European Review for Medical and Pharmacological Sciences 2023; 27: 88-97

How to end up on the podium after running a 6-days-run with type 1 diabetes mellitus – A case study and literature review

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Abstract. – BACKGROUND: An increasing number of people living with type 1 diabetes mellitus (T1DM) are pushing their physical limits to compete at the sport's highest level. Muscle, liver, and glycogen metabolism can be normal in athletes with diabetes with good glucose management, and modifications to insulin dose and nutrition can facilitate exercise performance.

CASE PRESENTATION: We report on a 66-year-old runner with insulin-dependent T1DM. He has run over 90 marathons and ultra-marathons. Thanks to an insulin pump and continuous glucose monitoring, he has completed forty-eight 24-hour runs with an average performance of 133.8 km.

Over the years, the runner increased his monthly running volume significantly and decreased his glycated Hemoglobin type A1C (hba1c) levels. Meanwhile, a significant association between monthly running kilometers and hba1c levels could be shown. At the age of 66 years, he finished his sixth 6-day-run in third place overall by covering a total distance of 467.424 km.

CONCLUSIONS: These findings show that it is possible to participate in ultra-endurance events while suffering from T1DM without glucose derailing. With a good understanding of the disease and its impact on an individual's body, we can curtail the preparation and execution phases of ultra-endurance events to allow athletes to compete with minimal risk.

Key Words:

Endurance performance, Running, Metabolic disorder, Diabetes mellitus type 1.

Introduction

Type 1 diabetes mellitus (T1DM) is characterized by a highly specific immune-mediated destruction of pancreatic β cells, resulting in chronic hyperglycemia[1]. Exogenous insulin has been considered one of the mainstays of T1DM therapies[2]. One hundred years after discovering insulin, people with T1DM can achieve a near-normal life expectancy and an overall high quality of life, but this requires constant monitoring of on-target blood glucose levels and good cardiovascular health[3]. Managing T1DM remains challenging even with access to specialized diabetes care[4]. Regular physical activity can improve cardiometabolic health[5] and is associated with increased longevity[6]. Furthermore, regular physical activity improves the vascular endothelial function[7], reduces blood pressure[8], improves lipid abnormalities[8], improves the cardiorespiratory function[9], and is associated with increased longevity[6].

Additionally, an increasing number of people living with T1DM are pushing their physical limits to compete at the sport's highest level. Athletes with T1DM can achieve normal muscle, liver, and glycogen metabolism[10]. Good glucose management and modifications to the insulin dosage and nutrition exercise performance can be facilitated. However, maintaining normal glucose levels during training, travel, and competition remains challenging for athletes living with T1DM[10]. Ath-

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letes with low-to-moderate levels of carbohydrate intake during training and rest days tend to benefit from high rates of carbohydrate feeding during long-distance events, both from a glucose and performance perspective[10].

Little attention was given to the post-exercise recovery routine within the scientific literature, which mainly focused on sporting performance. Most focus is on insulin or nutritional adaptations to manage glycaemia before and during the exercise phase[11]. The post-exercise recovery period presents an opportunity to maximize training adaption, recovery, and the management of glycaemia through the rest of the day[11].

T1DM results from precise immune-mediated destruction of pancreatic β cells, resulting in chronic hyperglycaemia[11]. Individuals living with T1DM require a regular exogenous insulin injection to survive[2]. With the advances in insulin therapy, delivery, and monitoring, individuals with T1DM are enjoying a rise in life expectancy[12] and can participate in the highest levels of competitive sports[13-15].

An ultra-marathon is a longer running distance than a classic marathon distance (42.195 km) or an endurance exercise that lasts more than 6 hours[16]. Ultra-marathons are divided into distance runs (in km or miles)[17] and limited time runs (6, 12, 24 hours, up to 10 days)[18].

The number of ultra-marathon competitions has increased significantly in the past few decades[19], and finishers have increased exponentially[20]. Particularly popular are the 100 km runs[21], the 100-mile runs[22], the runs in hours or days from 6 hours to 10 days[23], and multi-stage runs like the ones passing through a desert[24], a country[25] or an entire continent[26].

Ultra-runners differ from the general population. As a rule, ultra-runners are healthy, middle-aged people between 30 and 40 who invest much of their time in training and have significant experience in marathons and ultramarathons[27,28]. The prevalence of chronic diseases such as coronary heart disease or diabetes mellitus in ultra-runners is well below 1%[27], however, latest evidence suggests that there may also be potential long-term health risks associated with ultra-endurance running[29].

Nonetheless, isolated reports of endurance athletes with insulin-dependent diabetes mellitus participating in ultra-competitions in recent years have been emerging[30]. The number of T1DM athletes actively participating in competitive sports is increasing[31]. A more extensive study describing triathletes with insulin-dependent diabetes mellitus who completed an Ironman triathlon was already undertaken[32]. Even significantly longer distances are possible. Case reports discuss a triathlete with insulin-dependent diabetes mellitus completing a Double Iron ultra-triathlon (7.6 km swim, 360 km bike ride, and 84.4 km run)[23] and a triathlete with insulin-dependent diabetes mellitus completing an Ultraman-Triathlon (distance of a Double Iron ultra-triathlon divided into three daily stages)[33].

There are field studies[34-37] in the context of running with insulin-dependent diabetic patients that have completed endurance runs such as a half-marathon[34], a marathon[35,36], and even an ultra-marathon[37].

Literature shows that athletes with insulin-dependent diabetes mellitus manage long-running competitions up to ultramarathons. Nonetheless, we know nothing about endurance athletes' long-term progression and training. In particular, the connection between training and sugar metabolism [glycated Hemoglobin type A_{1C} (hba_{1c})] over the years is still unknown.

In the present case report, we report on a 66-year-old runner who has been diagnosed with juvenile T1DM. In particular, we can gain insight into the connection between training and the development of hba_{1c} values over the years. When planning training and competitions, these results are of interest to general practitioners and other athletes with insulin dependent T1DM.

Case Presentation

In this case report, we would like to present the case of the first T1DM patient to finish a 6-day-run on the podium.

Our male runner, born in 1955, was 66 years old at the examination. In 1976, at the age of 21, he was diagnosed with T1DM. In 1984, at the age of 29, he started running. He ran 2 to 3 km sessions a week and ran his first marathon at 32 and his first ultra-marathon at 34.

He weighed 133 kg at the age of 16 and reduced his weight to 110-115 kg by the age of 20, When diabetes mellitus was detected, he decreased his weight to 85-90 kg. His weight stabilized at around 80-85 kg in the next few decades.

Based on his training records, hba_{1c} values and competition results over several decades, we can demonstrate that it is possible to compete in marathons and ultra-marathons for decades even with insulin dependent T1DM. At the age of 66 years, he finished his sixth 6-days-run in third place overall by covering a total distance of 467.424 km.

Since the type of diabetes seemed quite unusual, and the runner had been extremely obese at the age of 16, the C-peptide value was checked in 2011. A 17.0 pmol/l with a normal value of 364-1,655 pmol/l indicated that he does not have type 2 diabetes mellitus.

His basic nutritional plan is a wholesome diet, according to Kollath/Bruker, with only two meals a day without snacks in between. He eats a fresh grain porridge made from 40 g of cereals with about 300 g of fruit and some sweetened cream for breakfast and fresh salads, cheese, vegetables, and whole meal bread with butter and apples for dessert in the evening. He gets about 30 CU/day (carbohydrate units), corresponding to approximately 300 g carbohydrates/day. The runner has been continuously recording his hba_{1c} values since 2001.

Since 1984, he has logged his training volume as kilometers run per month. He has trained out of concern for his well-being and does not do any specific running training. Instead, he has incorporated running as walking into everyday life, not following a strict training plan. Running and hiking training consists of continuous runs in mountainous terrain at 500-1,000 meters in altitude up to 2,500 meters. The high mountain runs up to 2,500 meters are only done in summer when the weather conditions are good, with the primary goal of reaching the summit. No emphasis is given to running speed because of the path's difficulty and environmental factors such as heat.

We divide the runner's previous running results into distance-limited (marathon, 100 km) and time-limited (6, 12, 24, 48, 72 h, 6 days) runs. Between 1987 and 2004, he ran 15 marathons with an average finish time of 4:22:33 h:min:s, and between 1989 and 2005, eleven 100 km ultra-marathons with an average finish time of 17:02:00 h:min:s. Focusing on the time-limited runs, he completed a 6-hour run in 1998 and 1999 with an average distance of 51.7 km. From 1991 to 1995, he ran two 12-hour runs with an average length of 80.4 km. From 1994 to 2017, he competed in forty-eight 24-hour runs, with an average performance of around 133 km and no significant change in performance over the years. Between 1999 and 2005, he completed 6 competitions over 48 hours with an average distance of 184.8 km. While he only competed in one competition of 288.9 km over 72 hours, between 2008 and 2016, he completed three 6-day runs with an average performance of 438 km.

We are focusing on the 24-hour runs since this form of competition has developed into a particular discipline for this runner. In the 24-hour races, he has a clear diet. Depending on the level of blood sugar, he takes pieces of cake or pretzel sticks from the official catering stand of the organizers and drinks conventional Coca-Cola®. The start of these competitions is usually at noon. After about 9 hours of running (at 9 p.m.), he eats a dinner of potatoes and vegetables (about 5 CU). After around 2 p.m. (early at 2 a.m.), he consumes coffee and cake (approx. 5 CU). Those quantities are about the same throughout the different competitions.

The runner used the Accu-Chek Mobile test device for regular blood sugar checks until 2015 (available at: www.accu-chek.ch). He was also able to measure his blood sugar when running without stopping. He carried the measuring device and the lancing device in a pouch around his neck. To measure his blood sugar, he pricked his finger, put the lancing device back in the pocket, took out the measuring device, applied the blood, and measured. Since September 2015, the measures have been carried out using CGM (Continuous Glucose Monitoring) with a Medtronic MiniMed 640G and an Enlite glucose sensor (available at: www.medtronic-diabetes.ch).

Insulin was delivered in conventional form until 2003, and since 2004, an insulin pump has been used. From 2004 to 2009, he used the Roche D-TRON, the Roche Spirit from 2009 to 2012, the Medtronic MiniMed 640G from 2013 to 2015, and the CGM from 2015 (Continuous Glucose Monitor-ring) (available at: www.medtronic-diabetes.ch/de/minimed-produkte/minimed-640 g-insulin pump). Additional injections were administered while running, depending on the situation.

The 640 G's hypo switch-off proved extremely useful to the runner. During training, the hypo switch-off is very often active with the advantage that the runner can focus on running and has to check his blood sugar level much less frequently. As soon as the blood sugar level drops, the pump switches off, significantly reducing hypoglycemia risk. If the blood sugar level rises, the pump starts up again, keeping the blood sugar level constantly in the range of 3.5-7 mmol/l. This is particularly useful in winter when it is cold, snowy, and raining, as the runner can keep his hands in the gloves and does not have to pull the pump out of his pocket to read the value and turn it off.

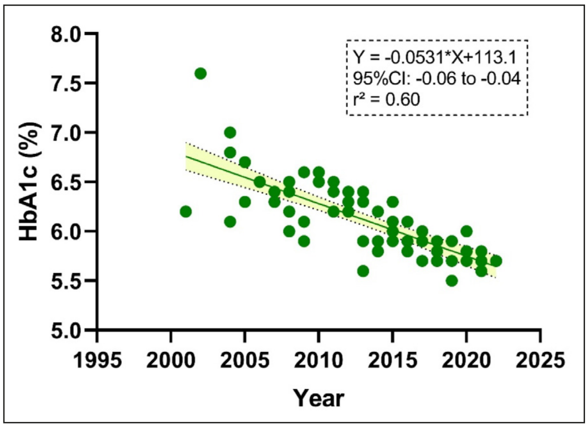

Figure 1. Association between glycated Hemoglobin type A_{1c} (hba_{1c}) over time.

Their daily insulin requirement is 35-45 units if the runner eats. However, the daily insulin requirement varies between 35 and 45 units, which he attributes to the different insulin absorption.

While not on CGM, the runner has reduced the pump's basal rate by 70% during a run, as long as the blood glucose values measured during exercise were within the norm. If a correction bolus became necessary, he did not have a fixed scheme, but dosed it according to his own experience. There was no hypoglycemia during the competition.

The very rare blood sugar imbalances would also be more typical of type 2 diabetes mellitus. The runner can assess blood sugar behavior based on his experience. He can easily run for ≥10 hours without eating and not lose efficiency. As a result, he can get by with very little insulin without a too high or too low bolus. The CGM is very helpful because it serves as an early warning if the hypo switch-off is insufficient and can be adjusted with a small sip of coke. It is the same with a rising blood sugar level, where just 0.5 IU of insulin can be administered to keep the levels in the optimal range.

Statistical Analysis

Data normality distribution was tested through the Kolmogorov-Smirnov test. Linear regression analysis was performed to verify the relationship between hba_{1c} and running volume over time, as well as the association between glucose, bolus, and the covered distance. 95% of the confidence interval was presented. Graphpad Prism (version 8.0.1, La Jolla, CA, USA) was used for all statistical and graphical analyses, adopting a significance level of $p<0.05$.

Results

Analyzing this exceptional 66-year-old runner with T1DM since the age of 21, several important points stand out, such as (i) the high number of 48 completed 24-hour runs, (ii) a significant increase in the monthly running volume, (iii) a significant decrease in hba_{1c} levels over the years, and (iv) a significant association between monthly running kilometers and hba_{1c} levels.

Our runner completed forty-eight 24-hour runs from 1994 to 2017, an average of two per year. He has also undertaken other runs, such as 100 km runs, and 6-hour runs up to 6-day runs.

The Decline in Hba1c Over the Years

We found a significant decrease in hba_{1c} over the past almost 20 years (Figure 1) and a significant association between the increase in monthly kilometers run and the reduction in hba_{1c}.

Consistent Competitive Performance and Increased Training Volume

The featured runner has significantly increased his monthly running volume over the past few decades (Figure 2).

Relationship Between Running Distance and Hba1c

If we compare the hba_{1c} values with the kilometers run in the three months before the measurement, we find an inverse correlation because an

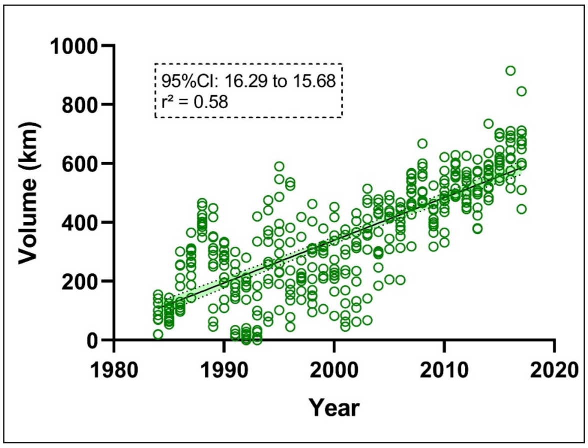

Figure 2. Monthly running volume over calendar years.

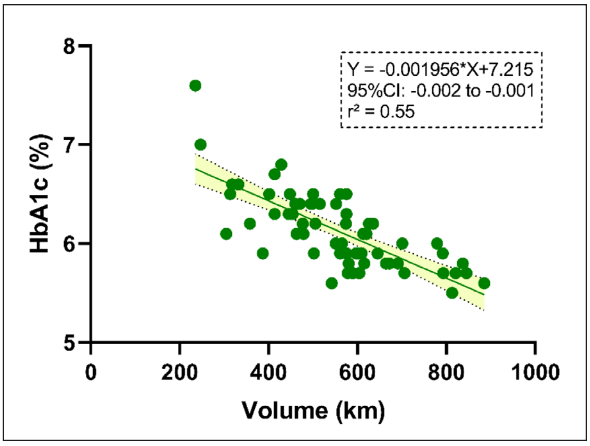

Figure 3. Association between glycated Hemoglobin type A_{1c} (hba_{1c}) and running training volume.

increase in running volume led to a decrease in the hba_{1c} value (Figure 3).

The 6-Day Run

Our runner kept approximately the same routine throughout the 6-day race. After waking up, he ran for ca. 1,5 hours and then ate breakfast which consisted of bread, marmalade, honey, sausages, cheese, and coffee. He ran for ca. 12 hours until the evening when he took a quick shower, changed clothes, and ate dinner, which consisted of cooked vegetables with potatoes, bread, cheese, sausage, and diet soda. He continued to run for ca. 5 hours after dinner and slept ca. 4 hours. Throughout the course, he corrected his blood sugar levels with regular coke. The blood sugar curve stayed at almost optimal levels with the CGM and the insulin pump, with the time in range (TIR) between 84 and 100% on running days.

The race started at 15 p.m. On his first day, our runner covered a distance of 103 km. He consumed 22 planned CUs (breakfast and dinner), 3.5 corrections CUs (coke), and administered a bolus twice. On the second day, he ran 79 km for 182 km covered, consumed 22 planned CUs and 4 corrections CUs and administered a bolus three times. On the third day, he ran 73 km for 255 km covered, consumed 22 planned CUs and 0.5 corrections CUs, and administered a bolus six times. On the fourth day, he ran 70 km for 325 km covered, consumed 22 planned CUs, 2 corrections CUs, and 3 CUs of birthday cake, and administered a bolus seven times. On the fifth day, he ran 77 km for 402 km covered, consumed 22 planned CUs, 1.5 corrections CUs and administered a bolus seven times. On the last day, he ran 65 km and finished third with a total of 467.502 km. He consumed 22 planned CUs, no correction CUs and administered a bolus six times while still running. Two more boluses were administered just after and before eating anything else.

As seen in Figure 4, average glucose levels over the whole distance covered grew but did not derail as the runner kept correcting when needed. A noticeable spike in blood sugar levels and bolus was recorded in the evening of day 4 (at 281 km) as the runner had eaten his birthday cake after dinner.

The rise in the average glucose levels can be directly linked to the times a correction CU or bolus had to be used. The need for correction CUs was also inversely related to the bolus application. In summary, the average glucose levels rose with the distance covered, as did the frequency of applying a correction bolus (Figure 5). At the same time, the frequency of the consumed correction CUs fell.

Literature Review

People with T1DM want to enjoy the benefits of sport and exercise, but the management of diabetes in this context is complex. Understanding the physiology of exercise in health, particularly the control of fuel mobilization and metabolism, highlights the problems in managing diabetes through sport and exercise.

Ratjen et al[38] assessed the individual experiences of competitive athletes with T1DM and compared those experiences with current recommendations. The results highlight the unique adaptations of the athlete's therapy undertaken during training and competition[37].

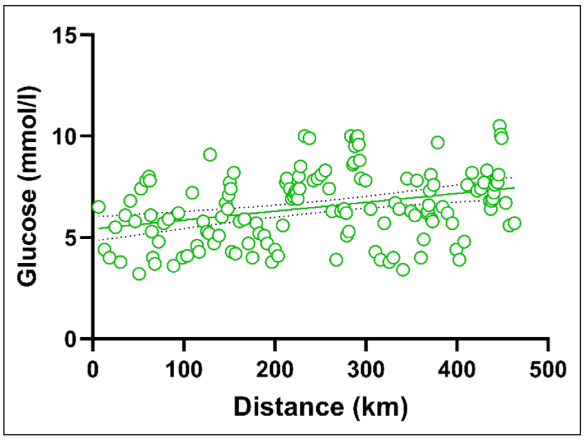

Figure 4. Association between glucose and distance.

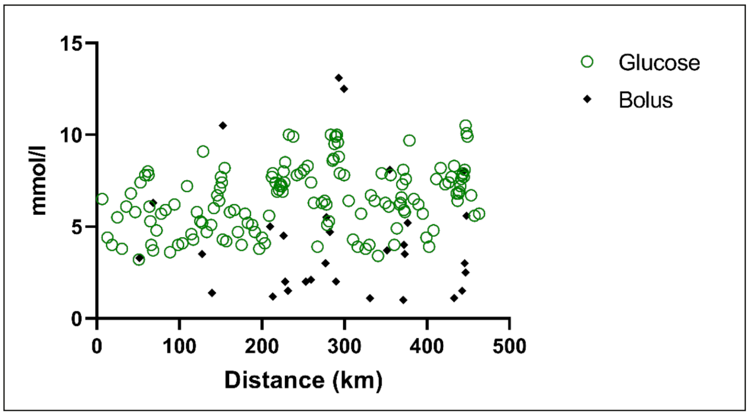

Figure 5. Glucose and Bolus over the race.

Athletes with diabetes need to be advised on an appropriate diet to maximize performance and reduce fatigue. In particular circumstances, exercise in diabetes is complicated by hypoglycemia and hyperglycemia, and explanations are advanced, which can provide a theoretical underpinning for possible management strategies. Management strategies are proposed to improve glycemic control and performance[39]. Such strategies include physical activity supported by medical technology advances and social support[40]. Furthermore, advanced monitoring tools provide information on exercise-related variables such as heart rate, step count, calories, and blood glucose[40].

In general, athletes with T1DM perform training and competition with elevated circulating insulin levels and blunted glucagon responses. They typically require a high rate of carbohydrate consumption in race events[10]. However, some athletes follow a low-to-moderate-carbohydrate diet on non-race days, which appears to improve overall glycemic control and preserve muscle glycogen storage capacity[10].

We assume that the outstanding performance achieved at the age of 66 years with T1DM a podium in 6 days run was due to the extensive experience of this runner and his discipline in monitoring blood glucose.

An analysis of 20,238 runs by women and 76,888 runs by men from runs ≥6 h up to 6 days between the years 1975-2013 showed that about 50% of the starters only had one such run, and only 10% had done seven or more runs in life[18]. This performance can only be described as exceptional, especially since he has a chronic metabolic disease. Nonetheless, this performance could be linked to the experience and increased training volume. As shown by Knechtle et al[41], the number of finishes gets higher with age, pointing out the impact of experience on course execution. At the same time, an increase in running volume directly impacts ultra-endurance performance[42]. We could now postulate that the increased running volume leads to an improvement in the diabetic metabolic situation. Intensive endurance training in type 2 diabetes mellitus effectively decreases the hba_{1c} value[24].

However, it is also possible that the reduced hba_{1c} values result from a therapy adjustment since the runner has had an insulin pump since 2004 and a CGM since 2015. With the insulin pump, an improvement in diabetes control could be possible[43]. With the use of the CGM, even further progress could be possible[26]. Managing blood glucose control and the possibility of hypoglycemia are the most significant challenges of regular exercise for individuals with T1DM. With an insulin pump and CGM, people with T1DM can keep their blood sugar constant under stress[43].

Another reason for decreasing hba_{1c} levels could be the reduction of the runner's weight over the years. Physical training has been shown to affect the severity of T1DM[44]. In people with type 2 diabetes mellitus, a reduction in adipose tissue and improved fitness decreases hba_{1c} levels[45].

However, the weight loss might also result from training since the runner has increased his running volume over the years. Ultra-runners gain less weight with age than the general population[46].

Notably, endurance athletes with T1DM report a more extraordinary hypoglycemia occurrence than their non-endurance sporting counterparts[31]. These athletes often require greater rigor in glucose management strategies that emphasize nutritional intake and insulin adjustment[47]. The complexity of the sport and its characteristics, alongside the pathological heterogeneity of T1DM, may explain the lack of athlete adherence to conventional glucose management recommendations of competitive exercise[48].

Hyperglycemia in T1DM athletes (blood glucose (BG) > 250 mg/dl) generally occurs as a result of low circulating insulin levels (commonly secondary to inadequate insulin administration), excessive food intake, physical inactivity, illness, stress, or injury[11].

In people with type 2 diabetes mellitus, it has been shown that long-term physical training benefits blood sugar control[49]. It has been shown that controlled and structured training, in contrast to unstructured physical activity, decreases the hba_{1c} value in type 2 diabetes mellitus[50].

We have figures over 23 years (1994-2017) that are hardly comparable with figures in the literature. In a case report[51], the training volume of a triathlete over half that time (17 years, 1995-2012) was compiled for swimming, running, and cycling. This triathlete has shown no increase in the volume of cycling and running over the years and has even reduced the swimming volume[51].

A possible explanation for the increased running volume in recent years could be participation in the three 6-day runs in 2008, 2010, and 2016. It has been shown that ultra-runners have a significantly higher training volume than marathon runners[22]. Our runner may have learned from the experience of the previous 24-hour runs and the 48-hour runs from 1999 to 2005 that he had to increase the running volume significantly for a 6-day run.

Hawgley et al[52] showed in a cross-sectional study design with a control group that adults with T1D did not have reduced oxidative capacity, muscle endurance, or muscle reperfusion rates compared to controls. Hba_{1c} also did not correlate with muscle endurance, mitochondrial capacity, or reperfusion rates[52].

Although our patient showed that a person with T1DM could participate in such a strenuous and long-lasting event, we would not go so far as to conclude that ultra-endurance events and extreme physiological conditions are generally safe for people who have diabetes. Also, there is a lack of data about the long-term consequences of such participation. Only a few reports[10,34,35,48,53-55] exist on T1DM patients participating in endurance events. Most of them report participation in shorter races such as marathons[35,53,54] and emphasize the dangers of hypoglycaemia[10,34,48,55]. In patients with T1DM, it has been observed that a medical support protocol monitoring glycemic balance and adjusting carbohydrate intake/insulin dose during endurance running (2h running for training and marathon race) was effective in preventing hypoglycemia during and after running[56]. In addition, a woman with well-controlled T1DM safely finished a half marathon using a hybrid closed-loop system therapy without changes in glycemic control when compared to the previous period[57].

Despite dangers and obstacles, the potential benefit for a person with T1DM involved in endurance sports could be considerable. Athletes maintain a healthy lifestyle, closely monitor their blood glucose status, and serve as motivation for other people living with diabetes to involve in regular moderate exercise. People with T1DM could benefit from exercise not only to improve blood glucose regulation but also to experience acute cardiovascular changes[58]. Moreover, exercise could improve parameters such as blood glucose control, physical fitness, endothelial function, insulin sensitivity, well-being, immune system, blood lipid profile, insulin resistance, cardiovascular diseases, insulin requirements, blood pressure, and life expectancy for people with T1DM[59].

Conclusions

We have noticed that T1DM patients can participate in ultra-endurance events without glucose derailing. With a good understanding of the disease and its impact on an individual's body, we can curtail the preparation and execution phases of ultra-endurance events to allow athletes to compete with minimal risk. As presented in our case, an experienced athlete can effectively manage glucose levels throughout the event. An appropriate diet and structured training regimen can improve health, maximize performance and reduce fatigue. More studies are needed to confirm the general safety of ultra-endurance events for type 1 diabetes patients and explore their long-term effects.

Conflict of Interest
The Authors declare that they have no conflict of interests.

Ethics Approval
All procedures applied in the study were approved by the Institutional Review Board of Kanton St. Gallen.

Informed Consent

The patient gave written informed consent to publish this case report and any accompanying images.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Funding

No funding was used to support this research and the preparation of the manuscript.

Authors' Contributions

Katja Weiss drafted the manuscript. Mabliny Thuany performed the data processing, and statistical analyses. Nejmeddine Ouerghi, Volker Scheer, Pantelis T. Nikolaidis, Marilia Andrade, Ivan Cuk and Beat Knechtle helped draft the manuscript. All authors approved the final version.

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