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Obesity and Diabetes as Accelerators of Functional Decline; Can Lifestyle Interventions Maintain Functional Status in High Risk Older Adults?

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Abstract

Obesity and diabetes are known risk factors for the development of physical disability among older adults. With the number of seniors with these conditions rising worldwide, the prevention and treatment of physical disability in these persons has become a major public health challenge. Sarcopenia, the progressive loss of muscle mass and strength, has been identified as a common pathway associated with the initial onset and progression of physical disability among older adults. A growing body of evidence suggests that metabolic dysregulation associated with obesity and diabetes accelerates the progression of sarcopenia, and subsequently functional decline in older adults. The focus of this brief review is on the contributions of obesity and diabetes in accelerating sarcopenia and functional decline among older adults. We also briefly discuss the underexplored interaction between obesity and diabetes that may further accelerate sarcopenia and place obese older adults with diabetes at particularly high risk of disability. Finally, we review findings from studies that have specifically tested the efficacy of lifestyle-based interventions in maintaining the functional status of older persons with obesity and/or diabetes.

Keywords

Physical Function; Obesity; Diabetes; Aging

Introduction

Physical disability resulting from declining health is becoming increasingly prevalent among older adults (age ≥> 65 years) in the United States. Functional decline is typically associated with the progressive loss of skeletal muscle mass and strength known as *sarcopenia* (Hyatt et al., 1990; Janssen et al., 2002). Some estimates indicate that approximately one-quarter to

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one-half of adults aged 65 and older are sarcopenic (Jansen et al., 2004), though the true prevalence is difficult to ascertain given that a consensus clinical definition of sarcopenia does not presently exist. In addition to muscle atrophy secondary to age-related physiological changes, approximately four out of five older adults have at least one chronic health condition, and one out of two older adults have two or more chronic health conditions (Houston et al., 2009). Obesity (Body Mass Index ≥ 30.0 kg/m^2) and diabetes mellitus (hereafter referred to as diabetes), have been identified as important contributors to the progression of sarcopenia (Villareal et al., 2004; Park et al., 2006; Park et al., 2007; Jarosz and Bellar, 2009) and physical disability (Lang et al., 2008; Figaro et al., 2006). Accordingly, the subset of older adults with both obesity and diabetes appears to be at highest risk of physical disability. By 2030, older adults are expected to comprise approximately one fourth of the U.S. population (Houston et al., 2009); thus, it is critical that interventions be developed to prevent or reduce risk of physical disability in seniors.

Physical function, a marker of performance in domains such as activities of daily living and mobility tasks, is a strong determinant of independent living and health (Guralnik and Simonsick, 1993). The maintenance of independent functioning is a central tenet of health-related quality of life for seniors (Muszalik et al., 2011). Moreover, the capacity to perform basic physical functions is also a key predictor of clinical outcomes including hospitalization, surgical recovery, and mortality (Penninx et al., 2000; Afilalo et al., 2010; Studenski et al., 2011). Notably, older adults with diabetes are significantly more likely to become physically disabled than their non-diabetic peers (Kalyani et al., 2010; Volpato et al., 2010; Volpato et al., 2003; De Rekeneire et al., 2003; Rodrigues-Saldaῆ a et al., 2002; Volpato et al., 2002). Accordingly, as compared to non-diabetic older adults, diabetic older adults reportedly experience a 9-year reduction in disability-free life expectancy (Andrade, 2010). Similarly, the relationship between obesity and physical function has been widely examined (Vincent et al., 2010; Coakley et al., 1998; Lang et al., 2008; Rejeski et al., 2010; Alley et al., 2008), and data show that high body weight and high BMI are associated with increased risk for functional impairment and disability. Functional impairments and disabilities in older adults can lead to a loss of independence (Mor et al., 1994), increased use of support services (Branch and Jette, 1982), hospitalization (Branch and Jette, 1981; Ostir et al., 2001), and mortality (Manton, 1988; Reuben and Siu, 1990). Therefore, both obesity and diabetes place older adults at high risk for adverse clinical outcomes including functional impairments in ADLs, disability, hospitalization, and ultimately mortality.

Previously, we reviewed the impact of multiple health conditions in accelerating the progression of sarcopenia and functional decline in older adults (Buford et al., 2010). Here we focus specifically on the contributions and potential mechanisms through which obesity and diabetes may contribute to accelerated sarcopenia and functional decline among older adult populations. We also briefly discuss the underexplored interaction among these conditions, which place the subset of obese older adults with diabetes at particularly high risk of disability. Finally, we review outcomes of clinical trials that have specifically tested lifestyle-based interventions (i.e., dietary and behavioral interventions) for improving or maintaining the functional status of older persons with obesity, diabetes, or both conditions combined. Confounding factors, such as the medical management of obesity and glycemic control, are important considerations when examining individuals with these conditions but are beyond the scope of this review.

Obesity

Recent estimates indicate that over two-thirds of persons aged 60 years and older are overweight, and that one-third of adults age 60 and older are obese (Flegal et al., 2010). These statistics are quite concerning as obesity dramatically increases risk of functional decline and the development of disability in aging populations (Alley et al., 2008; Peeters et al., 2004). With aging, a decrease in muscle mass is typically observed, which is coupled with an increase in fat mass, most notably central adipose tissue (Ferrucci and Alley, 2007). Previous studies have found higher fat mass is associated with lower functional ability in healthy, postmenopausal women (Lebrun et al., 2006), and older men (Broadwin et al., 2001). Compared to peers with a body mass index (BMI; kg/m^2) in the healthy range (i.e., 20 – 24.9 kg/m^2), obese older adults with a BMI $\geq 30 kg/m^2$ experience impairments in basic activities of daily living approximately five years earlier and are twice as likely to develop impairments in function and/or activities of daily living (Peeters et al., 2004). Such findings suggest that obese older adults represent a high risk group for the development of disability and associated negative health outcomes, such as frailty, pain, and functional impairment (Vincent et al., 2012).

In contrast to the working definition of sarcopenia used in non-obese populations, which is based on absolute muscle mass, sarcopenia in obese persons is often defined based on skeletal muscle mass relative to total body mass (Janssen et al., 2002; Penninx et al., 2000; Baumgartner et al., 2004). Relative muscle mass has recently been reported to decrease by 0.02 kg per year for every standard deviation increase in fat mass (i.e., SD = 7.1 kg for males and SD = 9.1 kg for females) (Koster et al., 2011). Importantly, previous studies have found that risk of functional impairment and disability in older adults dramatically increases if muscle loss progresses to the point where relative muscle mass declines below 30% of the mean for young adults (Janssen et al., 2002).

A review by Vincent and colleagues (2010) of 13 cross-sectional and 15 longitudinal studies examining the effect of obesity on mobility disability concluded that increased adiposity combined with low levels of skeletal muscle influences the development of functional impairments (Vincent et al., 2010). A key determinant of functional abilities is the relative relationship of muscle strength to body mass (Goodpaster et al., 2001; Manini et al., 2007; Visser et al., 1998). Evidence suggests that obese older adults typically possess a reduced strength to body mass ratio compared to non-obese older adults, particularly for tasks that require lower extremity strength, such as walking and rising from a chair (Stenholm et al., 2009; Bouchard and Janssen, 2010). Several different mechanisms may underlie the accelerated rate of muscle loss and strength observed in obese older adults. Some potential mechanisms likely include hormonal changes, fat accumulation in muscle, and increased pro-inflammatory load. Obesity is associated with the accumulation of adipose tissue and subsequent increases in both cortisol and pro-inflammatory cytokines (Kyrou and Tsigos, 2009). These physiological changes can promote abdominal fat accumulation, the development of insulin resistance, and skeletal muscle atrophy (Epel, 2009; Estrada et al., 2007). Furthermore, increased fat accumulation in the muscle commonly observed with aging has also been associated with decreased muscle function and quality (i.e., lower strength per muscle size) (Delmonico et al., 2009). Adipose tissue, which was previously thought to be inert, has been identified as an active metabolic tissue, producing and releasing more than 50 different protein molecules and inflammatory cytokines (Jarosz and Bellar, 2009). Thus, excess adipose tissue could disturb the surrounding muscle and other organs by secreting catabolic cytokines (e.g., TNF-α and IL-6) and ultimately lead to metabolic dysregulation (Ferrucci and Alley, 2007; Martha et al., 2012; DiStefano et al., 2007) and accelerated rates of sarcopenia (Meng and Yu, 2010).

Diabetes

Similar to obesity, diabetes is highly prevalent among older adults. Diabetes currently afflicts more than one in five adults age 65 years and older (Center for Disease Control and Prevention, 2007; Federal Interagency Forum on Aging-Related Statistics, 2008). Additionally, the prevalence of diabetes among older adults is rising and projected to reach 30% in the next three decades (Federal Interagency Forum on Aging-Related Statistics, 2008; Boyle et al., 2010). With the total number of older Americans expected to double from 40 to 80 million during this same time span (Federal Interagency Forum on Aging-Related Statistics, 2008), over 26 million older Americans are projected to have diabetes by 2040 with similar projections existing for numerous developed countries worldwide (Chiu et al., 2011; Fagot-Campagna et al., 2005).

Although obesity is a significant contributor to diabetes-related disability (de Rekeneire et al., 2003; Gregg et al., 2000; Volpato et al., 2002; Volpato et al., 2003), there appears to be a distinct effect of diabetes on risk for disability independent of BMI (Park et al., 2006; Volpato et al., 2002; Taijiri et al., 2010; Park et al., 2009). For example, investigators from the Women's Health and Aging Study reported that adjusting for obesity minimally reduced the association between diabetes and objective measures of physical function (Volpato et al., 2002). In addition, Park and colleagues (2006) found a linear relationship between duration of diabetes and poor glycemic control with changes in muscle quality (Park et al., 2006).

Previous studies have demonstrated that older adults with diabetes have a two to threefold higher risk of becoming disabled than their non-diabetic counterparts (de Rekeneire et al., 2003; Rodriguez-Saldañ a et al., 2002). For example, in a cross-sectional, population-based study, diabetic adults aged 65 years and older were significantly slower on two walking tests (4-m and 400-m), after adjusting for age and sex, compared to their non-diabetic peers (Volpato et al., 2012). Furthermore, data from a large community-based, case-control study showed that older adults with diabetes were significantly more likely to use some form of mobility aid (i.e., wheelchair, frame, or walking stick) compared with matched control subjects (Sinclair et al., 2008). In contrast to obese older adults without diabetes, non-obese older adults with diabetes often display an accelerated loss of absolute muscle mass (Park et al., 2006; Taijiri et al., 2010; Park et al., 2009; Kim et al., 2010). Data from an epidemiological study by Park and colleagues (2009) indicate that diabetic older adults lose 33% more muscle mass per year than their non-diabetic peers (Park et al., 2009). Thus, the phenotype of non-obese older adults with diabetes is markedly different than the phenotype of obese older adults. Specifically, non-obese diabetic older adults experience a loss in absolute muscle mass whereas obese older adults experience a loss in relative muscle mass.

Both systemic and cellular mechanisms are thought to accelerate the development of sarcopenia among older adults with diabetes. For example, insulin resistance is known to reduce skeletal muscle protein synthesis by decreasing the activity of anabolic hormones involved in regulating the phosphotidyl-inositol-3-kinase (PI3K) pathway (Morley, 2000; Guttridge, 2004; Figure 1). Other myocellular changes, such as mitochondrial dysfunction and increased myonuclear apoptosis, may also contribute to increased extramyocellular lipid content (and thus decreased muscle quality) in diabetic individuals (Lamson and Plaza, 2002; Sakkas et al., 2006). Various neuropathies associated with diabetes and the resultant decrease in motor end plates can cause weakness, ataxia, and poor coordination thereby playing an important role in the pathogenesis of physical function decline and sarcopenia (Morley, 2008). Additionally, diabetic patients often have accelerated progression of atherosclerosis (Morley, 2000), which can decrease peripheral blood flow, resulting in poor muscle perfusion. Importantly, this list of potentially contributory mechanisms is far from exhaustive as such a list would be beyond the scope of the present review. However, parceled findings do highlight the fact that an integrated understanding of the pathogenesis of sarcopenia among older diabetic individuals has yet to be developed.

Interactions between Obesity and Diabetes in Older Adults

Because obesity dramatically increases risk of diabetes in older adults (Roth et al., 2004), the increasing prevalence of diabetes directly tracks that of obesity over the past thirty years. Accordingly, the conditions have become known as "twin epidemics." As noted above, body fat redistribution occurs during aging and places older adults at increased risk for accumulation of abdominal fat, which contribute to unhealthy metabolic conditions and reductions in insulin sensitivity. Additionally, high levels of visceral fat have been associated with simultaneously increases in the production of pro-inflammatory cytokines and decreases in production of the anti-inflammatory cytokine, adiponectin (Xu et al., 2003). The metabolic disturbances associated with obesity can therefore place older adults at increased risk of diabetes, and the subsequent glucose dysregulation and insulin resistance associated with diabetes may adversely affect appetite regulation and lead to excessive food intake. Thus, the adverse metabolic effects of obesity may ultimately dysregulate appetite and further predispose obese older adults to develop diabetes (Anora and McFarlane, 2005). Since increased levels of inflammation have been shown to be detrimental to muscle (Anker et al., 1999), a negative cycle can occur whereby the pathophysiological effects of obesity and diabetes may interact in such a manner to dramatically increase risk of sarcopenia in this subpopulation of obese older adults with diabetes (Dominquez and Barbagallo, 2007). Additional research is needed to better understand the complex pathophysiologic processes through which obesity and diabetes may interact to increase risk of sarcopenia and subsequent disability in older adults.

An increased understanding of the mechanisms through which both obesity and diabetes interact to affect rates of sarcopenia and functional decline can help facilitate the development of targeted interventions specifically designed to improve the functional status of this high risk population. Findings from intervention studies conducted to date may help elucidate the important contribution that lifestyle factors have in the development and treatment of these chronic health conditions. In the sections below, we review outcomes of intervention studies that have specifically tested lifestyle strategies for improving or maintaining mobility and physical function in the at risk populations of obese older adults, non-obese diabetic older adults, and the high risk sub-population of obese older adults with diabetes. Mobility was selected as an independent outcome measure of physical function because recent reviews and meta-analyses have demonstrated the striking relationship between walking speed and mortality risk in older adults (Studenski et al., 2011; Nocera et al., 2011).

Effects of Lifestyle Interventions on Physical Function in Obese Older Adults

Effects of Dietary Interventions on Physical Function—Accumulating evidence indicates that diet-induced weight loss can improve physical function among obese older adults, independent of changes in physical activity. For example, a study by Jensen and colleagues (2004) examined changes in physical function after a three month low calorie weight loss program for obese older women (Jensen et al., 2004). A pedometer was provided to encourage physical activity but no formal exercise program was provided. After three months, participants achieved a significant reduction in body weight. This change paralleled significant improvements in physical performance, based on scores from a battery of physical tasks, including the 400-meter walk and stair climb, timed and scored on a rating scale. In line with these objectively measured findings, there was a significant improvement in self-reported physical functioning on the Short-Form 36 Health Status Survey.

Another study by Miller and colleagues (2006) found that, despite a decrease in lean muscle mass, a diet-induced weight loss intervention was more effective in improving all measured aspects of physical function compared to the weight stable control (Miller et al., 2006). After six months, the weight loss group showed greater walking distance and faster time in the stair climb task. Self-reported physical function, as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), was significantly higher for participants in the weight loss group.

Based on the findings of these two studies, low calorie dietary interventions alone appear to be effective for improving physical functioning levels in obese older adults. Thus, reductions in body fat and change in body composition may be key physiological changes leading to improved physical function in this group. More research is needed as the use of dietary restriction in older adult populations remains an area of significant debate due to concerns about lean muscle loss following low-calorie dietary regimens. In addition, the examination of specific nutrients (i.e., dietary protein or fish oil) that might influence muscle strength, quality, and retention may help inform recommendations for dietary restriction in this population; however, the role specific macro- and micronutrients may have in affecting muscle retention during weight loss is beyond the scope of the present review.

Effects of Exercise Interventions on Physical Function—Although age is considered a major risk factor for the development and progression of most chronic diseases, regular physical activity substantially attenuates these risks (American College of Sports Medicine, 2009). Unfortunately, the majority of older adults in the United States do not engage in the minimum physical activity recommendations, and older adults typically become more sedentary with advancing age (Pleis et al., 2000; Center for Disease Control and Prevention, 2008). Obesity-related co-morbidities and physical disability are strongly associated with physical inactivity (Chaput and Tremblay, 2009), thus making exercise an important but challenging, aspect of weight loss and physical function.

Few studies have examined the effect of exercise interventions alone on changes in physical function in obese older adults. Davidson and colleagues (2009) investigated functional limitations in sedentary, abdominally obese older adults randomized to an aerobic training, resistance training, combined training, or no-training control group for six months (Davidson et al., 2009). Improvements in functional limitations, measured by four tests including chair stands, two-minute step, Timed Up and Go Test, and seated arm curl, were significant across all exercise groups. Furthermore, improvements in the combined exercise group were greater than that in the aerobic exercise group, but not the resistance exercise group. Somewhat contradictory evidence has been presented by Manini and colleagues (2010), where one year of aerobic and resistance exercise performed twice per week was ineffective at improving long-distance walking speed in obese participants compared to non-obese (Manini et al., 2010). Although obese participants in the intervention group did not show improvements in walking speed compared to non-obese participants, clinically significant improvements on the Short Physical Performance Battery (SPPB) were observed in both groups after one year. Thus, this moderate intensity physical activity intervention improved physical function in older adults, but the positive benefits were attenuated with obesity.

Effects of Combined Dietary plus Exercise Interventions on Physical Function —Lifestyle interventions, designed to combine both diet and exercise, may improve physical function while simultaneously inducing weight loss. Based on evidence from the studies described below, these interventions are likely to be the most beneficial for obese older adults. Specifically, studies to date indicate combined lifestyle interventions have favorable effects in obese older adults on changes in walking speed (see Table 1), objective measures of physical function (see Table 2), and subjective measures of physical function (see Table 3).

Several studies have reported results supporting improved physical function in obese older adults with the combination of diet plus exercise. The Arthritis, Diet and Activity Promotion Trial (ADAPT) examined whether interventions in which diet-induced weight loss were combined with exercise were more effective, either separately or in combination, than usual care in improving physical function and mobility in sedentary overweight and obese older adults with knee osteoarthritis (Messier et al., 2004). The exercise intervention included both aerobic and resistance training activities on three days of the week performed either at home or a supervised facility. The diet intervention included group behavior-focused, skills based sessions. After 18 months, only participants in the diet plus exercise group significantly improved on both objective measures of mobility (i.e., 6-min walk and stair-climb time) and on the pain subscale of the WOMAC compared to usual care.

Anton and colleagues (2011) evaluated the effects of a comprehensive, lifestyle-based intervention by testing whether a reduced calorie diet (i.e., dietary restriction of approximately 750kcal/day) plus a multi-component exercise program could improve physical function in obese older women with mild to moderate physical impairments (Anton et al., 2011). Participants randomized to the treatment group received a six month weight loss program that included weekly group-based weight management sessions plus three supervised exercise sessions consisting of both aerobic activities and lower-body strength training. Compared to participants in the education control group, participants in the treatment group significantly increased walking speed and showed improvements in physical function, based on performance on the SPPB.

Villareal and colleagues (2006) also examined the effects of a multi-component program for weight loss on physical function in obese, frail older adults (Villareal et al., 2006). This 26-week intervention included caloric restriction of approximately 750kcals/day and group-based exercise training sessions with a physical therapist on three days/week including flexibility, endurance, strength training, and balance exercises. Compared to participants in the control group, participants in the treatment group had better outcomes on the Physical Performance Test (i.e., measuring seven timed subtests of physical function including 50-ft walk, chair stands, and standing balance), Functional Status Questionnaire, and specific objective measures of physical function including lower extremity strength, gait, and balance.

In another study by Villareal et al (2011), the independent and combined effects of diet-induced weight loss and exercise on physical function in obese older adults were examined (Villareal et al., 2011). This 52-week intervention included four groups: control group, diet only group (i.e., energy deficit of 500 to 750 kcal per day from their daily energy requirement), exercise only group (i.e., three multi-component, group-based exercise sessions per week), and a diet plus exercise group (i.e., both the diet and exercise programs). Significant weight loss was reported for the diet only and diet plus exercise groups (approximately 10% from baseline), but not the exercise only or control groups. Scores on the Physical Performance Test improved to a greater extent in the diet plus exercise group, indicating better functioning after 12 months, than the diet- or exercise only group. Additionally, gait speed (i.e., measured by time to walk 25 ft.) increased in the diet plus exercise and exercise only groups. Results from this study illustrate the benefits of both diet and exercise separately, but highlight the superiority of a combined treatment program.

Santanasto and colleagues (2011) examined physical function outcomes following six months of a physical activity program, with or without a weight loss intervention, in obese older adults (Santanasto et al., 2011). Participants randomized to the weight loss intervention received a physical activity program, including both aerobic and resistance exercise training, and a healthy-eating weight loss plan based on the Diabetes Prevention Program. Significant improvements on the SPPB at six months were achieved by the weight loss group only. Although some muscle strength was lost, as is expected with aging, changes in fat mass were more closely related to change in physical function compared to changes in lean mass.

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The Diet, Exercise, and Metabolism for Older Women (DEMO) study was a randomized trial comparing the effects of caloric restriction alone versus caloric restriction plus aerobic exercise at a moderate- or vigorous-intensity in obese postmenopausal women (Nicklas et al., 2009). This 20-week intervention included controlled feeding with caloric restriction of approximately 400 kcals/day and supervised aerobic exercise training (i.e., treadmill walking) on three days/week. Beavers and colleagues (2012) examined changes in physical functions in all participants engaged in intentional weight loss from the DEMO study (Beavers et al., 2012). Compared to baseline values, participants showed improvements in physical function based on increased walking speed and performance on the SPPB.

Bouchard and colleagues (2009) examined change in physical capacity in postmenopausal, obese, sedentary women after a 12-week resistance training intervention alone or with caloric restriction (Bouchard et al., 2009). The resistance training with calorie restriction (RT + CR) intervention included a nutrition information session for supervised weight loss plus three supervised resistance-training exercise sessions per week. Physical capacity was measured by a battery of 11 physical tasks of variable difficulty, adapted from the SPPB, and a cumulative score was calculated to yield a summary score of global physical capacity. Observed changes in physical function differed between the resistance training alone and the RT + CR groups such that only participants in the resistance training alone group significantly improved on the global physical capacity score compared to control. However, further examination of the subscales revealed that only participants in the RT + CR group significantly improved on both the 6-min walk and one-leg stand tests.

Similarly, Sénéchal and colleagues (2012) studied the impact of resistance training alone or with caloric restriction on changes in physical function after 12-weeks in dynapenic-obese postmenopausal women (Sénéchal et al., 2012). No significant changes in gait speed were observed, but significant improvements in physical function were noted on two of three validated measures; participants in the resistance training only group improved on the chair stand test while participants in the RT + CR group improved on the one-leg stand test.

Most recently, Straight and colleagues (2012) designed an eight-week community-based resistance training intervention combined with a dietary intervention using a modified version of the Dietary Approaches to Stop Hypertension (DASH) program to improve body composition and physical function in overweight and obese older adults (Straight et al., 2012). Physical function was measured by the SPPB and outcomes indicated that participants significantly improved their performance following the intervention; however, there was no increase in walking speed on the 4-m walk test. These findings are in contrast to those by Avila and colleagues (2010) which examined changes in physical function among participants randomized to DASH for weight loss or DASH plus moderate intensity resistance training for ten weeks (Avila et al., 2010). Walking speed improved on both the 4-m and 400-m walk test for participants in both groups, but no changes on the SPPB were observed in either group.

Effects of Lifestyle Interventions on Physical Function in Older Adults with Diabetes

Evidence has repeatedly shown that weight loss through reduction in caloric intake decreases body weight and improves insulin sensitivity and glucose tolerance in older adults with impaired glucose tolerance (Colman et al., 1995). Limited data exists, however, on the effects of dietary interventions alone on physical function in older adults with diabetes. To our knowledge, no studies have examined the effects of dietary interventions on changes in physical function in older diabetic adults. In addition, lifestyle interventions (i.e., diet plus exercise) have demonstrated efficacy for weight loss (Ryan et al., 2012; Daly et al, 2005) and improved metabolic function (Kelly et al., 2011; Mason et al., 2011; Castaneda et al., 2002) in overweight and obese older adults at risk for diabetes or with overt diabetes, but little is known about the effects of these interventions on measures of mobility and physical function. Thus, in the section below, we limit our discussion to the effects of exercise interventions and combined interventions on changes in physical function in older adults with diabetes.

Effects of Exercise Interventions on Physical Function—To our knowledge, only four studies to date have specifically examined the effects of exercise interventions on changes in physical function in older adults with diabetes. Physical function was assessed in a study by Allet and colleagues (2009) which evaluated the effects of a circuit training regimen on gait and balance in individuals with diabetes (Allet et al., 2010). Participants were randomized to a 12-week exercise intervention, consisting of group-based physiotherapeutic training, or no-treatment control. Based on outcomes of several functional tests, including the Performance-Oriented Mobility Assessment (POMA; 16 items measuring balance and gait), gait assessment, and dynamic and static balance tests, participants in the exercise intervention group showed significant improvements in habitual walking speed, dynamic balance, and the POMA compared to participants in the control group after 12 weeks. A six-month follow-up revealed a decrease in gains made during the intervention in both gait and balance; however, analyses showed the results of these variables remained significantly better than control.

A recent study by Geirsdottir and colleagues (2012) examined the effects of a 12-week exercise intervention designed to increase strength, muscle mass, and physical function in healthy, pre-diabetic, and diabetic older adults (Geirsdottir et al., 2012). Significant improvements in physical function, as measured by the Timed Up and Go Test and 6-min walk test, were observed following the intervention in both healthy and metabolically impaired groups. Thus, the findings of this study support the efficacy of exercise training for improving physical function in older adults with diabetes and pre-diabetes.

Due to potential barriers to exercise in older adults with diabetes (Nied and Franklin, 2002), some researchers have examined the effects of alternative forms of physical activity for improving physical function. Tsang and colleagues (2007) tested the efficacy of a Tai Chi program on mobility in older adults with diabetes (Tsang et al., 2007). Groups met for two supervised hour-long sessions per week for 16 weeks. Significant improvements in maximal gait speed and balance were observed in both groups. Song and colleagues (2011) examined the effects of a balance exercise program on mobility in non-obese older adults with diabetic neuropathies (Song et al., 2011). Participants engaged in balance exercises twice a week for eight weeks, and results showed the Timed Up and Go Test and 10-m walk time both significantly decreased. These findings are in line with the effects of traditional exercise training programs on physical function in older adults with diabetes.

Effects of Lifestyle Interventions on Physical Function in Obese Older Adults with Diabetes

To our knowledge, no studies have specifically evaluated the impact of lifestyle interventions on physical function targeting the high risk group of obese older adults (age > 65 years) with diabetes. All studies to date have examined the effects of combined interventions on changes in functional outcomes in obese adults with diabetes or who at risk for diabetes; thus we limit our discussion in the section below to the effects of two studies in which combined lifestyle interventions were tested in this high risk population.

Effects of Combined Dietary plus Exercise Interventions on Physical Function —The Diabetes Prevention Program (DPP) was a large, randomized controlled trial examining the effects of a lifestyle intervention on preventing or delaying the development

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of type 2 diabetes in non-diabetic adults with elevated fasting and post-load plasma glucose concentrations (The Diabetes Prevention Program Research Group, 2002). Participants were randomly assigned to one of three interventions: lifestyle modification program, metformin (850 mg/bid), or placebo. The weight loss goal for all DPP participants was to lose 7% of initial body weight within the first 6 months and to maintain this weight loss over four years. The lifestyle modification program consisted of an energy decrease of 500–1,000 calories/day (depending on initial body weight), at least 150 min of moderate physical activities (i.e., brisk walking), and individual counseling sessions. Notably, of the 1, 079 participants randomized to the lifestyle intervention, the average age was 51 years old and 20% of the sample in this group was 60 years and older. On average, participants were followed for 2.8 years and the average weight loss reported at the last visit was 0.1, 2.1, and 5.6 kg in the placebo, metformin, and lifestyle-intervention groups, respectively. Overall, participants in the lifestyle intervention group reduced their risk of developing diabetes by 58% as compared to control; this increased to a 71% risk reduction for participants aged 60 years and older in the lifestyle intervention group as compared to control (The Diabetes Prevention Program Research Group, 2002). Thus, the DPP results indicate that a lifestyle intervention consisting of dietary modification, physical activity, and behavioral counseling can delay or prevent the development of type 2 diabetes in the high risk population of obese older adults with impaired glucose regulation.

The Look AHEAD (Action for Health in Diabetes) trial compared the impact of an intensive lifestyle intervention combining a calorie restriction diet plus exercise program to a diabetes support and education group in over 5,000 overweight or obese individuals with diabetes between the ages of 45 to 74 years old (Look AHEAD Research Group, 2007). A standardized treatment protocol was delivered to participants in the intensive lifestyle intervention, utilizing behavioral strategies for weight loss, a portion-controlled diet, and an activity goal of at least 175 minutes per week. The goal of the intensive lifestyle intervention program was to achieve a 7% weight loss in the first year and maintenance of this weight loss over three years. Aerobic fitness, assessed using a submaximal graded exercise test, was significantly greater in the intensive lifestyle intervention group compared to the diabetes support and education group after year one. Although fitness gains declined over time in both groups, participants in the intensive lifestyle intervention group maintained an overall positive change in fitness at year four. In contrast, fitness levels declined among participants in the education group and were below baseline levels at year four.

Foy et al (2011) examined a subset of participants (n = 1203; mean age = 58.8 years old) from the Look AHEAD study with self-reported knee pain to assess changes in physical function, knee pain, and stiffness after one year (Foy et al., 2011). Changes were measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which assesses function, pain, stiffness, and overall summary score. Analyses were conducted to determine the relationship between the intensive lifestyle intervention and WOMAC scores, as well as to discover any relationships between the intensive lifestyle intervention and potential mediator variables. Results showed that participants in the intensive lifestyle intervention group reported more favorable change in WOMAC pain, function, and summary scores compared to the diabetes support and education group, and increased weight was associated with poorer outcomes on all subscales of the WOMAC. Other variables negatively associated with all WOMAC subscales included age, female gender, baseline weight, and use of non-steroidal anti-inflammatory drugs.

Notably, a recent publication by Rejeski et al (2012) also examined participants in the Look AHEAD trial and assessed the degree to which mobility was influenced by the intervention and if weight loss or improvements in fitness mediated that change (Rejeski et al., 2012). Based on a sequential and progressive model of disability, participants were characterized by one of four states ranging from "good mobility" to "severe limitations." Mobility was assessed by self-report on the Physical Functioning subscale of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). At baseline, average BMI and number of comorbid medical conditions increased progressively from the "good mobility" group to the "severe limitations" group. Regarding changes in the risk of loss of mobility, participants in the lifestyle intervention group reduced their risk by nearly half as compared to the education group. Moreover, fewer participants in the education group had good mobility and more had severe limitations compared to the intervention group. Both weight loss and improved fitness were found to be significant mediators of these functional changes.

Conclusions and Future Directions

Age-related changes in body composition play a central role in metabolic dysregulation, functional decline, and risk for disability. Both obesity and diabetes have been found to accelerate the progression of sarcopenia and physical disability in older adults. Obese older adults frequently exhibit low relative muscle mass and increased intramuscular adipose tissue compared to non-obese older adults. In contrast, diabetic older adults show greater muscle atrophy compared to non-diabetic peers. To date, the adverse effects of obesity and diabetes on physical function have primarily been studied independently. The interaction among these conditions, however, may lead to a particularly high risk subpopulation of obese older adults with diabetes who may experience greatly accelerated rates of sarcopenia and functional decline. This is of significant concern, as the prevalence of older adults with both obesity and diabetes is accelerating.

Our review indicates that lifestyle interventions involving either dietary change (i.e., caloric restriction) or exercise can improve functional outcomes in obese older adults as well as older adults with diabetes. Combined lifestyle approaches appear to produce the largest improvements in physical function. The optimal strategy for intervening in these high risk populations, however, is currently unknown. To our knowledge, no study has tested the effects of either dietary or exercise interventions alone on changes in physical function specifically in obese older adults with diabetes. Findings from at least one study indicate that a combined lifestyle approach can produce functional improvements in obese adults with diabetes, though obese older adults with diabetes were not specifically targeted in this study. Thus, there is an urgent need for intervention studies testing lifestyle strategies for improving or maintaining functional status in the extremely high risk group of obese older adults with diabetes.

If left unimpeded, the rising prevalence of the co-morbid conditions of obesity and diabetes will undoubtedly contribute to the increasing prevalence of disability among older populations, which could have grim health and economic consequences in the United States and other developed countries. As such, identification of older adults at high risk for sarcopenic due to obesity or diabetes or the combination of both conditions will be important in clinical practice. Moreover, new comprehensive prevention and treatment strategies will be needed to combat escalating rates of physical disability among obese older adults with diabetes.

Although findings from clinical trials are critical to inform healthcare practice for older adults with obesity and/or diabetes, there are a number of challenges that must be overcome to successfully conduct such trials (Anton et al., 2012). Among these challenges, adherence to lifestyle interventions and other aspects of experimental protocols are among the top factors that need to be considered since poor adherence can have a significant adverse effect on interpretation of study outcomes (Shumaker and Rejeski, 2000). Thus, significant efforts should be made during the study planning process to design trials so as to facilitate adherence and maximize participant retention. As compared to many other populations, adherence and retention are likely to be an even greater challenge among older adults with obesity and diabetes for a number of reasons including: (1) increased risk of disease conditions, such as illness and disability, that could interfere with study participation, (2) similar to physical functioning, cognitive functioning may decline over the course of a trial, particularly in trials in which the length of the intervention is greater than one year, which could adversely affect a participant's ability to function and engage in key aspects of a study intervention, and (3) increased levels of depression and other psychological concerns may lead participants to avoid initiation and/or continued engagement in recommended lifestyle changes in experimental protocols. Strategies for handling each of these specific challenges are beyond the scope of the present review but have been recently reviewed elsewhere (Anton et al., 2012).

Future research is warranted regarding differences in the development of sarcopenia and functional decline among obese and non-obese, diabetic older adults. Additional research is clearly needed to better characterize the underlying causes of accelerated muscle atrophy in this population and to develop subsequent therapeutic treatments specifically designed to combat sarcopenia and prevent functional decline among the high risk population of obese older adults with diabetes. Such research should include information regarding the biological mechanisms that exacerbate muscle atrophy in obese and non-obese older adults with and without diabetes. Finally, more research is needed to determine the best methods for intervening to reduce risk of functional decline and physical disability in the high risk population of obese older adults with diabetes.

Abbreviations

DASH	Dietary Approaches to Stop Hypertension
POMA	Performance-Oriented Mobility Assessment
RT + CR	Resistance Training plus Calorie Restriction
SPPB	Short Physical Performance Battery
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

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Highlights

- Age-related physical disability is an important public health concern
- Obesity and diabetes each independently increase the risk of disability in seniors
- Obese, diabetic older adults appear to be among highest risk for becoming disabled
- Lifestyle-based interventions have shown efficacy for improving physical function
- Questions remain regarding functional decline in obese vs. non-obese diabetics

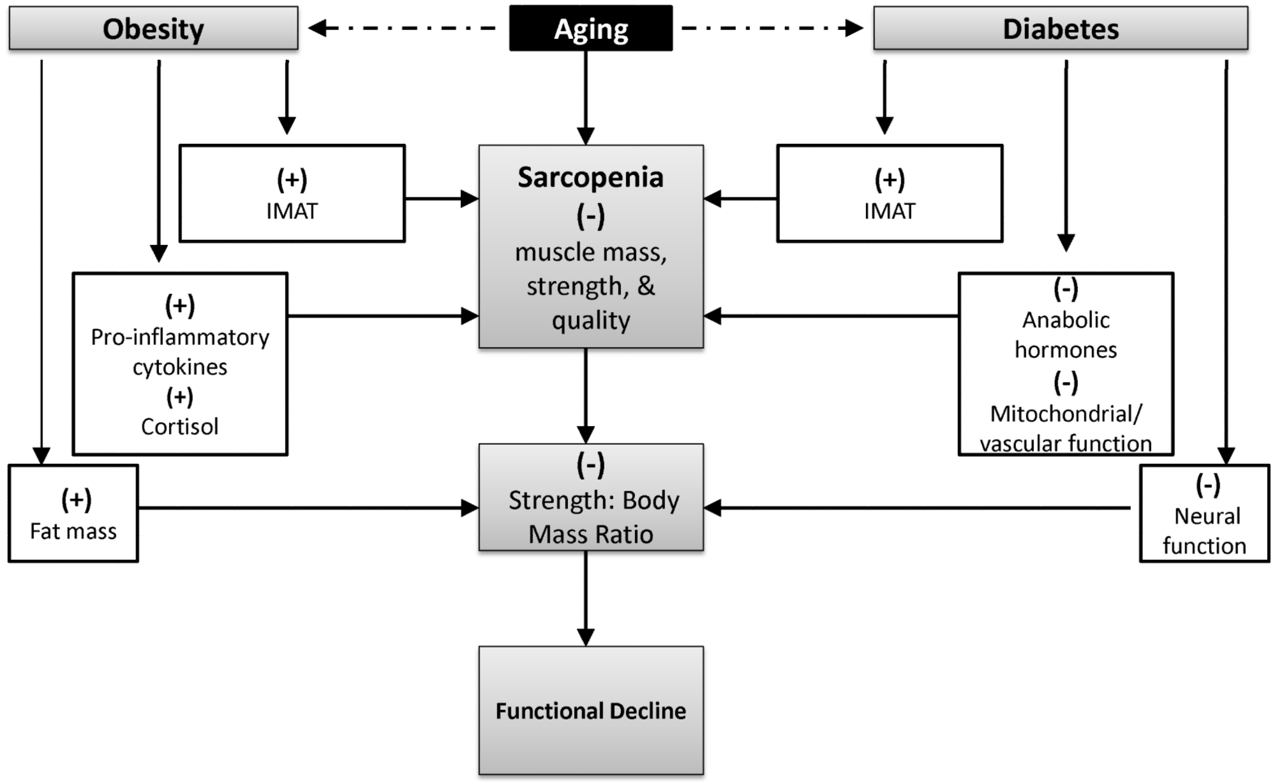

Figure 1.

Potential mechanisms through which obesity and diabetes may accelerate functional decline among older adults.

[1] A negative cycle can occur whereby the pathophysiological effects of obesity and diabetes may interact in such a manner to dramatically increase risk of sarcopenia in this subpopulation of obese older adults with diabetes (Dominquez and Barbagallo, 2007).

Table 1

Effects of Lifestyle Interventions on Changes in Walking Speed in Obese Older Adults

Study	N	Age Range (years)	BMI Range (kg/m^2)	Intervention	Contact Frequency	Length (weeks)	Physical Function Measure	Δ in Speed (m/s)	p-value
Anton *et al.* (2011)	34	55–79	>28.0	CR+PA	wk	24	400-m Walk *	0.16	n/a
Avila *et al.* (2010)	31	60–75	25.0 – 39.9	CR+RT	wk	10	4-m Walk	0.11	*ns*
							400-m Walk	0.10	<.001
Bouchard *et al.* (2009)	48	55–75	27.0 – 38.0	CR	wk	12	6-min Walk	0.03	<.01
				CR+RT				0.06	*ns*
				RT				0.08	*ns*
Manini *et al.* (2010)	424	70–88	≥30.0	PA	wk	52	400-m Walk	0.04	n/a
Messier *et al.* (2004)	316	≥60	≥28.0	PA	wk/bi-wk	78	6-min Walk *	0.13	n/a
				CR				0.03	n/a
				CR+PA				0.17	n/a
Miller *et al.* (2006)	87	≥60	≥30.0	CR+PA	wk	26	6-min Walk **	0.20	n/a
Nicklas *et al.* (2004) †	112	50–70	25.0 – 40.0	CR+PA	wk	20	4-m Walk	0.01	n/a
Sénéchal *et al.* (2012)	48	55–75	27.0 – 38.0	CR	wk	12	6-min Walk	0.06	*ns*
				RET				0.09	*ns*
				CR+RT				0.06	*ns*
Straight *et al.* (2012)	109	55–80	25.0 – 39.9	CR + RT	wk	8	4-m Walk	0.04	<.001
Villareal *et al.* (2006)	27	≥65	≥30.0	CR+PA	wk	26	25ft Walk *	0.08	<.05
Villareal *et al.* (2011)	107	≥65	≥30.0	CR	wk	52	25ft Walk *	0.08	*ns*
				PA				0.14	*ns*
				CR+PA				0.28	<.01

CR= Caloric Restriction; PA= Physical Activity; RT= Resistance Training; wk= weekly; m/s = meters per second; Δ= change

Change data are defined as the follow-up minus the baseline value.

* Significant Between Group Difference p<.05;

** Significant Between Group Difference p<.01

† Data on physical function from Beavers *et al* (2012)

Table 2

Effects of Lifestyle Interventions on Changes in Physical Function in Obese Older Adults

Study	N	Age Range (years)	BMI Range (kg/m^2)	Intervention	Contact Frequency	Length (weeks)	Physical Function Measure	Δ in Score	p-value
Anton *et al.* (2011)	34	55–79	>28.0	CR+PA	wk	24	SPPB*	1.8	<.001
Avila *et al.* (2010)	31	60–75	25.0 – 39.9	CR+RT	wk	10	SPPB	0.1	*ns*
Bouchard *et al.* (2009)	48	55–75	27.0 – 38.0	CR	wk	12	Global	0.0	*ns*
				CR+RT			Physical	2.0	*ns*
				RT			Capacity score*	4.0	<.05
Jensen *et al.* (2004)	26	≥60	≥30.0	CR	wk	12	PPT	1.1	<.05
Manini *et al.* (2010)	424	70–88	≥30.0	PA	wk	52	SPPB	0.7	<.05
Nicklas *et al.* (2004)†	112	50–70	25.0 – 40.0	CR+PA	wk	20	SPPB	0.4	n/a
Santanasto *et al.* (2011)	36	≥60	28.0 – 39.9	CR+PA	wk	52	SPPB	0.7	<.05
				PA				0.5	*ns*
Straight *et al.* (2012)	109	55–80	25.0 – 39.9	CR + R	wk	8	SPPB	0.5	<.001
Villareal *et al.* (2006)	27	≥65	≥30.0	CR+PA	wk	26	PPT**	2.6	<.001
Villareal *et al.* (2011)	107	≥65	≥30.0	CR	wk	52	PPT*	3.1	<.001
				PA				4.0	<.001
				CR+PA				5.4	<.001

CR= Caloric Restriction; PA=Physical Activity; RT= Resistance Training; wk= weekly; PPT= Physical Performance Test; SPPB= Short Physical Performance Battery; Global Physical Capacity score= sum of 11 physical capacity tests; Δ= change

Change data are defined as the follow-up minus the baseline value.

* Significant Between Group Difference p<.05;

** Significant Between Group Difference p<.01

† Data on physical function from Beavers *et al* (2012)

Table 3

Effects of Lifestyle Interventions on Perceived Changes in Functional Status Measured by Self-Report Assessments in Obese Older Adults.

Study	N	Age Range (years)	BMI Range (kg/m^2)	Intervention	Contact Frequency	Length (weeks)	Physical Function Measure	Self-Report Improvements	p-value
Jensen *et al.* (2004)	26	≥60	≥30.0	CR	wk	12	SF36		
							-Physical Function	8.7%	<.05
Messier *et al.* (2004)	316	≥60	≥28.0	PA	wk/bi-wk	78	WOMAC	12%	*ns*
				CR				18%	<.05
				CR+PA				24%	<.05
Miller *et al.* (2006)	87	≥60	≥30.0	CR+PA	wk	26	WOMAC		
							-Sum*	11.2%	n/a
							-Physical Function*	12.4%	n/a
Villareal *et al.* (2006)	27	≥65	≥30.0	CR+PA	wk	26	FSQ*	4.7%	.005
							SF36		
							-Physical Function*	23.2%	<.001
							-Role Limitations*	23.6%	<.05
							-Bodily Pain*	10.4%	.001
Villareal *et al.* (2011)	107	≥65	≥30.0	CR	wk	52	FSQ*	3.6%	<.001
				PA				5.0%	<.01
				CR+PA				7.5%	<.001

CR= Caloric Restriction; PA=Physical Activity; wk= weekly; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SF36= Medical Outcomes Survey 36-Item Short-Form Health Survey; FSQ= Functional Status Questionnaire.

*Significant Between Group Difference p<.05;

**Significant Between Group Difference p<.01