



Artigo Revisão

## Type 1 Diabetes and Exercise Management among Children and Adolescents: An Overview



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### A B S T R A C T

Exercise is determinant to the management of type 1 diabetes mellitus. Despite being crucial for a healthy development, it brings several challenges for patients, families and professionals that deal with insulin therapy. In fact, the type, duration, intensity of the exercise (among several other factors) can have an important impact on glycemic control. For that reason, this paper aims to present an overview of some basic concepts related with exercise in children and adolescents with type 1 diabetic patients, that will be useful for clinicians to develop an effective management that enables this activity while avoiding hypo and hyperglycemia.

### Diabetes Tipo 1 e Gestão da Prática de Exercício Físico em Idade Pediátrica

#### R E S U M O

O exercício é determinante para a abordagem terapêutica da diabetes *mellitus* tipo 1. Apesar de ser crucial para um desenvolvimento saudável, a sua prática dá origem a diversos desafios para doentes, familiares e profissionais que lidam com a terapêutica insulínica. De facto, o tipo, duração, intensidade do exercício (entre vários outros fatores) podem ter um impacto importante no controlo glicémico. Por esse motivo, este artigo tem como objetivo apresentar uma visão geral de alguns conceitos básicos relativos ao exercício em doentes com diabetes tipo 1, que serão úteis para que os clínicos desenvolvam uma gestão terapêutica eficaz que possibilite esta atividade, evitando hipo e hiperglicemias.

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## Introduction

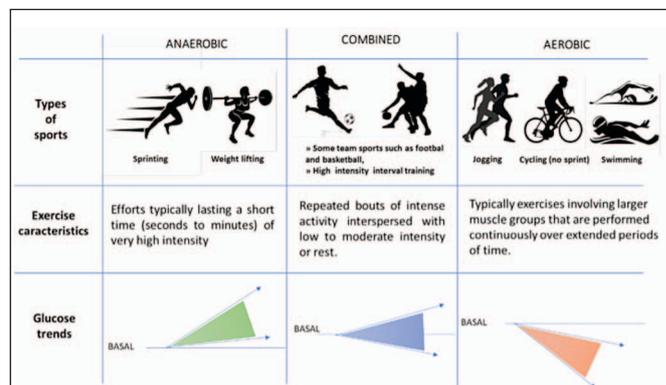
The management of type 1 diabetes mellitus (T1D) settles in three main pillars: (1) insulin, (2) proper nutritional guidance and (3) regular exercise. This activity presents several benefits among children and adolescents: improves body composition, cardiorespiratory fitness, blood lipid profile and psychological well-being while decreases total daily insulin needs, episodes of severe hypo- or hyperglycemia and end-organ damage. The relevance of this therapeutic pillar becomes even clearer when considering that many T1D patients are overweight/ obese and that cardiovascular disease remains the leading cause of mortality and morbidity among young T1D patients.<sup>1-4</sup> Therefore, it is unsurprising that all T1D pediatric patients with 6 years or more are advised to engage in at least 60 minutes of physical exercise daily, similarly to healthy children. This should encompass moderate to vigorous aerobic activities most of the time, but also musculoskeletal strengthening exercises.<sup>4</sup>

Although exercise is essential for a healthy development, it poses several challenges for families and professionals that manage insulin therapy in T1D patients.<sup>5</sup> For instance, planned adjustments of carbohydrates or insulin are challenging in young children because physical activity is frequently based around play, which is usually unplanned and variable from day to day. Conversely, older children and adolescents usually engage in more structured exercise (school sports, or other extracurricular activities, such as competitive ones), where exercise strategies to prevent hypo- or hypoglycemia are more easily applied.<sup>6</sup> In addition, growth and pubertal development influence glucose levels,<sup>7</sup> adding to a myriad of factors that also impact glycemic response to exercise (including type, duration of the exercise, intensity, amount of active insulin, anxious behavior, among others).<sup>6</sup>

Thus, this paper aims to summarize the physiological mechanisms and basic practical concepts surrounding exercise in pediatric T1D patients, providing the necessary tools to the clinician for the development of an effective diabetes management plan.

## The physiology of exercise in type 1 diabetes and its clinical consequences

The key for a successful therapeutic management strategy lies on a thorough knowledge of the exercise physiology. Exercise can be classified into three main groups: aerobic, anaerobic or combined exercises. Aerobic activities comprise repeated sequences of light to vigorous intensity exercise for extended periods (at least 10 minutes), involving large muscle groups and being usually associated with blood glucose reductions in T1D patients. In contrast, anaerobic activities are typically very high intensity efforts lasting for a short time (seconds to minutes). These activities are fueled by energy sources located within the muscles that are independent of the use of inhaled oxygen, being frequently associated with elevations in blood glucose.<sup>8,9</sup> Combined exercises encompass repeated bouts of intense activities interspersed with low to moderate intensity or rest; these include multiple common playground activities, such as soccer or other team sports, that usually produce moderating effects on glycemia (Fig. 1).<sup>1,10</sup> In a first phase, the main sources of energy for prolonged aerobic exercise are carbohydrates and lipids derived from within the muscle cells but also from other organs such as the adipose tissue stores and liver. Carbohydrates ingested during physical activity are particularly more useful as its intensity increase, the same being true regarding exercise duration. During prolonged exercise, the pre-



**Figure 1.** Blood glucose trends according to different types of exercise in type 1 diabetic patients.

Adapted from: Riddell MC, *et al.* Exercise management in type 1 diabetes: a consensus statement. *Lancet Diabetes Endocrinol.* 2017;5:377-90; Mascarenhas LP. Physical exercise in type 1 diabetes: recommendations and care. *Rev Educ Física.* 2016;22: 223-30.<sup>1,2</sup>

sented sources act to rapidly restore circulating glucose levels and to maintain normoglycemia.<sup>11-12</sup> But how does this happen?

In healthy individuals, blood glucose is maintained within a tight range (70-110 mg/dL) regardless of exercise type (aerobic or anaerobic). In these persons, the reduction in glycemic levels induced by muscle cell glucose uptake during exercise is effectively counteracted by several neuroendocrine mechanisms.<sup>13</sup> The first of them - activated when blood glucose drops to less than 80 mg/dL - is the reduction of insulin secretion. As glycemia progressively decreases, this is followed by increased secretion of glucagon, epinephrine, norepinephrine, growth hormone and cortisol.<sup>10</sup> These hormonal changes lead to increased hepatic glucose output due to increased glycogenolysis (breakdown of hepatic glycogen stores) and gluconeogenesis (conversion of non-carbohydrate precursors such as aminoacids, lactate and glycerol into glucose). By balancing the glucose uptake by muscle cells with the subsequently increased hepatic glucose secretion, these metabolic pathways prevent exercise-induced hypoglycemia and promote stable glycemic levels.<sup>14</sup> During prolonged aerobic exercise, the described hormonal response also contributes to increased lipolysis, as non-esterified fatty acids are mobilized from the adipose tissue and used as energy sources, thus sparing blood glucose.<sup>10,14</sup> Unfortunately, T1D patients deviate from this counter-regulatory response because their pancreas cannot regulate insulin levels during and after exercise: plasma insulin levels are often too high for the intensity of a given exercise, ultimately leading to hypoglycemia - the main exercise-related problem in these patients. In addition, exercise increases insulin sensitivity and also non-insulin mediated glucose uptake through the translocation of glucose transporter type-4 (GLUT-4) to the cell membrane while promoting subcutaneous insulin absorption, further lowering plasma glucose.<sup>4,15</sup> Low glucose levels also occur due to an impaired/ absent hyperglycemic response to hypoglycemia (through glucagon production and sympathoadrenal hyperglycemic responses) in T1D patients. In fact, these blunted counterregulatory hormone responses are even more common among young athletes with a hypoglycemia in the 24-48 hours prior to exercise. This “perfect storm” favors the occurrence of repeated hypoglycemia episodes, resulting in hypoglycemia-associated autonomic failure in some patients who do not experience and respond properly to the potentially life-saving warning symptoms.<sup>4,13</sup> These hypoglycemia-related symptoms include sweating, chills, dizziness, palpitations, fatigue, and im-

paired cognitive processing, which ultimately contribute to poor exercise performance. If not treated, low blood sugars are also associated with falls, coma, or even death.<sup>15</sup>

The timing of exercise is also important to predict hypoglycemia. It is known that when it is performed early in the day, a sustained increase in insulin sensitivity is observed for at least 11 hours after the exercise. On the other hand, exercise that is performed late in the day (such as during the afternoon) elicits a biphasic response in insulin sensitivity, with a first peak during the exercise and the second one 7 to 11 hours later (usually overnight, when the child is sleeping). This is obviously a factor of great anxiety for the patient and their family, that can be avoided with a correct management strategy.<sup>10,16</sup>

Despite the main focus in T1D – exercise relationship being on hypoglycemia avoidance, exercise can also be associated with hyperglycemia.<sup>17</sup> One of the causes is physiological stress of competition: by inducing the secretion of cortisol, catecholamines and interleukin 6, promotes insulin resistance and hyperglycemia before and during exercise, resulting in the need of additional insulin. Other players with putative hyperglycemic effect are multiple environmental factors, such as temperature or humidity. It is thought that warm and humid environments tend to elevate blood glucose levels through excessive production of counterregulatory hyperglycemic hormones, an effect that is counterbalanced by increased subcutaneous insulin absorption due to heat-induced vasodilatation. Insufficient insulin administration and/or excessive carbohydrate intake are also two of the main factors related with high blood glucose values during or after exercise.<sup>10,18</sup> Finally, the type of exercise is also important in this context as described above, since anaerobic exercises may promote hyperglycemia. This fact raised increased interest among the research community because it has been hypothesized that the inclusion of anaerobic intervals in aerobic exercise sessions may provide additional protection against hypoglycemia.<sup>19-21</sup>

### Practical concepts for therapy management in type 1 diabetes among children and adolescents

Despite being advised to engage in a wide variety of exercises, there are some issues that T1D patients need to address before, during and after exercise. The knowledge of these considerations is important to achieve a healthy lifestyle and exercise safely while avoiding hypoglycemia and hyperglycemia/ketoacidosis.

#### 1. Contraindications for exercise

##### » Recent episode of severe hypoglycemia

Exercise is contraindicated if the patient had an episode of severe hypoglycemia (blood glucose under 50 mg/dL or hypoglycemia requiring external assistance for correction due to cognitive impairment) within the 24 hours prior to exercise. It is known that the risk of recurrent hypoglycemia is increased in these cases due to a subsequent deterioration of the protective hormonal counterregulation.<sup>22</sup> Those patients with a mild hypoglycemia prior to exercise should be treated before beginning and carefully monitored (with frequent blood glucose checks) during the activity.<sup>4</sup>

##### » Severe hyperglycemia with elevated levels of ketones

T1D patients presenting blood glucose (BG) levels > 250 mg/dL should check their ketone levels through blood beta-hydroxybutyrate (BOHB) testing. If ketone levels are >1.5 mmol/L or BG

> 350 mg/dL, they must not engage in exercise practice but habitual physical activity included in daily routine should be kept. The cause of these alterations needs to be identified (high carbohydrate intake, insulin omission, illness, among others) and rapidly corrected with insulin administration, hydration, and carbohydrate intake if necessary (depending on the cause). Blood ketone levels  $\geq 3.0$  mmol/L must be evaluated and treated by a qualified health-care professional due to the risk of occurrence of diabetic ketoacidosis.<sup>10</sup>

##### » Inadequate training or logistics to deal with exercise-related hypoglycemia

Patients with T1D should be proficient in self-monitoring of blood glucose and hypoglycemia correction before starting any type of exercise. Before the activity, they should check their starting glucose concentration (also monitored regularly during and after exercising) and need to carry blood glucose monitoring equipment and carbohydrate snacks to correct hypoglycemia. If these conditions are not met, exercise is not safe in these patients. Additionally, T1D children and adolescents should be encouraged to have some kind of diabetes identification. It is also essential that a responsible adult monitor exercise practice of younger children.<sup>4</sup>

##### » Injuries

Injuries may contribute to higher blood glucose levels in T1D patients as a response to increased catecholamine and cortisol production in this context. Hyperglycemic states delay the recovery from an injury while hypoglycemic states may contribute to falls, increasing the risk of sustained injuries. For these reasons, exercise is not recommended in this setting.<sup>10</sup>

#### 2. Glycemic management prior and during exercise: practical advice

Glycemic responses to the different types, intensities, and duration of exercise present great variability between and within T1D patients. For this reason, blood glucose management is based on frequent glucose self-monitoring, adjustments in the administered insulin doses (both pre-prandial and prandial) and also in the intake of carbohydrates before, during and after exercise (if needed).<sup>1,23</sup> To avoid blood glucose disturbances (mainly hypoglycemia) during and after exercise, some basic rules should be met. The first of them is to initiate exercise within target glycemic control.<sup>24</sup> To achieve this goal, BG levels should always be evaluated in T1D patients before starting exercise. The target range for BG levels prior to this activity is between 90-250 mg/dL, and ketones should be checked when BG >250 mg/dL or if the patient has symptoms of nausea/vomiting (Table 1).<sup>19</sup>

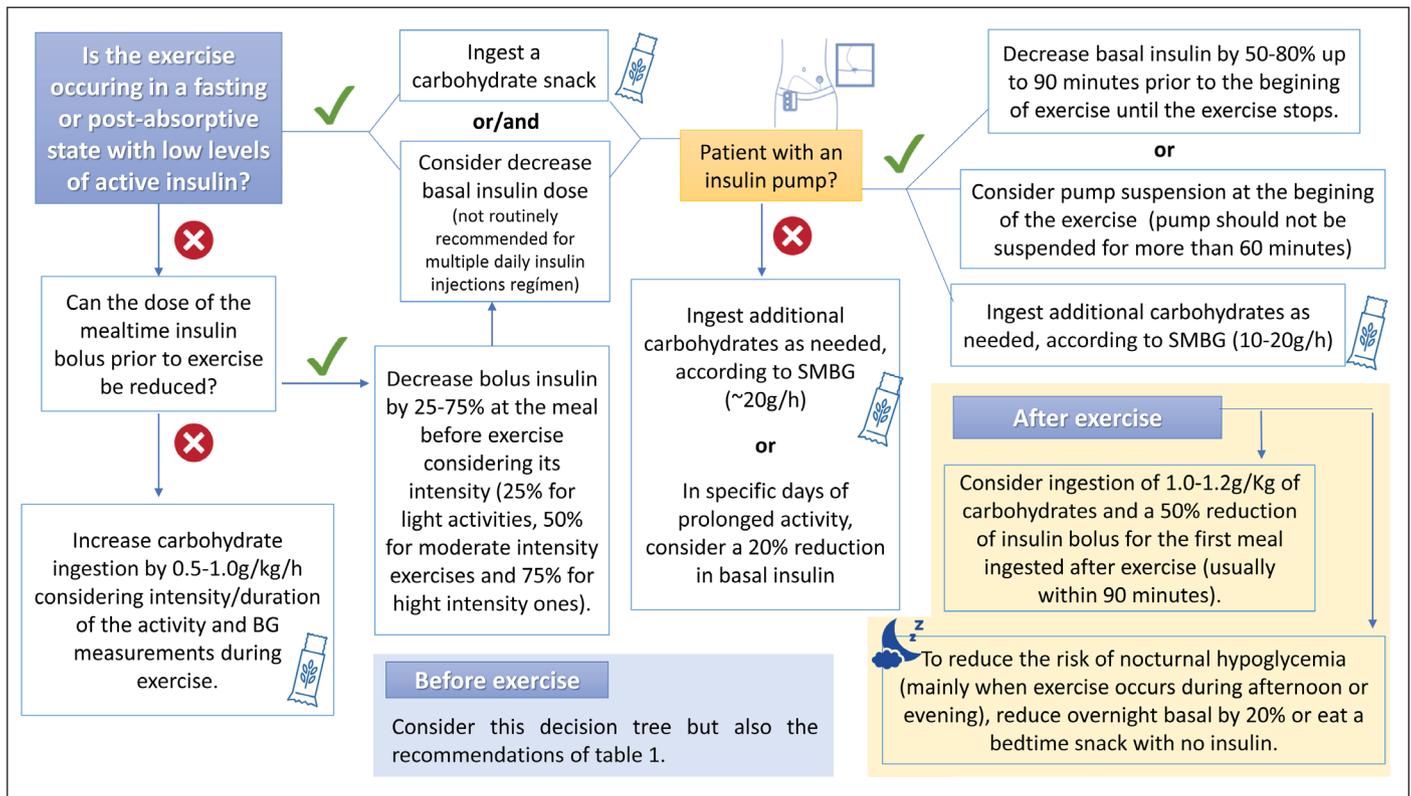
The child/adolescent should always bring fast-acting carbohydrates to the activity and ingest slowly absorbing ones in the hours prior to exercise (to avoid hypoglycemia). These fast-acting carbohydrates taken during exercise should not be accompanied by insulin and are used to stabilize glucose levels in patients in risk of hypoglycemia or to correct it. This is especially important in some particular cases (such as in patients not able to reduce mealtime insulin bolus prior to exercise). The slowly absorbing carbohydrates may be ingested in the hours prior to exercise as part of a meal with insulin, but accounting for the expected insulin dose reductions (Fig. 2).<sup>25</sup>

The site of insulin administration should not be the one that will be exercised (by increasing blood flow to the exercised area,

**Table 1.** Recommended glucose management strategy before starting an exercise. This strategy intends to stabilize glycemia at the beginning of the exercise, and aerobic exercise will probably demand additional carbohydrates. Glycemia should always be checked regularly during exercise. This plan can be modified based on several factors such as patient's previous responses to exercise, recent boluses of insulin or the trend arrow on continuous glucose monitoring.

Blood glucose	How to proceed?
<90 mg/dL	Ingest 10-20 g of fast-acting carbohydrates and delay the beginning of exercise until BG>90 mg/dL.
90-125 mg/dL	Consume 10-20 g of fast-acting carbohydrates before starting aerobic exercise.
126-180 mg/dL	Proceed with aerobic or anaerobic exercise. The patient should ingest supplemental carbohydrates after beginning exercise if it lasts for more than 30 minutes.
181-250 mg/dL	Proceed with aerobic or anaerobic exercise.
<b>Measure ketones:</b>	
<b>BOHB ≥3.0 mmol/L:</b>	
Exercise is contra-indicated. Look for a qualified health-care professional due to the risk of diabetic ketoacidosis.	
<b>BOHB ≥1.5-2.9 mmol/L:</b>	
Exercise is contra-indicated. Give ½ correction dose of insulin with pen/syringe. Follow sick-day rules to manage hyperglycemia/ketosis.	
<b>BOHB 1.1-1.4 mmol/L:</b>	
Give ½ correction dose of insulin with pen/syringe, wait 60 minutes after correction and proceed exercise only after ensuring decreased BG.	
<b>BOHB 0.6-1.0 mmol/L:</b>	
Give ½ correction dose of insulin with pen/syringe, wait 15 minutes after correction and proceed exercise.	
<b>BOHB &lt;0.6 mmol/L:</b>	
Ok to proceed exercise	

Adapted from: 1. Riddell MC, *et al.* Exercise management in type 1 diabetes: a consensus statement. *Lancet Diabetes Endocrinol.* 2017;5:377-90; Adolfsson P, *et al.* ISPAD Clinical Practice Consensus Guidelines 2018: Exercise in children and adolescents with diabetes. *Pediatr Diabetes.* 2018;19:205-26; Colberg SR, *et al.* Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. *Diabetes Care.* 2016;39:2065-79.<sup>14,19</sup>



**Figure 2.** Decision tree for type 1 diabetes management before, during and after exercise.

Adapted from: Riddell MC, *et al.* Exercise management in type 1 diabetes: a consensus statement. *Lancet Diabetes Endocrinol.* 2017;5:377-90; Mascarenhas LP. Physical exercise in type 1 diabetes: recommendations and care. *Rev Educ Fisica.* 2016;22: 223-30.<sup>1,2</sup>

SMBG: Self-monitoring blood glucose; BG: Blood glucose

it will also increase insulin absorption and favor hypoglycemia occurrence).<sup>26</sup> In the case of prolonged exercise, the patient needs to increase the intensity/ duration of the exercise progressively

and consider the introduction of solid or liquid carbohydrates before, during and after the activity. In addition, when the physical activity is planned to be performed at the time of insulin peak

action, its dose should be reduced. The patient or his family also need to make others aware of the procedures regarding a severe hypoglycemia.<sup>1,27</sup> In patients with continuous glucose monitoring, the alerts regarding low glucose values (and low glucose suspend mode in newer pumps) may be also a valuable tool to avoid exercise-related hypoglycemia.<sup>28</sup> Finally, the BG value measured before bedtime on the evening after relevant physical activity should be evaluated; slow-absorbing extra- carbohydrates should be added at bedtime and/or basal insulin should be reduced to avoid nocturnal hypoglycemia (usually when the patient is asleep).<sup>29</sup>

It should also be stressed the importance of patients and their families having access to simple and written information regarding the procedures to be carried out before, during and after exercise. This will be a precious help to avoid glycemic disturbances related with exercise, that are many times associated with patient frustration or even exercise abandonment.<sup>30,31</sup> In addition, monitoring blood glucose before, during and after exercise is of great importance to adjust the therapeutic approach and promote exercise practice with less glycemic disturbances.<sup>1,4</sup>

One of the factors influencing the therapeutic approach is the timing of exercise in relation to the last meal. If the exercise is occurring in a fasting or pos-absorptive state with low levels of insulin, the patient should take a snack or/and consider decreasing the dose of basal insulin (in the case of insulin pumps, the basal rate infusion can be reduced in 50%-80% up to 90 minutes prior to the beginning of exercise or even be suspended temporarily). If the exercise is occurring postprandially, the insulin bolus of that previous meal should be reduced between 25% and 75% taking into account the intensity of the exercise (greater reductions for higher intensity exercises). If this previous meal is already taken with insulin, the patient should ingest carbohydrates by 0.5-1.0 g/kg/h according to intensity/duration of the activity and BG measurements. After exercise, the patient should consider the ingestion of 1.0-1.2 g/kg/ of carbohydrates and a 50% reduction of insulin bolus for the first meal ingested after exercise. Nocturnal hypoglycemia can be avoided by reducing overnight basal by 20% or by eating a snack at bedtime with no insulin.<sup>1,4</sup> Fig. 2 displays a proposed decision tree which must be taken into consideration to help these patients to successfully manage their glycemic profile while practicing exercise and with increased relevance in situations of prolonged exercise (more than 30 minutes).

It is important to understand that these recommendations are just a starting point and that every individual with diabetes is unique. For this reason, the effect of every modification in insulin dose or carbohydrate change should be carefully evaluated and adapted taking into account the patient's needs. Thus, BG monitoring plays a central role in this process by allowing the identification of metabolic adaptations and appropriate interventions. After the adaptation period to these new situations (with eventual understanding of glucose patterns related with that particular type of exercise), monitoring follows the recommendations already mentioned in the paper. The increasingly used continuous glucose monitoring devices (CGMs) are also a major breakthrough to help these patients maintaining normoglycemia. These devices measure glucose in the interstitial fluid, providing real-time sensor glucose data, and some of them are equipped with alarms for hyper and hypoglycemia, which is reassuring for patients and their families. For children and adolescents that will exercise, the alarms of hypo and hyperglycemia alarms should be set at 100 mg/dL and 180 mg/dL (giving time to the patient to address the problem properly), or individualized if required. Despite the great advantages in glucose pattern identification and diabetes control,

a self-monitored confirmatory blood glucose should be performed in glycemic extremes (hypo and marked hyperglycemia) or when the symptoms do not add up with the glycemic value provided by CGM. In addition, a lag time exists between the glucose value in the vasculature and in the interstitial fluid. A consensus statement regarding CGM monitoring for exercise among individuals with type 1 diabetes was published recently and addresses this issue in more detail.<sup>33</sup>

Lastly, it should be addressed that there is a lack of evidence regarding exercise management among pediatric patients (when compared with adult ones). For this reason, the authors would like to draw attention for the fact that some recommendations followed nowadays regarding pediatric patients in this context might be based in adult ones. This stresses the importance of more research dedicated to this particular issue.

## Conclusion

Physical activity is a fundamental pillar in controlling diabetes, in addition to having multiple other benefits.<sup>32</sup> Precisely for this reason, it is necessary that the follow-up teams of children and young people with T1DM know how to deal with the challenges of exercising, in order to help patients and their families. In this way, it will be avoided that potentially demotivating situations arise and that contribute to the abandonment of such an important activity. The knowledge of the glycemic impact of different types of exercise (anaerobic, aerobic and combined) and exercise physiology is important to predict glycemic trends and to understand how a particular exercise affect glycemic control. This can be effectively measured with glucometers or with new CGM devices, that provide valuable information to the patient but also to the physician. The main therapeutic approaches usually encompass insulin dose reductions and/or carbohydrate ingestion (according to the monitored glycemia), aiming to the maintenance of normoglycemia during this important activity.

## Contributorship Statement / Declaração de Contribuição:

FM - conceptualization, writing and review.

SF,CC,SBS,CC- conceptualization and review.

## Responsabilidades Éticas

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