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Relationships between physical activity metrics of intensity and diabetes

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Introduction

Diabetes is a serious metabolic health problem that currently affects approximately 37.3 million or 11.3% of U.S. adults, with another 23% who are undiagnosed.[1] The global prevalence of diabetes continues to expand[2] with an expected increase from 451 million in 2017 to 693 million by 2045.[3] Costs for diagnosis and treatment increased by 26% in the last 5 years alone,[4] of which approximately 19 to 34% are attributed to diabetic foot ulcers (DFUs).[5] Lifestyle interventions such as physical activity (PA) and the maintenance of a recommended body weight improve insulin sensitivity, pancreatic ß-cell function, glycemic control, prevent obesity[2] and decrease the propensity for atherosclerosis.[3] An estimated 31 to 37% of those with diabetes engage in quantities of PA consistent with the recommended guidelines.[6] While improving anthropometric and metabolic (i.e., HbA_{1C}) parameters helps to prevent the insidious complications associated with diabetes, [2, 7] numerous challenges exist when attempting to increase quantities of PA, such as the risk for DFUs.[5]

Background

Physical activity is considered a cornerstone in the prevention and treatment of prediabetes and type 2 diabetes (T2D) and the treatment of type 1 diabetes (T1D).[7] Moderate intensity PA improves insulin resistance and reduces the risk for cardiovascular (CV) morbidity and mortality in individuals with diabetes.[7] Individuals with diabetes typically have diminished fitness;[8] however, PA can prevent the development of such complications as DFUs.[6-7] The current PA Guidelines for Americans[9] are applicable to all adults with diabetes with consideration to age and existing co-morbidities. The importance of high-intensity interval exercise (HIIE) for individuals with T2D was recently validated by the American College of Sports Medicine (ACSM)[2] in a consensus statement that updated the 2010 joint

ACSM/American Diabetes Association position statement on PA and exercise in individuals with T2D.[10] The ACSM recommends engaging in HIIE regimens involving aerobic training between 65% and 90% VO_2peak or 75% and 95% heart rate peak for 10 seconds to 4 minutes with 12 seconds to 5 minutes of active or passive recovery, in addition to various PA modes, flexibility and balancing exercises, and reducing sedentary time.[2] Compared with PA performed at lower intensities, HIIE provides CV health benefits by improving fitness, body composition (BMI) and reducing HbA_{1C} levels in individuals with T2D.[11]

PA metrics such as cadence and the 6-minute walk test (6MWT) reflect PA intensity.[13] Cadence is measured in steps per minute.[12] Walking cadence has a strong relationship with PA and is measured in in metabolic equivalents (METs).[12, 15] Slow walking cadence is 60 – 79 steps per minute, medium cadence is 80–99 steps per minute, and brisk cadence is 100–119 steps per minute.[12] An appropriate intensity of PA is especially important to consider as heart rate and blood pressure readings have been found to be higher in those with T2D compared to controls after performing a 6MWT.[14] Moreover, an association was found between CV response and higher cardiac work in individuals with T2D who experienced the same rating of perceived exertion (RPE) that was attributed to diabetes rather than body composition, PA or fitness levels.[14] Cardiometabolic risk decreased when steps per day was combined with cadence during higher intensity PA (peak 30-min cadence expressed in steps/min).[16] Grace et al.,[17] found higher intensity training was superior to low-intensity training for individuals with T2D consistent with ACSM recommendations. To successfully configure an effective PA intervention, it is important to understand factors associated with the PA response in diabetes. Identifying those factors associated with efficacy of PA interventions will provide insight into targeting resources to prevent diabetes-related complications such as DFUs for the development of effective exercise prescriptions in diabetes. The purpose of this study was to examine relationships between baseline and post-intervention clinical variables (HbA1c, weight, max steps per episode, cadence, daily step count and 6-minute walk test) to increase PA in adults at risk for DFUs.[18] We hypothesized that post-clinical metrics of PA intensity measured by cadence and max steps per episode would be more strongly associated with weight and HbA_{1C} than metrics of PA quantity.

Methods

Research Design and Participants

The current study was performed as a secondary analysis of a previous outpatient population study conducted as a feasibility study.[18] Briefly, the feasibility study[18] involved sedentary adults with T1D or T2D to explore the feasibility of increasing PA without increasing the incidence of DFUs. Study criteria included participants who were (a) $\geq$ 21 years of age, (b) diagnosed with diabetes (T1D or T2D, $HbA_{1C} > 6.5$), (c) had evidence of peripheral neuropathy by a loss of protective sensation (identified by 10-gram Semms Weistein Monofilament in either foot at one of four sites tested [1st, 3rd, 5th metatarsal heads, and plantar surface of hallux]),[6] (d) were able to speak and read English, (e) had physician approval, and (f) had internet access. Those who had evidence of a (a) foot ulcer; (b) self-report of at least 2 bouts (20+ minutes) of weekly physical activity; (c) a diagnosed significant medical illness (renal, liver, or thromboembolic disease); (d) proliferative retinopathy or an ankle brachial index (ABI) < 0.6; (e) inability to engage in PA without assistance; (f) autonomic neuropathy as evidenced by tachycardia (at rest) OR orthostatic hypotension; or (g) pregnant or planning pregnancy in next 3 months. Two institutions were involved in conducting the study which was approved by both institutional review boards. Eleven of the twelve initial participants completed (91.67%) the study, and the outcomes are included in the analysis. Subjects were recruited from a university affiliated outpatient clinic and a local VA podiatry clinic and through flyers posted at a university located in a Chicago suburb. All supervised PA sessions were supervised by trained medical researchers in the gait lab of a university setting.

Measures

The variables of age, fasting glucose, HbA_{1C}, weight, 6MWT, steps per day, max steps per episode and cadence, were obtained during screening and at baseline in the feasibility study and were extracted for use in this secondary analysis. The same variables were also examined following the 10-week PA intervention phase of the study.

Age. Demographics to include age, were obtained.

Glucose. Baseline fasting blood glucose was obtained following a 24-hour fast by the research assistant (phlebotomist) and evaluated by Quest Diagnostic Laboratory.

HbA_{1C}. HbA_{1C} was obtained in the same vial as fasting glucose.

BMI. BMI was calculated from height and weight (weight[kg]/height^2[meters]).[19] Participants wore only light clothing and no shoes.

Participants wore a PA monitor called a PAMSys™(BIOSENSICS) device that uses kinematic sensors for a 7-day step count assessment of PA metrics.

PA Intensity. Cadence and maximum steps per episode were measured by PAMsys for 7 days at baseline and following the intervention.

6-Minute Walk Performance (Distance). The 6MWT is a measure of PA intensity that was not measured by PAMSys. This test was performed in the gait lab during the baseline visit. Participants walked back and forth for six minutes; they were allowed to slow down, stop, and rest when necessary and received verbal encouragement every minute, and a 15 second warning before it was time to stop.

PA Quantity. Steps per Day. Daily step count was measured by FitBit during the 10-week PA intervention period.

Procedures

All assessments were completed during the screening, baseline, and the follow-up visit. A flowchart of the procedures is detailed in Figure 1, including the 10-week PA intervention phase.

****INSERT FIGURE 1 HERE****

Visit 1: Screening

During screening, ethical considerations and study proceedings were reviewed, and each participant provided written informed consent following an initial assessment to determine eligibility. Participant data were obtained in the following order: demographic data and medical history, height, weight, degree of peripheral neuropathy, fasting glucose and HbA_{1C}. Participants completed the Revised Physical Activity Readiness Questionnaire to establish safe exercise ability[19] and were given the PAMSys^{TM} for a 7-day step count assessment of PA metrics.

Visit 2: Baseline

A 6MWT distance (meters) was performed to establish baseline fitness, DFU prevention strategies were implemented, and all participants received an activity monitor (Zip, FitBit Inc.) and were invited to join a Fitbit support group to meet step count goal. Step count was measured via Fitbit based on a pre-determined PA prescription.

Physical Activity Intervention: Visits 3 through 6 and Remote Phase

During visits 3 through 6, participants walked for 5-20 min on a treadmill to assess CV response during four supervised PA sessions (2 weeks) and set goals to increase daily step count.

During the remote phase (8 weeks) of the 10-week intervention, participants gradually increased steps per day (by 50 steps) after first receiving training to assess plantar foot temperature and blood glucose for safety. A digital thermometer was used to assess the surface of each foot to see if the difference between two plantar sites (i.e., left great toe vs right great toe) exceeded 4° F for 2 consecutive days. If so, participants were advised to reduce activity until temperatures normalized.

Final Post-Intervention: Visit 7

Following the 10-week PA intervention, assessment of fasting glucose HbA_{1C}, weight, 6MWT performance and 7-day PA metric assessment by PAMSys were completed. Participants received modest compensation ($175.00 gift cards) after completing screening, baseline, and following the PA intervention.

Data Analyses

Nonparametric methods, Wilcoxon Rank test, and permutation test were utilized to determine the differences in mean scores of the clinical variables, average cadence, max steps per episode, 6MWT and steps per day. Spearman correlation was employed to identify associations among weight, HbA_{1C}, and PA metrics. Data were analyzed using SAS 9.4 (SAS Institute Inc., Carry, NC) and R version 4.1.0 (R Foundation for Statistical Computing).

Results

Demographic

Of the twelve adult participants between 48 to 74 years of age (average 59.92, SD = 8.68) who began the study, 11 (91.7%) completed all measures. The majority were female (n = 8, 72.7%) from the ethnic groups of non-Hispanic (n=11, 100%), Caucasian (n=9, 81.1%), African

American (n=2). Most participants had T2D (92%) with an average duration of diabetes of 13 years (range, 1 to 21 years, SD = 6.63).

Anthropometric and Weight

The participants' average BMI was 38.15 kg/m^2 to qualify as obese, class 2.[20] Average baseline weight decreased by 4% from 240.3 pounds (SD = 49.5) at baseline to 230.4 pounds (SD = 36.6) post-intervention, although the difference was not statistically significant (p=0.55).

Physical Activity Metrics

Average steps per day and max steps per episode increased by 21 and 24%, respectively. Average step count increased by 21% (p=0.151) or 971 steps per day, from 3867 (SD = 1493.15) steps at baseline to 4661.73 (SD = 1516.24) at post-intervention. This increase is notable for a 10-week period, especially considering participants had neuropathy. The average distance walked in six minutes improved by 15 meters (4.5%) from 334.83 (SD = 80.73) from baseline to 349.93 (SD = 111.95, p=0.689) post-study although this increase was not significant. The average pre- to post-max steps per episode increased by 24% (109 steps), from 746.83 (SD = 621.20) at baseline to 925.64 (SD = 729.95) post-intervention, although this increase was not significant.

HbA$_{1C}$ and Glucose

HbA$_{1C}$ decreased from an average of 8.43% (SD = 1.40) at baseline to 8.19% (SD = 1.37) post-study (p=0.289, $d_m = -0.235$). While the improvement in HbA$_{1C}$ was not significant, average fasting glucose decreased by 25.6% ($p = 0.018$, $d_m = -52.93$) ($p < .05$) from a baseline level of 208 mg/dl (SD = 107.25) to 154.72 (SD = 69.32) mg/dl following the PA intervention.

Correlations Between HbA$_{1C}$, Weight and PA Metrics

A correlation analysis was performed to determine associations between PA metrics, HbA_{1C} and weight. Spearman correlation coefficients of baseline variables demonstrated (Table 1) Pre-HbA_{1C} was not associated with max steps per episode (r=0.026, p=0.93), 6MWT (r=-0.09, p=0.78) or average cadence (steps/min) (r=-0.024, p=0.93). Following the PA intervention, HbA_{1C} was associated with max steps per episode (r=-0.63, p=0.03) and 6-minute walk test (r=-0.50, p=0.09) but not with average cadence (r=-0.37, p=0.23). Steps per day was not associated with HbA_{1C} (r=0.19, p=0.55) before or after the intervention (r=-0.03, p=0.92). Weight assessed during screening was associated with average cadence (r=-0.76, p=0.007) but not with max steps per episode (r=-0.41, p=0.18) 6MWT (r=-0.30, p=0.34) or steps per day (-0.097, p=0.98). Post-intervention weight was related to max steps per episode (r=-0.62, p=0.03) and average cadence (r=-0.60, p=0.04) but not 6MWT (r=-0.13, p=0.69) or steps per day (r=-0.034, p=0.98).

****INSERT TABLE 1 HERE****

Discussion

The purpose of this study was to explore relationships between clinical predictor variables pre and post a 10-week PA intervention in adults with diabetes. Consistent with our hypothesis, HbA_{1C} and weight were associated more strongly with metrics of PA intensity (cadence, max steps per episode, and 6MWT) than with steps per day. We, therefore, conclude that an increase in PA intensity may be more beneficial in individuals with diabetes to improve glycemic control and weight, consistent with the recent ACSM consensus statement.[2] It is well-established that HbA_{1C} levels are more strongly associated with PA intensity than quantity.[2, 7] Consistent with our findings, HbA_{1C} was associated with max steps per episode and the 6MWT following the PA intervention – both PA metrics reflecting intensity. Before the intervention, HbA_{1C} was not associated with max steps per episode, 6MWT, average cadence or steps per day suggesting the PA intervention was beneficial. Steps per day, a PA metric not specific to intensity, was not associated with HbA_{1C} before or after the PA intervention. Nor was weight associated with steps per day before or after the PA intervention, yet the average daily step count increased by 971 steps post-study.[18] The lack of significance between HbA_{1C} and certain metrics of PA may have been due in part to the duration of 10 weeks as HbA_{1C} reflects average glucose levels for 90-120 days. A longer study duration may provide a more accurate reflection of the HbA_{1C} response, especially to PA metrics of intensity. In addition, the decrease in average HbA_{1C} following the 10-week intervention was not significant, therefore, average fasting glucose levels may have been more reflective of participants' metabolic state. Glucose levels decreased significantly following the PA intervention by 25.6% (208 [±107.25] mg/dl to 154.72 [±69.32] mg/dl) which corresponded with the increased step count and intensity. Baseline glucose (fasting = 208 mg/dl) was mildly elevated considering the diabetes diagnostic criteria (fasting = 126 mg/dl); therefore, even gradual increases in PA may influence glucose control.

Participants' average baseline weight represented class 2 obesity but decreased following the PA intervention. The ACSM recommends moderate to high-intensity PA four to five days per week for weight loss and weight loss improves glycemic control.[6] A relationship was observed between PA metrics associated with intensity and weight in our participants although weight was not associated with step count before or after the PA intervention. A negative association between step intensity and mortality was observed by Saint-Maurice et al.,[15] and Yates and colleagues found higher gait speeds and higher self-reported walking pace was associated with a lower mortality risk.[21]

Cadence[12, 22] was associated with weight and max steps per episode in our findings after the 10-week PA intervention consistent with the outcomes of Saint-Maurice et al.[15] Higher weights and BMIs also influenced cadence in the findings of Retory and colleagues.[23] The 4% decrease in participants' average weight (12.9 pounds) following the PA intervention may have influenced participants' average cadence post-study. Retory and colleagues[23] found cadence, step length and 6MWT were significantly lower in subjects who had higher BMIs compared to controls. Gill also found excess weight influenced gait in overweight adults with slower cadences compared to normal-weight adults.[24] The lack of association between weight and 6MWT in our findings may have been due to the methodology used to administer the test.

Implications for Diabetes Care and Lifestyle Management

The findings of our study demonstrate important clinical implications for preventing and mitigating CV complications in those with diabetes. The pathogenesis of diabetes involves microvascular and macrovascular complications, including CV disease and neuropathy leading to DFUs. For those with diabetes who typically have lower VO_2peaks[8], exercise prescriptions should be individualized to include a gradual increase in intensity to improve metabolic outcomes.[25] The ACSM consensus statement[2] currently prioritizes PA intensity over quantity as an update ADA recommendations in addition to[7, 10] interrupting sitting time with PA to improve blood glucose and insulin levels.[2] Rather than vigorous regimens during exercise, Schwaab and colleagues[8] recommend a 'comfort zone' during PA in which 'walking and talking' are 'comfortable' to encourage PA adherence and sustainability.[25] While participants had diminished glucose control (average HbA_{1C}, 8.43%; average glucose level, 208 mg/dl) at baseline, increases in PA quantity and intensity occurred without DFU incidence. Those with worse glucose control, either in the form of glucose modulations or higher fasting glucose levels, may require more in-person support to derive benefit from PA interventions.

Limitations

This secondary analysis had certain limitations. The sample size was small due to limited enrollment, not completing visits or failure to meet inclusion criteria. The small sample and participant homogeneity decreased the likelihood of detecting differences in the outcomes. The lack of a control in the original study tempered the conclusions. Additional research with similar hypotheses and a larger and more diverse sample size is warranted to determine the relationships among HbA_{1C}, weight and metrics of PA. In spite of small sample, the study demonstrated the importance of correlating PA with comorbidities in adults with diabetes.

Conclusions

PA is an effective treatment and prevention strategy in adults with diabetes although increasing quantities of PA may pose significant challenges. PA metrics reflecting intensity, cadence and max steps per episode, more strongly influenced HbA_{1C} and weight than did steps per day indicating the potential for CV benefits in diabetes. Future research to identify factors that predict the response to PA interventions in individuals with diabetes will allow for refinement of interventions and the targeting of resources to prevent diabetes-associated complications for those in greatest need of support.

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