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REVIEW ARTICLE

Effects of high-intensity interval training on patients with type 2 diabetes mellitus: A narrative review

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ABSTRACT

Diabetes Mellitus (DM) which is characterized by pancreatic beta-cell dysfunction, peripheral insulin resistance, or both, is one of the most relevant cardiovascular risk factors worldwide. Its most prevalent and studied form is type 2 diabetes mellitus (DM2), a chronic multifunctional condition linked to physical inactivity and lifestyle. The purpose of this narrative review is to explore the implications of high intensity interval training on different hemodynamic, biochemical and anthropometric parameters of DM2 patients. Findings yielded that high-intensity interval training is a safe and recommended training method to improve functional capacity and certain parameters such as body weight and body mass index (BMI), systolic blood pressure (SBP), VO_2 maximum (peak) and Hb1Ac, compared to moderate and low intensity training, and passive controls. Moreover, the benefits of physical exercise are independent of weight loss and there is no nutritional protocol or drug to replace them.
Keywords: High intensity interval training; HIIT; Type 2 diabetes mellitus; Health.

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INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disease characterized by inappropriate high levels of glucose in the bloodstream. Moreover, chronic DM has been linked to different complications as polyneuropathy, chronic kidney disease, cardiovascular disease, cerebrovascular disease, loss of vision and immunosuppression (Galicia-Garcia et al., 2020). The International Diabetes Federation estimates on 425 million the number of people affected worldwide by DM (Colberg et al., 2016; Khan et al., 2019). On the other hand, DM is originated by a pancreatic beta-cell dysfunction (DM1), peripheral insulin resistance (DM2), or both (Iglay et al., 2016). Between the different DM types, its most prevalent and studied form (approximately 90%) is DM2 (Khan et al., 2019; Lin et al., 2020), which will be explored in this review.

In the last years, a β-cell-centred model of DM has been proposed for a functional assessment of DM (Cerf, 2013). Accordingly, it is suggested that β-cell disfunction as well as its interactions with genetics, insulin resistance, environmental factors and inflammation are the key mechanisms of DM onset (Galicia-Garcia et al., 2020). The risk of developing DM2 follows a continuum through all abnormal blood glucose levels (Banday et al., 2020). However, the highest risk patients include those with altered basal blood glucose, impaired glucose tolerance, or a glycosylated haemoglobin (HbA1c) between 5.7- 6.4% (Galicia-Garcia et al., 2020). The progression towards DM2 is determined by a group of factors (Paulweber et al., 2010),of which some are "non-modifiable" and others are "modifiable". Regarding non-modifiable risk factors, the most prevalent are (a) age, (b) race / ethnicity, (c) history of DM2 in first-degree relatives or with gestational diabetes, and (d) the presence of a polycystic ovary (Livadas et al., 2022; Wu et al., 2014). However, under a lifestyle approach, the most interesting factor are those defined as modifiable risk factors (Reddy, 2018). In addition, under this classification are included obesity, overweight and abdominal obesity, sedentary lifestyle, smoking, dietary patterns, as well as other disorders in glucose regulation which can be modulated under lifestyle interventions (Joseph et al., 2017). Thus, obesity and overweight increase the risk of impairment of glucose tolerance and DM2 at all ages, through an increment in insulin resistance (Cerf, 2013; Wondmkun, 2020). In addition, research confirms that more than 80% of DM2 cases can be attributed to obesity (Golay & Ybarra, 2005). Consequently, overweight reduction or conversion to normal weight also decrease DM2 onset risk, improving glycaemic control in patients with established diabetes (Wondmkun, 2020).

Moreover, a sedentary lifestyle entails a reduction in caloric expenditure, promotes weight gain, reduces aerobic capacity and muscle strength (Newton et al., 2013). Thus, sedentarism favours obesity and therefore increase the risk of DM2 (Langleite et al., 2016). Lifestyle modifications based on daily physical activity, avoiding tobacco and nutritional improvements, learning about health comorbidities according to obesity and DM2, as well as the study of these modifiable risk factors, are key interventions to reorient this prevalent pathology (Chester et al., 2018). Health education will be key for a successful treatment of this pathology (Chester et al., 2018). The establishment of pharmacological treatment in many occasions will be necessary but it will never replace the hygienic-dietary recommendations and physical activity (Raveendran, 2018). Certainly, physical activity improves insulin sensitivity, thus, it improves blood glucose levels to values in the normal range (Colberg et al., 2016; Hordern et al., 2012). To enhance glycaemic control, reduce or maintain body weight and/or reduce the risk of cardiovascular diseases, a plan of at least 150 minutes a week is recommended, developed in 3 to 5 weekly sessions of moderate to vigorous aerobic activity, at the 50-70% of your maximum heart rate with no more than 2 consecutive days of no activity (Colberg et al., 2016). However, shorter durations (minimum 75 min / week) of vigorous intensity or interval training (HIIT) may be sufficient for younger and more physically fit people (Colberg et al., 2010; Yang et al., 2014). However, previous research suggests that exercise programs may be designed according to specific modalities (Fritz et al., 2021). In this sense, Umpierre et al. (2011) concluded that aerobic exercise achieves a reduction in

HbA1c of 0.73% compared to 0.57% for strength training. However, when both training modalities were studied in combination, the total decrement of HbA1c was 0.51%.

Currently, medical guidelines have not well aggregated if new training methods as high-intensity interval training (HIIT) are an effective cost-benefit intervention in this patients (Paternina-de la Osa et al., 2017). Therefore, the objective of this review was to examine the effects of HIIT as part of the therapy of DM2. Specifically, it was intended to clarify whether the HITT causes an improvement in hemodynamic, analytical and anthropometric outcomes of DM2 patients, compared to other types of training, other physical activity or none at all.

SYSTEMATIC REVIEWS AND META-ANALYSIS ABOUT HIIT AND DM2

Regarding systematic reviews and/or meta-analysis, 5 articles have been published in the last five years (da Silva et al., 2019; De Nardi et al., 2018; Jiménez-Maldonado et al., 2020; Liu et al., 2019; Lora-Pozo et al., 2019; Picard et al., 2021):

In a recent systematic review with meta-analysis, (Picard et al., 2021), it was evaluated the effect of physical exercise on heart rate variability (HRV) in DM2 patients. Between the primary outcomes studied, it was found a usual comorbidity called cardiac autonomic neuropathy (CAN), which can trigger autonomous nervous system damage, coronary ischemia, arrhythmia, stroke, orthostatic hypotension and sudden death syndrome. Data included 21 interventions, where only 4 of the selected studies reported a HIIT protocol. Results, regarding HIIT elicit improvements in each exercise group, however, HIIT groups exerts more benefits in functional capacities than traditional resistance training, but not in VFC variables. Exercise enhanced essential biomarkers of DM2 including glycaemic control, insulin resistance, fat body mass, blood pressure, strength and lean body mass, despite of the insufficient number of non-resistance training protocols. Moreover, meta-analysis of the 4 HIIT studies reported benefits on HbA1c, BMI, total cholesterol, HDL, LDL, TGs and VO_2.

In other systematic review (Jiménez-Maldonado et al., 2020) found a primary role of glycemia in the prevention of comorbidities related to metabolic syndrome in DM2. HIIT alone or imbedded in a resistance training intervention exerts a positive impact on glycaemic in DM2 and non-dysmetabolic subjects comparable to aerobic training, which was fixed as the comparative reference.

Lora-Pozo et al. (2019) in a systematic review with meta-analysis of randomized control trials, explored the effects of HIIT compared to passive controls and other exercise interventions (e.g., aerobic exercise) in DM2 patients. Collected data reported anthropometric, cardio-pulmonary and metabolic measurements. After statistical analysis, obtained results favoured HIIT interventions, compared to passive controls: (Weight: standardized mean difference (SMD) = -2.09; 95% confidence interval (CI): (−3.41; −0.78); BMI: SMD = −3.73; 95% CI: (-5.53; -1.93); Systolic blood pressure: SMD = −4.55; 95% CI: (−8.44; −0.65); VO_{2max}: SMD = 12.20; 95%CI: (0.26; 24.14); HbA1c: SMD = -3.72; 95%CI: (−7.34; −0.10)]). Concerning HIIT effects compared to other interventions, this meta-analysis manifested positive improvements in weight loss, BMI, systolic blood pressure, VO_{2max} and HbA1c. This study also suggested better results in the moderate intensity exercise in contrast to lower intensities groups.

In a 5 RCTs systematic review (da Silva et al., 2019), authors examined the effects of a HIIT intervention in comparison to low or moderate interval training on blood glucose in DM2 patients. This review was characterized for being the first one analysing the impact of HIIT in DM2 with a RCT eligibility criteria. Most

studies reported significant differences for weight and BMI in HIIT interventions. Metabolic profile measurements (SBP, DBP, cholesterol, TGs, fasting glucose and HbAC1) related to HIIT protocols were examined in only 1 study; significant differences were found for SBP and HDL cholesterol in 2 studies. Only 1 study reported data for medium intensity interval, showing improvements in LDL levels. Blood glucose was examined in 4 studies; all the selected interventions obtained significant differences for HIIT and moderate intensity training protocols.

Liu et al. (2019) developed a systematic review with meta-analysis of 13 studies (n = 345) exploring the effectiveness of HIIT on glycaemic control and cardio-pulmonary fitness. In this review HIIT was compared with moderate intensity interval training and a passive control in DM2 patients. HIIT protocols resulted in a positive reduction in fat body mass, HbA1c (SMD: - 0.37, 95% CI: - 0.55 ; - 0.19, $p < .0001$); VO_2 relative peak (SMD: 3.37 ml / kg / min, 95% CI: 1.88 ; 4.87, $p < .0001$); VO_2 absolute peak (SMD: 0.37/ min, 95% CI: 0.28 ; 0.45, $p < .00001$) fasting insulin, weight (SMD: - 1.22 kg, 95% CI: - 2.23 ; - 0.18, $p = .02$) and BMI (SMD: - 0.40 kg / m^2, 95% CI - 0.78 ; - 0.02, $p = .04$) compared to moderate intensity training.

In a meta-analysis of 7 low of risk bias studies (De Nardi et al., 2018), explored the impact of HIIT in comparison to continuum training in metabolic biomarkers of pre-DM2 and DM2 patients. HIIT increased significantly in 3.02 ml / kg / min (CI 95% 1.42-4.61) VO_{2max} in contrast to moderate intensity training. No differences were found between both training modalities for A1c, SBP, DPB, total cholesterol, LDL, HDL, BMI and waist to hip ratio (WHR).

Clinical guidelines concerning HIIT and DM2

Clinical practice guidelines targeting DM2 were also reviewed. HIIT was only mentioned in the Canadian Clinical Practice Guidelines (2018) and in the evidence summary of Dynamed (2018).

The Canadian Clinical Practice Guidelines (2018) discussed the benefits of HIIT within the chapter dedicated to physical activity and diabetes. It is known that HIIT induces greater cardiorespiratory functional adaptations but, when talking about patients with DM2, HIIT also seems to be more effective to improve glycaemic control compared to lower intensity continuous exercise. It is recommended for DM2 patients to perform interval trainings (short periods of vigorous exercise alternating with short recovery periods at low-to-moderate intensity or rest from 30 seconds to 3 minute each) aiming to improve their cardiorespiratory fitness (Grade B, Level 2).

In the evidence summary of Dynamed (2018) targeting alternative treatments for diabetes, HIIT is included as a plausible exercise protocol to reduce fasting glucose levels and HbA1c in patients with DM2 (Evidence level 3) based the findings reported by a randomized clinical trial.

Summary of the effects of HIIT on patients with DM2

Lingvay et al (2021) declared that obesity management should be the primary treatment for remission of DM2. In a recent study (Taheri et al., 2020), randomly assigned 158 patients with DM2 to an intervention (n = 79) and a control group (n = 79). The intervention group underwent lifestyle modifications with physical activity and nutrition interventions and was compared to another group based on general recommendations (passive control group). The intervention group lost 11.98 kg (95% IC: 9.72 a 14.23) while the control group lost 3.98 kg (95% IC: 2.78 a 5.18). Besides, the intervention group achieved a significantly greater remission of type 2 diabetes mellitus (61 vs. 12%).

High intensity training improves health parameters regardless of the induced weight loss (Gaesser & Angadi, 2021). In the latest guidelines for the management of heart failure by the European Society of Cardiology (McDonagh et al., 2021), it is recommended to perform 75-150 minutes of high intensity physical exercise per week aiming to reduce all causes of mortality, cardiovascular mortality and morbidity (IA evidence). In fact, Gaesser et al. (2020) state that the treatment of obesity (key for the treatment of type 2 DM) should focus on physical exercise due to its benefits regardless of weight loss: (1) The risk of mortality associated to obesity is attenuated or eliminated by moderate-high levels of cardiorespiratory fitness (measured by VO_{2max}) or high levels of physical activity (measured by number of steps per day, among others); (2) Most of the cardiometabolic risk markers associated to obesity can be improved with physical exercise independently of weight loss (Colberg et al., 2010). Improved cardiorespiratory fitness or elevated levels of physical activity are associated with greater reductions in mortality compared to weight loss alone (McDonagh et al., 2021).

At physiological and molecular levels, HIIT would regulate both lipid and glycaemic metabolism (Sabag et al., 2021). Focusing on glycaemic metabolism, HIIT would improve the quantity and quality of mitochondria organelles, which are key in the beta oxidation of fatty acids (Sabag et al., 2021). These effects would reduce the accumulation of ceramides and diacylglycerides, lipids that decrease insulin sensitivity by several mechanisms. In addition to the inhibition of protein kinase C resulting from physical exercise, it would induce an increase in the translocation of GLUT4 receptors at the muscle level, increasing peripheral glucose uptake and increasing the storage capacity of muscle glycogen (Banday et al., 2020; Sabag et al., 2021).

HIIT provides greater benefits to functional capacity compared to resistance training (Jiménez-Maldonado et al., 2020; Picard et al., 2021). Both, resistance training and HIIT improve glycaemic control, insulin resistance, fat mass, blood pressure, strength and lean body mass (Jiménez-Maldonado et al., 2020). Combining resistance training and HIIT improved only some results (Jiménez-Maldonado et al., 2020). On the other hand, HIIT and sprint interval training improve glycaemic control to a similar or greater degree than aerobic exercise in populations without metabolic syndrome or DM2 (Jiménez-Maldonado et al., 2020). HIIT improves body weight and significantly reduces BMI (da Silva et al., 2019; Lora-Pozo et al., 2019). Despite this, HIIT does not seem to induce greater effects compared to other exercise interventions. On the other hand, HIIT improves VO_{2max} absorption in DM2 patients, which indicates the maximum capacity of the cells of our body to absorb and use oxygen, also predicting glucose clearance by plasma insulin (De Nardi et al., 2018).

CONCLUSIONS

In conclusion, HIIT is a safe and recommended effective exercise for patients with DM2 to improve their functional capacities, body weight, BMI, blood pressure, VO_{2max} and Hb1Ac. There is no drug or nutritional intervention that could replace physical exercise benefits. Physical exercise is applicable to the entire population regardless of their financial resources. Further research is needed to clarify the most effective HIIT protocol depending on the targeted population.

AUTHOR CONTRIBUTIONS

All authors have worked in the development of this study. The study was conceived by AKR and APC, the literature search and reviewed was performed by AKR, PJM, APC and CAF, all authors participated in writing and the final critical revision of the manuscript.

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DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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