D remains uncertain. One study found that insulin sensitivity remained unchanged 12 and 36 hours post-resistance exercise, suggesting that resistance training might not induce as much of post-exercise hypoglycemic effect compared to aerobic exercise [27]. Yang et al. found that aerobic exercise led to a slightly greater reduction in glycosylated hemoglobin (HbA1c) compared to resistance exercise, with a difference of 0,18%. However, this difference was not significant in sensitivity analysis ($p=0.14$) [28].

High Intensity Training (HIIT) is considered as an another type of anaerobic training due to its high-intensity, short-duration intervals, making it a form of exercise that emphasizes anaerobic metabolism. During HIIT sessions, individuals perform short, intense bursts of exercise followed by periods of rest and lower intensity exercise. The intense bursts typically last from a few seconds to several minutes and are repeated throughout the whole workout. Recent research has highlighted HIIT as a promising exercise regimen to mitigate nocturnal hypoglycemia risk, particularly if performed early in the morning. Sleep disturbances adversely impact both mental, physical well-being and diminish the overall quality of life in individuals with T1D. HIIT could be theorized as a beneficial approach to exercise enjoyment, enhancing sleep quality as it reduces post-exercise and nocturnal low blood sugar episodes, which prevents night-time awakenings and thereby potentially improve Health-Related Quality of Life [37].

3. Limitations of Using Continuous Glucose Monitoring During Physical Activity

There is a wide array of technologies currently available for people with T1D that enhance PA, providing comprehensive support and monitoring to manage their condition effectively. Despite fingerstick blood glucose monitoring being the standard for many years, rapid advancement of technology has led to the increasing adoption of continuous glucose monitoring (CGM) and closed-loop systems [29].

CGM is a modern technology used to track glucose levels in real time throughout the day and night.

Most common CGM systems measure glucose levels in the interstitial fluid using electrochemical sensor that is inserted under the skin, typically in the abdomen or upper arm. The sensor measures glucose repeatedly, usually every five minutes, providing real-time glucose data, and transmit this information to a skin applied transmitter that relays readings wirelessly to a compatible insulin pump.

Before CGM was widely used, research on exercise effects in T1D was limited to the exercise periods, with few studies monitoring overnight due to budget constraints. Nowadays, CGM is commonly used in exercise studies, enabling researchers to track the late post-exercise period [20, 21, 22]. CGM extends the duration of euglycemia and lessens severe hypoglycemia in individuals with impaired hypoglycemia awareness. It also lowers HbA1c and improves overall glycemic control, as it was proved in various randomized studies [22, 23, 35]. Additionally, it serves as a crucial tool in mitigating adverse outcomes related to PA in individuals with T1D, including hypoglycemia and hyperglycemia. By visualizing immediate improvements in glycemic regulation, individuals can boost their motivation to maintain the enhanced exercise behavior [23]. In one study, using CGM systems for three days per month over a 12-week period led to increased PA and an additional 1% decrease in HbA1c among individuals with previously suboptimal glycemic control [24].

There are several limitations that should be taken into consideration before the use during PA. CGM measures glucose levels in interstitial fluid, which can occur delay and lead to a 5 to 15 minutes lag time between current blood glucose and sensor readings, which can result in discrepancies during exercise when glucose levels can change rapidly. The performance of CGM sensors can vary based on the type and intensity of exercise and so rapid changes in glucose levels during exercise can make it challenging to interpret CGM data in real-time, requiring users to rely on additional blood glucose tests to confirm readings. For example high-intensity interval training and aerobic exercises may cause fluctuations in glucose levels that are not accurately captured by CGM devices. Physical exercise also poses a challenge for CGM accuracy due to alterations in blood flow within subcutaneous tissue, rises in body temperature, fluctuations in blood oxygen levels [23].

Sweat and increased PA can affect the adhesion of the CGM, potentially causing the sensor to dislodge [32]. In Houlder et al. ascertained that CGM reading can either overestimate or underestimate actual glucose levels depending on the type and intensity of exercise [20].

4. New Technologies in Physical Activity Management

Recent advancements in new technologies have significantly improved the management of T1D, particularly in the context of PA. Closed-loop systems (CLS), also known as artificial pancreas systems, have revolutionized diabetes management by enhancing time-in range for glucose levels and improving HbA1c while minimizing hypoglycemic episodes. These systems typically consist of a continuous interstitial glucose sensor, a control algorithm that calculates insulin requirements based on sensor data and past insulin delivery, and an insulin pump which delivers rapid-acting insulin. The addition of an automatic correction bolus feature, which adjusts insulin delivery based on real-time glucose readings, is a novel advancement and contributed to the system being classified as an advanced hybrid closed-loop (AHCL).

Commercially available AHCL systems include: Minimed 780 G (SmartGuard), Tandem's T X2 with Control-IQ and Insulet's Omnipod5 (Automated mode with HypoProtect) [29, 30].
Studies have indicated no rise in the incidence of nocturnal hypoglycemia following exercise, with overall hypoglycemia frequency being similar or reduced during closed-loop administration compared to open-loop control [25].
For instance, Breton et al. (2014) found that incorporating a heart rate signal to a control-to-range CLS system decreased hypoglycemia during exercise in T1D. The use of CLS significantly decreased hypoglycemic events during exercise. This integration enhances the system's ability to manage blood glucose fluctuations more effectively, thereby increasing safety and confidence in engaging in PA. Moreover, the development of next-generation wearables and applications that provide real-time feedback on glucose levels changes, enables people with T1D to make proper decisions about their insulin dosing and carbohydrate ingest before, during, and after the physical exercise, contributing to overall glucose control and helps overcome barriers to engaging in regular PA [26].

5. Discussion

Patients with T1D require daily intensive insulin therapy, which is administered through multiple injections or continuous infusion via an insulin pump. This can lead to many complications, such as severe hypoglycemia, with the risk being increased during PA. Therefore, PA poses a significant challenge for them and their healthcare providers. Other barriers to engage in PA include difficulties in glucose management, inadequate knowledge about the relationship between different types of physical exercise and their impact on blood glucose levels, and lack of motivation. The effects of different types of PA on glucose control are multifaceted, reflecting the varied impacts of aerobic and anaerobic exercises on blood glucose fluctuations. Understanding these limitations and effects is crucial for optimizing exercise regiments to balance the benefits of PA with the management of T1D and can enhance motivation to engage in regular PA among patients with T1D which is highly desirable. Additionally, increasing awareness of the complexities associated with engaging in regular PA among non-diabetologist doctors can help them better understand patients and reduce criticism. Consequently, patients may receive better support from these doctors.

Authors' contribution.
Conceptualization: Karina Lissak
Methodology: Olgierd Dróżdż, Bianka Nowińska
Software: Bartosz Siudek, Wiktoria Bińczyk, Anna Wiśniewska
Check: Agata Konopka, Zuzanna Szczepaniak
Formal analysis: Karina Lissak, Agata Konopka, Klaudia Włodarczyk
Investigation: Karina Lissak, Zuzanna Szczepaniak, Milena Orzeł, Maria Myślicka
Resources: Anna Wiśniewska, Olgierd Dróżdż, Bartłomiej Orzeł
Data curation: Karina Lissak
Writing - rough preparation: Karina Lissak, Wiktoria Bińczyk
Writing - review and editing: Karina Lissak, Milena Orzeł, Bartłomiej Orzeł
Visualization: Karina Lissak, Bartosz Siudek
Supervision: Karina Lissak
Project administration: Karina Lissak, Bianka Nowińska, Klaudia Włodarczyk, Maria Myślicka
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