Effect of Exercise on Disorders of Carbohydrate and Lipid Metabolism in Adults With Traumatic Spinal Cord Injury: Systematic Review of the Evidence

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Abstract

Background/Objective: Carbohydrate and lipid metabolism disorders may affect adults with spinal cord injuries (SCIs) differently than able-bodied individuals because of reduced physical activity in the SCI population. The objective of this study was to conduct a systematic review to determine the effectiveness of exercise to improve carbohydrate and lipid metabolism disorders in adults with chronic SCI.

Methods: Studies were identified in MEDLINE (1996–2008), Cochrane Library, bibliographies of identified articles, and expert recommendations. English language articles were included if they evaluated adults with chronic SCI; evaluated exercise; and reported carbohydrate-, lipid-, and/or cardiovascular disease-related outcomes.

Results: Twenty-two studies met inclusion criteria, including 15 intervention case-series and 7 cross-sectional surveys using self-reported physical activity measures. Intervention protocols involved active ($n = 7$) or electrically stimulated ($n = 7$) exercise or an educational program ($n = 1$) from 8 to 52 weeks in duration. Frequency of exercise was typically 2 to 3 sessions/week, lasting 30 to 60 minutes/session. Totals of 150 and 369 subjects participated in studies with carbohydrate ($n = 12$) or lipid and cardiovascular ($n = 16$) outcomes, respectively; 78% were men. Level of SCI ranged from C4 to L5 and included both incomplete and complete lesions. Outcomes measures included fasting and postload blood glucose and insulin concentrations and serum cholesterol levels. Small sample sizes and variations in study design, intervention, SCI characteristics, and reported outcomes precluded quantitative pooling of results or reliable assessment of metabolic efficacy. No intervention studies assessed cardiovascular outcomes.

Conclusions: Evidence is insufficient to determine whether exercise improves carbohydrate and lipid metabolism disorders among adults with SCI. Expert consensus, based on the preliminary evidence, is needed to inform future studies.

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Key Words: Spinal cord injuries; Tetraplegia; Paraplegia; Exercise; Functional electrical stimulation; Lipid metabolism; Carbohydrate metabolism; Systematic review; Outcomes research

INTRODUCTION

New spinal cord injuries (SCIs) result in 11,000 hospitalizations annually in the United States (1,2). More than 240,000 Americans live with SCI-related disability, and the estimated annual cost of SCI in the United States

averages \$9.7 billion (1,3,4). Cardiovascular diseases (CVDs) are the most common cause of death in adults with chronic SCI (5–8). Risk factors among individuals with SCI include behaviors such as smoking or inactivity and metabolic abnormalities such as obesity, metabolic syndrome, and diabetes (7,9,10). Diabetes (11,12), dyslipidemia (13,14), and coronary heart disease (6,12) are believed to be more prevalent and to occur earlier in adults with SCI compared with the general population. However, a recent systematic review was unable to find strong evidence to support this belief (15). This review also found little evidence supporting development of

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different practice guidelines for SCI populations in defining carbohydrate and lipid metabolism disorders (15).

In able-bodied individuals, exercise programs are important in the prevention and control of many metabolic syndrome-related disorders, particularly carbohydrate and lipid metabolism disorders. Moderate to rigorous physical activity has been shown to prevent diabetes mellitus in at-risk individuals (16,17) and, among adults with diabetes mellitus, aerobic and resistance training was shown to improve glycemic control in a recent randomized trial (18). Systematic reviews have also identified strong evidence that exercise can improve lipoprotein levels in diabetic and/or overweight able-bodied individuals (19,20). Biochemically, it is hypothesized that exercise-induced increases in AMP-activated protein kinase (AMPK), an enzyme that, among many other functions, stimulates glucose uptake and fatty acid oxidation while decreasing lipid synthesis, may explain the observed associations between exercise and reduced metabolic disease (21). Although present in all human cells, AMPK is notably activated by exercise in skeletal muscle fibers (21).

Through associated increases in skeletal muscle, overall improvements in physiologic condition, and multiple other mechanisms, it is expected that exercise training programs will impart the same metabolic benefits to those with SCI as they do for able-bodied individuals. However, SCIs create unique challenges that are not experienced by the able-bodied population. For one, individuals with SCI have reduced access to appropriate exercise facilities and equipment (4). This population also experiences physiologic risks of exercise including autonomic and circulatory dysregulation (22). Furthermore, individuals have reduced muscle mass with which to exercise (22), and fractures, joint dislocation, and overuse injuries are common (23). Therefore, although exercise may improve metabolic functioning in individuals with SCI, it is important to weigh this potential benefit vs such potential harm.

To date, no evidence-based guidelines have been developed pertinent to exercise in the SCI population (24). The American College of Sports Medicine's endurance training recommendations for individuals with SCI are similar to advice directed toward the able-bodied population. Generally, the recommended exercise prescription, at least for those with paraplegia, is 3 to 5 weekly sessions, 20 to 60 minutes in duration, at an intensity of 50% to 80% of peak heart rate (25). Suggested modes of exercise include arm cranking, wheelchair propulsion, swimming, wheelchair sports, circuit resistance training, electrically stimulated cycling, and electrically stimulated walking.

We conducted a systematic review of published evidence to determine the effects of different forms (active, electrically stimulated, and passive) or measures (interventional and self-reported physical activity) of

exercise on carbohydrate and lipid measures and cardiovascular outcomes in adults with chronic, traumatic SCI. This report is part of a larger evidence report conducted for the Agency for Healthcare Research and Quality (AHRQ) (15).

METHODS

Literature Search Strategy

We first searched MEDLINE, using the terms "spinal cord injury" combined with "hyperinsulinemia" or "hyperinsulinism" or "insulin resistance" or "Metabolic Syndrome X" or "metabolic syndrome;" "diabetes mellitus" or "glucose intolerance" or "impaired glucose tolerance;" "hyperlipidemias" or "HDL cholesterol" or "low HDL cholesterol;" and "obesity." The search was limited to articles published in English from 1990 to May 2007. The resulting Endnote library ($n = 2,212$) was searched for articles published since 1996, with abstracts that included the words "fitness," "physical activity," or "exercise." We also examined the Cochrane Database of Systematic Reviews of Effectiveness, examined bibliographies of published articles, and contacted technical experts for recommendations. This process yielded a subtotal of 305 citations. For this study, we updated our prior search through July 2008. This updated search identified 2 additional original studies published since our full AHRQ report (15).

Inclusion/Exclusion Criteria

Our study flow diagram is presented in Figure 1. We included any study evaluating exercise interventions, regardless of design, sample size, or duration, if it reported serum glucose, serum insulin, glucose tolerance, total cholesterol, triglyceride, low-density lipoprotein (LDL)- or high-density lipoprotein (HDL)-cholesterol, or cardiovascular-related outcomes for adults with chronic SCI. Other intermediate measures (eg, adiposity, blood pressure, cardiorespiratory fitness) were excluded.

Data Extraction

We extracted and reported individual study characteristics and results with tests of significance, as reported by authors. We evaluated studies separately by outcomes of interest (carbohydrate-related, and lipid- or cardiovascular-related). A summary of individual studies was conducted, stratified by type of exercise intervention (active, functional electrical stimulation, passive) or self-reported physical activity. Variation in study design, population, intervention, and outcomes did not permit pooling of study results.

RESULTS

Twenty-two studies met inclusion criteria for this review. Studies were excluded because: patient population did not include adults with chronic SCI ($n = 38$); lack of exercise program or measure of self-reported physical activity ($n = 18$); and lack of relevant carbohydrate-,

Figure 1. Data search and selection.

lipid-, or cardiovascular-related outcome measures ($n = 231$).

Most studies were preliminary in nature and involved either small, uncontrolled intervention trials (case series) or cross-sectional surveys using measures of self-reported physical activity. The only included study that involved random assignment of subjects to an intervention compared high-intensity vs low-intensity exercise (26). Only 3 subjects were assigned to each group, and no control group was included for comparison. There were 12 studies that reported carbohydrate-related outcomes (9,10,26–35) (Table 1) and 15 that reported lipid-related outcomes (9,10,26,27,30,35–44) (Table 2). Only 1 study included cardiovascular morbidity as an endpoint (Table 2), and this was assessed using a survey instrument with variable levels of sensitivity and specificity when tested in able-bodied populations (45).

Description of Studies

The types/measures and duration of exercise examined across all studies, and characteristics of enrolled subjects, were as follows.

- (A) Active Exercise: Seven studies of 57 unique individuals (9 individuals were subjects in 2 studies) (70% male, 9% female, 21% unreported; 40% paraplegic, 5% tetraplegic, 39% unclassified, 16% other; 35% com-

- plete lesions, 40% incomplete lesions, 9% unclassified, 16% other) (duration, 8–24 weeks of exercise)
- (B) Functional Electrical Stimulation (FES) Exercise: Seven studies of 78 individuals (51% male, 13% female; 36% unreported; 41% paraplegic, 14% tetraplegic, 45% unclassified; 35% complete lesions, 17% incomplete lesions, 48% unclassified) (duration, 8–52 weeks of exercise)
- (C) Passive Exercise: No studies identified
- (D) Self-Reported Physical Activity: Seven studies of 250 individuals (88% male, 12% female; 50% paraplegic, 37% tetraplegic, 6% unclassified, 7% able-bodied; 43% complete lesions, 35% incomplete lesions, 15% unclassified, 7% able-bodied) (only 1 study reported exercise duration of 1–5 years in a varsity athletic program)
- (E) Other: One study of 16 individuals (56% male, 44% female; 75% paraplegic, 25% tetraplegic; 56% complete lesions, 44% incomplete lesions) (12-week weight management program that included exercise curriculum)

Description of Exercise Studies With Carbohydrate-Related Outcomes

We identified 12 studies involving 150 individuals that reported carbohydrate-related outcomes (9,10,26–35)

Table 1. Description of Exercise Studies With Carbohydrate-Related Outcomes in People With SCI

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
A. Active exercise					
de Groot 2003 (26) Case series n = 6 Random assignment to high- vs low-intensity	Arm crank exercise	3 sessions/wk; 60 min/session; High-intensity (HI; 70–80% heart rate reserve [HRR]) vs low-intensity (LI; 40–50% HRR); 8 wks of training	4 males, 2 females; Age range 19–54 y; Mean duration since injury 116 d; 6 paraplegic (C5–L1); 1 complete, 5 incomplete	Insulin sensitivity (mean ± SD posttest/pretest)	Significant ($P < 0.05$) decline in HI group ($67 \pm 9\%$) and nonsignificant improvement in LI group ($156 \pm$ 55%) from baseline
Midha 1999 (27) Case series n = 12	Wheelchair aerobic fitness trainer (WAFT) training program	2–3 sessions/wk; 20–30 min, until target heart rate of 90% age- predicted maximum reached; Mean intensity 177 W; 10 wks of training	11 males, 1 female; Age range 22–58 y; Duration since injury range 4–29 y; 3 tetraplegic, 7 paraplegic, 1 stroke, 1 amputee; 3 complete, 7 incomplete	Fasting serum glucose (mean ± SD mg/dL)	No change from pretraining to post- training (86 ± 35 to 85 ± 32)
Phillips 2004 (28) Case series n = 9	Body weight- supported treadmill training program	68 sessions (2.8 ± 0.2 sessions/wk); Velocity and percent weight supported varied for each participant; 6.0 ± 0.3 mo of training	8 males, 1 female; Mean age 31 y; Mean duration since injury 8.1 y; 9 incomplete (C4–T12)	A. Plasma glucose during oral glucose tolerance test B. Glucose tolerance (mean ± SE area under glucose × time curve) C. Plasma insulin during oral glucose tolerance test D. Insulin response (mean ± SE area under insulin × time curve)	A. Significant decreases ($P < 0.05$) from pretraining to posttraining at times = 20, 40, 60, 80, and 140 min B. $15 \pm 4\%$ (range 6–26%) reduction from baseline ($P < 0.05$) C. Significant decreases ($P < 0.05$) from pretraining to posttraining at times = 120 and 180 min D. $33 \pm 8\%$ (range 17–47%) reduction from baseline ($P < 0.01$)
B. Functional electrical stimulation exercise					
Chilibeck 1999 (29) Case series n = 5	Electrically stimulated leg cycling program	3 sessions/wk; 30 min/session; Power 6.0 W, increased as possible each session; 50 revolutions/min; 8 wks of training	4 males, 1 female; Age range 31–50 y; Duration since injury range 3–25 y; 5 complete (C5–T8)	A. Glucose tolerance (area under glucose × time curve) B. Insulin response (area under insulin × time curve) C. Insulin sensitivity index (determined from OGTT)	A. Nonsignificant decreases from pretraining to posttraining B. Nonsignificant decreases from pretraining to posttraining C. Improved from pretraining (~0.9) to posttraining (~1.3) ($P < 0.05$)

Table 1. Continued

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
Griffin 2008 (30) Case series n = 18	Electrically stimulated leg cycling program	2–3 sessions/wk; 30 min/session; 50-Hz stimulation frequency; 49 RPM; 10 wks of training	13 males, 5 females; Mean age 40 y (range 25–57 y); Mean duration since injury 11 y (range 1–53 y); 5 complete, 13 incomplete (C4–T7)	A. Blood glucose levels during oral glucose tolerance test B. Plasma insulin levels during oral glucose tolerance test	A. Significant decreases ($P \leq 0.05$) from pretraining to posttraining at times = 30, 60, and 120 min postload B. Significant decreases ($P \leq 0.05$) from pretraining to posttraining at times = 60 and 120 min postload
Hjeltnes 1998 (31) Case series n = 5	Electrically stimulated leg cycling program	7 sessions/wk; 30 min/session or until fatigued; Power 6.0 W, increased by 6.1 W each session; 50 revolutions/min; 8 wks of training	5 males, 0 females; Mean age 35 y; Mean duration since injury 10.2 y; 5 tetraplegic; 5 complete (C5–C7)	A. Insulin-mediated glucose disposal (mean $\pm$ SE posttest/pretest values)	A. $33 \pm 13\%$ increase from baseline ($P < 0.05$)
Jeon 2002 (32) Case series n = 7	Electrically stimulated leg cycling program	3 sessions/wk; 30 min/session; 50–60% VO_2max ; 8 wks of training	5 males, 2 females; Age range 30–53 y; Duration since injury range 3–40 y; 7 complete (C5–T10)	A. 2-h postload plasma glucose levels (mean $\pm$ SE mg/dL) B. 2-h postload serum insulin levels (mean $\pm$ SE uU/mL)	A. Reduction from pretraining to posttraining (139.9 ± 16 to $122.4 \pm$ 10 ; $P = 0.014$) B. Nonsignificant reduction from pretraining to posttraining (118.4 ± 42.6 to 87.5 ± 10)
Mahoney 2005 (33) Case series n = 5	Resistance exercise training program	2 sessions/wk; 4 sets of 10 unilateral, dynamic knee extensions; 12 wks of training	5 males, 0 females; Mean age 35.6 y; Mean duration since injury 13.4 y; 5 chronic complete (C5–T9)	A. Plasma glucose levels during oral glucose tolerance test B. Plasma insulin concentration	A. No significant differences at times = 0, 60, 90, or 120 min from pretraining to posttraining, but trend for reduced levels ($P = 0.074$) B. No significant differences from pretraining to posttraining
Mohr 2001 (34) Case series n = 10	Electrically stimulated leg cycling program	3 sessions/wk; 30 min/session; 50 revolutions/min; 1 y of training	8 males, 2 females; Mean age 35 y; Mean duration since injury 12 y; 6 tetraplegic (C6), 4 paraplegic (T4)	A. 2-h postload plasma glucose levels and areas under glucose curves B. 2-h postload plasma insulin levels and areas under insulin curves C. Insulin-stimulated glucose uptake rates (mean $\pm$ SE mg/min/kg)	A. No change from pretraining to posttraining B. No change from pretraining to posttraining C. 28% increase from pretraining to posttraining (4.9 ± 0.5 to 6.2 ± 0.6 ; $P < 0.05$)

Table 1. Continued

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
C. Passive exercise: No eligible studies					
D. Self-reported physical activity					
Jones 2004 (10) Cross-sectional survey n = 20	NA Assessed physical activity levels (min/wk) and metabolic variables	NA Subjects reported 376 ± 59 (mean ± SE) min per wk of mild, moderate, and strenuous physical activity	20 males, 0 females; Age range 16–52 y; Mean duration since injury 10.3 y; 11 tetraplegic (C4–C7), 9 paraplegic (T5–L5)	Correlation between physical activity and: A. Fasting plasma glucose B. Log 2-h postload glucose C. Log fasting plasma insulin D. Log 2-h postload insulin	A. Nonsignificant inverse correlation ($r = -0.40$) B. Inverse correlation ($r = -0.59$; $P < 0.01$) C. No correlation ($r = -0.07$) D. Inverse correlation ($r = -0.79$; $P < 0.01$)
Manns 2005 (9) Cross-sectional survey n = 22	NA Assessed physical activity levels and metabolic variables	NA Subjects completed a comprehensive physical activity questionnaire specialized for persons with disabilities; Reported 88.7 ± 80.6 (mean ± SD) arbitrary units of physical activity	22 males, 0 females; Mean age 39 y; Mean duration since injury 17 y; 22 paraplegic (T2–L2); 22 complete	Partial correlation (controlled for age, duration of injury, and medication use) between physical activity and: A. Fasting serum glucose B. 2-h postload glucose C. Fasting plasma insulin D. 2-h postload insulin	A. Inverse correlation ($r = -0.525$; $P < 0.05$) B. Nonsignificant inverse correlation ($r = -0.344$) C. Nonsignificant inverse correlation ($r = -0.397$) D. No correlation ($r = -0.155$)
Mojtahedi 2008 (35) Cross-sectional survey n = 31	NA Compared metabolic outcomes between college athletes with SCI and sedentary able-bodied (AB) subjects (age- and BMI-matched)	NA SCI subjects participated in varsity athletic program for 1–5 y, involving 12 h of sport and 3 h of resistance training per wk; AB subjects participated in <1 h of physical activity per wk for prior 6 mo	15 males, 16 females; Mean age 22.5 y; 14 SCI (T5–L5); Mean duration since injury 16.5 y; 17 able-bodied	A. Fasting plasma glucose (mean ± SE mg/dL) B. Glucose area under curve (mean ± SE mg/dL/min) C. Fasting plasma insulin (mean ± SE uIU/ml) D. Insulin area under curve (mean ± SE uIU/ml/min) E. Insulin sensitivity index (mean ± SE)	A. No difference between SCI (87.1 ± 5.0) and AB (89.1 ± 6.2) B. No significant difference between SCI (104.9 ± 21.7) and AB (118.2 ± 22.2) C. No significant difference between SCI (13.8 ± 5.3) and AB (16.3 ± 5.6) D. No significant difference between SCI (64.0 ± 27.1) and AB (86.8 ± 39.8) E. No significant difference between SCI (4.0 ± 1.4) and AB (3.1 ± 1.3)

Table 2. Description of Exercise Studies With Lipid- and Cardiovascular-Related Outcomes in People With SCI

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
A. Active exercise					
Durán 2001 (36) Case series n = 13	Training program including mobility, strength, coordination, aerobic resistance, and relaxation activities	3 sessions/wk; 120 min/session; Target HR 40–80% of maximal HR; 16 wks of training	12 males, 1 female; Mean age 26.3 y; Duration since injury range 2–120 mo; 4 subjects T6 or higher, 9 subjects T6 or lower; 11 complete, 2 incomplete	A. HDL-C (mean $\pm$ SD mg/dL) B. LDL-C (mean $\pm$ SD mg/dL) C. TC/HDL-C (mean $\pm$ SD)	A. No change from pretraining (38 $\pm$ 11.6) to posttraining ($P = 0.08$) B. No change from pretraining (94 $\pm$ 39.8) to posttraining ($P = 0.25$) C. No change from pretraining (4.75 $\pm$ 2.15) to posttraining ($P = 0.076$)
de Groot 2003 (26) Case series n = 6 Random assignment to high- vs low-intensity	Arm crank exercise program	3 sessions/wk; 60 min/session; High-intensity (HI; 70–80% heart rate reserve [HRR]) vs low-intensity (LI; 40–50% HRR); 8 wks of training	4 males, 2 females; Age range 19–54 y; Mean duration since injury 116 d; 6 paraplegic (C5–L1); 1 complete, 5 incomplete	A. TC (% posttest/pretest $\pm$ SD) B. HDL-C (% posttest/pretest $\pm$ SD) C. LDL-C (% posttest/pretest $\pm$ SD) D. TC/HDL-C (% posttest/pretest $\pm$ SD) F. TG (% posttest/pretest $\pm$ SD)	A. No significant differences for HI (87 $\pm$ 9) or LI (94 $\pm$ 13) groups B. No significant differences for HI (113 $\pm$ 12) or LI (95 $\pm$ 6) groups C. No significant differences for HI (86 $\pm$ 9) or LI (95 $\pm$ 22) groups D. Reduction in HI (77 $\pm$ 6) but not LI (100 $\pm$ 20) group F. Reduction in HI (69 $\pm$ 7) but not LI (95 $\pm$ 14) group
El-Sayed 2005 (37) Controlled case series n = 12	Arm crank exercise program	3 sessions/wk; 30 min/session; 60–65% VO ₂ peak; 12 wks of training	Mean age 31 y for SCI; Mean age 32 y for AB; 5 paraplegic (SCI), 7 able-bodied (AB)	A. TC B. HDL-C C. TG	A. No change from pretraining to posttraining in AB or SCI B. Increase ($P < 0.05$) from pretraining to posttraining in SCI C. No change from pretraining to posttraining in AB or SCI
Midha 1999 (27) Case series n = 12	Wheelchair aerobic fitness trainer (WAFIT) training program	2–3 sessions/wk; 20–30 min, until target heart rate of 90% age-predicted maximum reached; Mean intensity 177 watts; 10 wks of training	11 males, 1 female; Age range 22–58; Duration since injury range 4–29 y; 3 tetraplegic, 7 paraplegic, 1 stroke, 1 amputee; 3 complete, 7 incomplete	A. TC (mean $\pm$ SD mg/dL) B. HDL-C (mean $\pm$ SD mg/dL) C. TC/HDL-C (mean $\pm$ SD) D. TG (mean $\pm$ SD mg/dL)	A. Reduction from pretraining to posttraining (185 $\pm$ 42 to 170 $\pm$ 32; $P = 0.04$) B. No change from pretraining to posttraining (48 $\pm$ 10 to 48 $\pm$ 10) C. No change from pretraining to posttraining (4.0 $\pm$ 1 to 3.8 $\pm$ 1) D. No change from pretraining to posttraining (117 $\pm$ 52 to 110 $\pm$ 60)

Table 2. Continued

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
Nash 2001 (38) Case series n = 5	Arm crank exercise program, with focus on resistance and endurance	3 sessions/wk; 45 min/session; Power output 400 + 100 kpm every 3 min until peak VO ₂ max; 3 mo of training	5 males, 0 females; Age range 34–43 y; Mean duration since injury 4.8 ± 1.4 y; 5 paraplegic; 5 complete (T6–L1)	A. TC (mean ± SD mg/dL) B. HDL-C (mean ± SD mg/dL) C. LDL-C (mean ± SD mg/dL) D. TC/HDL-C E. TG (mean ± SD mg/dL)	A. Nonsignificant decrease pretraining to posttraining (183 ± 26 to 167 ± 33) B. Nonsignificant increase pretraining to posttraining (41 ± 5 to 45 ± 12) C. Decrease pretraining to posttraining (118 ± 22 to 88 ± 30; $P = 0.05$) D. Decrease pretraining to posttraining (5.0 ± 1.1 to 3.9 ± 0.7; $P = 0.05$) E. Nonsignificant decrease pretraining to posttraining (202 ± 120 to 190 ± 91)
Stewart 2004 (39) Case series n = 9	Body weight-supported treadmill training program	68 sessions (2.8 ± 0.2 sessions/wk); Velocity and percent weight support varied for each participant; 6.0 ± 0.3 mo of training	8 males, 1 female; Mean age 31 ± 3 y; Mean duration since injury 8.1 y; 9 incomplete (C4–T12)	A. TC (mean ± SE mM) B. HDL-C (mean ± SE mM) C. LDL-C (mean ± SE mM) D. TC/HDL-C (mean ± SE) E. TG (mean ± SE mM)	A. Decrease from pretraining to posttraining (4.9 ± 0.2 to 4.4 ± 0.1; $P = 0.021$) B. Nonsignificant increase pretraining to posttraining (1.3 ± 0.2 to 1.4 ± 0.3; $P = 0.19$) C. Decrease from pretraining to posttraining (3.3 ± 0.2 to 2.8 ± 0.3; $P = 0.046$) D. Decrease from pretraining to posttraining (3.8 ± 0.3 to 3.1 ± 0.3; $P = 0.041$) E. Nonsignificant decrease pretraining to posttraining (1.5 ± 0.2 to 1.3 ± 0.2; $P = 0.17$)

Table 2. Continued

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
B. Functional electrical stimulation exercise					
Griffin 2008 (30) Case series n = 18	Electrically stimulated leg cycling program	2–3 sessions/wk; 30 min/session; 50-Hz stimulation frequency; 49 RPM; 10 wks of training	13 males, 5 females; Mean age 40 y (range 25–57 y); Mean duration since injury 11 y (range 1–53 y); 5 complete, 13 incomplete (C4–T7)	A. TC (mean $\pm$ SE mg/dL) B. HDL-C (mean $\pm$ SE mg/dL) C. LDL-C (mean $\pm$ SE mg/dL) D. TG (mean $\pm$ SE mg/dL)	A. No change from pretraining to posttraining (157.91 ± 6.36 to 156.32 ± 6.65) B. Reduction from pretraining to posttraining (34.27 ± 2.00 to 30.56 ± 2.11 ; $p < 0.05$) C. No significant change from pretraining to posttraining (102.65 ± 6.20 to 105.54 ± 5.49) D. No significant change from pretraining to posttraining (104.92 ± 26.90 to 101.07 ± 25.46)
Solomonow 1997 (40) Case series n = 28	Training program with reciprocating gait orthosis powered with electrical muscle stimulation	3 sessions/wk; 60 min/session; Average 14.6 wks of training among those with high TC at baseline; Average 15.6 wks of training among those with normal TC at baseline	28 paraplegic; 8 high TC at baseline (>200 mg/dL), 20 normal TC at baseline (<200 mg/dL)	A. TC among n = 8 with high baseline TC (mean mg/dL) B. HDL-C among n = 8 with high baseline TC (mean mg/dL) C. LDL-C among n = 8 with high baseline TC (mean mg/dL) D. TC/HDL-C among n = 8 with high baseline TC (mean) E. TC, HDL-C, LDL-C, TC/HDL-C among n = 20 with normal baseline levels of TC	A. Significant decrease from pretraining to posttraining ($231-196$; $P = 0.02$) B. No significant change from pretraining to posttraining C. Significant decrease from pretraining to posttraining ($160-130$; $P = 0.009$) D. Significant decrease from pretraining to posttraining (~ 3.7 to ~ 3.0 ; $P = 0.04$) E. No significant changes from pretraining to posttraining
C. Passive exercise: No eligible studies					
D. Self-reported physical activity					

Table 2. Continued

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
Dallmeijer 1999 (41) Case-series survey n = 19	NA Assessed risk profiles at t1 (during rehab) and risk profiles and sport activity at t2 (1 y postdischarge)	NA Subjects reported 2.6 ± 3.0 (mean $\pm$ SD) h per wk of sport activity during the y preceding t2	15 males, 4 females; Mean age at t1 40.7 y; Mean duration since injury at t2 760 d; 9 tetraplegic, 10 paraplegic; 12 complete, 7 incomplete	Sport activity as determinant of change (t1 to t2) in: A. TC B. HDL-C C. LDL-C D. TC/HDL-C E. TG	A. Most important determinant of lower levels at t2 ($r^2 = 0.34$; $P = 0.008$) B. No significant change in levels from t1 to t2 C. Most important determinant of lower levels at t2 ($r^2 = 0.47$; $P = 0.003$) D. Most important determinant of lower levels at t2 ($r^2 = 0.29$; $P = 0.035$) E. No change in levels from t1 to t2
Dallmeijer 1997 (42) Cross-sectional survey n = 24	NA Compared lipid levels between SCI patients who were sedentary and those who were physically active for at least 6 mo before study	NA Physically active subjects reported 3.0 ± 1.7 (mean $\pm$ SD) h per wk (range 1.5–6.0) of sport activity	24 males, 0 females; 11 physically active, 13 sedentary; 24 tetraplegic; 20 complete, 4 incomplete	A. TC (mean $\pm$ SD mM/L) B. HDL-C (mean $\pm$ SD mM/L) C. LDL-C (mean $\pm$ SD mM/L) D. TC/HDL-C (mean $\pm$ SD) E. TG (mean $\pm$ SD mM/L)	A. No difference between physically active (4.6 ± 1.1) and sedentary (4.9 ± 1.3) ($P = 0.537$) B. Higher for physically active (1.13 ± 0.21) than sedentary (0.95 ± 0.20) ($P = 0.049$) C. No difference between physically active (2.9 ± 0.9) and sedentary (3.2 ± 1.1) ($P = 0.609$) D. Lower for physically active (4.2 ± 0.8) than sedentary (5.3 ± 1.5) ($P = 0.036$) E. Nonsignificantly lower for physically active (1.34 ± 0.67) than sedentary (1.96 ± 1.01) ($P = 0.115$) No association with physical activity at $P < 0.25$ level
Davies 2002 (45) Cross-sectional survey n = 97	NA Assessed physical activity and cardiovascular morbidity	NA Subjects reported $9.17 \pm$ 6.96 (mean $\pm$ SD) units (range 0–26) of physical activity; 13 of 97 subjects reported cardiovascular morbidity	87 males, 10 females; Mean age 47.5 y; Mean duration since injury 15.9 y; 41 tetraplegic, 55 paraplegic, 1 undetermined; 32 complete, 62 incomplete, 3 undetermined	Cardiovascular morbidity	No association with physical activity at $P < 0.25$ level

Table 2. Continued

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
Janssen 1997 (43) Cross-sectional survey n = 37	NA Assessed sport participation and lipid profiles	NA Subjects reported 2.9 ± 3.4 (mean ± SD) h per wk of sport participation	37 males, 0 females; Age range 19–71 y; Duration since injury range 4–33 y; 8 tetraplegic; 29 paraplegic; 23 complete, 14 incomplete	Correlation between sport participation and: A. TC B. HDL-C C. LDL-C D. TC/HDL-C E. TG	A. Inverse correlation ($r = -0.33$; $P < 0.05$) B. No correlation ($r = -0.14$) C. Inverse correlation ($r = -0.40$; $P < 0.01$) D. No correlation ($r = -0.17$) E. No correlation ($r = 0.06$)
Jones 2004 (10) Cross-sectional survey n = 20	NA Assessed physical activity levels and lipid profiles	NA Subjects reported 376 ± 59 (mean ± SE) min per wk of mild, moderate, and strenuous physical activity	20 males, 0 females; Age range 16–52 y; Mean duration since injury 10.3 y; 11 tetraplegic (C4–C7), 9 paraplegic (T5–L5)	Correlation between physical activity and: A. Log HDL-C B. TC/HDL-C	A. Direct correlation ($r = 0.46$; $P < 0.05$) B. Inverse correlation ($r = -0.49$; $P < 0.05$)
Manns 2005 (9) Cross-sectional survey n = 22	NA Assessed physical activity levels and lipid profiles	NA Subjects completed a comprehensive physical activity questionnaire specialized for persons with disabilities; reported 88.7 ± 80.6 (mean ± SD) arbitrary units of physical activity	22 males, 0 females; Mean age 39 y; Mean duration since injury 17 y; 22 paraplegic (T2–L2); 22 complete	Correlation between physical activity and: A. HDL-C B. TG	A. Direct correlation ($r = 0.625$; $P < 0.01$) B. No correlation ($r = -0.256$)
Mojtahedi 2008 (35) Cross-sectional survey n = 31	NA Compared lipid profiles between college athletes with SCI and sedentary able bodied (AB) subjects (age- and BMI-matched)	NA SCI subjects participated in varsity athletic program for 1–5 y, involving 12 h of sport and 3 h of resistance training per wk; AB subjects participated in <1 h of physical activity per wk for prior 6 mo	15 males, 16 females; Mean age 22.5 y; 14 SCI (T5–L5); Mean duration since injury 16.5 y; 17 able-bodied	A. TC (mean ± SE mg/dL) B. HDL-C (mean ± SE mg/dL) C. LDL-C (mean ± SE mg/dL)	A. No significant difference between SCI (150.7 ± 51.2) and AB (158.6 ± 41.8) B. No significant difference between SCI (53.1 ± 15.7) and AB (46.2 ± 11.0) C. No significant difference between SCI (86.2 ± 44.3) and AB (104.2 ± 35.7)

Table 2. Continued

Reference; Study Design; Sample Size	Intervention Type	Frequency; Intensity; Duration	Subject Characteristics	Outcomes of Interest	Findings
E. Other					
Chen 2006 (44) Case series n = 16	NA Participation in weight management program where exercise behavior was taught	NA Follow-up testing at 12 and 24 wks	9 males, 7 females; Age range 21–66 y; Mean duration 17.5 y since injury (15) or illness (1); 4 tetraplegic; 12 paraplegic; 9 complete; 7 incomplete	A. TC (mean $\pm$ SD mg/dL) B. HDL-C (mean $\pm$ SD mg/dL) C. LDL-C (mean $\pm$ SD mg/dL)	A. No change preprogram to postprogram (-5.8 ± 20.9 ; $P = 0.28$) B. Decrease from pre-program to postprogram (-3.2 ± 5.4 ; $P = 0.03$) C. No change preprogram to postprogram (-1.8 ± 22.1 ; $P = 0.76$)

(Table 1). Based on a widely accepted approach that grades study design, quality, consistency, and directness (46,47), the overall quality of SCI-specific evidence in support of exercise as an intervention for carbohydrate metabolism disorders was low. Studies were small in size, short in duration, and frequently lacked control groups. Study characteristics ranged from a case series using pre-post assessment of outcomes for 6 individuals randomly assigned to 8 weeks of high- vs low-intensity arm crank exercise (26), to a cross-sectional survey of 22 individuals who provided self-assessed physical activity levels and blood samples for metabolic measurements (9).

The type, frequency, intensity, and duration of exercise varied considerably across studies. Most intervention studies involved several sessions of supervised exercise per week with a study duration ranging from 8 weeks to 1 year. SCI level and severity and duration since injury varied across studies. Injury level ranged from C4 to L5 and included both incomplete and complete lesions. Eighty percent of subjects were men. Three studies examined the effects of active exercise (26–28), whereas 6 examined the effects of FES exercise (29–34) on carbohydrate-related measures. Of these, only 2 considered baseline glucose or insulin measures in analysis or discussion (32,33). Three survey studies assessed the association between self-reported physical activity and carbohydrate-related measures (9,10,35). The most commonly assessed carbohydrate-related measures involved oral glucose tolerance tests (OGTTs), measuring post-oral load levels of glucose and insulin.

Impact of Exercise on Carbohydrate-Related Outcomes

Blood Glucose Levels. There is inconsistent evidence that a program of exercise can improve blood glucose levels. Four studies (1 active; 3 survey) reported fasting blood glucose measures. The active exercise study found no difference between fasting serum glucose before and after a 10-week training program (27). Of the 3 survey studies, one identified a statistically significant inverse correlation ($r = -0.53$; $P < 0.05$) between reported levels of physical activity and fasting serum glucose (9). Another identified an inverse correlation ($r = -0.40$) that was not statistically significant (10), whereas the third found no difference in glucose levels between athletes with SCI and a sedentary, able-bodied population (35).

Nine studies (1 active; 5 FES; 3 survey) reported results of OGTTs. Reports included levels of blood glucose at various times following oral load, as well as calculations of the area under “glucose $\times$ time” curves as an indicator of glucose tolerance. The active exercise study identified statistically significant ($P < 0.05$) decreases in plasma glucose after a 6-month training program with 9 participants at 20, 40, 60, 80, and 140 minutes postload (28). This study also calculated a 15% average reduction in area under the curve ($P < 0.05$). One FES study identified

statistically significant ($P \leq 0.05$) decreases in blood glucose levels from pretraining to post-training (10 weeks) at 30, 60, and 120 minutes postload (30). Another FES study found differences pre- to post-training (12 weeks) that did not reach statistical significance, but a test for trend was also suggestive of reduced levels ($P = 0.07$) (33). Two additional FES studies reported glucose levels at 2 hours postload: 1 identified a statistically significant ($P = 0.014$) reduction after an 8-week training program (32), whereas the other found no change after 1 year of training (34). This latter study (34) also found no difference in area under the “glucose $\times$ time” curve, whereas another 8-week FES study observed decreases in area under the curve that were not statistically significant (29). Of the 3 survey studies, 1 identified an inverse correlation between levels of physical activity and 2-hour postload glucose ($r = -0.59$; $P < 0.01$), whereas another identified an inverse correlation that was not statistically significant ($r = -0.34$). The third reported no difference in areas under the curve between SCI athletes and a sedentary, able-bodied population.

Plasma Insulin Levels. Measures of insulin and insulin sensitivity were also variable across studies. Most studies (1 active; 5 FES; 3 survey) assessed either fasting plasma insulin levels or plasma insulin at incremental times after an OGTT. The active exercise study reported statistically significant ($P < 0.05$) decreases in plasma insulin levels at 2- and 3-hours after glucose load after a 6-month training program (28). This corresponded with an average 33% reduction ($P < 0.01$) in area under the “insulin $\times$ time” curves for participants in this study ($n = 9$). Of the five FES studies that reported insulin levels before and after the programs of exercise, 1 reported a significant decrease ($P \leq 0.05$) at 1 and 2 hours after oral glucose load (30); 2 reported nonstatistically significant reductions in 2-hour postload insulin (32) or area under the “insulin $\times$ time” curve (29); and 2 reported no changes in plasma insulin concentrations after 12 weeks of training (33) or 2-hour postload plasma insulin and area under the “insulin $\times$ time” curve after 1 year of training (34).

Similarly, 2 survey studies reported fasting plasma insulin levels and 2-hour postload levels. Although 1 identified a nonstatistically significant inverse correlation ($r = -0.397$) between self-reported physical activity and fasting plasma insulin (9), the other found no correlation (10). However, the latter study did identify a statistically significant inverse correlation ($r = -0.79$; $P < 0.01$) between physical activity and 2-hour postload insulin (10), whereas the former study did not ($r = -0.155$). The third survey identified no significant differences in fasting plasma insulin levels, insulin area under the curve, or in insulin sensitivity index between athletes with SCI and a sedentary, able-bodied population (35).

Insulin sensitivity index was also calculated in 1 active exercise and 1 FES study. The active exercise study (26) identified a statistically significant decline in insulin

sensitivity among 3 participants randomly assigned to a high-intensity arm crank exercise program, but a nonsignificant improvement among 3 participants assigned to a low-intensity program. The FES study reported an improvement in insulin sensitivity index among 5 subjects who participated in an 8-week leg cycling program (29). Two additional FES studies identified average pre- to post-training increases of 33% (31) and 28% (34) in rates of insulin-stimulated glucose disposal after 8 weeks and 1 year, respectively, of participation in leg cycling programs.

Description of Exercise Studies With Lipid- or Cardiovascular-Related Outcomes

We identified 16 studies involving 369 individuals that reported lipid- (9,10,26,27,30,35–44) or cardiovascular- (45) related outcomes (Table 2). The overall quality of SCI-specific evidence supporting exercise as a therapy for lipid metabolism disorders was low (46,47). Study designs were primarily reports of small, short-duration case series and cross-sectional surveys. Intervention type, frequency, intensity, and duration varied. More than three fourths of subjects were men, with injury levels again ranging from C4 to L5 and including both incomplete and complete lesions. Six studies examined the effects of active exercise on lipid-related measures (26,27,36–39). Only 2 studies examined FES exercise (30,40). Of the intervention studies, only 4 considered baseline lipid levels in analysis or discussion (30,36,38,40). There were 6 survey studies that assessed the association between self-reported physical activity and lipid measures (9,10,35,41–43). One survey examined the association between physical activity and cardiovascular morbidity, with both variables measured using a self-report survey instrument (45). One study, categorized as “other,” examined the effects of a weight management training program, including an exercise-related curriculum, on lipid outcomes (44).

Impact of Exercise Programs on Lipid- and Cardiovascular-Related Measures

Total Cholesterol Levels. Evidence pertaining to improved levels of total cholesterol (TC) after an exercise training intervention is inconclusive. Of the 5 studies examining effects of active exercise interventions, 2 identified statistically significant reductions in TC levels after training (on average, 8% and 10% less than pretraining) (27,39). These involved programs averaging 6 months and 10 weeks, respectively, with either a body weight-supported treadmill (39) or a wheelchair aerobic fitness trainer (27). Two studies reported decreases in TC that were not statistically significant: 1 identified a 9% reduction among 5 participants after 3 months of arm-crank exercise (38), and the other identified 11% and 6% reductions, respectively, among participants randomized to high-intensity ($n = 3$) or low-intensity ($n = 3$) arm crank programs (26). Only 1 study showed no change in

TC in $n = 12$ subjects after 12 weeks of arm crank training (37).

Similarly, 1 FES study showed no change in total cholesterol after 10 weeks of leg cycling (30), whereas the other identified a statistically significant ($P = 0.02$) average decrease of 15% among participants with high baseline TC (>200 mg/dL) after 14.6 weeks of training (40). This study showed no change in TC levels among participants with normal baseline values (<200 mg/dL).

Of the 4 survey studies that examined self-reported physical activity and TC, 1 identified a statistically significant inverse correlation ($r = -0.33$; $P < 0.05$) between the 2 variables (43), and another reported hours per week of sports activity to be the most important determinant examined of decreased levels of TC from time 1 to time 2 (41). However, 2 additional survey studies showed no difference in TC levels between SCI patients who were physically active and those who were sedentary (42) or between SCI athletes and sedentary, able-bodied subjects (35). The study examining the weight management training program found no significant change in TC after training (44).

HDL-Cholesterol Levels. Similar to total TC levels, studies had mixed results pertaining to levels of HDL-cholesterol (HDL-C). Across studies, reports included elevated and reduced levels of HDL-C in relation to participation in exercise programs or physical activity, and several studies found no associations. Six active exercise studies reported outcomes for HDL-C. Although 2 reported no changes in levels from pretraining to post-training (27,36), 1 reported a statistically significant ($P < 0.05$) increase in HDL-C after 12 weeks of training (37), and 2 reported nonsignificant increases of 10% and 8% after 3 and 6 months of training, respectively (38,39). The study that randomly assigned subjects to high- vs low-intensity arm crank programs observed a 13% increase in the high-intensity group but a 5% decrease in the low-intensity group; neither were statistically significant changes (26).

Five survey studies reported HDL-C levels; 1 identified statistically significant higher levels ($P < 0.05$) among individuals with SCI who were physically active compared with those who were sedentary (42). Two studies identified direct correlations between physical activity levels and HDL-C ($r = 0.46$ and 0.63 ; $P < 0.05$ and 0.01 , respectively) (9,10), whereas 1 other reported no correlation (43). There was no difference in HDL-C levels between athletes with SCI and sedentary, able-bodied subjects (35). Surprisingly, 1 FES study reported a statistically significant reduction in HDL-C after a 10-week leg cycling program (30), as did the weight management study (44). Another FES study identified no changes in HDL-C among participants with either high or normal baseline levels of TC (40).

Measures for TC/HDL-C were similarly inconclusive. Of 5 active exercise studies, 2 reported no changes (27,36), whereas 3 reported statistically significant

reductions in values ranging from 18% to 23% (26,38,39). One FES study identified a statistically significant ($P = 0.04$) 19% decrease among participants with high baseline TC, but no change among participants with normal baseline TC (40). Two survey studies identified significant inverse associations between physical activity and levels of (10), or declines in (41), TC/HDL-C. One survey study identified statistically significant lower values ($P < 0.05$) among patients with SCI who were physically active compared with those who were sedentary (42), and 1 showed no correlation (43).

LDL-Cholesterol Levels. No consistent trends were observed across studies pertaining to LDL-cholesterol (LDL-C). In 2 of 4 active exercise studies reporting LDL-C measures, levels were decreased by 15% and 25% ($P \leq 0.05$ for both) after 6 months of body weight-supported treadmill training (39) or 3 months of arm crank exercise, respectively (37,38). No changes were observed in the other studies involving 2 and 4 months of training (26,36). One FES study identified no change in levels after 10 weeks of leg cycling (30), whereas the other identified a significant ($P = 0.009$) 19% decrease among participants with high baseline levels of TC after 14.6 weeks of training (40). No changes were observed among participants with normal baseline TC (40). Four survey studies reported LDL-C values; 1 identified a statistically significant inverse correlation with self-reported physical activity ($r = -0.40$; $P < 0.01$) (43), and 1 reported sport activity to be the most important determinant of decreased LDL-C levels over time (41). The other 2 studies reported no significant differences between athletes with SCI and sedentary, able-bodied subjects (35) or between physically active and sedentary SCI patient groups (42). Similarly, the weight management program was not associated with decreased LDL-C levels (44).

Triglyceride Levels. Studies reported inconclusive results for triglycerides (TGs) as well. Although 1 active exercise study identified a statistically significant 31% average decrease in TG among 3 subjects assigned a high-intensity arm crank training protocol (26), 2 others showed decreases that were nonsignificant (38,39), and 2 studies found no changes in TG levels (27,37). The FES study found no change in TG levels after 10 weeks of training (30). Among the 3 self-report surveys reporting TG values, 1 identified a nonsignificant 32% decrease among patients with SCI who were physically active compared with those who were sedentary (42). Two studies identified no correlation between physical activity and TG levels (9,43).

Cardiovascular Morbidity. In the only study reporting cardiovascular outcomes, no association was observed between physical activity levels and self-reported cardiovascular morbidity (45). This was a small, cross-sectional study involving 97 individuals with SCI and was not adequately designed to assess these outcomes.

DISCUSSION

Evidence to date is insufficient to determine whether exercise programs favorably alter carbohydrate and lipid metabolism in adults with chronic SCI. We were unable to identify consistency in findings across studies relevant to measures of blood glucose, insulin, TC, HDL-C, LDL-C, or TGs. Inconsistency in study results could be caused by the considerable variation in patient populations, exercise programs, and outcome measures used. The studies published from 1996 through July 2008 have been few in number ($n = 22$), small in size, and short in duration and have frequently lacked control subjects. Because studies to date have been preliminary and heterogeneous in nature, pooling of data was not possible.

Results of pilot studies may be informative for development of future research. Individual studies frequently indicated some overall post-training benefits, which could be used as the basis for high-quality but resource-intensive randomized controlled trials (RCTs) or large, prospective epidemiologic studies. Authors of the identified studies, and past reviews (48–51), often suggest that exercise training and/or physical activity are important determinants of carbohydrate and lipid metabolism among individuals with SCI; however, we urge caution in drawing conclusions or implementing policies until this next step in research is conducted. Although exercise may ultimately be shown to be effective, this caution is warranted in light of the potential risks of physical activity among denervated individuals (22,23).

Although data from the able-bodied population are promising, we identified no equivalent high-quality data pertinent to the population with SCI. A major purpose of this review that was originally requested by the Consortium for Spinal Cord Medicine to assist in developing their practice guidelines was to specifically focus on evidence in individuals with SCI. Studies in this population have been based on short-term exercise intervention case series or cross-sectional studies, study designs that are highly susceptible to systematic bias and confounding. Furthermore, the exercise intervention programs varied considerably from 1 study to the next, with little consistency in duration, mode, frequency, or intensity. The length of program protocols ranged from 8 to 52 weeks; most were only 8 to 16 weeks in duration. Interventions of this length are likely not long enough to impart consistent and measurable metabolic benefits to study participants.

In the cross-sectional surveys, parameters of physical activity were generally self-reported by survey participants. Self-report responses can be biased because of social desirability and recall error. Even if measurement of physical activity is accurate, potential confounding can also bias results. For example, underlying carbohydrate and/or lipid metabolism disorders, and poor cardiovascular health in general, may be the reason some subjects participated in little physical activity. This would make

physical activity positively correlated with better carbohydrate and lipid levels, but not necessarily a determinant of better levels.

The diversity of physical activity and exercise programs described across studies may also explain the lack of consistent findings. For example, exercise modes included functional electrical stimulation, arm crank ergometers, body weight-supported treadmills, wheelchair ergometers, and assorted strength and resistance training activities. Additionally, normal vs abnormal baseline measures were reported and/or discussed in only a few of the studies. It may be that exercise has a greater potential for therapeutic benefit among individuals with higher risk for metabolic disorders at baseline than among those with normal risk profiles. However, because baseline measures are not consistently reported, this theory cannot be substantiated in the current body of literature.

The published intervention studies have not yet considered challenges with implementation or sustainability of exercise programs in community settings. In general, study participants have consisted of carefully recruited, hospital- and/or clinic-based patients. It is unknown whether exercise intervention programs would be sustainable over time in a community-based population of individuals with SCI.

Given the heterogeneity of the SCI population, including, among other things, individuals' levels of injury and the corresponding exercise options available, the lack of consistency we observed across studies is not surprising. In general, participation in sports and physical activity is associated with improved quality of life for people with disabilities (52), and we therefore laud researchers who have worked to establish and test programs that increase fitness among patients with SCI. It is clear, however, that prior to any widespread endorsement of exercise therapies for the prevention and/or treatment of carbohydrate and lipid metabolism disorders, consistent and higher-quality studies are needed to understand levels of risk vs benefit for this population.

RECOMMENDATIONS

Ultimately, higher-quality RCTs and/or prospective, epidemiologic studies with large, well-characterized cohorts would contribute the most reliable knowledge to the current evidence base on exercise therapy for the prevention or control of metabolic disorders and cardiovascular morbidity. The identified studies could help inform design of this future research. To start, expert consensus and prioritization of study parameters (including the study population, exercise interventions, and outcomes measures) are needed. For example, what individuals are most likely to benefit from exercise? Which types of interventions (including mode, frequency, intensity, and duration) are the most likely to impart physiological benefits? Initial RCTs might look at the

feasibility and long-term sustainability of these interventions in the most clinically relevant individuals, as determined by an expert panel.

RCTs and prospective epidemiologic studies are resource intensive, and the pool of potential study participants is small, yet heterogeneous, relative to other populations. Thus, accomplishing the program of research needed will likely require the pooling of resources, both by funding agencies and by researchers through multiple site collaborations. Cooperative research groups could determine the most appropriate and pragmatic study parameters, including intervention type and outcomes measures, and also identify persons willing to participate from multiple geographic locations.

Observational studies will be more definitive if important subject demographic and injury parameters are considered and carefully controlled. Key variables that should be considered are subject age, race, and sex; comorbid conditions; baseline carbohydrate- and lipid-related values; baseline physical activity; duration, level, and completeness of SCI; functional status; and life satisfaction and other important psychosocial variables. Glycated hemoglobin (A1C) value is an additional important variable to measure at baseline. Because A1C is highly correlated with mean plasma glucose levels and reflects the integrated effects of blood glucose over time (53), it may also be a more meaningful outcome variable than fasting plasma glucose. RCTs and prospective epidemiologic studies with adequate numbers of participants can provide the least confounded evidence for or against exercise programs if the intervention and control groups are appropriately balanced and/or stratified by these multiple variables.

In the case that higher-quality studies provide consistent evidence for exercise as an effective intervention, it will remain to be seen if exercise programs are feasible in a community setting, and if the interventions, as well as health outcomes, are sustainable over time. Further evidence on translation of exercise interventions, including how best to motivate individuals to maintain a program of exercise and how best to identify and manage potential risks, will ultimately be needed.

CONCLUSIONS

Evidence is insufficient to assess the effects of exercise on lipid and carbohydrate metabolism and corresponding clinical outcomes in adults with chronic SCI. Future collaborative research is needed to better understand the risks vs benefits of exercise in adults with chronic SCIs.

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