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Exercise Regimen Recommendations in Type II Diabetics and Their Effects on Glucose Control

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Abstract

The most effective non-pharmacologic method of reducing the hemoglobin A1c (HgbA1c) levels in type II diabetic patients is still debated. Clinicians evaluating and treating Type II Diabetics (T2DM) generally recommend diet and lifestyle modifications as initial therapy. The medical literature comparing different types of exercise and their effects on glucose control was reviewed with the goal of determining whether aerobic or resistance exercise was more effective for reducing HgbA1c levels in type II diabetics. The more effective form of exercise, if any, could then be recommended in addition to diet and other lifestyle changes. Although the studies were heterogeneous in their methods of comparison, no significant differences in their overall reductions in HgbA1c measures were found between aerobic and resistance training. Moreover, the greatest decreases in HgbA1c levels changes were observed with a combination of aerobic and resistance training. More extensive research is needed to determine the long-term effects of exercise programs on HgbA1c levels.

Introduction

One in three Americans will develop type II diabetes (T2DM) in their lifetime, with current projections estimating closer to 50% of the population will develop a form of diabetes or insulin resistance.[1] Diabetes is associated with greater costs and use of medical resources than any other medical diagnosis alone.[2] This financial burden is due to both primary and secondary complications associated with poorly controlled diabetes. Diabetic control is commonly assessed by blood glucose determinations. Hemoglobin A1c (HgbA1c) measurements capture average glucose levels over a 90-day period and provide important data about a patient's glucose control. Furthermore, high HgbA1c levels are associated with increased risks of diabetes complications.

A one percent decrease in this value is associated with a 15-20% decrease in cardiovascular event risk and a 37% decrease in microvascular diabetes complications.[3] These facts alone are motivation for clinicians to encourage patients to engage in preemptive measures to prevent both the development of diabetes and, when it is already present, to prevent its progression and complications.

Exercise has been established as beneficial for assisting blood glucose control in diabetes. Mechanisms for improved control include the short-term changes of glycogen store breakdown to glucose and the long-term effects in the upregulation of GLUT-4 receptors induced by muscle contractions.[4] This upregulation subsequently increases insulin sensitivity in peripheral receptor sites in muscles and tissues, ultimately supporting better glucose control. Aerobic exercise particularly increases oxidative capacity, blood vessel compliance, lung function, and cardiac output.[5] Resistance (strength) training has been shown to increase oxidative muscle capacity, insulin sensitivity, and glycemic control as well, though this form of exercise has not been as extensively studied as aerobic exercise.

Aerobic exercise incorporates the use of large muscle groups to move the body in the form of walking, jogging, swimming, or biking. Resistance exercise involves more isolated muscle movement against a sustained force using free weights, body weight, weight machines, or elastic bands. Sustained physical activity shows improvements in weight loss, cardiopulmonary fitness, blood glucose control, blood pressure, lipid control, and microvascular complications of diabetes. Ultimately, these physiologic changes amount to reductions of approximately 40-70% of the complications associated with T2DM**.** The American Diabetes Association currently recommends that adults with diabetes should engage in at least 150 minutes of exercise, of

moderate to vigorous intensity, to be spread out over three days with no more than two consecutive days without exercise.[6] Diabetics should also include two to three sessions per week of resistance training on nonconsecutive days.[6]

More time and resources have been dedicated to studying the effects of aerobic, rather than resistance, exercise training. In diabetics, aerobic exercise has been promoted for its cardiovascular effects, HgbA1c lowering effects, and general ease of performance. Recent research suggests a role for resistance exercise training in diabetic patients; it increases muscle mass and may be a preferable option for patients who are not able to perform aerobic training programs. Previous evidence has not indicated whether one form of exercise was superior to another. For that reason, glucose control, over at least 12 weeks duration, resulting from specific aerobic or resistance training compared with standard diabetic treatment will be examined**.**

Recommendations for exercise programs in diabetics should incorporate individual patient factors: their functional status and ability to perform exercise, interests and motivations for exercising, and their baseline status as a diabetic. Compliance with an exercise program is an important consideration and is enhanced by considering these patient factors. Generally, both aerobic and resistance exercises are recommended to patients with diabetes. Thus, clinicians should first recognize which forms of exercise would most likely produce maximal results for patients. Then clear and achievable exercise goals reflecting patient preferences and abilities could be recommended. With individualized exercise instructions, patient adherence rates may increase, thus potentially improving glucose control.

Discussion

Each of the studies examined utilized unique approaches to evaluate metabolic control. Nonetheless, all studies measured hemoglobin A1c as an outcome of exercise effectiveness. Most of the randomized control trials (RCTs) used similar exercise regimens to compare HgbA1c measures. The methods included aerobic exercise in the form of walking, jogging, swimming, and biking**,** while resistance exercise regimens utilized weight lifting or resistance machines. Supervised training regimens in a controlled, indoor environment was common to all the studies in order to control for extraneous variables associated with independent exercise programs. Training regimens generally consisted of exercise for at least three days per week, similar to ADA guidelines. Additionally, studies were all at least three months in duration to ensure appropriate evaluation of HgbA1c changes.

Aerobic Exercise

Aerobic exercise training programs have long been studied and recommended for both glycemic control and cardiovascular benefits for diabetic patients. A systematic review and meta-analysis by Yang et al. comparing 12 randomized control trials including 626 type II diabetic participants found greater reductions in HgbA1c measurements among participants in the aerobic exercise category, -0.46%, compared with -0.32% in the resistance training group.[7] However, this difference was statistically insignificant. Additionally, the average study duration was only 16 weeks, which limited assessment of the long-term effects of each type of exercise on HgbA1c levels. The heterogeneity of the RCTs made it difficult to draw significant conclusions for clinical practice, specifically whether to emphasize aerobic training over resistance training.

The Diabetes Aerobic and Resistance Exercise (DARE) Trial, a large randomized control trial comparing 251 previously inactive diabetic adults, ages 39-70, found overall a slightly greater HgbA1c reduction in aerobic training regimens (-0.51%) compared with resistance training (-0.38%).[3] After 22 weeks of supervised exercise training, reductions were observed in both aerobic and resistance exercise training participants, though the combined exercise training group experienced even greater reductions in A1c levels compared to either type of training alone. Although overall aerobic training produced slightly greater reductions in HgbA1c compared to resistance training, only the combined exercise training group produced significant changes when the baseline A1c was greater than 7.5%, indicating superior benefit from combined training.

The DARE Trial was later referenced in the Resistance versus Aerobic Exercise in Type 2 Diabetes (RAED2) trial, which produced comparable data for HgbA1c levels between aerobic (-0.40%) and resistance (-0.35%) training regimens.[5] This 16-week trial also revealed an inverse relationship between insulin sensitivity and reductions in A1c levels, with no significant difference between the aerobic and resistance training regimens. This finding may be due to the different physiological impacts of aerobic and resistance training. Synergistic benefits of glucose control were observed in the combined training group, though these superior results may be due to the increased time spent completing both full exercise regimens. Aerobic and resistance exercise training sessions were each one hour in duration; therefore, the combined training group performed two hours of exercise to complete both regimens, doubling the overall benefit from the exercise training programs.

Additionally, the DARE trial was included as a major contributing study in a systematic review and meta-analysis comparing eight globally published articles and included 276

participants. This analysis found similar results to the DARE trial since the greatest HgbA1c reductions were observed in the combined training program participants.[8] Small differences in HgbA1c levels were observed when comparing aerobic to resistance training exercise regimens, -0.40% to -0.35% respectively. After applying the GRADE system for determining the quality of evidence to these studies, the evidence for suggesting a difference between aerobic and resistance exercise training regimens was determined to be low-quality. Ultimately, the conclusions from this study are not easily extrapolated to the general population due to the risk of bias (not providing full descriptions of results) and the overall heterogeneity of the studies included in the review.

Comparing low intensity and high intensity aerobic exercise, an overall decrease in HgbA1c by 0.3 +/- 0.2% was observed with no significant difference observed between the intensity of the groups according to Hansen et al.[9] For six months duration, 37 obese males with controlled T2DM (A1c <7%) were randomly assigned and engaged in supervised low intensity or high intensity exercise groups for three days per week. Though these results were limited due to the exclusively male participant enrollment and overall small sample size, the extended duration and lack of significant difference between the intensities provide data to support the premise that the intensity of exercise does not have a significant effect on the improvement in metabolic outcomes. This concept is particularly important when considering patient adherence to an exercise program; an inverse relationship was observed between the increasing intensity of exercise and program adherence. Low intensity exercise can be recommended for patients to effectively reduce HgbA1c measurements.

Resistance Exercise

Although aerobic training has long been studied and promoted as effective for improving metabolic outcomes in diabetics, resistance training more recently provided evidence with similar results and has been endorsed for diabetic patients. High intensity interval training (HIIT) has become popular as a form of exercise and has been highlighted to improve metabolic outcomes better than aerobic exercise alone. A parallel randomized control trial of 80 adult diabetic participants compared the effectiveness of HIIT paired with resistance training versus moderate continuous training (aerobic) combined with resistance training on HgbA1c measures.[10] Ultimately, the evidence did not confirm that HIIT training was more effective for reducing A1c compared with moderate continuous training. Instead, the authors concluded that after one year of training, the moderate continuous training combined with resistance exercise was the only group that experienced significant reductions in A1c measurements. Though this study had an adequate duration of follow-up and an appropriate number of participants to strengthen its evidence, the profile of the participants, the average age of 58.5 years, and baseline HgbA1c values of 7.2% may not represent the typical diabetic patient.

In an RCT that included patients with an average baseline HgbA1c of <7.6%, statistically significant differences were not observed among aerobic, resistance, combined, and controlled group interventions.[11] Nonetheless, the resistance training group showed the greatest overall reduction in HgbA1c (-0.23%) over the course of the 12-week study, which may have been due to the higher average baseline HgbA1c values in this group. This study reinforces the concept that greater reductions in metabolic outcomes are generally observed with higher baseline HgbA1c values**;** otherwise no significant differences between the types of exercise performed were observed.

This assumption that higher baseline HgbA1c and fasting blood sugar correlate with greater changes in HgbA1c after exercise training was further supported by a 16-week trial of 43 adult diabetics with an average baseline A1c of 8.7%. Resistance training reduced HgbA1c levels by 1.2% compared to a reduction of 0.3% in the endurance training group.[12] Published in 2005, this trial was one of the premier studies promoting resistance training over aerobic training in order to produce greater reductions in HgbA1c, though the authors acknowledged that the higher baseline HgbA1c levels do limit the generalizability of these findings.

Authors Castaneda et al. recognized that minority populations are disproportionately outnumbered in terms of T2DM diagnoses compared to majority racial groups.[13] A 16-week RCT with 60 Latino participants examined the effects of resistance training programs on HgbA1c measures. Progressive resistance training was shown to improve HgbA1c levels from baseline by 1.2% compared to the control group, Latinos who did not engage in resistance exercise training. The baseline glucose control in the progressive resistance training group (~8.7%) was slightly less than the control group (~8.4%), which may have contributed to the significant reductions. Although this study did not include an aerobic training group, the overall effectiveness of resistance training was demonstrated in the Latino population, who make up a disproportionately high percentage of the diabetic population.

A systematic review and meta-analysis by Snowling and Hopkins with 1,003 participants initially revealed that the greatest HgbA1c reductions occurred in resistance and combined training groups with average reductions of 0.8 +/- 0.3% in both groups.[14] Upon further weighted mean analysis, however, differences among the training modalities were not significant. This conclusion was drawn by reviewing 27 randomized, parallel-group controlled trials of training programs including resistance, aerobic, combined training, and control modalities in diabetic

patients for a minimum of 12 weeks duration. Even though these results gave credit to the benefits of resistance training, the findings of the analysis were limited due to the heterogeneity of the studies' designs, populations, and descriptions of exercise methods. The disproportionately high number of aerobic training regimens compared with resistance training programs may have skewed the data as well. Hence, the overall average HgbA1c reduction might have been affected either positively or negatively by this heterogeneity.

Similarly, in a short 10-week randomized control trial, greater reductions were observed in the resistance training group (-1.8%) compared to the aerobic training group (-1.1%).[15] The difference in HgbA1c control between these groups, however, was not significant. Furthermore, this study's findings were limited due to the short duration and the small sample size, (n=14)**.** In addition, compared with the aerobic training group, the resistance training group had higher baseline HgbA1c values, which disparity might have resulted in the greater reductions of A1c values in this group. Nonetheless, this tightly controlled RCT did provide evidence supporting the recommendation of either aerobic or resistance training, and imputed a slight advantage with resistance training.

Combined Training

A large (n=262) randomized control trial found that significant reductions in HgbA1c levels were only observed in the combined training group, reducing HgbA1c by approximately -0.34% over a nine month exercise intervention period.[17] Study participants had an average baseline HgbA1c of 7.7%, and were previously sedentary. Many had co-morbidities in addition to diabetes. The characteristics of this study design, including duration, population, and sample size, imparted high external validity by more accurately representing an average diabetic patient.

Additionally, these results were significant since exercise duration remained essentially equal among all training groups, opposed to completing more exercise in the combined training group. This finding deconstructs the argument that differences in HgbA1c levels in the combined training group are solely due to additional time spent exercising.

Comparable findings were observed in a meta-analysis of 32 RCTs from global sources comparing supervised and unsupervised forms of aerobic, resistance, or combined exercise models; combined supervised training programs significantly and clinically reduced HgbA1c by approximately 0.53%.[4] This result compares to supervised aerobic or resistance training that reduced HgbA1c measurements approximately -0.30%. Unsupervised training programs did not significantly reduce HgbA1c measurements compared to supervised programs. The authors recognized that while combined supervised training produced the greatest health benefits for diabetic patients overall, either aerobic or resistance training could be recommended for individual regimens with similar effects on glycemic control.

All the studies discussed herein created ideal study environments by controlling for outside variables and requiring participants to complete scheduled, supervised training sessions. While this requirement is ideal for study purposes, it does not engender high external validity because some patients do not have the monetary means or choose not to participate in supervised training programs. This limitation highlights the crucial role of patient adherence to an exercise program because studies show that patients are more likely to be compliant with an exercise program through direct supervision.[5] Additionally, many studies excluded participants on insulin therapy, which currently comprises roughly 30% of the diabetic population, further limiting the external validity.[12] Most of the current literature on diabetic exercise regimens involves studies with a duration of six months or less, limiting the generalizability for understanding the long-

term effects of specific exercise regimens on glycemic control. Though the present literature suggests that combined aerobic and resistance training produces the greatest changes in HgbA1c levels, the specific parameters for this recommendation are not yet determined.

Conclusion

Currently available studies lack evidence to establish that either aerobic or resistance training alone is superior for improving glucose control in diabetes. Aerobic and resistance regimens target different metabolic pathways to improve glucose utilization and insulin resistance in the body; theoretically, the most ideal training program should involve both types of exercise. This concept was substantiated by numerous studies that demonstrated the correlation between combined exercise training regimens and the greatest HgbA1c reductions. Additional research should be undertaken to determine more specifically the proportions of each type of exercise necessary and the ideal duration of exercise to produce A1c changes during combined exercise training with a focus on determining if this finding is related solely to increased time spent exercising or if combined training of the same duration as either aerobic or resistance training would produce similar reductions in A1c levels.

Practitioners need to be cognizant of the motivations and limitations of each individual patient when prescribing exercise programs. Practically, the best exercise program is one that is adhered to by patients. With the current information indicating that there is not a significant difference between types of exercise, either can be recommended to diabetics based on their individual abilities and limitations. However, our data also suggests that the best regimen to improve HgbA1c should include both resistance and exercise training. This conclusion agrees with current ADA guidelines that indicate that a combination of aerobic and resistance exercise

programs should be performed by diabetics to effectively reduce HgbA1c levels.

References

1. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and Type 2 Diabetes: The American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes Care*. 2010;33(12):e147-e167. doi:10.2337/dc10-9990

2. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and Type 2 Diabetes. *Diabetes Care*. 2010;33(12):e147-e167. doi:10.2337/dc10-9990

3. Sigal RJ, Kenny GP, Boulé NG, et al. Effects of Aerobic Training, Resistance Training, or Both on Glycemic Control in Type 2 Diabetes: A Randomized Trial. *Ann Intern Med*. 2007;147(6):357. doi:10.7326/0003-4819-147-6-200709180-00005

4. Pan B, Ge L, Xun Y, et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. *Int J Behav Nutr Phys Act*. 2018;15. doi:10.1186/s12966-018-0703-3

5. Bacchi E, Negri C, Zanolin ME, et al. Metabolic Effects of Aerobic Training and Resistance Training in Type 2 Diabetic Subjects. *Diabetes Care*. 2012;35(4):676-682. doi:10.2337/dc11-1655

6. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach: Update to a Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2015;38(1):140-149. doi:10.2337/dc14-2441

7. Yang Z, Scott CA, Mao C, Tang J, Farmer AJ. Resistance exercise versus aerobic exercise for type 2 diabetes: a systematic review and meta-analysis. *Sports Med Auckl NZ*. 2014;44(4):487-499. doi:10.1007/s40279-013-0128-8

8. Nery C, Moraes SRAD, Novaes KA, Bezerra MA, Silveira PVDC, Lemos A. Effectiveness of resistance exercise compared to aerobic exercise without insulin therapy in patients with type 2 diabetes mellitus: a meta-analysis. *Braz J Phys Ther*. 2017;21(6):400-415. doi:10.1016/j.bjpt.2017.06.004

9. Hansen D, Peeters S, Zwaenepoel B, et al. Exercise Assessment and Prescription in Patients With Type 2 Diabetes in the Private and Home Care Setting: Clinical Recommendations From AXXON (Belgian Physical Therapy Association). *Phys Ther*. 2013;93(5):597-610. doi:10.2522/ptj.20120400

10. Magalhães JP, Júdice PB, Ribeiro R, et al. Effectiveness of high-intensity interval training combined with resistance training versus continuous moderate-intensity training combined with resistance training in patients with type 2 diabetes: A one-year randomized controlled trial. *Diabetes Obes Metab*. 2019;21(3):550-559. doi:10.1111/dom.13551

11. Jorge MLMP, de Oliveira VN, Resende NM, et al. The effects of aerobic, resistance, and combined exercise on metabolic control, inflammatory markers, adipocytokines, and muscle

insulin signaling in patients with type 2 diabetes mellitus. *Metabolism*. 2011;60(9):1244-1252. doi:10.1016/j.metabol.2011.01.006

12. Cauza E, Hanusch-Enserer U, Strasser B, et al. The Relative Benefits of Endurance and Strength Training on the Metabolic Factors and Muscle Function of People With Type 2 Diabetes Mellitus. *Arch Phys Med Rehabil*. 2005;86(8):1527-1533. doi:10.1016/j.apmr.2005.01.007

13. Castaneda C, Layne JE, Munoz-Orians L, et al. A Randomized Controlled Trial of Resistance Exercise Training to Improve Glycemic Control in Older Adults With Type 2 Diabetes. *Diabetes Care*. 2002;25(12):2335-2341. doi:10.2337/diacare.25.12.2335

14. Snowling NJ, Hopkins WG. Effects of Different Modes of Exercise Training on Glucose Control and Risk Factors for Complications in Type 2 Diabetic Patients: A meta-analysis. *Diabetes Care*. 2006;29(11):2518-2527. doi:10.2337/dc06-1317

15. de Lade CG, Marins JCB, Lima LM, et al. Effects of different exercise programs and minimal detectable changes in hemoglobin A1c in patients with type 2 diabetes. *Diabetol Metab Syndr*. 2016;8. doi:10.1186/s13098-016-0123-y

16. Reid RD, Tulloch HE, Sigal RJ, et al. Effects of aerobic exercise, resistance exercise or both, on patient-reported health status and well-being in type 2 diabetes mellitus: a randomised trial. *Diabetologia*. 2010;53(4):632-640. doi:10.1007/s00125-009-1631-1

17. Church TS, Blair SN, Cocreham S, et al. Effects of Aerobic and Resistance Training on Hemoglobin A1c Levels in Patients With Type 2 Diabetes. *JAMA J Am Med Assoc*. 2010;304(20):2253-2262. doi:10.1001/jama.2010.1710