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Original Research

Muscle strengthening activities and retinopathy

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ABSTRACT

Background: Participation in muscle strengthening activities (MSA) is a neglected health behavior that can have substantive health benefits. **Objective:** We evaluated the specific association between MSA and retinopathy among a national sample of the broader U.S. adult population, which has yet to be investigated in the literature. **Results:** Compared to those with no retinopathy, those who engaged in MSA had a 36% (odds ratio [OR] = 0.64; 95% confidence interval [CI] = 0.49-0.85; $P = 0.004$) reduced odds of having mild retinopathy. MSA was not statistically significantly associated with reduced odds of moderate-to-severe retinopathy (OR = 0.85; 95% CI = 0.13-5.32; $P = 0.85$). **Conclusion:** Promotion of MSA is of major public health interest.

KEY WORDS: Chronic disease, diabetes, epidemiology, physical activity, public health, vision

INTRODUCTION

Previous research has examined associations between aerobic-based physical activities and their preventive effect on retinopathy [1-3]. Although the utility of physical activity as a moderator in the pathogenesis of retinopathy is widely disputed in the literature [1,3-6]. Evidence has suggested physical activity may not completely attenuate the deleterious health outcomes of nonproliferative retinopathy [4]. In contrast, studies have also demonstrated the efficacy of physical activity as a valuable prescription in the management of diabetes, regardless of potential improvements in microvascular complications [5]. Our recent work, indeed, demonstrates independent associations of sedentary behavior and physical activity on retinopathy [3,7,8]. We also demonstrate survival benefits of physical activity among those with mild retinopathy, but not more severe retinopathy [2].

Recent work also describes the rationale for physical activity to play a pivotal role in reducing the progressive severity of diabetes [9] and diabetic retinopathy [6,8]. Specifically, physical activity may reduce glycosylated hemoglobin concentration (HbA1c) and body mass index (BMI) [6] via improved control of circulating plasma glucose and body composition. In addition to a reduction in HbA1c, physical activity also aids blood pressure regulation by enhancing endothelial function, namely, vasodilatory capacity [8]. These favorable changes in blood pressure, BMI, and HbA1c are instrumental prerequisites for eliminating poor health outcomes and risks linked with the development of microvascular disease, which ultimately may influence retinopathy incidence [3,10-12].

Emerging work demonstrates that muscle strengthening activities (MSA), particularly resistance training, exert an independently beneficial effect on health; an effect which may be distinct from aerobic-based physical activity [10,11,13-18]. Resistance training is believed to reduce fat mass, while increasing lean tissue distribution, more effectively than aerobic training [10]. Aerobic-based physical activities have been shown to induce lipolysis [19], with little effect on muscle growth [20].

To our knowledge, no studies have specifically explored the association between MSA on retinopathy. This association is, of course, plausible, as MSA, just like aerobic-based physical activities, could facilitate glucose uptake and clearance via contraction-mediated glucose uptake pathways [21]. Resistance training-induced increases in glucose metabolism may regulate the translocation of glucose transporter 4 (GLUT-4) signaling proteins and increase glucose delivery to trained skeletal muscles, independent of associated increases in muscle mass [21]. This

enhanced glycemic control of MSA engagement may play a critical role in the prevention of retinopathy incidence [3,11]. The integration of MSA into public health agendas aiming to prevent or attenuate diabetic complications may be particularly justifiable for individuals with mobility concerns [22]. Thus, the objective of this brief report was to explore the relationship between MSA and retinopathy in a representative sample of the United States population.

METHODS

Design

Data from the 2005 to 2006 National Health and Nutrition Examination Survey (NHANES) were used. Study procedures were approved by the National Center for Health Statistics ethics review board, with informed consent obtained before data collection.

The NHANES is an ongoing survey conducted by the centers for disease control and prevention that uses a representative sample of non-institutionalized United States civilians selected by a complex, multistage, stratified, and clustered probability design. The multistage design consists of four stages, including the identification of counties, segments (city blocks), random selection of households within the segments, and random selection of individuals within the households. Further information on NHANES methodology and data collection is available on the NHANES website (http://www.cdc.gov/nchs/nhanes.htm).

Participants

The analyzed sample included 2047 participants with complete data on the study variables and who did not have a physician diagnosis of coronary artery disease, congestive heart failure, heart attack or stroke; participants were excluded if they had these conditions as these parameters may confounded our investigated association between MSA and retinopathy. The participants ranged in age between 40 and 85 years.

Measurement of MSA

Participants were asked, "Over the past 30 days, did you do any physical activities specifically designed to strengthen your muscles such as lifting weights, push-ups or sit-ups?" (response option: Yes or no). This exact NHANES muscular strength activities item has provided evidence of convergent validity (e.g. shown to associate with cardiovascular-related parameters [18] and insulin sensitivity [23]). Further, we calculated knee extremity strength (using Kin Com MP dynamometer) among those reporting and not reporting engagement in MSA (≥50 years); those reporting engagement in MSA (unweighted mean: 296.9 N) had greater knee extensor strength than those not reporting engagement in MSA (unweighted mean: 266.0 N) ($P < 0.05$), providing some evidence of construct validity for this MSA item. Notably, these estimates were not from the NHANES cycle in this study (2005-2006) but rather were from the 1999 to 2002 NHANES cycles because 1999-2002 are the only cycles with lower extremity strength data.

Retinopathy

As we have described elsewhere [3,8], retinal imaging was performed using the Canon Non-Mydriatic Retinal Camera CR6-45NM (Canon, Tokyo, Japan). The presence of nonproliferative retinopathy (mild or moderate/severe retinopathy) was determined using the early treatment diabetic retinopathy study grading criteria [24]. Thus, participants were classified as no retinopathy, mild nonproliferative retinopathy or moderate-to-severe nonproliferative retinopathy.

Analysis

All statistical analyses, computed in Stata (v. 12), accounted for the complex survey design employed in NHANES. A weighted multivariable multinomial model was used, adjusting for age (years; continuous), gender, race-ethnicity (Mexican American, non-Hispanic White, non-Hispanic Black, other), self-reported smoking status (current, former, and never smoker), self-reported physical activity (continuous; MET-min-month), measured BMI (continuous; kg/m^2), diabetes status (yes/no), physician-diagnosed hypertension (yes/no), and objectively-measured visual acuity [25] (normal vision, uncorrected refractive effort, and vision impairment). With regard to diabetes status, participants were defined as having diabetes if they had a physician diagnosis, had a fasting blood glucose of 126 mg/dL or higher, had an HbA1c of 6.5% or higher or were taking any diabetes medications. Significance was set at $P < 0.05$.

RESULTS

Table 1 displays the weighted characteristics of the measured variables. Table 2 displays the weighted multinomial regression results. Compared to those with no retinopathy, those who engaged in MSA had a 36% (odds ratio [OR] = 0.64; 95% confidence interval [CI] = 0.49-0.85; $P = 0.004$) reduced odds of having mild retinopathy; MSA was not statistically significantly associated with reduced odds of moderate-to-severe retinopathy (OR = 0.85; 95% CI = 0.13-5.32; $P = 0.85$). This latter finding may be due to the few ($N = 39$) participants who had moderate-to-severe retinopathy. Thus, we computed another model that collapsed moderate-to-severe retinopathy with mild retinopathy. This model showed that those engaging in MSA had a 33% (OR = 0.67; 95% CI = 0.48-0.93; $P = 0.02$) reduced odds of having any retinopathy (i.e., mild-to-severe retinopathy).

DISCUSSION

Despite early contention, emerging work on this topic has demonstrated that regular engagement in aerobic-based physical activity and minimizing sedentary behavior is associated with reduced odds of retinopathy [3,8]. The purpose of our brief report was to extend recent findings by evaluating the

Table 1: Weighted characteristics of the study variables across retinopathy status (*N*=2,047)

Variable	Point estimate (SE)		
	No retinopathy	Mild retinopathy	Moderate or greater retinopathy
N	1830	178	39
Age, mean (years)	54.8 (0.6)	56.8 (1.6)	57.1 (1.4)
BMI, mean (kg/m^2)	29.0 (0.2)	28.8 (0.5)	32.7 (2.5)
Gender, % female	54.3	44.0	36.7
Race-ethnicity, %			
Non-Hispanic white	79.4	67.8	54.1
Current smoker, %			
MVPA, mean MET-min-month	4042 (184)	4207 (884)	2581 (906)
Diabetic, %	9.1	25.3	86.9
Hypertension, %	36.6	41.6	54.1
Vision impairment, %	0.7	2.1	2.6
Smoker, %	21.1	29.8	7.5
Engaging in MSA, %	28.5	19.0	21.6

MSA: Muscle strengthening activities, MVPA: Moderate-to-vigorous physical activity, SE: Standard error

Table 2: Weighted multinomial regression is examining the association between MSA and retinopathy (*N*=2,047)

Variable	OR (95% CI)		
	No retinopathy	Mild retinopathy	Moderate or greater retinopathy
Engaging in MSA versus not	Referent	0.64 (0.49-0.85)	0.85 (0.13-5.32)

MSA: Muscle strengthening activities, CI: Confidence interval, BMI: Body mass index, OR: Odds ratio. †Adjusted for age (years; continuous), gender, race-ethnicity (Mexican American, non-Hispanic White, non-Hispanic Black, other), self-reported smoking status (current, former, and never smoker), self-reported physical activity (continuous; MET-min-month), measured body mass index (continuous; kg/m^2), diabetes status (yes/no), hypertension (yes/no), and objectively-measured visual acuity (normal vision, uncorrected refractive effort and vision impairment)

plausibility for MSA to exert an independently beneficial effect on the degree of retinopathy in a representative cohort of Americans. The main finding was that among individuals susceptible to mild and moderate-to-severe retinopathy, those who engaged in MSA reduced their risk of being diagnosed with nonproliferative retinopathy by one-third.

MSA may provide individuals with an alternative mode of exercise as individuals with retinopathy may be disinclined to engage in aerobic-based activity. This disinclination may stem from the mobility limitations often associated with retinopathy. For example, those with retinopathy often have worse visual acuity, which is associated with reduced balance and increase the risk of injurious falls. Further, the advantageous impact of MSA on proteins associated with GLUT-4 expression, principally protein kinase B, mitogen-activated protein kinase, and glycogen synthase, may be achievable with modest training loads [21,26]. This suggests that even individuals with substantive barriers to aerobic physical activity may benefit from low-volume MSA. In addition, enhanced glucose delivery to trained skeletal muscle has been shown to improve blood flow [21]. Increases in circulation may promote angiogenesis or direct flow to under-perfused capillaries; however more work in needed in this area [21]. Therefore, the results of this brief report should forerun subsequent longitudinal work investigating the novelty of MSA with respect to ocular health; perhaps with special attention given to training-mediated alterations in perfusion pressure and retinal blood flow, which have been shown to increase with exercise [27].

The retina is a vascularized, neural structure heavily reliant on glycolysis. Impaired glucose metabolism, in diabetes or prediabetic conditions, initiates an attack on the neural tissue of the retina. This process of retinal degradation occurs similar to disrupted insulin signaling in peripheral tissues and presents before vascular lesions characteristic of retinopathy [28]. Physical activity may be protective against the development of motor and sensory neuropathy [1]. Future research is needed to illustrate the effects of MSA alone on neuropathy.

In conclusion, this paper emphasizes the independent association between MSA and retinopathy among aging individuals within the broader United States population. Our novel findings extend the previous research exploring the relation between physical activity and retinopathy through an examination of the plausibility for resistance training applications to promote the quality of life among those with existing nonproliferative retinopathy. Future work should overcome the limitations of our study, which include the cross-sectional study design and relatively crude, subjective measure of MSA.

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REFERENCES

1. Balducci S, Iacobellis G, Parisi L, Di Biase N, Calandriello E, Leonetti F, *et al.* Exercise training can modify the natural history of diabetic peripheral neuropathy. J Diabetes Complications 2006;20:216-23.
2. Loprinzi PD. Effect of physical activity on mortality risk among Americans with retinopathy. Health Promot Perspect 2016;6:171-3.
3. Loprinzi PD, Brodowicz GR, Sengupta S, Solomon SD, Ramulu PY. Accelerometer-assessed physical activity and diabetic retinopathy in the United States. JAMA Ophthalmol 2014;132:1017-9.
4. Cruickshanks KJ, Moss SE, Klein R, Klein BE. Physical activity and the risk of progression of retinopathy or the development of proliferative retinopathy. Ophthalmology 1995;102:1177-82.
5. Makura CB, Nirantharakumar K, Girling AJ, Saravanan P, Narendran P. Effects of physical activity on the development and progression

of microvascular complications in Type 1 diabetes: Retrospective analysis of the DCCT study. BMC Endocr Disord 2013;13:37.
6. Praidou A, Harris M, Niakas D, Labiris G. Physical activity and its correlation to diabetic retinopathy. J Diabetes Complications 2017;31:456-61.
7. Loprinzi PD. Concurrent healthy behavior adoption and diabetic retinopathy in the United States. Prev Med Rep 2015;2:591-4.
8. Loprinzi PD. Association of accelerometer-assessed sedentary behavior with diabetic retinopathy in the United States. JAMA Ophthalmol 2016;134:1197-8.
9. Loprinzi PD, Ramulu PY. Objectively measured physical activity and inflammatory markers among US adults with diabetes: Implications for attenuating disease progression. Mayo Clin Proc 2013;88:942-51.
10. Castaneda C, Layne JE, Munoz-Orians L, Gordon PL, Walsmith J, Foldvari M, *et al.* A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with Type 2 diabetes. Diabetes Care 2002;25:2335-41.
11. Church TS, Blair SN, Cocreham S, Johannsen N, Johnson W, Kramer K, *et al.* Effects of aerobic and resistance training on hemoglobin A1c levels in patients with Type 2 diabetes: A randomized controlled trial. JAMA 2010;304:2253-62.
12. van Leiden HA, Dekker JM, Moll AC, Nijpels G, Heine RJ, Bouter LM, *et al.* Risk factors for incident retinopathy in a diabetic and nondiabetic population: The Hoorn study. Arch Ophthalmol 2003;121:245-51.
13. Buckner SL, Loenneke JP, Loprinzi PD. Single and combined associations of accelerometer-assessed physical activity and muscle-strengthening activities on plasma homocysteine in a national sample. Clin Physiol Funct Imaging 2016.
14. Dankel SJ, Loenneke JP, Loprinzi PD. Participation in muscle-strengthening activities as an alternative method for the prevention of multimorbidity. Prev Med 2015;81:54-7.
15. Dankel SJ, Loenneke JP, Loprinzi PD. The individual, joint, and additive interaction associations of aerobic-based physical activity and muscle strengthening activities on metabolic syndrome. Int J Behav Med 2016;23:707-13.
16. Dankel SJ, Loenneke JP, Loprinzi PD. Determining the importance of meeting muscle-strengthening activity guidelines: Is the behavior or the outcome of the behavior (strength) a more important determinant of all-cause mortality? Mayo Clin Proc 2016;91:166-74.
17. Dankel SJ, Loenneke JP, Loprinzi PD. Combined associations of muscle-strengthening activities and accelerometer-assessed physical activity on multimorbidity: Findings from NHANES. Am J Health Promot 2016.
18. Loprinzi PD, Loenneke JP, Abe T. The association between muscle strengthening activities and red blood cell distribution width among a national sample of U.S. Adults. Prev Med 2015;73:130-2.
19. Stich V, de Glisezinski I, Galitzky J, Hejnova J, Crampes F, Rivière D, *et al.* Endurance training increases the beta-adrenergic lipolytic response in subcutaneous adipose tissue in obese subjects. Int J Obes Relat Metab Disord 1999;23:374-81.
20. Holloszy JO, Booth FW. Biochemical adaptations to endurance exercise in muscle. Annu Rev Physiol 1976;38:273-91.
21. Holten MK, Zacho M, Gaster M, Juel C, Wojtaszewski JF, Dela F. Strength training increases insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with Type 2 diabetes. Diabetes 2004;53:294-305.
22. Yki-Jarvinen H. Exercise in the treatment of Type 2 and type 1 diabetes. In: Kjær KM, Magnusson P, Engebretsen L, Roos H, Takala T, Woo SL, editors. Textbook of Sports Medicine. Basic Science and Clinical Aspects of Sports Injury and Physical Activity. Oxford, UK: Blackwell Science; 2003. p. 435-50.
23. Cheng YJ, Gregg EW, De Rekeneire N, Williams DE, Imperatore G, Caspersen CJ, *et al.* Muscle-strengthening activity and its association with insulin sensitivity. Diabetes Care 2007;30:2264-70.
24. Grading diabetic retinopathy from stereoscopic color fundus photographs--an extension of the modified Airlie House classification. ETDRS report number 10. Early Treatment Diabetic Retinopathy Study Research Group. Ophthalmology 1991;98 5 Suppl:786-806.
25. Loprinzi PD, Pariser G, Ramulu PY. Accelerometer-assessed sedentary and physical activity behavior and its association with vision among U.S. Adults with diabetes. J Phys Act Health 2014;11:1156-61.
26. Ryder JW, Chibalin AV, Zierath JR. Intracellular mechanisms underlying increases in glucose uptake in response to insulin or exercise in skeletal muscle. Acta Physiol Scand 2001;171:249-57.
27. Wylegala A. The effects of physical exercises on ocular physiology: A review. J Glaucoma 2016;25:e843-9.
28. Antonetti DA, Barber AJ, Bronson SK, Freeman WM, Gardner TW, Jefferson LS, *et al.* Diabetic retinopathy: Seeing beyond glucose-induced microvascular disease. Diabetes 2006;55:2401-11.

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