Obstructive Sleep Apnea Risk in Abdominal Aortic Aneurysm Disease Patients: Associations with Physical Activity Status, Metabolic Syndrome, and Exercise Tolerance

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ABSTRACT

Obstructive sleep apnea (OSA) is common in older U.S. adults and the prevalence is anticipated to rise in this age group along with obesity, a prominent risk factor for OSA. Recently, OSA was determined to be highly prevalent among patients with abdominal aortic aneurysm (AAA) disease. **Objectives:** Examine associations between OSA risk and physical activity (PA), metabolic syndrome (MetSyn), and exercise responses to cardiopulmonary exercise testing (CPET) in elderly patients with AAA disease. **Methods:** Elderly patients (*n*=326 for Studies 1 and 2; *n*=114 for Study 3) newly diagnosed with small AAAs (aortic diameter ≥2.5 and < 5.5 cm) were recruited. Data collection for all participants included: extraction of medical history and drug information from medical records; completion of a physical examination to assess resting vital signs and anthropometrics; fasting blood draw for several biochemical analyses; completion of a cardiopulmonary exercise test (CPET); and completion of interviews and questionnaires for health history, PA, and OSA risk. **Results:** 57% of subjects were High-risk for OSA and 17% were classified in the highest-risk Berlin Risk Score (BRS) 3 group; these subjects reported fewer blocks walked/day, flights of stairs climbed/day, and expended fewer Calories when engaged in these activities compared to Low-risk counterparts, independent of obesity. Among those at High-risk for OSA, 45% had MetSyn. Subjects with the highest BRS also had the highest prevalence of MetSyn and values for the MetSyn component biomarkers. Exercise capacity and physiological responses at rest, during exercise, and recovery were similar between groups at High- and Low-risk for OSA. **Conclusions:** Reduced levels of PA among elderly AAA patients at High-risk for OSA could have unfavorable implications for cardiovascular disease (CVD) risk and all-cause and CVD mortality. Subjects demonstrating the most clinical symptoms of OSA showed a significantly higher prevalence for MetSyn and several of the biomarkers that determine MetSyn. In clinical practice, the BRS may be useful for identifying those AAA patients at increased risk for both OSA and MetSyn.

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INTRODUCTION

The prevalence of obesity is increasing in the U.S., with more than one-third of adults qualifying as obese in 2009-2010 [1]; by the year 2030, it is projected that 42% of Americans will be obese [2]. Due to the physiological effects of aging on body weight and body composition, in addition to potential declines in the activity habits of older adults, it is not surprising that a greater percentage of adults age 60 and over are obese in comparison to younger adults, with nearly 40% of older adults qualifying as obese [1, 3]. Greater attention to positive health culture and advances in medical care has contributed to an increasing elderly population as people are living longer. By 2030, the number of U.S. adults age 65 and older is anticipated to double to about 71 million [4].

Abdominal aortic aneurysm (AAA) disease is prevalent in the elderly, most often occurring in people age 60 years and old. AAA disease is a common and morbid disease in which the lower part of the aorta is weakened and bulging. Risk factors for AAA disease include advancing age, history of cigarette smoking, male gender and family history. Recently, obstructive sleep apnea (OSA), the most common sleep related breathing disorder that affects an estimated 20% of the U.S. adult population [5], was determined to be highly prevalent among patients with AAA disease [6] and may not only be a risk for factor for aortic disease [7], but a causal factor for advanced AAA expansion [6]. Surgical repair is currently the only effective method of AAA treatment and is usually recommended when the aneurysm is large enough that the risk of surgery is less than the risk of rupture; however, participation in regular exercise has been shown to reduce the risk of developing AAA disease [8] and may limit progression of early AAA disease [9].

OSA is characterized by repetitive bouts of upper airway occlusion or collapse during sleep, resulting in intermittent periods of hypoxia, hypercapnia, and fragmented sleep [10]. OSA is diagnosed in individuals who have at least 5 apnea or hypopnea events per hour of sleep (Apnea/Hypopnea Index, AHI). OSA is prevalent in older adults with at least 1 in 10 people older than 65 years of age having diagnosed OSA (compared to 1 in 20 adults in the general population) and the prevalence of the disorder is anticipated to rise as an increasing proportion of Americans are obese and elderly, both of which are risk factors for OSA [5, 11]. It is estimated that up to 90% of people with OSA remain undiagnosed, likely due to poor awareness of the disorder, lack of routine screening, and limited diagnostic sleep study facilities. A hallmark symptom of OSA is excessive daytime sleepiness (EDS), which may reduce physical activity (PA) due to fatigue and sleepiness during the day. Consequently, reduced PA may further exacerbate OSA through its influence on obesity, a major correlate of OSA (approximately 80% of people suffering from OSA are obese) [12]. Untreated OSA can increase risk for several chronic diseases and disorders including obesity, hypertension (HTN) and cardiovascular disease (CVD), metabolic disorders, depression, and aortic disease [7, 13-20].

Metabolic syndrome (MetSyn) is the clustering of central obesity, insulin resistance (IR) or glucose intolerance, HTN, and dyslipidemia; important consequences of MetSyn include increased risk of CVD and type II diabetes [21, 22]. OSA may contribute to development of MetSyn and subsequently to type II diabetes through inflammation exacerbated by chronic intermittent hypoxia and sleep fragmentation associated with OSA [22, 23]. Repetitive episodes of intermittent hypoxia followed by re-oxygenation, as seen in OSA, may result in the generation of reactive oxygen species which can up-regulate transcription factors that control inflammatory pathways that have downstream effects on the cardio-metabolic factors in MetSyn [24-27].

Furthermore, sleep deprivation may modulate neuro-humoral pathways [28, 29], activate systemic inflammation [30], and increase susceptibility to oxidative stress [31], thereby potentially encouraging the development of metabolic abnormalities through multiple feedback mechanisms [32]. While the exact pathophysiology remains unclear, untreated OSA in association with obesity, is linked to impaired glucose regulation, HTN, and increased cardiovascular mortality in adults [33]. Age is a risk factor for both OSA and MetSyn, with OSA occurring 2-3 times more often in older adults and MetSyn affecting 20% of people in their 60s [34]. Studies suggest that the clinical implications of OSA differ in the elderly. Follow-up studies of middle-aged cohorts have shown that OSA severity worsens over time and increases risk for associated comorbidities [35]; however, in the elderly, OSA severity appears to decrease with age [36] and presence of comorbidities may not be associated as strongly with OSA [37-39]. Furthermore, markers that are strong predictors of OSA in middle-aged adults, such as increased body anthropometrics and snoring, are less strongly associated with OSA in the elderly [40]. The untoward associations between OSA and clinical risk of MetSyn has been elucidated in pre-elderly populations [41, 42], but not systematically examined in the elderly [32].

Physical activity has significant health benefits on not only weight control, but also independently reduces risk for chronic health diseases and disorders including type II diabetes, HTN, CVD, OSA, depression and osteoporosis [43, 44]. Consequently, a sedentary lifestyle often accompanies and promotes obesity, further increasing risk for developing chronic illnesses. EDS, a consequence of untreated OSA, may further limit PA behavior beyond the influence of obesity alone. Findings from several studies indicate that OSA is associated with decreased PA in young and pre-elderly populations [45-47]; however, upon review of the literature, this has not been systematically examined in an elderly population with diagnosed small AAA disease who may already demonstrate lower levels of PA due to aging and AAA disease.

Activities of daily living (ADLs) refer to daily self-care activities performed within an individual's daily environment, and include activities such as bathing, dressing and feeding one's self, homemaking, functional mobility, and leisure activities [48]. A fundamental requirement for many ADLs is the ability to perform aerobic work, requiring the efforts of the heart, lungs, and circulation to deliver oxygen to metabolically active muscles. The assessment of exercise capacity and tolerance also provides important diagnostic and prognostic information in a clinical setting [49]; exercise capacity and PA status are well- established predictors of cardiovascular and overall mortality [50, 51], supporting the value of cardiopulmonary exercise testing (CPET) as a clinical tool that provides clinically relevant diagnostic and prognostic information in both healthy persons and those with chronic health conditions, including OSA [52].

LITERATURE REVIEW

Aging in the United States

Improved medical care and prevention efforts have contributed to dramatic increases in life expectancy and population rates of older adults in the United States over the past century. The life expectancy for adults in the U.S. increased from 68.2 yrs in 1950, to 73.7 yrs in 1980, and reached 78.5 yrs in 2009 [53]. Longer life spans and aging baby boomers are anticipated to double the population of older Americans (age 65 years and older) during the next quarter century. By 2030, there will be more than 70 million older adults, accounting for about 20% of the U.S. population [54]. Longer life expectancy is accompanied by increases in chronic disease development in older adults. Approximately 80% of older Americans have at least one chronic condition and 50% have at least two chronic conditions, such as CVD, type II diabetes, or cancer [4]. People living longer have also resulted in a shift in the leading cause of death for all age groups, including older adults, from infectious diseases and acute illnesses to chronic and degenerative illnesses. In 2011 the leading cause of death was heart disease, while respiratory diseases, cerebrovascular diseases, and diabetes were among the top ten leading causes of death in the U.S [55].

Abdominal Aortic Aneurysm (AAA) Disease

AAA disease is a common and morbid condition of older adults in which the lower part of the aorta is weakened and bulging. AAA disease is prevalent in the elderly, most often occurring in people age 60 years and older, and AAA presence is associated with overweight and obesity [56]. AAAs tend to cause no symptoms, though occasionally pain in the abdomen and back, due to pressure on surrounding tissues, or leg discomfort, due to reduced blood flow, may be experienced. Most small and slow-growing AAAs don't rupture, but size and rate of growth should be watched carefully. The aorta enlarges with age normally, but is considered aneurysmal when the diameter exceeds 3cm (normal diameter of the aorta is approximately 2cm). Risk factors for AAA include advancing age, history of cigarette smoking, male gender and family history. Risk of AAA rupture is significant for AAAs with diameters greater than 6cm. Surgical repair is currently the only effective method of AAA treatment and is usually recommended when the aneurysm is large enough that the risk of surgery is less than the risk of rupture. The major complication of AAAs is rupture, in which large amounts of blood spill into the abdominal cavity and can result in death within minutes.

The pathophysiology of AAA formation is complex and not fully understood. Currently, there are thought to be four mechanisms relevant to AAA formation, including: 1) proteolytic degradation of aortic wall connective tissue; 2) inflammation and immune responses; 3) biochemical wall stress; and 4) molecular genetics [57]. Aneurysm formation involves a complex process of destruction of the aortic wall through degradation of elastin and collagen. This leads to a decrease in tensile strength in the aortic wall which can lead to formation of an aneurysm. Differences in aortic structure, biology, and stress along the length of the aorta can also make sites more susceptible to AAA formation. Animal and human models suggest a critical role for the matrix metalloproteinase proteinases (MMPs) in aneurysm formation [58]. The MMPs play a role in the control of inflammation, as well as breakdown of the aortic wall. MMP9 appears to play a particularly critical role in AAA formation, expansion, and rupture. Family history also plays a role in predisposition to AAA disease. It is estimated that approximately 15% of patients with AAA disease have a positive family history. There are many candidate genes that could be linked to AAA formation; however, no single genetic polymorphism or defect has been identified as positively being linked with AAA formation.

Obesity

Obesity is becoming a global epidemic and in the past 10 years in the United States, dramatic increases in obesity have occurred in all demographics. Overweight and obesity are classified by body mass index (BMI), a factor of weight for height. In adults, overweight is defined by a BMI of 25.0 to 29.9 kg/m^2; obesity is defined as a BMI $\geq$ 30.0 kg/m^2. The prevalence of obesity is increasing in the U.S for older adults, age 60 years and over, of which 40% are obese [3] compared to the 35.7% of all American adults age 20 years and older who are considered obese according to data from the National Center for Health Statistics from the 2009/2010 National Health and Nutrition Examination Survey (NHANES) [1]. Older women have higher obesity rates compared to men, with 42.3% of women age 60 years and older meeting or exceeding obesity thresholds compared to 36.6% of older men. The prevalence of obesity in the U.S. has increased over the past several decades. From the 1988-1994 NHANES report to the 1999-2000 report, the prevalence of obesity increased from 22.9% to 30.5% among adult men and women. Prevalence of obesity continued to rise and by 2010 the prevalence of obesity increased to 35% among men and 35.8% among women. By the year 2030, it is projected that 42% of Americans will be obese and this proportion will likely be even greater for older adults considering the trends of obesity [59].

Obesity and Chronic Diseases

The health consequences of obesity are significant and include cardiovascular diseases, metabolic diseases, cancers, dyslipidemia, sleep apnea and respiratory disorders, and mental health conditions [60]. Obesity increases the risk of CVD due to negative effects on blood lipids, blood pressure (BP), atherosclerosis and inflammation. Metabolic consequences of obesity include development of type II diabetes, insulin resistance (IR), and impaired glucose tolerance, in response to the inability of the body to produce enough insulin in the blood or resistance to the insulin produced. Body mass and type II diabetes are highly associated, as more than 80% of people with diabetes are obese or overweight (CDC). Obesity is the strongest risk factors for development of OSA, a common chronic sleep disorder characterized by recurrent occlusion of the upper airway during sleep. It is estimated that 80% of OSA patients are obese [12]. Obesity is also strongly associated with poor mental health, particularly depression. Adults with depression or with a history of depression are 60% more likely to be obese than those with positive mental health. One study concluded that clinically significant depression is up to four times higher in severely obese individuals than in similar, non-obese individuals [61]. Sixty percent of the nation's obese population reported having at least one of these chronic conditions compared to 33% of normal-weight adults [62]. Excess weight is also associated with increased early mortality, as shown in follow-up studies from the Framingham Heart Study and the NHANES III cohort [63, 64] and it is well documented that all-cause mortality is increased in overweight and obese individuals [65-67]. Obesity is also a financially costly disorder. In 2008, overall medical care costs related to obesity for U.S. adults were estimated to be approximately $147 billion [68]. Additional costs related to obesity include loss of worker productivity due to absenteeism, disability, and death. Researchers have estimated that if U.S. obesity trends continue, obesity-related medical costs alone could increase by as much as $66 billion annually by the year 2030 [69].

Aging and Obesity

Due to the physiological effects of aging on body weight and body composition, in addition to potential declines in the activity habits of older adults, it is not surprising that a greater percentage of adults age 60 and over are obese in comparison to younger adults, with nearly 40% of older adults qualifying as obese [1, 3]. Aging is associated with changes in body composition, whereby fat-free mass progressively decreases and fat mass increases. Body fat mass is determined by relation between energy intake and expenditure. Studies suggest that energy intake does not change or may decline with advancing age, proposing that a decrease in energy expenditure is a primary contributor to the gradual increase in body fat with advancing age [70, 71]. Aging is associated with a decrease in all the major components of total energy expenditure, including resting metabolic rate and thermic effect of food, along with PA which accounts for about half of the decrease in the total energy expenditure that occurs with aging [72]. Hormonal changes that accompany aging may also contribute to alterations in fat distribution, favoring increased fat mass in the elderly. These include, but are not limited to, thyroid hormones, insulin, glucose, and reproductive hormones including estrogen, progesterone, and testosterone. Serum thyroid stimulating hormones decrease in healthy elderly subjects due to age-related decreases in the secretion of these hormones by the pituitary [73]. Thyroid hormones influence body metabolism, thereby slowing metabolism as secretion of thyroid hormones declines with age. Glucose tolerance progressively declines with age, potentially leading to IR in older adults [74]. Age-related insulin secretory dysfunction may have play a role in the alterations in glucose metabolism with age, contributing to the high rates of impaired glucose tolerance in older adults (more than 40% of Americans age 65 years and older meet the diagnostic criteria for type II diabetes or impaired glucose tolerance) [75]. Additionally, aging is accompanied by a decrease in testosterone, estrogen, and progesterone, all of which can contribute to fat gain with age due to influences on muscle mass, metabolic rate, fat synthesization, and fluid retention, respectively.

Aging and Chronic Diseases

Increases in chronic diseases and disabilities that often accompany aging may limit the daily activities of older adults and reduce health-related quality of life. Chronic illness may also attribute to the reductions in PA and exercise capacity seen in older adults. A 2003 study found that nearly 57% of older adults did not meet the recommended guidelines for PA [76]. The

Centers for Disease Control and Prevention (CDC) recommends that older adults who are generally fit and have no limiting health conditions engage in 150 minutes of moderate intensity aerobic activity each week, or 75 minutes of vigorous intensity aerobic activity, in addition to two days each week of muscle-strengthening activities that work all major muscle groups [77]. Conversely, physical inactivity and a sedentary lifestyle contribute to and exacerbate many chronic diseases that are the leading causes of death in the U.S, including cardiovascular and metabolic diseases. In 2002, the primary causes of death for older adults in the U.S. included heart disease (accounting for 32% of all deaths), cancer (accounting for 22% of all deaths), and stroke (accounting for 8% of all deaths). These accounted for 61% of all deaths in American adults, age 65 years and older [2]. A study published in 1993 demonstrated that 14% of deaths in the U.S. were attributed to activity patterns and diet [78] while another study linked sedentary lifestyles to 23% of deaths from major chronic diseases [79]. In 2007, three negative health behaviors, including smoking, poor diet, and physical inactivity, were the root cause of nearly 35% of deaths in the U.S [54]. These negative health behaviors primarily attribute to the development of obesity, heart disease, cancer, stroke, and diabetes, which are the nation’s leading chronic disease killers.

Obstructive Sleep Apnea

OSA is the most common sleep related breathing disorder, affecting an estimated 20% of the U.S. adult population [5]. The prevalence of OSA is anticipated to rise as an increasing proportion of Americans are obese and elderly, both of which are risk factors for OSA. OSA is prevalent in older adults; the Sleep Heart Health Study found that among 6,400 older adults, sleep disordered breathing (SDB) prevalence rates for mild to severe SDB ranged from 19-36%

for adults 60-98 years old [40]. These rates far outpace those for middle aged adults, age 30-60 years old, whose SDB rates were 2-4% for women and men [11]. In a large population-based study of older adults (65 to 95 years of age), Ancoli-Israel and colleagues [38] found that 70% of the men and 56% of the women had OSA as defined by an AHI of 10 or more. Bixler and colleagues [36] found that men and women 65 to 100 years of age had a prevalence of OSA that was twice as high as the OSA prevalence among middle age persons. Both of these studies, however, suggest that most of the age-related prevalence increase occurs before age 65 and plateaus at some point after age 65. Obesity is the primary risk factor for OSA and is reported in more than 40% of OSA cases; furthermore, more than 80% of individuals with OSA are also obese [12]. Body mass directly influences OSA risk, as one study suggests a 10% increase in body weight increases risk for OSA 6-fold [17]. In addition to obesity, several anthropometric and physical features are indicative of OSA, including a large neck circumference and retrognathia, or a small or recessed jaw. A large neck circumference can indicate excess adipose tissue around the upper airway which can reduce the patency of the airway during sleep. Some studies have concluded that neck circumference is a more useful predictor for OSA than general obesity [80]. Craniofacial abnormalities, such as a small jaw or recessed chin, can also affect the affect the airway and result in SDB. Major signs and symptoms of OSA include loud and chronic snoring, choking or gasping during sleep, and EDS due to poor sleep quality and quantity. One retrospective, cross-sectional study found that EDS was demonstrated in 87.2% of patients with OSA [81]. It is estimated that up to 90% of people with OSA remain undiagnosed, likely due to poor awareness of OSA, lack of routine screening, and limited diagnostic sleep study facilities.

The “gold standard” for diagnosing OSA is laboratory polysomnography (PSG); however, sleep health questionnaires that stratify patients based on clinical symptoms, physical examinations, and risk factors, are often employed as a first step assessment to screen for OSA. Questionnaires that are commonly used to screen for OSA and have been validated against PSG, include the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Berlin Questionnaire (BQ), and most recently, the STOP-Bang questionnaire. Sleep screening questionnaires do not require complicated calculations to identify high risk patients, and they are relatively easy and cost-effective to apply clinically; however, there are also limitations. Sleep questionnaires rely on self-report and disclosure of signs and symptoms, as well as the patient's memory and ability and willingness to follow instructions. Additionally, many of the signs and symptoms of OSA may be difficult for the patient to self-identify, such as snoring and choking during sleep, and can be misinterpreted as other conditions. A recent review and meta-analysis of OSA screening questionnaires concluded that the BQ had the highest specificity for predicting the existence of OSA and the BQ and STOP Bang questionnaire had the highest specificity and sensitivity, respectively, for predicting moderate or severe OSA [82]. Another meta-analysis also concluded that BQ was among the most accurate questionnaires overall to screen for SDB, and that the ESS was the least accurate [83].

Untreated OSA can increase risk for several chronic diseases and disorders including obesity, HTN and CVD, metabolic disorders, depression, and aortic disease [7, 13-20]; however, the mechanism linking OSA to HTN and CVD remains undetermined. Repetitive nighttime apneas and hypopneas (cessations and pauses in breathing) result in activation of the sympathetic nervous system (SNS) and stressful arousals to reestablish breathing. It has been determined that OSA patients demonstrate an exaggerated activation of the SNS that persists into waking hours that can lead to elevations in HR and BP [84]. Over time, activation of the baroreceptors, which respond to normalize these HR and BP oscillations, become altered and depressed in OSA patients [85], suggesting an impairment of the cardiovascular autonomic system, thereby increasing risk for HTN and CVD.

OSA is an independent risk factor for HTN and CVD [86] and has been associated with endothelial dysfunction and increases in inflammatory markers associated with the development of atherosclerosis [25, 87, 88]. OSA has also been associated with IR and altered glucose metabolism [41, 89]. OSA is also linked with depression; a European study concluded that people with depression were five times more likely to suffer from sleep disordered breathing, including OSA [15]. Recently, OSA was determined to be highly prevalent among patients with AAA disease [6] and may not only be a risk for factor for aortic disease [7], but a causal factor for faster AAA expansion [6]. EDS caused by OSA may reduce PA due to fatigue and sleepiness during the day. Findings from several studies using subjective measures of activity indicate that increased OSA severity is associated with decreased PA in young and pre-elderly populations [45-47]. A recent cross-sectional study by Chasens and colleagues is consistent with previous research, finding that OSA severity is associated with decreased objective PA in middle-aged adults and that subjective sleepiness is associated with perceived difficulty of activity. Consequently, reduced PA may further exacerbate OSA through its influence on obesity, a major correlate of OSA [90].

Some data suggest that OSA in older age may be a condition distinct from that of middle age. Follow-up studies of middle-aged cohorts have shown that OSA severity worsens with time [35]; however, in the elderly, associations of these comorbidities may not be linked to severity of OSA, but may actually decrease with age [39]. The authors found that although mild SDB is exceptionally prevalent among elderly adults, the disorder in this population is weakly associated with common signs and symptoms and may be difficult to detect. Furthermore, markers that are strong predictors of OSA in middle-aged adults, such as increased body anthropometrics and snoring, are less strongly associated with OSA in the elderly [40]. Studies of OSA in older populations report little or no association of OSA with sleepiness, HTN, or declines in cognitive function, all of which are common correlates of OSA in middle age adults [37, 91-94]. The association of obesity with OSA severity is weaker in older compared to middle-aged adults and the prevalence of snoring, a strong marker for OSA, decreases beyond middle aged. The untoward associations between OSA and risk of MetSyn has been elucidated in pre-elderly populations [41, 42] but not systematically examined in the elderly [32].

Physical Activity

Regular PA is important for improving the health and wellbeing of people of all ages. PA, defined as any movement that involves physical effort and increased metabolic demand for energy, is not synonymous with exercise but also includes lifestyle activity. Unfortunately, few older adults achieve the minimum recommendation for PA; up to 34% of adults age 65-74 years and up to 44% of adults ages 75 years and older are inactive [76]. Physical inactivity and cardiovascular mortality are directly related and physical inactivity is an independent risk factor for the development of coronary artery disease [95, 96]. Research has demonstrated that all individuals benefit from regular PA, whether it be vigorous exercise or mild-level exertion activities. PA increases cardiovascular functional capacity and decreases myocardial oxygen demand at any level of exertion by increasing both maximum cardiac output and the ability of muscles to extract and utilize oxygen from the blood [97]. Beneficial changes in hemodynamic, hormonal, metabolic, neurological, and respiratory function also occur with increased exercise capacity [98-101]. Regular PA also helps to control blood lipid and carbohydrate metabolisms, blood sugar regulation, insulin sensitivity, BP, and is recommended to prevent and treat osteoporosis [102-104]. Developing and maintaining aerobic endurance, joint flexibility, and muscle strength is especially important for aging individuals [105]. Resistance training aids carbohydrate metabolism through the development or maintenance of muscle mass and effects on basal metabolism [106, 107]. Resistance training is also of critical importance for the elderly due to its beneficial effects on strength and flexibility, bone mineral density, functional capacity, and musculoskeletal benefits [108, 109]. For older adults, PA can improve mobility and physical functioning and ability to complete ADLs, in addition to having mental health benefits and improving quality of life. On average, people who are physically active outlive their inactive counterparts [110]. PA reduces the risk of developing or dying from a host of chronic diseases, including heart disease, diabetes, colon cancer, and high BP [43, 44]. There is an inverse dose-response relationship between the amount of energy expended through PA and all-cause mortality and CVD mortality in middle-aged and elderly populations [111, 112]. Participation in regular exercise also has been shown to reduce the risk of developing AAA disease [8] and may limit progression of early AAA disease [9].

Epidemiological cross-sectional studies have shown that increased PA is associated with better sleep [113-115] and a lower prevalence of sleep disorders [116]. A recent study that involved a nationally representative sample of more than 2,600 men and women, age 18-85 years, found that individuals who participated in at least 150 minutes of moderate to vigorous activity a week, improved their sleep quality by 65% and reported feeling less sleepy during the day [117]. Recently, cross-sectional studies have shown reduced odds of SDB with increasing PA independent of body habitus [46]. Additionally, PA, particularly vigorous PA, appears to be protective against the presences of SDB; researchers found that increasing amounts of PA were associated with less severe SDB [46, 118]. Findings from several studies using subjective measures of activity indicate that increased OSA severity is associated with decreased PA in young and pre-elderly populations [45-47]. Additionally, EDS, a frequent symptom of OSA, has been associated with both obesity and decreased functional activity in areas sensitive to sleep disruption [119]. A recent cross-sectional study by Chasens and colleagues is consistent with previous research, also finding that OSA severity is associated with decreased objective PA in middle-aged adults; however, this group also found that subjective sleepiness is associated with perceived difficulty in activity, but not with objectively measured activity [120]. Upon review of the literature, associations between OSA and PA have not been systematically examined in an elderly population who may already demonstrate lower levels of PA due to aging and AAA disease.

Metabolic Syndrome

The term "metabolic syndrome" (MetSyn) was first coined in the late 1960's by Avogaro and colleagues [121] and described the frequent simultaneous presence of obesity, hyperlipidemia, type II diabetes, and HTN. Since the identification of MetSyn, several other terms and similar but slightly varying definitions have been proposed, including "Syndrome X" and "insulin resistance syndrome." The most commonly used definitions are those of the World Health Organization (WHO) and the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III) [21, 22], though several other definitions are recognized (Table 1).

Table 1. Common Definitions and Criteria of the Metabolic Syndrome

Component	WHO (1999)	NCEP ATP III (2001)	AACE (2003)	AHA/NHLBI (2005)	ADF (2006)
IR (presence)	Yes	_	_	_	_
IGT (mmol/L)	≥ 6.1	_	≥ 6.9	_	_
Fasting Plasma Glucose (mmol/L)	≥ 5.6 or Type II Diabetes	≥ 6.1/5.6	≥ 6.1	≥ 5.6 or Rx	≥ 5.6 or Rx
BMI (kg/m^2)	≥ 30	_	_	_	_
WC (cm) Male; Female	WHR > 0.90; > 0.85	> 102; > 88	_	> 102; > 88	Ethnicity specific
Blood Pressure (mm Hg)	≥ 140/90	≥ 130/85	≥ 130/85 or Rx	≥ 130/85 or Rx	≥ 130/85 or Rx
Triglycerides (mmol/L)	≥ 1.7	≥1.7	≥1.7	≥1.7	≥1.7 or Rx
HDL-C (mmol/L) Male; Female	< 0.9; <1.0	<1.03; <1.3	<1.03; <1.3	<1.03; <1.3 or Rx	<1.03; <1.3 or Rx
Microalbuminuria *	≥ 20 mg/min; ≥ 30 mg/g	_	_	_	_
Required number of components for MetSyn diagnosis	IR or IGT plus ≥ 2 other components	≥ 3	Diagnosis dependent on clinical judgment	≥ 3	WC plus ≥ 2 other components

* Indicates urinary albumin excretion rate or albumin/creatinin ratio. Abbreviations: IR-insulin resistance; IGT-impaired glucose tolerance; BMI-body mass index; WC-waist circumference; WHR-waist/hip ratio; HDL-C-high density lipoprotein cholesterol; Rx-prescription.

Based on the NCEP ATP III guidelines, more than one-third of American adults may have MetSyn, characterized by the presence of at least three of the following risk factors: waist circumference ≥ 102 cm in males and ≥ 88 cm in females; BP levels ≥ 130/ ≥ 85 mmHg; serum TG levels ≥ 150 mg/dl; fasting blood glucose ≥ 110 mg/dl; and serum HDL-C levels < 40 mg/dl in males and < 50 mg/dl in females. The National Health Statistics Reports examined the prevalence of the individual risk factors for MetSyn, as well as the prevalence of MetSyn using the NHANES 2003-2006. NHANES is a cross-sectional nationally representative health and nutrition examination survey conducted by the Center for Disease Prevention and Control (CDC)'s National Center for Health Statistics [21]. Age-adjusted estimates indicate that 34% of the U.S. population 20 years of age and over meets the NCEP ATP III criteria for MetSyn. This survey also found that abdominal obesity, HTN, and hyperglycemia are the most frequently occurring risk factors for MetSyn, with prevalence rates of 53%, 40%, and 39%, respectively. Elevated TG and low HDL-C were noted less frequently in the NHANES report, with U.S. prevalence rates of 31% and 25%, respectively. These findings also indicate that MetSyn increases with age and BMI. Males and females 60 years of age and over were more than four times and six times as likely as the youngest group (20-39 years) to meet the criteria for MetSyn, respectively. Obese male and female adults, regardless of age, were about 32 and 17 times as likely as their normal weight counterparts to meet the criteria for MetSyn, respectively [21].

The pathogenesis of the MetSyn is complex and not yet fully elucidated but appears to have two primary points of origin that include obesity and IR. Other factors that have been implicated as contributors to the development of MetSyn include age, pro-inflammatory state, and abnormalities in hormones such as C-reactive protein (CRP). The

NCEP ATP III considers obesity the main contributing factor for the development of MetSyn. Obesity contributes to HTN, dyslipidemia, hyperglycemia, and is associated with risk for CVD. Abdominal obesity, specifically, is associated with metabolic dysregulation, as excess adipose tissue in the abdominal region releases adipocytokines that can intensify metabolic risk factors, causing IR, which in turn exacerbates these metabolic risk factors, thereby promoting a continuous cycle of metabolic dysregulation [122]. IR is also prevalent in people with MetSyn and is strongly associated with risk for DM and CVD, independent of obesity [23].

Individuals with MetSyn are at increased risk for CVD; researchers found that the MetSyn alone predicted 25% of all new-onset CVD [123]. Additionally, the primary outcome of MetSyn is CVD, according to the NCEP ATP III [22]. This is not surprising considering the components that comprise the MetSyn also are cardinal risk factors for CVD; however, research supports that it is the clustering of several of these cardiovascular risk factors, or MetSyn, that further increases risk for CVD, beyond that of the individual risk factors alone. Golden and colleagues [124] concluded that having several combinations of risk factors associated with MetSyn puts individuals at greater risk for CVD beyond the risk associated with singular risk factors that are MetSyn components. Furthermore, as the number of MetSyn components increases, CVD risk also increases.

Many predisposing conditions which increased in prevalence with age, such as obesity, IR, inflammation, and HTN, contribute to the increase prevalence of MetSyn that accompanies aging. MetSyn in an elderly population is a risk factor for cardiovascular morbidity, especially stroke and coronary heart disease, and mortality [125]. Inflammation is one of the main mechanisms underlying endothelial dysfunction and, therefore, plays an important role in atherosclerosis and other metabolic and cardiovascular disorders, including HTN, IR, dyslipidemia, and obesity [126-129]. Inflammation is also a key factor in the progressive loss of lean tissue and impaired immune function observed in aging. Aging in adults is associated with marked and sustained increases in sympathetic nervous system (SNS) activity to peripheral tissues. This stimulates thermogenesis and prevents further fat storage in response to increasing adiposity that accompanies aging; however, this chronic activation of the peripheral SNS has adverse consequences to the cardiovascular system and increases risk of developing clinical cardiovascular and metabolic diseases in older adults [130].

OSA and MetSyn

Studies indicate that OSA may be a manifestation of the MetSyn [131, 132], in fact, individuals with OSA are more than twice as likely to have MetSyn as compared to obese controls [41]. It appears that OSA and the MetSyn are characterized by the same pathophysiologic environment, which increases risk for developing CVD [133]. Increased visceral fat and the IR that accompanies it seem to be the main characteristics responsible for the development of OSA and the MetSyn [5, 134]. OSA is often accompanied by the same disorders which characterize the MetSyn, including HTN, elevated fasting blood glucose, IR, abdominal obesity, and dyslipidemia. Other characteristics shared between OSA and MetSyn, include increased SNS activation, endothelial dysfunction, and systemic inflammation [5, 135]. Elevated levels of inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha, which also increase with age, are common features of both OSA and MetSyn [135-137]. One study found that the prevalence of MetSyn (according to the ATP-III criteria) is almost 40% greater in patients with OSA [41]. It is unclear whether OSA is observed as part of the basic pathophysiology of the MetSyn or whether OSA, through repetitive hypoxemia events during apneas and other mechanisms, induces the derangements that constitute the MetSyn.

Exercise Capacity

A fundamental requirement for many ADLs is the ability to perform aerobic work, requiring the efforts of the heart, lungs, and circulation to deliver oxygen to metabolically active muscles. The maximal capacity to perform aerobic work is defined by the maximal oxygen consumption ($V0_2$max), which is the product of cardiac output (Q) and arterio-venous oxygen (a-vO_2) difference at maximal exercise. Q is the volume of blood being pumped by the heart per minute and is indicative of the health of the heart. CVDs, including HTN and congestive

heart failure, can result in low Q. a-vO_2 difference is the difference in the oxygen content of the blood between the arterial blood and the venous blood and is indicative of how much oxygen is removed from the blood as it circulates the body. a-vO_2 difference increases with PA and training. A more realistic variable achieved during CPET in most populations is peak VO_2, rather than VO_2max [49]. VO_2peak is measured in liters per minute, but is usually expressed as a function of body weight. Functional capacity is often expressed in metabolic equivalents (METs), where one MET represents resting energy expenditure and 3.5 ml O_2 per kilogram body weight per minute.

Exercise capacity is affected by age, sex, conditioning status, presence of diseases, or medications that can influence VO_2peak [49]. Aerobic capacity declines approximately 10% per decade in nonathletic persons, largely due to attenuations in maximal heart rate and a-vO_2

difference [138]. This rate may decrease to approximately 5% per decade in persons who endurance train and exercise vigorously, due to augmentations in maximal stroke volume and AVO_2 difference [139]. Stroke volume is a measure of the blood pumped from one ventricle of the heart with each beat. Stroke volume is an important determinant of Q, along with heart rate (HR), and correlates with Q, decreasing in certain conditions and disease states. Exercise capacity is 10-20% greater in men than women at any age due to muscle mass, greater stroke volume, and higher hemoglobin concentrations [49]. Previous studies have shown that elderly individuals experience changes in the cardiac autonomic control, due to aging, demonstrating a marked reduction in parasympathetic modulation [140]; therefore, this population demonstrates a reduction in Q, peripheral blood flow, and muscle metabolism, which can promote changes related to the transport and use of oxygen in the body [141]. During CPET, elderly persons demonstrate lower values for maximal power (cycle ergometry), and peak HR, as well as ventilatory and metabolic variables, compared to younger populations; this is primarily due to muscular and cardiorespiratory changes caused by aging [141].

Cardiopulmonary Exercise Testing (CPET)

The assessment of exercise capacity and physiological responses during CPET provides important diagnostic and prognostic information in a clinical setting [49] and is an effective tool for identifying those at high risk for CVD [142]. Exercise capacity and PA status are well- established predictors of cardiovascular and overall mortality [50-52], supporting the value of CPET as a clinical tool that provides clinically relevant diagnostic and prognostic information in both healthy persons and those with cardiovascular conditions [52]. Researchers found that having an exercise capacity of less than 4 METs was an important predictor for increased cardiovascular morbidity and mortality among a cohort of patients with coronary artery disease [143]. CPET is frequently used to assess integrated response of cardiovascular, respiratory, and muscular systems to graded physical exercise. In addition to exercise capacity, other physiological responses during CPET are of clinical utility, including responses at the ventilatory threshold (VT) and during exercise recovery. The VT, defined by the exercise level at which ventilation begins to increase exponentially for a given increment in oxygen consumption ($V0_2$), can predict exercise performance and intensity. Recently, researchers identified VO_2 at the VT as a comparable parameter to VO_{2peak} for identifying patients at increased mortality risk [144]. Ventilatory efficiency (VE/VCO_2) demonstrates the relationship between minute ventilation and carbon dioxide production and also appears to have clinical value for predicting mortality [145, 146]. Additionally, recovery responses after exercise are markers of autonomic function; abnormal HR or BP responses during exercise recovery may indicate impairment in autonomic regulation and have been shown to predict future CVD [147] and mortality [148, 149]. CPET has been shown to be safe and effective for evaluating AAA patients [150].

Patients with OSA are also characterized by excessive daytime sleepiness (EDS), fatigue, and decreased daily PA which may also impair muscle energy metabolism and decrease exercise tolerance [151]. Obesity is often a co-morbid condition in individuals with OSA and may also influence exercise capacity through abnormalities in lung function and increases in ventilatory stress [152]. Decreased exercise capacity, an independent predictor for all-cause mortality in older men [52], has been demonstrated in middle-aged adults with OSA [153-155]; however, the mechanisms by which have not been determined. Possible causes include cardiovascular [86], respiratory [156], and peripheral muscular abnormalities

[151]. Autonomic nervous system dysfunction has been hypothesized to link OSA to CVDs such as HTN, heart failure, myocardial infarction, and stroke [157]. Przybylowski and colleagues found that exercise capacity can be limited due to HTN response during exercise in middle-age OSA patients; they also found that those with severe OSA have exaggerated hemodynamic response to exercise and delayed post- exercise BP recovery [152]. Kaleth and colleagues found that middle-age OSA patients have a distinctive response to CPET, characterized by a blunted HR response, delayed systolic BP recovery, and elevated diastolic BP in both exercise and early recovery [158]. Hargens and colleagues determined that OSA elicits alterations in cardiovascular responses post exercise in young adult men, reflected by an attenuated HR recovery, which may indicate an autonomic regulation imbalance [159]. Aron *et al.* [155] published a review of the literature examining exercise testing in OSA patients and reported that several studies found that patients with OSA have a reduced exercise capacity, blunted HR response during exercise, and atypical BP response during exercise and recovery. Aron highlighted possible explanations for these responses, including cardiac dysfunction, impaired muscle metabolism, chronic sympathetic over-activation, and endothelial dysfunction [155]. Exercise capacity may also be influenced by presence of AAAs in this subject sample, as physical inactivity, a correlate of exercise capacity, is a risk factor for the development of AAAs. Myers and colleagues evaluated exercise capacity and responses to CPET in elderly patients with small AAAs and found that they demonstrate similar exercise capacities, as assessed by peak $V0_2$, as the age-matched referral group; however AAA patients demonstrated a slightly higher incidence of hyper- and hypotensive responses to exercise than the referral group, suggestive of potential autonomic imbalance [150]. Myers et al. concluded that AAA patients can safely undergo maximal CPET and supports its routine use for risk evaluation and functional assessment of patients with AAA.

The relationship between exercise capacity and mortality has yet to be established in the elderly at risk for OSA. Furthermore, the influence of OSA risk on exercise capacity and physiological responses during exercise has been examined in pre-elderly populations with OSA [152, 158, 159] but not systematically examined in an elderly population at risk for OSA with newly diagnosed AAAs.

RESEARCH AIMS

Study 1

An aim of Study 1 was to evaluate the risk of OSA, as assessed from the clinical interpretation of the BQ, among elderly patients with newly diagnosed AAA disease. To further examine gradations in OSA risk, subjects were also classified by their Berlin Risk Score (BRS), the sum of the three categorical scores from the BQ. Subjects were grouped into one of four BRS groups which equated to the number of categories that were scored positive from their BQ (BRS 0, 1, 2, or 3). OSA risk among the elderly AAA subjects was then compared to OSA risk reported for younger and middle-age groups, as well as elderly populations without AAA disease. The primary aim of Study 1 was to examine associations between OSA risk and self-report PA behavior in our subject sample. I hypothesized older adults at High- risk for OSA from the BQ and with higher BRS would report engaging in less PA than their lower-risk counterparts.

Study 2

An aim of Study 2 was to examine the cardio-metabolic profile related to MetSyn and the constituent markers of MetSyn, as defined by the NCEP ATP III criteria, among elderly patients with newly diagnosed AAA disease. The primary aim of Study 2 was to assess how biomarkers of MetSyn and MetSyn status may be associated with risk for OSA (High- vs.

Low- OSA Risk; Berlin Risk Score classifications), as assessed by the Berlin Questionnaire. I hypothesized that subjects at High-risk for OSA and those with higher BRS would have more features of MetSyn and higher rates of MetSyn compared to lower risk counterparts.

Study 3

The aim of Study 3 was to examine and compare and contrast exercise capacity and physiological responses to CPET in elderly patients with AAA disease relative to OSA risk as assessed from the clinical BQ and BRS classifications. I hypothesized that OSA risk would be associated with reduced exercise capacity and with physiological responses to exercise suggestive of autonomic imbalance during exercise and recovery.

METHODS

A total of 396 subjects (*n*=326 for Studies 1 and 2; *n*=114 for Study 3) with newly diagnosed small AAAs (aortic diameter ≥2.5 and < 5.5 cm) were recruited from Stanford University Medical Center, the Veterans Affairs Palo Alto Health Care System (VAPAHCS) and Kaiser Permanente of Northern California. Recruitment procedures and all study-related activities were reviewed and approved in advance by Institutional Review Boards (IRBs) at Stanford University (including VAPAHCS) as well as the Kaiser Permanente Division of Research and an independent Data Safety Monitoring Board (DSMB) organized by the NHLBI and are discussed in greater detail in Appendix A. The ancillary study for the analyses pertaining to this dissertation was approved by the IRB at Virginia Tech (Appendix B). Study methods for all participants included extraction of medical history and drug information from medical records; completion of a physical examination with study personnel to assess resting systolic and diastolic BP, as well as anthropometrics including height and weight for body mass index (BMI) calculation and waist and hip circumference measurements; fasting blood draw and analysis for complete lipid panel and fasting insulin and glucose levels (serum); and completion of questionnaires with verification of responses completed by interviews with study staff to assess health history, PA behavior and habits, and OSA risk. In addition, subjects included in Study 3 completed a symptom-limited CPET with gas exchange using an individualized ramp treadmill protocol, as previously described by Myers *et al*. [160] and according to standard protocols and recommended procedures as outlined by the *American College of Sports Medicine's Guidelines for Exercise Testing and Prescription* to assess exercise capacity and physiological responses during CPET [142]. Additional details regarding the methodology utilized in this dissertation is included in Appendix A. This dissertation was derived from an ancillary research project that is part of a large National Heart, Lung and Blood Institute (NHLBI) sponsored study, conducted at the Specialized Center of Clinically Oriented Research Program (SCCOR) in AAA disease at Stanford University and the VA Palo Alto Health Care System (VAPAHCS), titled "Evaluation of Exercise Therapy for Small Abdominal Aortic Aneurysms."

Berlin Questionnaire

The modified Berlin Questionnaire (BQ) is a 12-item self-report questionnaire that includes questions about risk factors for OSA that can be identified with three discrete sign/symptom categories of 1) snoring behavior, 2) wake time sleepiness and fatigue, and 3) obesity and HTN. The modified BQ, an extension of the original BQ, includes three additional questions regarding choking behavior and wake-time sleepiness. The modified BQ is a validated instrument used to identify individuals who are at risk for OSA with a sensitivity (86%) and specificity (95%) comparable to the original BQ [161-164]; positive and negative predictive values of 96% and 82%, respectively, were reported for the modified BQ [164].

Veterans Affairs Physical Activity Questionnaire

The quantification of PA was recorded by use of the Veterans Affairs Physical Activity Questionnaire (VAPAQ), modeled after the Harvard Alumni studies of Paffenbarger and colleagues [165]. A copy of the VAPAQ is included in Appendix C. The VAPAQ has been validated and successfully used in large numbers of veteran patients and others as reported in previous publications and has been useful in predicting all-cause mortality [9,168].

Physical Examination

Subjects underwent a clinical and physical examination with study personnel to assess resting systolic and diastolic BP, as well as measures of body habitus, including height and weight for BMI calculation and waist (WC) and hip circumference (HC) measurements, which were also used to calculate waist/hip (W/H) ratio. Detailed assessment protocols for these measures are included in Appendix A. Subjects also completed a health history questionnaire which included self-report medication use to assess medically controlled HTN, dyslipidemia, type II diabetes, and other diseases and disorders.

Metabolic and Cardiovascular Biomarkers

Fasting serum blood was collected from participants and evaluated for biomarkers of metabolic and cardiovascular diseases, including serum insulin and glucose, and lipid profile, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). Detailed collection procedures for these measures are included in Appendix A.

Metabolic Syndrome

Presence of MetSyn among the subject sample was determined based on the NCEP ATP III guidelines [22], characterized by presence of at least three of the five risk factors outlined in Chapter 3. Prescription medication use was also taken into consideration when identifying the presence or absence of each of the MetSyn risk factors. Detailed procedures for assessment of MetSyn are included in Appendix A.

Cardiopulmonary Exercise Testing

Participants completed a symptom-limited CPET with gas exchange using an individualized ramp treadmill protocol, as previously described by Myers *et al*. [160] and according to standard protocols and recommended procedures as outlined by the *American College of Sports Medicine's Guidelines for Exercise Testing and Prescription* to assess exercise capacity and physiological responses during CPET [142]. Detailed protocols and procedures for these measures are discussed by Myers *et.al* in a previous publication that evaluated exercise training in patients with AAA disease [9] and are discussed in Appendix A.

Statistical Analyses

Data were stored electronically in a SPSS® (SPSS, Inc., Chicago, IL) database

(Version 20.0). Statistical significance was determined *a priori* for all experimental analyses as a p value < 0.05. Missing data points were excluded on a case by case basis for all analyses.

Study 1

The subject sample for Study 1 includes 326 patients from the larger AAA study and subjects were similar based on diagnosed small AAAs. To address the research question, *"What fraction of these elderly AAA patients are at risk for OSA, as assessed by the Berlin Questionnaire?"*, responses to the BQ were scored for subjects using the instructions adapted from Netzer and colleagues [162] and subjects were classified as High-Risk or Low-Risk for OSA, using the clinical interpretation of the BQ. To further stratify subjects by OSA-risk, they also were assigned a BRS, which was determined by summing the number of sub-scores for each of the three categories (snoring, EDS, and HTN/BMI) of the BQ. Subjects thus were grouped into one of four BRS groups for further analyses (BRS 0-3).

To address the primary research question, *"Is OSA risk in the elderly with AAA disease associated with recent and lifetime physical activity behavior?"* descriptive statistics were assessed to observe means, standard deviations, and ranges for variables by group (BQ High- vs. Low-Risk and BRS classifications). An independent sample t-test was used to compare means between High- vs. Low-Risk groups for all dependent variables of interest related to self-report recreational and occupational PA. To compare means between and within BRS groups, a one- way analysis of variance (ANOVA) was performed; Bonferroni post hoc analysis was performed to further examine differences between groups for all dependent variables of interest related to self-report recreational and occupational PA. Although the subject sample was similar, group differences existed for BMI that may affect relationships between dependent variables of interest related to PA and OSA risk; therefore, when appropriate, a general linear model univariate procedure was performed, controlling for BMI as a covariate.

Study 2

The subject sample for Study 2 includes 326 patients from the larger AAA study and subjects were similar based on diagnosed small AAAs. To address the primary research question, *"how is MetSyn and the constituent biomarkers of MetSyn associated with risk for OSA, as assessed by the Berlin Questionnaire?"*, subjects were classified as High-Risk or Low-Risk for OSA, using the clinical interpretation of the BQ [162].To further examine gradations in OSA risk, subjects were also classified by their BRS, the sum of the three categorical scores from the BQ. Descriptive statistics were assessed to observe means, standard deviations, and ranges for variables of interest by group. To compare means between and within groups, independent sample t-tests and ANOVA were performed, for two- and four-group comparisons, respectively; Bonferroni post hoc analysis were used to further examine differences between four-group comparisons for all dependent variables of interest related to metabolic and cardiovascular biomarkers. Although the subject sample was similar, group differences existed for BMI that may affect relationships between dependent variables of interest related to MetSyn constituents and OSA risk; therefore, when statistically significant differences between groups were observed for variables of interest related to biomarkers of the MetSyn, a general linear model univariate procedure was performed, controlling for BMI as a covariate.

Study 3

The subject sample includes 114 patients from the larger AAA study and subjects were similar based on diagnosed small AAAs. To examine the research question, *"Is OSA risk in the elderly with AAA disease associated with reduced exercise capacity and unique physiological responses during CPET?"* subjects were classified as High-Risk or Low-Risk for OSA using the clinical interpretation of the BQ [162] and by their BRS. Descriptive statistics were assessed for each group to observe means, standard deviations, and ranges for variables of interest related to physiological responses at rest, during exercise, at peak exercise, and during recovery. To compare means between groups, independent student t-tests and ANOVA were performed, for two- and four-group comparisons, respectively; Bonferroni post hoc analysis were used to further examine differences between four-group comparisons for all dependent variables of interest. Although the subject sample was similar, group differences existed for BMI that may affect relationships between dependent variables of interest related to exercise capacity or physiological exercise responses, a general linear model univariate procedure was performed, controlling for BMI as a covariate.

DELIMITATIONS AND LIMITATIONS

Delimitations

1. The AAA study provides a large sample of middle-aged and elderly patients, both male and female, constituting a rich and unique resource for conducting cross-sectional studies representative of the older adult population.
2. The Berlin Questionnaire is the most widely used questionnaire for assessing OSA risk. The sensitivity and specificity of the BQ ranges from 54-86% and 43-87% among primary care patients, respectively [161-163]. Subjects completed the BQ and responses were confirmed and clarified by one-on-one interview between subject and study personnel. To further examine gradations in OSA risk, subjects were also classified by

their Berlin Risk Score (BRS), the sum of the three categorical scores from the BQ. Subjects were grouped into one of four BRS groups which equated to the number of categories that were scored positive from their BQ (BRS 0, 1, 2, or 3). It should be noted that this is not a validated interpretation of the BQ, but simply an approach to examine a more detailed analysis of risk for OSA from patient responses to the individual questions and risk factor categories that comprise the BQ.

3. Study participants completed a detailed self-report of their recent and lifetime PA habits using the VAPAQ. Standard parameters include: number of blocks walked/day; number of stair flights climbed/day; blocks walked/stairs climbed/day (kcals); occupational activity/week (kcals); combined occupational and recreational activities/week (kcals); recreational activity/week, last year; and recreational activity/week, lifetime. Activity type, frequency and duration were recorded for their participation in sports and recreational activities. Activities were further classified according to intensity and duration. The VAPAQ has been validated and successfully used in large numbers of veteran patients and others [168].
4. Study participants completed a physical examination with study personnel to evaluate vitals and anthropometric information; a fasting blood draw was also processed and analyzed to evaluate metabolic and cardiovascular biomarkers. Additionally, participants completed a detailed health status questionnaire which included information on their medication use, including anti-hypertensives, statins, fibrates, niacins, and medications to control diabetes, and other disorders.
5. Participants completed a symptom-limited CPET with gas exchange using an individualized ramp treadmill protocol, as previously described by Myers *et al*. [160] and according to standard protocols and recommended procedures as outlined by the

American College of Sports Medicine's Guidelines for Exercise Testing and Prescription to assess exercise capacity and physiological responses during CPET [142]. Myers *et al.* concluded that AAA patients can safely undergo maximal CPET and supports its routine use for risk evaluation and functional assessment of patients with AAA [150].

Limitations

1. OSA was not clinically diagnosed but rather risk of the disorder was determined by interview and self-reports, using the BQ, the most widely used questionnaire for assessing OSA risk. The sensitivity and specificity of the BQ ranges from 54-86% and 43-87% among primary care patients, respectively [161-163]. Despite these limitations, a strength of our methodology is that study staff administered the BQ to participants via interview rather than the participants completing them alone. This allowed participants to ask questions or clarify statements with research staff, if needed, and reduced individual interpretation that can be a limitation with self-report assessments.
2. The Berlin Questionnaire may not provide a high level of diagnostic specificity to discriminate OSA in an elderly population. One group that assessed the accuracy of the Berlin to diagnose OSA in a large healthy elderly population found that the Berlin had a sensitivity of 77% and a specificity of 39% for predicting moderate and severe OSA and a positive and negative predictive value of 63% and 55%, respectively [170].
3. Participation in PA was assessed through self-report questionnaire, one of the most

practical and widely used methods for assessing PA; however, a limitation is that subjects may misclassify and over report PA behavior due to recall and social desirability biases (Sallis and Saelens 2000; Aadahl, Kjaer et al. 2007). Klesges and colleagues investigated the accuracy of self-report PA compared to observational activity and found that subjects underestimate sedentary activities and overestimate aerobic activities by over 300% (Klesges, Eck et al. 1990). This limitation was addressed by having study staff administer the BQ to participants via interview rather than the participants completing them independently. This allowed participants to ask questions or clarify statements with research staff, if needed, and reduced individual interpretation that can be a limitation with self-report assessments. PA habits were self-reported from study participants, posing concerns about the accuracy of the PA variables.

4. Because this study included a convenience sample of subjects with AAA disease, results may not be generalizable to an elderly population; however, due to the high prevalence of undiagnosed AAA disease in the elderly observed by Singh and colleagues, who found a prevalence rate of nearly 34% for AAA disease among adults 65-84 years of age [171], the findings of this dissertation may be more generalizable to the elderly population than originally thought.

DEFINITIONS

Abdominal Aortic Aneurysm (AAA) – a bulging or weakened area in the wall of the aorta, resulting in an abnormal widening or ballooning greater than 50% of the normal diameter.

Activities of Daily Living (ADL) – daily self-care activities, such as feeding and grooming oneself, work and leisure activities. Often used as a measurement of a person's functional status, particularly in regards to people with disabilities and the elderly [172].

Apnea – the cessation of airflow at the nostrils and mouth for at least 10 seconds [173].

Apnea/Hypopnea Index (AHI) – the number of apneas and hypopneas per hour [173].

Berlin Questionnaire – a sleep apnea screening questionnaire used to identify the risk of sleep disordered breathing.

Body Mass Index (BMI) – indice of body habitus calculated from weight and height

Cardiac output (CO) – the volume of blood pumped by the heart in one minute [142].

Cytokine – a chemical messenger that can induce or inhibit a variety of local and systemic physiological processes, e.g. inflammation.

Exercise Capacity – the maximum amount of physical exertion that a patient can sustain [174].

Heart Rate (HR) – number of heart beats per minute [142].

Homeostasis Model of Assessment (HOMA) – a calculated index of insulin resistance typically used in non-invasive studies, defined as the product of fasting insulin and glucose divided by a constant (22.5) [175].

Hypercapnia – increased levels of carbon dioxide in arterial blood [173].

Hypopnea – a significant reduction in airflow characterized by 50% reduction in airflow; <50% reduction in airflow coupled with a >4% reduction in oxygen saturation; OR 50% reduction in airflow coupled by EEG evidence of arousal [173].

Insulin Resistance (IR) – impaired biological response to insulin, causing a subsequent decrease in insulin mediated disposal of glucose and desensitization of peripheral tissues to insulin [176].

Metabolic Syndrome (MetSyn) – clustering of traditional cardiovascular risk factors which increases risk for cardiovascular morbidity and mortality, and is present in individuals who have three or more of the following risk factors according to the NCEP ATP III definition: waist circumference of ≥ 102 cm in males and ≥ 88 cm in females, BP levels of ≥ 130/ ≥ 85 mmHg, TG levels of ≥ 150 mg/dl, fasting blood glucose of ≥ 100mg/dl, and HDL-C levels < 40mg/dl in males and <50 mg/dl in females [22].

Metabolic Equivalent of Task (MET) – a physiological measure of the energy cost of physical activities; used as a means of expressing the intensity and energy expenditure of activities without considering individual body mass [142].

Obstructive Sleep Apnea (OSA) – a sleep disorder characterized by periodic complete or partial obstructions of the upper airway during sleep, leading to intermittent cessations of breathing or reductions in airflow to the lungs despite ongoing respiratory effort [173].

Polysomnogram (PSG) – the gold standard test used to diagnose sleep disorders that involves continuous recording and monitoring of physiological variables during sleep, including brain activity, cardiac activity, respiratory activity, lower limb movement, and other physiological variables.

Respiratory Exchange Ratio (RER) – ratio between the amount of CO_2 exhaled and O_2 inhaled in one breath

Stroke Volume (SV) – volume of blood pumped from the left ventricle of the heart with each beat [142].

Ventilatory Threshold (VT) – the peak oxygen consumption at which the energy demands exceed circulatory ability to sustain aerobic metabolism [142].

Veterans Affairs Physical Activity Questionnaire (VAPAQ) – validated questionnaire for quantifying physical activity

Peak oxygen consumption (VO_2peak) – the maximum capacity of an individual's body to transport and use oxygen during exercise [142].

ABBREVIATIONS OF TERMS

AAA – Abdominal Aortic Aneurysm

AHI – Apnea/Hypopnea Index

ANOVA – Analysis of Variance

BMI – Body Mass Index

BRS – Berlin Risk Score

BQ – Berlin Questionnaire

CDC – Centers for Disease Control and Prevention

CPET – Cardiopulmonary Exercise Testing

CVD – Cardiovascular Disease

DBP – Diastolic Blood Pressure

EDS – Excessive Daytime Sleepiness

HC – Hip circumference

HDL-C – High Density Lipoprotein-Cholesterol

HOMA – Homeostasis Model of Assessment

HR – Heart rate

HRR – Heart rate recovery

HTN – Hypertension

LDL-C – Low Density Lipoprotein – Cholesterol

MetSyn – Metabolic Syndrome

MET – Metabolic Equivalent

NCEP ATP – National Cholesterol Education Program Adult Treatment Panel

NHANES – National Health and Nutrition Examination Survey

OSA – Obstructive Sleep Apnea

PA - Physical Activity

RER – Respiratory Exchange Ratio

ROS – Reactive Oxygen Species

Rx – Prescription

SDB – Sleep Disordered Breathing

SBP – Systolic Blood Pressure

SBPR – Systolic Blood Pressure Recovery

TC – Total Cholesterol

TEE – Total Energy Expenditure

TG – Triglycerides

VAPAQ – Veterans Affairs Physical Activity Questionnaire

VCO_2 – carbon dioxide production

VO_2 – Oxygen consumption

VT – Ventilatory Threshold

WC – Waist Circumference

W/H Ratio – Waist to Hip Ratio

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CHAPTER TWO

OBSTRUCTIVE SLEEP APNEA RISK IN ABDOMINAL AORTIC ANEURYSM DISEASE PATIENTS: ASSOCIATIONS WITH PHYSICAL ACTIVITY STATUS

ABSTRACT

Objectives: Evaluate risk of obstructive sleep apnea (OSA) in a sample of elderly adults with abdominal aortic aneurysm (AAA) disease and examine associations between OSA risk and self-report physical activity (PA). **Methods:** 326 elderly volunteer subjects with newly diagnosed small AAAs participated. Study methods for all participants included extraction of medical history and drug information from medical records; completion of a physical examination with study personnel to assess resting vitals and measures of body habitus including body mass index (BMI) calculation; and completion of questionnaires with verification of responses completed by interviews with study staff, to assess PA behavior and OSA risk. Subjects were classified as High-Risk or Low-Risk for OSA, using the Berlin Questionnaire (BQ); to further examine gradations in OSA risk, subjects were also classified by their Berlin Risk Score (BRS), as determined by summing the three categorical scores from the BQ (BRS 0, 1, 2, or 3).

Results: A high proportion of study patients (57%) were at increased risk for OSA; these subjects had higher body mass indexes (BMIs) and measures of body habitus (waist and hip circumferences and waist/hip ratio) and a higher proportion were taking anti-hypertensive medications than Low-risk subjects. Subjects at High- Risk for OSA reported fewer blocks walked/day, flights of stairs climbed/day, and expended fewer kilo-calories engaging in these activities compared to their Low-risk counterparts, independent of obesity. **Discussion:** Elderly AAA patients at High-risk for OSA demonstrated higher measures of body habitus and controlled HTN and report engaging in less daily moderate and vigorous PA, compared to their low-risk counterparts, independent of obesity. These findings may have important implications

for cardiovascular fitness and mortality, as well as all-cause mortality for elderly AAA disease patients at risk for OSA. The importance of daily moderate to vigorous PA should be stressed to elderly patients at risk for OSA and they should strive to meet the recommended levels for daily PA.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by repetitive bouts of upper airway occlusion or collapse during sleep, resulting in intermittent periods of hypoxia, hypercapnia, and fragmented sleep [1]. OSA is the most common sleep related breathing disorder, affecting an estimated 20% of the U.S. adult population [2]; Prevalence of OSA is difficult to quantify, as up to 90% of people with the disorder remain undiagnosed [3], though it is anticipated to rise as an increasing proportion of Americans are obese and elderly, both of which are risk factors for OSA. Obesity is the primary risk factor for OSA; OSA is present in 40% of obese persons and more than 80% of individuals with OSA are also obese [4]. Untreated OSA can increase risk for several chronic diseases and disorders including obesity, hypertension (HTN) and cardiovascular disease (CVD), metabolic disorders, depression, and aortic disease [5-13]; however, the mechanism(s) linking OSA to HTN and CVD remains undetermined. Repetitive nighttime apneas and hypopneas (cessations and pauses in breathing) result in activation of the sympathetic nervous system (SNS) and stressful arousals to reestablish breathing. It has been determined that OSA patients demonstrate an exaggerated activation of the SNS that persists into waking hours that can lead to elevations in HR and BP [14]. Over time, activation of the baroreceptors, which respond to normalize these HR and BP oscillations, become altered and depressed in OSA patients [15], suggesting an impairment of the cardiovascular autonomic system, thereby increasing risk for HTN and CVD.

The “gold standard” for diagnosing OSA is laboratory polysomnography (PSG); however, sleep health questionnaires that stratify patients based on clinical symptoms, physical examinations, and risk factors, are often employed as a first step assessment to screen for OSA. Questionnaires that are commonly used to screen for OSA and have been validated against PSG, include the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Berlin Questionnaire (BQ), and most recently, the STOP-Bang questionnaire. Sleep screening questionnaires do not require complicated calculations to identify high risk patients, and they are relatively easy and cost-effective to apply clinically; however, there are also limitations. Sleep questionnaires rely on self-report and disclosure of signs and symptoms, as well as the patient's memory and ability and willingness to follow instructions. Additionally, many of the signs and symptoms of OSA may be difficult for the patient to self-identify, such as snoring and choking during sleep, and can be misinterpreted as other conditions; however, the BQ is regarded for its high specificity and sensitivity for predicting moderate to severe OSA [16] and is also among the most accurate screening questionnaires for OSA [17].

Sleep disorders, specifically OSA, are highly prevalent in older adults; the Sleep Heart Health Study found that among 6,400 older adults, sleep disordered breathing (SDB) prevalence rates for mild to severe SDB ranged from 19-36% for adults 60-98 years old [18]. These rates far outpace those for middle aged adults, age 30-60 years old, whose SDB rates were 2-4% for women and men [19]. One cohort study found that for adults 71-100 years, the prevalence of mild OSA was 80% and moderate OSA was 49% for women and 57% for men [20, 21]. Despite these high prevalence rates, studies have suggested that most of the age-related increase in prevalence of OSA occurs before age 65 and plateaus at some point after age 65 [22, 23].

Recently, OSA was determined to be highly prevalent among patients with AAA disease, a disease of the elderly in which the lower part of the aorta is weakened and bulging. Moderate or severe OSA was present in 42% of subjects with AAA disease [24]. One very recent report suggests that OSA may not only be a risk for factor for aortic disease [10], but a causal factor for AAA expansion [24]. AAA disease is prevalent in the elderly, most often occurring in people age 60 years and older, and AAA presence is associated with overweight and obesity [25].

Increases in chronic diseases and disabilities that often accompany aging, in addition to AAA disease, may limit the daily activities of older adults and reduce health-related quality of life. Approximately 80% of older Americans have at least one and 50% have at least two chronic conditions, such as obesity, cardiovascular disease (CVD), type II diabetes, or cancer [26]. Chronic diseases and disabilities that often accompany aging may limit the daily activities of older adults, reduce health-related quality of life and attribute to the reductions in physical activity (PA) seen in older adults. A 2003 study found that nearly 57% of older adults did not meet the guidelines for PA recommended by the Centers for Disease Control and Prevention [27] for older adults, which includes 150 minutes of moderate intensity aerobic activity each week, or 75 minutes of vigorous intensity aerobic activity, in addition to two days each week of muscle-strengthening activities that work all major muscle groups [28]. Conversely, physical inactivity and a sedentary lifestyle contribute to and exacerbate many chronic diseases that are the leading causes of death in the U.S [29]. Three studies from the last two decades clearly point to poor health behaviors, including diet, physical inactivity, and smoking, as accountable for somewhere between 14-35% of the deaths each year that are attributable chronic diseases [30-32].

Regular PA is important for improving the health and wellbeing of people of all ages. PA, defined as any movement that involves physical effort, is not synonymous with exercise but also includes lifestyle activity. Physical inactivity and cardiovascular mortality are directly related and physical inactivity is an independent risk factor for the development of coronary artery disease [33, 34]. Research has demonstrated that all individuals benefit from regular PA, whether it be vigorous exercise or mild-level exertion activities. For older adults, PA can improve mobility and physical functioning and ability to complete activities of daily living (ADLs), in addition to having mental health benefits and improving quality of life. PA reduces the risk of developing or dying from a host of chronic diseases, including CVD, diabetes, colon cancer, and HTN [35, 36] and a dose-response relationship exists between the energy expended through PA and all-cause mortality and CVD mortality in middle-aged and elderly populations [37, 38]. Participation in regular exercise also has been shown to reduce the risk of developing AAA disease [39] and may limit progression of early AAA disease [40].

Epidemiological cross-sectional studies have shown that increased PA is associated with better sleep [41-43] and a lower prevalence of sleep disorders [44]. Cross-sectional studies have shown reduced odds of sleep disordered breathing (SDB) with increasing PA independent of body habitus [45]. Additionally, PA, particularly vigorous PA, appears to be protective against the presence of SDB [45, 46]. Findings from several studies using subjective measures of activity indicate that increased OSA severity is associated with decreased PA in young and pre-elderly populations [45, 47, 48]. Thus far, associations between OSA and PA have not been systematically studied in an elderly population, particularly not among those expected to be habitually less active due to influences of aging and AAA disease.

OBJECTIVES

The purpose of this study was two-fold: to determine the proportion of patients at risk for OSA, as assessed from the Berlin Questionnaire (BQ), in a convenience sample of elderly patients with newly diagnosed AAA disease and; to examine the possible associations between OSA risk and self-report PA behavior in this group.

METHODS

Subjects

Patients (*n*=326) with newly diagnosed small AAAs (aortic diameter ≥2.5 and < 5.5 cm) were recruited from Stanford University Medical Center, the Veterans Affairs Palo Alto Health Care System (VAPAHCS) and Kaiser Permanente of Northern California. Subjects were 50 years of age or older, agreed to comply with study protocols and procedures, and provided voluntary consent to participate. Recruitment procedures and all study-related activities were reviewed and approved in advance by Institutional Review Boards (IRBs) at Stanford University (including VAPAHCS), Kaiser Permanente Division of Research, Virginia Polytechnic Institute and State University (VPISU), and an independent Data Safety Monitoring Board (DSMB) organized by the National Heart, Lung and Blood Institute (NHLBI). Additional details on recruitment procedures can be found in Appendix A. Study methods for all participants included extraction of medical history and drug information from medical records; physical assessment to collect body habitus and resting BP measurements; completion of questionnaires, with verification of subject answers completed by interview with study staff, for health history, lifetime and recent occupational and recreational PA, and OSA risk.

Physical Examination and Health History

Subjects underwent a physical examination and medical history with study personnel to assess resting systolic and diastolic blood pressure (BP), as well as measures of body habitus, including height and weight for body mass index (BMI) calculation and waist (WC) and hip circumference (HC) measurements, which were also used to calculate waist/hip (W/H) ratio. Detailed assessment protocols for these measures are included in Appendix A. Subjects also provided information on prescriptive medications they were receiving to determine the extent of medically managed HTN, dyslipidemia, type II diabetes, and other diseases and disorders in the sample.

Berlin Questionnaire

The modified Berlin Questionnaire (BQ) is a 12-item self-report questionnaire that includes questions about risk factors for OSA that can be identified with three discrete sign/symptom categories of 1.) snoring behavior, 2.) wake time sleepiness and fatigue, and 3.) obesity and HTN. The modified BQ, an extension of the original BQ, includes three additional questions regarding choking behavior and wake-time sleepiness. The modified BQ is a validated instrument used to identify individuals who are at risk for OSA with a sensitivity (86%) and specificity (95%) comparable to the original BQ [49-52]; positive and negative predictive values of 96% and 82%, respectively, were reported for the modified BQ [52]. Subjects completed the BQ and responses were confirmed and clarified by one-on-one interview between subject and study personnel.

Patients were classified as Low- or High -Risk for OSA based on their responses to the individual items on the BQ and their overall scores in the three symptom categories, according to the scoring instructions detailed by Netzer and colleagues [50]. To further examine gradations in OSA risk, subjects were also classified by their Berlin Risk Score (BRS), the sum of the three categorical scores from the BQ. Subjects were grouped into one of four BRS groups which equated to the number of categories that were scored positive from their BQ (BRS 0, 1, 2, or 3). It should be noted that this is not a validated interpretation of the BQ, but simply an approach to examine a more detailed analysis of risk for OSA from patient responses to the individual questions and risk factor categories that comprise the BQ.

Veterans Affairs Physical Activity Questionnaire

The quantification of PA was recorded by use of the Veterans Affairs Physical Activity Questionnaire (VAPAQ), modeled after the Harvard Alumni studies of Paffenbarger and colleagues [34]. Respondents were asked to self-report the number of city blocks they walk and the number of flights of stairs they climb on a typical day, as well as the occupational and recreational activities they regularly participate in and responses were confirmed and clarified by one-on-one interview between subject and study personnel. Energy cost of stairs climbed per week was calculated using the estimation of Basset and associates [53]. One flight of stairs equals 10 steps, and 12 blocks is considered 1 mile. Energy costs of activities were estimated from the compendium of activities developed by Ainsworth and associates [54]. Energy expenditure is expressed in terms of lifetime adulthood recreational and occupational PA. Recreational PA is also expressed separately as energy expended during the previous year (recent activity). The VAPAQ has been validated and successfully used in large numbers of veteran patients and others as reported in previous publications and has been useful in predicting all-cause mortality [40, 55].

Statistical Analyses

Data were stored electronically in a SPSS® (SPSS, Inc., Chicago, IL) database (Version 20.0). Statistical significance was determined *a priori* for all experimental analyses as a p value < 0.05. Subject responses to the BQ were scored for subjects using the instructions adapted from

Netzer and colleagues [50] and used to classify subjects as High-Risk or Low-Risk for OSA, using the clinical interpretation of the BQ. To further stratify subjects by OSA-risk, they also were assigned a BRS, which was determined by summing the number of sub-scores for each of the three categories (snoring, EDS, and HTN/BMI) of the BQ. Subjects thus were grouped into one of four BRS groups for further analyses (BRS 0-3). Descriptive statistics were assessed to observe means, standard deviations, and ranges for variables by group (BQ High- vs. Low-Risk and BRS classifications) and independent sample t-test and one-way analysis of variance (ANOVA) were used to compare means between two and four group comparisons, respectively, for all dependent variables of interest related to self-report recreational and occupational PA. Bonferroni post hoc analysis was performed to further examine differences between BRS groups for all dependent variables of interest related to self-report recreational and occupational PA. Although the subject sample was similar, group differences existed for BMI that may affect relationships between dependent variables of interest related to PA and OSA risk; therefore, when appropriate, a general linear model univariate procedure was performed, controlling for BMI as a covariate.

RESULTS

Characteristics of Study Participants

Characteristics of the subject sample are displayed in Table 1. Characteristics by gender can be found in Appendix D but are not presented here since characteristics were similar between men and women, other than body habitus characteristics influenced by gender differences. The majority of the subject sample was male (83%), mean age was 73.3 (8.5) yr, and the group was overweight with a BMI of 29.3 (6.1) kg/m^2 and demonstrated high values for additional indices of body habitus, including WC, HC, and W/H ratio. Participants demonstrated a slightly elevated systolic BP and a significant proportion of the subject sample was taking anti-hypertensive medications (89%) and anti-lipemic medications (79%), respectively. Fewer subjects were taking medications to control diabetes (21%).

OSA Risk and Characteristics of Study Participants by OSA Risk

Table 1 demonstrates the OSA risk classifications for the subject sample according to the clinical interpretation of the BQ (Low- vs. High-risk for OSA). Men and women demonstrated similar risk rates for OSA Risk Classification; a table detailing these proportions can be found in Appendix D. A high proportion of the study sample was considered High-risk for OSA according to the criteria for a clinically positive BQ score (57%).

The characteristics of the subject sample by High- and Low-risk for OSA as determined from the clinical interpretation of the BQ are shown in Table 1. AAA size was similar between BQ OSA-risk groups. The BQ High-risk group was younger and had an increased BMI compared to the Low-risk group; additional indices of body habitus, including WC, HC, and W/H ratio were higher in the BQ High-risk group compared to the BQ Low-risk group ($p<0.01$). There was a significant relationship and correlation between age and BMI ($F=13.5$, $p<0.01$; $r=-0.20$, $p<0.01$)); therefore, BMI was selected as the covariate and controlled for in the analyses of PA, where appropriate. Resting BP was similar between groups, although a higher proportion of the BQ High-risk OSA group was taking anti-hypertensive medications to control BP (92% vs. 84%; $p=0.05$). Other classes of medications including anti-lipemics and diabetic medications were similar between BQ High- and Low-risk OSA groups, respectively.

Table 1. Subject Characteristics by Clinical Berlin OSA Risk

Characteristic	**Subject Sample, n=326**	**BQ Low-Risk, n=139**	**BQ High- Risk, n=187**	***t* statistic**	**Pearson Chi-Square**	***p* value**
Proportion (%)	–	43	57	–	7.07	<0.01
Age (yr)	73.3 (8.5)	74.5 (8.6)	72.3 (8.3)	2.30	–	<0.01
AAA size (cm)	3.5 (0.8)	3.5 (0.7)	3.5 (0.8)	-0.69	–	0.49
BMI (kg/m^2)	29.3 (6.1)	27.6 (5.1)	30.5 (6.5)	-4.35	–	<0.01
WC (cm)	100.7 (15.2)	97.0 (14.2)	103.4 (15.2)	-3.69	–	<0.01
HC (cm)	105.4 (12.2)	102.8 (10.2)	107.2 (13.0)	-3.13	–	<0.01
W/H Ratio	0.95 (0.08)	0.94 (0.07)	0.96 (0.08)	-2.68	–	<0.01

SBP rest (mmHg)	142.3 (17.5)	143.3 (17.5)	141.6 (17.6)	0.83	–	0.41
DBP rest (mmHg)	76.6 (10.4)	76.3 (9.8)	76.8 (10.8)	-0.39	–	0.69
Anti-HTN Med (%)	89	84	92	-2.30	5.2	0.02
Anti-lipemic Med (%)	79	79	80	-3.32	0.11	0.74
Diabetic Med (%)	21	17	24	-1.43	2.03	0.15

Data are expressed as group Mean (Standard Deviation-SD). *p* values and *t* statistics for statistical differences between groups are expressed. Medication data is presented as a group percentage (%) taking each class of medication. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H-waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

Table 2 demonstrates the stratification of the subject sample by BRS, a function of the sum of the three categorical scores from the BQ. Subjects were grouped into one of four BRS groups which equated to the number of categories that were scored positive from their BQ (BRS 0, 1, 2, or 3). Men and women demonstrated similar risk rates for each OSA Risk Classification; a table detailing these proportions can be found in Appendix D. Few subjects were classified in BRS 0 group (6%), while a moderate proportion of subjects were classified as BRS 1 or 2 (37% and 41%), respectively. Approximately 17% of subjects were classified in the BRS 3 group. The characteristics of the subject sample by BRS for OSA are also shown in Table 2. Age and AAA size did not differ across the four BRS groups. BMI was higher among the BRS 3 group vs. Berlin Risk Score 0, 1 and 2 groups, and was controlled for in the analyses of PA (p<0.01). Additional indices of body habitus, including WC, HC, and W/H ratio were also higher among the BRS 3 group (p<0.01). Resting BP did not differ across the four BRS groups; though a lesser proportion of the BRS 0 group was taking anti-hypertensive medications to control BP compared to the all other group (p<0.01). Use of medications to control diabetes and lipids increased with BRS; diabetic medication use was significantly higher for the BRS 3 group (p=0.02), but anti-lipemics was non-significant.

Table 2. Subject Characteristics by Berlin Risk Score

Characteristic	BRS 0, n=18	BRS 1, n=121	BRS 2, n=133	BRS 3, n=54	*F* ratio	Pearson Chi Square	*p* value
Proportion (%)	6	37	41	17		110.4	<0.01
Age (yrs)	72.6 (9.5)	74.8 (8.5)	72.3 (7.9)	72.4 (9.4)	2.10	–	0.10
AAA size (cm)	3.2 (0.8)	3.5 (0.7)	3.6 (0.7)	3.4 (0.9)	1.32	–	0.27
BMI (kg/m^2)	24.4 (3.2) [d]	28.1 (5.2)	29.8 (6.3) [ab]	32.5 (6.6) [e]	11.5	–	<0.01
WC (cm)	89.6 (12.1) [d]	98.2 (14.2) [b]	101.8 (15.8) [a]	107.2 (13.2) [c]	8.05	–	<0.01
HC (cm)	97.8 (9.8) [d]	103.7 (10.1)	106.5 (13.6) [a]	109.0 (11.5) [a]	5.10	–	<0.01

W/H Ratio	0.91 (0.06) [b]	0.95 (0.08) [b]	0.96 (0.07)	0.99 (0.09) [c]	8.05	–	<0.01
SBP rest (mmHg)	144.7 (17.4)	143.1 (17.6)	140.5 (15.7)	144.3 (21.4)	0.82	–	0.48
DBP rest (mmHg)	77.8 (11.8)	76.1 (9.4)	76.6 (11.0)	77.2 (10.4)	0.23	–	0.88
Anti-HTN Med (%)	50	90 [a]	92 [a]	94 [a]	3.0	31.1	<0.01
Anti-lipemic Med (%)	72	80	77	88	0.95	2.88	0.41
Diabetic Med(%)	11[b]	18 [b]	18 [b]	38 [e]	3.47	10.2	0.02

Data are expressed as group Mean (SD). Medication data is presented as a group percentage (%) taking each class of medication. *p* values and *F* ratios for statistical differences between groups are expressed. Bonferroni post-hoc comparisons were used to investigate differences between BRS groups. [a] =different from BRS 0, [b] =different from BRS 3, [c] =different from BRS 0 and 1, [d] =different from

BRS 2 and 3, and [e] =different from BRS 0, 1 and 2. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H-waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

Physical Activity by OSA Risk

Tables 3 and 4 show the PA indices by Clinical BQ and BRS, respectively. After controlling for group differences in BMI, High-Risk OSA subjects, as indicated from the clinical interpretation of the BQ, demonstrated fewer blocks walked/day ($p<0.02$), flights of stairs climbed/day ($p=0.03$), and expended fewer daily kcals ($p<0.01$) engaging in these activities compared to their Low-risk counterparts. BQ High- and Low-risk OSA groups did not differ on other indices of occupational or recreational PA. Although use of anti-HTN medications was higher among the BQ High-Risk OSA group, it was not a significant predictor of OSA-risk group assignment ($p=0.12$) and was therefore not controlled for in these analyses.

After controlling for group differences in BMI, subjects classified in the BRS 3 group demonstrated significantly fewer blocks walked/day ($p<0.03$), flights of stairs climbed/day ($p=0.02$), and expended fewer daily kcals ($p=0.02$) engaging in these activities compared to participants in the BRS 0 and 1 groups, respectively. Group classification by BRS did not influence other indices of occupational and recreational PA. Although use of diabetic medications differed among BRS groups, it was not a significant predictor of BRS group assignment ($p=0.26$) and was therefore not controlled for in these analyses.

Table 3. Physical Activity by Clinical Berlin Risk

VAPAQ Variable	**BQ Low-Risk, *n*=139**	**BQ High- Risk, *n*=187**	***t* statistic/*F* ratio**	***p* value**
Blocks Walked/Day	7.5 (11.3)	4.9 (7.9)	2.34 / 5.59	0.02 / 0.02
Stair Flights Climbed/Day	2.8 (6.4)	1.4 (2.8)	2.14 / 4.53	0.03 / 0.03
Blocks and Stairs/Day (kcals)	82 (102)	49 (69)	2.39 / 8.70	<0.01 / <0.01
Occupational Activity/Week (kcals)	7400 (3136)	7618 (3015)	-0.56	0.59
Occupational and Recreational Activity/Week (kcals)	8251 (3301)	8509 (3162)	-0.62	0.53

Last Year Recreational Activity (kcals/week)	1272 (1035)	1150 (1018)	0.89	0.38
Lifetime Recreational Activity (kcals/week)	933 (878)	914 (985)	0.15	0.88

Data are expressed as group Mean and Standard Deviation (SD). BMI was controlled for in the analyses; *p* values and *F* ratios for statistical significance between groups are expressed as without the covariate / with the covariate, where appropriate. Abbreviations: VAPAQ-Veterans Affairs Physical Activity Questionnaire; BQ-Berlin Questionnaire; kcals-kilocalories.

Table 4. Physical Activity by Berlin Risk Score

VAPAQ Variable	BRS 0, n=18	BRS 1, n=121	BRS 2, n=133	BRS 3, n=54	*F* ratio	*p* value
Blocks Walked/Day	11.3 (11.6) [b]	7.0 (11.2)	5.2 (8.4)	4.2 (6.4) [a]	3.29 / 3.07	0.02 / 0.03
Stair Flights Climbed/Day	1.2 (2.8)	3.1 (6.8) [b]	1.6 (3.1)	0.9 (2.0)	3.13 / 2.82	0.03 / 0.04
Blocks and Stairs/Day (kcals)	102 (95) [b]	78 (103)	53 (74)	40 (55) [a]	3.97 / 3.50	<0.01 / 0.02
Occupational Activity/Week (kcals)	7799 (3052)	7321(3164)	7769 (3188)	7284 (2590)	0.49	0.69
Occupational and Recreational Activity/Week (kcals)	8385 (3203)	8225 (3337)	8675 (3308)	8133 (2811)	0.45	0.72
Last Year Recreational Activity (kcals)	1135 (877)	1297 (1064)	1255 (1072)	881 (818)	1.47	0.22

Lifetime Recreational Activity (kcals)	556 (457)	995 (916)	932 (1053)	865 (774)	1.06	0.37

Data are expressed as group Mean and Standard Deviation (SD). BMI was controlled for in the analyses; *p* values and *F* ratios are expressed as without the covariate / with the covariate, where appropriate. Bonferroni post-hoc comparisons were used to investigate differences between BRS groups. [a] =different from BRS 0, and [b] =different from BRS 3. Abbreviations: VAPAQ-Veterans Affairs Physical Activity Questionnaire; BRS-Berlin Risk Score; kcals-kilocalories.

DISCUSSION

OSA Prevalence and Risk

Findings from this study indicate that approximately 57% of older adult subjects with AAA disease were at High-risk for OSA according to the clinical interpretation of the BQ. Though not a true prevalence rate since OSA was not clinically diagnosed, the BQ is considered a surrogate indicator for OSA for the purposes of this study due to the validity of the BQ for identifying individuals at risk for OSA [49-51]. These findings appear to be consistent with the literature, demonstrating that OSA prevalence increases with age and is higher among people older than 65 years.

Several large cohort studies have examined the prevalence rates of OSA among adults using in-laboratory PSG. The Wisconsin Sleep Cohort Study, Southern Pennsylvania Cohort Study, and the Vitoria-Gasteiz Spain Cohort Study evaluated large groups of adults between the ages of 20-99 years and estimated the prevalence of OSA (as defined by an AHI greater than 5 events/hr) to be 9-24%, 17%, and 26-28%, respectively [19] [23, 56] [20]. Davies and Stradling analyzed 12 studies of OSA prevalence in Western populations and estimated that 1 to 5% of adult men have OSA [57].

OSA prevalence appears to increase with age and several studies have reported high prevalence of OSA among people older than 65 years. Ancoli-Israel and colleagues evaluated more than 400 men and women age 65 to 95 years and found that 70% of men and 56% of women had an AHI of 10 or greater [22]. The Vitorio-Gasteiz, Spain Cohort study found that for ages 71-100 years, the prevalence of mild OSA was 80% and moderate OSA was 49% for women and 57% for men [20, 21]. The Cleveland Family Study reported OSA prevalence rates of 32% for women and 42% for men over 60 years of age in their study [58]. Mason and colleagues investigated the prevalence of OSA in 127 individuals with AAA disease and determined that 40% of their subject sample had an oxygen desaturation index (ODI) of greater than 10. Their subject sample was slightly younger (mean 67.9 yr) than the subjects in this study and patients older than 75 years were excluded.

Although prevalence of OSA in the elderly is high, several authors have suggested that most of the age-related increase occurs before age 65 and then plateaus. Bixler and colleagues conducted a cohort study and found that OSA increases in prevalence from 20 to 59 years of age, peaking at a prevalence rate of 5.4%, after which it plateaus or decreases for patients 60 and older [23]. The authors concluded that OSA in older patients is less severe than OSA in the young. Similarly, Ancoli-Israel and colleagues found that AHI and RDI decreased by decade in elderly subjects 65-95 years of age, concluding that the increase in apnea indices associated with aging occurs before age 65 [22]. The Sleep Heart Health Study showed that although the proportion of people with moderate to severe OSA was approximately 1.7-fold higher in older (60-99 years) compared to middle-age (40-60 years) adults, most of this increase occurred before age 65, after which it plateaued or slightly increased [59]. These trends suggest that either a relative increase in mortality rate from OSA or a remission of OSA with aging exists. Further research is needed to better understand the long term impact of OSA and the clinical implications for the elderly with OSA.

Clinical Indicators of OSA

Results of this study indicate that AAA size was similar between BQ OSA-risk groups, in contrast to the literature that suggests a relationship exists between OSA risk and AAA disease. Subject selection criteria to only include patients with small AAA disease (aortic diameter $\geq$2.5 and < 5.5 cm) may explain the lack of association between OSA risk and AAA size in this study. Findings indicate that anthropometric markers of excess body mass or central adiposity were consistent with the clinical signature of OSA among patterns reported for the general population; participants at High-risk for OSA had greater BMIs, WC, HC, and W/H ratios than their Low-risk counterparts. When stratified by BRS, only the BRS 3 group was higher on indices of body habitus, suggesting that this group of High-risk subjects (17%) contributes to the majority of the difference observed in body habitus between High- and Low-risk groups.

Some data suggest that OSA in older individuals may be a distinctly different disorder than that suffered by those of middle age. Although mild OSA is exceptionally prevalent among elderly adults, it seems to be weakly associated with signs and symptoms commonly found in younger adults with the disorder and thus may be more difficult to detect. Furthermore, markers that are strong predictors of OSA in middle-aged adults, such as increased body mass, central fat accumulation and snoring, are less strongly associated with OSA in the elderly [59]. Ancoli-Israel and colleagues conducted a follow-up study with older adults with OSA and found that changes in BMI were weakly associated with changes in AHI [60]. Similarly, several studies have shown that the association between obesity and OSA severity is weaker in older adults compared to middle-aged adults in the Sleep Heart Health Study [23, 56, 59]. Studies of OSA in older populations also report little or no association of OSA with sleepiness, HTN, or declines in cognitive function, all of which are common correlates of OSA in middle-aged adults [61-64].

Findings from this study indicate the proportion of participants taking anti-HTN medications was significantly higher in the groups at High-risk for OSA. Approximately 82% of the subjects classified as High-risk for OSA by those methods were receiving anti-HTN medications, indicating greater incidence of diagnosed HTN. When stratified by BRS, the BRS 3 group was significantly higher on the proportion of subjects taking these medications, indicating a greater incidence of diagnosed diabetes in this High-risk OSA group.

Influences of OSA Risk on Physical Activity

Findings indicate that High-Risk OSA subjects, as indicated from the clinical BQ and the BRS, reported engaging in fewer blocks walked/day, flights of stairs climbed/day, and expended less energy engaging in these activities compared to their Low-risk counterparts. Again, when stratified by BRS, only the BRS 3 group was less active, suggesting that this small group of High-risk subjects (17%) contributes to the majority of the differences observed in PA habits between High- and Low-risk groups. These differences remained statistically significant even after controlling for differences in BMI. This is an interesting finding suggesting OSA is associated with reduced daily moderate and vigorous PA, independent of obesity. BQ High- and Low-risk OSA groups and BRS groups did not differ on other indices of occupational and recreational PA, including weekly occupational and recreational activity, yearly and lifetime recreational activity. These findings demonstrate that participants at High-risk for OSA report engaging in less daily PA, such as moderate walking and more vigorous stair climbing than their low-risk counterparts. The inability to walk four blocks and climb two flights of stairs has been shown to be an independent predictor of peri-operative and post-operative complications and even death following major, non-cardiac surgery [65, 66]. Additionally, Jain and colleagues demonstrated that the inability to climb stairs was associated with higher all-cause and CVD mortality among a large group of patients with peripheral arterial disease [67]. This group also suggests that stair climbing is a more precise indication of overall cardiovascular fitness compared to walking distance and speed, which were not associated with all-cause or CVD mortality in their study. Stair climbing ability is also considered a reliable surrogate of peak oxygen consumption, a powerful predictor of cardiovascular morbidity and premature cardiovascular mortality [68]. Contrastingly, OSA risk did not influence participants self-reported activities related to occupation and recreation, neither recent nor lifetime. It is unclear whether the reduced daily PA observed in our subject sample at High-risk for OSA is a result of their OSA risk or a contributing factor to it. It may be that patients with OSA are neither psychologically motivated nor physically able to engage in regular PA due in part to fatigue and EDS. Or perhaps this groups' sedentary behavior has over time contributed to their OSA risk, in part through influences on obesity.

Research in young and middle-age populations has shown that increased OSA severity is associated with decreased subjective measures of PA [45, 47, 48]. A recent cross-sectional study by Chasens and colleagues is consistent with previous research, finding that OSA severity is associated with decreased PA in middle-aged adults [69]. This group observed negative associations between AHI and objective measures of PA, including total energy expenditure, steps walked, and average METS; they also concluded that subjective sleepiness is associated with perceived difficulty in activity, but not with objectively measured activity. Using cross-sectional data collected from the Sleep Heart Health Study, Quan and colleagues observed the associations between PA and sleep disordered breathing in 4,275 middle-aged adults and found significant associations between decreased moderate to moderately vigorous PA and increased severity of OSA [45].

Research has demonstrated that all individuals benefit from regular PA, whether it be vigorous exercise or mild-level exertion activities. Developing and maintaining aerobic endurance, joint flexibility, and muscle strength is especially important for aging individuals [70] as it aids in maintenance of muscle mass, flexibility, bone mineral density, basal metabolism, and functional capacity, all of which naturally decline with aging. Physically active individuals also tend to outlive their inactive counterparts, as there is a dose-response relationship between the amount of energy expended through PA and mortality in middle-age and elderly populations [37, 38]. Participation in regular exercise also has been shown to reduce the risk of developing AAA disease [39] and may limit progression of early AAA disease [40].

PA may further benefit people with OSA by promoting physical and psychological wellbeing in patients by improving sleep architecture. Epidemiological, cross-sectional, and experimental studies have suggested that both acute and chronic exercise influences sleep. Epidemiological cross-sectional studies have shown that increased PA is associated with a reduced prevalence of sleep disturbance [9, 44, 59, 71] and SDB [46].Quan and colleagues took their analyses one step further, concluding that vigorous PA was more highly associated with a decrease in the prevalence of SDB than modest intensity PA [45].

However, it is unclear whether PA has a direct influence on psychological states or indirect effects by influencing other risk factors associated with OSA, including obesity and hypertension. Norman and colleagues demonstrated that patients with OSA showed reduced respiratory disturbance index with increased total sleep time, decreased awakenings and arousals during sleep, and improved mood following a 6 month exercise program [72]. These subjects also lost weight and improved their exercise tolerance. Another group evaluated a 6 month exercise intervention for OSA patients and found that despite no changes in body weight or physical status, subjects reduced their RDIs and reported less fatigue and improvements in energy [73]. Hong and colleagues examined the relationship between OSA severity, PA, and psychological well-being in middle-age OSA patients and concluded that PA level better predicted perceptions of energy and fatigue than OSA severity [74]. The authors also concluded that regular PA was significantly correlated with subjective well-being, even after controlling for OSA severity and BMI, suggesting that mood-enhancing effects of exercise may also be evident in OSA patients.

A limitation of this study is that OSA was not clinically diagnosed but rather risk of the disorder was determined by interview and self-reports, using the BQ, the most widely used questionnaire for assessing OSA risk. A second limitation is that the BQ may not provide a high level of diagnostic specificity to discriminate OSA in an elderly population, as indicated by recent findings [75]. Despite these limitations, a strength of this methodology is that study staff administered the BQ to participants via interview rather than the participants completing them independently. This allowed participants to ask questions or clarify statements with research staff, if needed, and reduced individual interpretation that can be a limitation with self-report assessments.

Participation in PA was assessed through self-report questionnaire, one of the most practical and widely used methods for assessing PA; however, a limitation is that subjects may misclassify and over report PA behavior due to recall and social desirability biases [76, 77]. This limitation was addressed by having study staff administer the BQ to participants via interview rather than the participants completing them independently. This allowed participants to ask questions or clarify statements with research staff, if needed, and reduced individual interpretation that can be a limitation with self-report assessments.

A final limitation of this study is that because subjects were a convenience sample of patients with AAA disease, results may not be generalizable to an elderly population; however, due to the high prevalence of undiagnosed AAA disease in the elderly observed by Singh and colleagues, these findings may be more generalizable to the elderly population than originally thought [78]. This study did not include a control group of elderly adults without AAA disease; therefore, it was not possible to determine how much of the high prevalence of OSA risk in this study is attributed to AAA disease; however, because high prevalence of OSA has been documented among older adults without documented AAA disease [20, 22, 58], it is not suspected that the high prevalence of OSA-risk in this study to be primarily attributed to presence of AAA disease.

In conclusion, findings from this study indicate that approximately 57% of older adults subjects with AAA disease were at High-risk for OSA according to the clinical interpretation of the BQ. Elderly participants at High-risk for OSA have greater BMIs and other indices of body habitus consistent with the clinical signature of OSA. Only the BRS 3 group was higher on measures of body habitus, suggesting that this subset of subjects at High-risk for OSA (17%) contributes to the majority of the difference observed in body habitus between High- and Low-risk groups. Findings from this study also indicate a greater incidence of diagnosed HTN in the High-risk OSA groups (BQ High-risk and BRS 2 and 3). Although previous studies of OSA in older populations report little association between OSA and HTN [79], our results are more consistent with OSA symptomology in the general population, in which OSA and HTN are highly associated [6, 9].

This study is the first to examine the associations between OSA risk and self-report PA behavior among an elderly population with newly diagnosed small AAA disease. Findings indicate that subjects at High-risk for OSA report engaging in less daily moderate and vigorous PA, including block walking and stair climbing, and expend less energy engaging in these activities compared to their Low-risk counterparts, even after controlling for differences in body habitus. Contrastingly, OSA risk did not influence participants' self-reported PA behavior related to recent and lifetime occupation and recreation. Further studies are needed to examine the causal relationship between OSA and PA, as it is unknown whether reduced PA among OSA patients is a result of their OSA, contributes to their OSA, or both.

Finally, the BRS may prove a useful interpretation of the BQ for clinical purposes, as additional information was revealed when subjects were stratified by BRS that was not observed when subjects were classified by the clinical interpretation of the BQ (High vs. Low-risk for OSA). The BRS may provide additional information by identifying subjects at increased risk for OSA and at risk for associated comorbid chronic diseases.

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CHAPTER THREE

OBSTRUCTIVE SLEEP APNEA RISK IN ABDOMINAL AORTIC ANEURYSM DISEASE PATIENTS: ASSOCIATIONS WITH METABOLIC SYNDROME

ABSTRACT

Study Objectives: Examine the prevalence of metabolic syndrome (MetSyn) and its constituent markers in a large sample of elderly patients with newly diagnosed small AAA disease and assess how MetSyn may be associated with risk for obstructive sleep apnea (OSA). **Methods:** Study methods included extraction of medical history and drug information from medical records; completion of a physical examination to assess resting blood pressure (BP) and anthropometrics; fasting serum blood analyses for glucose, insulin, and lipid profile; and completion of the Berlin Questionnaire (BQ) with verification of responses completed by interviews with study staff, to assess OSA risk. To further examine gradations in OSA risk, subjects were also classified by Berlin Risk Score (BRS), the sum of the three categorical scores from the BQ. **Results:** The prevalence of MetSyn among subjects in this sample was 41%, with hypertension being the most prevalent component (94%), followed by elevated fasting glucose (55%), low high-density lipoprotein cholesterol (HDL-C; 52%), increased waist circumference (WC; 45%), and elevated triglycerides (TG; 13%). In addition, of those subjects at High-risk for OSA according to the BQ, 45% also had MetSyn according to the NCEP ATP III criteria [1], whereas only 35% of those at Low-risk for OSA had MetSyn. Subjects with the highest BRS had an increased prevalence of MetSyn and MetSyn components, including increased WC and reduced HDL-C, independent of obesity. No other associations between OSA risk and other cardio-metabolic risk factor of interest were observed. **Conclusions:** OSA risk was associated with prevalence of MetSyn and several of its components, including increased WC and HDL-C, independent of obesity; however, this association was only observed in those patients with the

highest BRS, suggesting the BRS may prove a useful interpretation of the BQ for clinical purposes. No associations between OSA risk and any other cardio-metabolic risk factor of interest were observed, suggesting that there is not a significant association between OSA and cardio-metabolic risk factors, beyond the effects of obesity, among our elderly sample of AAA patients. Additional research to better understand the manifestation of OSA in the elderly is crucial for proper clinical management of older patients.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by repetitive bouts of upper airway occlusion or collapse during sleep, resulting in intermittent periods of hypoxia, hypercapnia, and fragmented sleep [2]. OSA is the most common sleep related breathing disorder, affecting an estimated 20% of the U.S. adult population [3]; Prevalence of OSA is difficult to report, as up to 90% of people with the disorder remain undiagnosed [4], though it is anticipated to rise as an increasing proportion of Americans are obese and elderly, both of which are risk factors for OSA. Obesity is the primary risk factor for OSA and is reported in more than 40% of OSA cases; furthermore, more than 80% of individuals with OSA are also obese [5]. Untreated OSA can increase risk for several chronic diseases and disorders including obesity, HTN and CVD, metabolic disorders, depression, and aortic disease [6-14]; however, the mechanism(s) linking OSA to HTN and CVD remains undetermined. Repetitive nighttime apneas and hypopneas (cessations and pauses in breathing) result in activation of the sympathetic nervous system (SNS) and stressful arousals to reestablish breathing. It has been determined that OSA patients demonstrate an exaggerated activation of the SNS that persists into waking hours [15]. Over time, activation of the baroreceptors, which respond to normalize these SNS oscillations, become altered and depressed in OSA patients [16], suggesting an impairment of the cardiovascular autonomic system, thereby increasing risk for HTN and CVD.

The “gold standard” for diagnosing OSA is laboratory polysomnography (PSG); however, sleep health questionnaires that stratify patients based on clinical symptoms, physical examinations, and risk factors, are often employed as a first step assessment to screen for OSA. Questionnaires that are commonly used to screen for OSA and have been validated against PSG, include the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Berlin

Questionnaire (BQ), and most recently, the STOP-Bang questionnaire. Sleep screening questionnaires do not require complicated calculations to identify high risk patients, and they are relatively easy and cost-effective to apply clinically; however, their accuracy relies on self-report and disclosure of signs and symptoms, as well as the patient's memory and ability and willingness to follow instructions. The BQ is regarded for its high specificity and sensitivity for predicting moderate to severe OSA [17] and is among the most accurate screening questionnaires for OSA [18].

Sleep disorders, specifically OSA, are highly prevalent in older adults; the Sleep Heart Health Study found that among 6,400 older adults, sleep disordered breathing (SDB) prevalence rates for mild to severe SDB ranged from 19-36% for adults 60-98 years old [19]. These rates far outpace those for middle aged adults, age 30-60 years old, whose SDB rates were 2-4% for women and men [20]. One cohort study found that for adults 71-100 years, the prevalence of mild OSA was 80% and moderate OSA was 49% for women and 57% for men [21, 22]. Despite these high prevalence rates, studies have suggested that most of the age-related increase in prevalence of OSA occurs before age 65 and plateaus at some point after age 65 [23, 24].

Recently, OSA was determined to be highly prevalent among patients with AAA disease, a disease of the elderly in which the lower part of the aorta is weakened and bulging. Moderate or severe OSA was present in 42% of their subjects with AAA disease [25]. One very recent report suggested that OSA may not only be a risk for factor for aortic disease [11], but a causal factor for faster AAA expansion [25]. AAA disease is prevalent in the elderly, most often occurring in people age 60 years and older, and AAA presence is associated with overweight and obesity [26].

The metabolic syndrome (MetSyn) describes the frequent simultaneous presence of obesity, hyperlipidemia, type II diabetes, and HTN [27]. One of the most commonly used definitions of the MetSyn is that of National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III) [1] (Table 1). More than one-third of American adults may have MetSyn [28], characterized by the presence of at least three of the five risk factors outlined in Table 1. MetSyn increases significantly with age and BMI; older adults were 4-6 times more to meet the criteria for MetSyn as young adults, and obese individuals were 17-32 times more likely than normal weight counterparts to meet the criteria for MetSyn [28].

The pathogenesis of the MetSyn is complex and not yet fully elucidated but appears to have two primary points of origin that include obesity and IR. Other factors that have been implicated as contributors to the development of MetSyn include age, and a pro-inflammatory state; however, the NCEP ATP III considers obesity, specifically abdominal obesity, the main contributing factor for the development of MetSyn as it contributes to HTN, dyslipidemia, hyperglycemia, and is associated with risk for CVD. Researchers found that the MetSyn alone predicted 25% of all new-onset CVD [29] and the primary outcome of MetSyn is CVD [1]. MetSyn has also been associated with advanced vascular damage in AAA patients [30].

Studies indicate that OSA may be a manifestation of the MetSyn [31, 32]; in fact, individuals with OSA are more than twice as likely to have MetSyn as compared to obese controls [33]. OSA and the MetSyn may be characterized by the same pathophysiologic environment, which increases risk for developing CVD [34]. Increased visceral fat and the IR that accompanies it seem to be the main characteristics responsible for the development of OSA and the MetSyn [3, 35]. OSA is often accompanied by the same disorders which characterize the MetSyn, including HTN, elevated fasting blood glucose, IR, abdominal obesity, and dyslipidemia. Other characteristics shared between OSA and MetSyn, include increased sympathetic nervous system activation, endothelial dysfunction, and systemic inflammation [3, 36]. One study found that the prevalence of MetSyn is almost 40% greater in patients with OSA [33]. It is unclear whether OSA is observed as part of the basic pathophysiology of the MetSyn or whether OSA, through repetitive hypoxemia events during apneas and other mechanisms, induces the derangements that constitute the MetSyn.

Research suggests that OSA in older age may be a condition distinct from that of middle age. Many of the cardiovascular and metabolic abnormalities that are associated with OSA are less associated in older adults and comorbidities that worsen with time in untreated middle-age cohorts with OSA may be less associated with severity of OSA in the elderly but more attributed to aging [37]. Furthermore, risk factors and predictors of OSA in middle-aged adults are less strongly associated with OSA in the elderly [19, 24, 38-44]. The untoward associations between OSA and clinical markers of MetSyn has been elucidated in pre-elderly populations [33, 45] but not systematically examined in the elderly [46]. Furthermore, AAA disease has been associated with MetSyn and OSA independently, but to our knowledge these disorders have not been examined together.

OBJECTIVES

One aim of this study was to examine the cardio-metabolic profile related to MetSyn and the constituent markers of MetSyn, as defined by the NCEP ATP III criteria, among elderly patients with newly diagnosed AAA disease. The second aim was to assess in this sample how biomarkers of MetSyn and MetSyn status may be associated with risk for OSA, as assessed by the BQ.

METHODS

Subjects (n=326) with newly diagnosed small AAAs (aortic diameter ≥2.5 and < 5.5 cm) were recruited from Stanford University Medical Center, the Veterans Affairs Palo Alto Health Care System (VAPAHCS) and Kaiser Permanente of Northern California. Subjects were 50 years of age or older, agreed to comply with study protocols and procedures, and provided voluntary consent to participate. Recruitment procedures and all study-related activities were reviewed and approved in advance by Institutional Review Boards (IRBs) at Stanford University (including VAPAHCS) as well as the Kaiser Permanente Division of Research and an independent Data Safety Monitoring Board (DSMB) organized by the NHLBI. Additional details on recruitment procedures can be found in Appendix A. Study methods for all participants included extraction of medical history and drug information from medical records; completion of a physical examination with study personnel to assess resting systolic and diastolic BP, as well as measures of body habitus including height and weight for BMI calculation and waist (WC) and hip (HC) circumference measurements; fasting blood analysis for complete lipid panels and serum insulin and glucose levels; and completion of questionnaires, with verification of subject answers completed by interview with study staff, regarding health history, and OSA risk.

Physical Examination and Health History

Subjects underwent a physical examination with study personnel to assess resting systolic and diastolic blood pressure (BP), as well as measures of body habitus, including height and weight for body mass index (BMI) calculation and waist (WC) and hip circumference (HC) measurements, which were also used to calculate waist/hip (W/H) ratio. Detailed assessment protocols for these measures are included in Appendix

A. Subjects also provided information on prescriptive medications they were receiving to determine the extent of medically managed HTN, dyslipidemia, type II diabetes, and other diseases and disorders in the sample.

Berlin Questionnaire

The modified Berlin Questionnaire (BQ) is a 12-item self-report questionnaire that includes questions about risk factors for OSA that can be identified with three discrete sign/symptom categories of 1.) snoring behavior, 2.) wake time sleepiness and fatigue, and 3.) obesity and HTN. The modified BQ, an extension of the original BQ, includes three additional questions regarding choking behavior and wake-time sleepiness. The modified BQ is a validated instrument used to identify individuals who are at risk for OSA with a sensitivity (86%) and specificity (95%) comparable to the original BQ [47-50]; positive and negative predictive values of 96% and 82%, respectively, were reported for the modified BQ [50]. Subjects completed the BQ and responses were confirmed and clarified by one-on-one interview between subject and study personnel.

Patients were classified as Low- or High -Risk for OSA based on their responses to the individual items on the BQ and their overall scores in the three symptom categories, according to the scoring instructions detailed by Netzer and colleagues [48]. To further examine gradations in OSA risk, subjects were also classified by their Berlin Risk Score (BRS), the sum of the three categorical scores from the BQ. Subjects were grouped into one of four BRS groups which equated to the number of categories that were scored positive from their BQ (BRS 0, 1, 2, or 3). It should be noted that this is not a validated interpretation of the BQ, but simply an approach to examine a more detailed analysis of risk for OSA from patient responses to the individual questions and risk factor categories that comprise the BQ.

Biomarkers for Metabolic and Cardiovascular Disease Risk

Overnight fasting serum blood was collected from participants and evaluated for biomarkers of metabolic and cardiovascular diseases, including serum insulin and glucose, lipid profile, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). Detailed collection procedures for these measures can be found in Appendix A.

Metabolic Syndrome

Presence of MetSyn was determined using criteria from the NCEP ATP III guidelines [1], which defines MetSyn as the presence of at least three of the five risk factors outlined in Table 1. Prescription medication use was also taken into consideration when identifying the presence or absence of each of the MetSyn risk factors. Subjects taking an anti-HTN medication to control BP were identified as positive for having an elevated BP according to the ATP III MetSyn criteria. Similarly, patients taking an anti-diabetic medication were identified as positive for having an elevated fasting glucose, one of the five risk factors that constitute MetSyn. Taking a fibrate or niacin medication to control elevated TGs and HDL-C, respectively, was also considered when examining the presence of MetSyn risk factors and the disorder among the subject sample.

Statistical Analyses

Data were stored electronically in a SPSS® (SPSS, Inc., Chicago, IL) database (Version 20.0). Statistical significance was determined *a priori* for all experimental analyses as a p value < 0.05. To examine the occurrence of MetSyn and the cardio-metabolic profile, related to the constituent biomarkers of MetSyn, among elderly AAA patients, descriptive statistics of the subject sample were assessed to observe means, standard deviations, and ranges for variables of interest related to clinical and physical measurements and metabolic and cardiovascular biomarkers. To examine associations between MetSyn and constituent biomarkers and risk for OSA, subjects were classified as High-Risk or Low-Risk for OSA, using the clinical interpretation of the BQ [48]. To further examine gradations in OSA risk, subjects were also classified by their BRS, which for this investigation, was defined as the sum of the three categorical scores from the BQ. Descriptive statistics were assessed to observe means, standard deviations, and ranges for variables of interest by group. To compare means between and within groups, independent sample t-tests and ANOVA were performed, for two- and four-group comparisons, respectively; Bonferroni post hoc analysis were used to further examine differences between BRS group comparisons for all dependent variables of interest related to metabolic and cardiovascular biomarkers. Although the subject sample was similar, group differences existed for BMI that may affect relationships between dependent variables of interest related to MetSyn constituents and OSA risk; therefore, a general linear model univariate procedure was performed, when appropriate, to control for BMI as a covariate.

RESULTS

Characteristics, Cardiovascular and Metabolic Biomarkers, and MetSyn Profile of Study Participants

Characteristics of the subject sample are displayed in Table 2. Characteristics by gender can be found in Appendix D but are not presented here since characteristics were similar between men and women, other than anthropometric characteristics influenced by gender differences. All values are expressed as group means (standard deviation-SD). The majority of the subject sample was male (83%), mean age was 73.3 (8.5) yr, and the group was overweight with a BMI of 29.3 (6.1) kg/m^2.

Constituent markers of MetSyn for the subject sample are also included in Table 2. Participants had a high WC (gender specific) and demonstrated elevated levels for systolic BP and fasting glucose. Mean values for HDL-C levels (gender specific) and TGs were within a range considered within clinically normal limits, per the NCEP ATP III criteria. Regarding additional markers of cardio- metabolic risk, the subject sample had a normal level for fasting insulin level, slightly elevated value for HOMA-IR, and desirable levels for TC and LDL-C. A significant proportion of the subject sample was taking anti-hypertensive medications (89%) and anti-lipemic medications (79%), respectively. Fewer subjects were taking medications to control diabetes (21%).

Table 3 and Figure 1 demonstrate the prevalence of MetSyn and the individual components of the disorder, as defined by the NCEP ATP III criteria, among the subject sample of elderly adults with AAA disease. As a group, they demonstrated a MetSyn prevalence of 41%. The most prevalent MetSyn component was HTN or taking a prescribed anti-HTN medication (95%) followed by elevated fasting glucose or taking a prescribed medication to control diabetes (55%), low HDL-C level or taking a prescribed niacin medication (52%), high WC (45%), and elevated TG level or taking a prescribed fibrate medication (13%) Prevalence rates of MetSyn and the individual components of the disorder by gender did not differ and are presented in Appendix D.

Cardiovascular and Metabolic Biomarkers and MetSyn Profile by OSA-Risk

Table 4 displays group characteristics and cardiovascular and metabolic biomarkers of the subject sample by OSA-risk according to the clinical interpretation of the BQ (High- vs. Low-risk for OSA). A high proportion of the study sample was considered High-risk for OSA by the BQ (57%). AAA size was similar between OSA-risk groups. The BQ High-risk group was slightly younger and had a greater BMI compared to the BQ Low-risk Group. There was a significant relationship between age and BMI (F=13.5, p<0.01); therefore, BMI was selected as the covariate and controlled for in the analyses, where appropriate.

Regarding constituent markers of MetSyn using the NCEP ATP III criteria, WC was higher among the BQ High-risk group, though not significant when controlled for BMI. Resting BP was similar between BQ OSA risk groups, though a higher proportion of the BQ High-risk group was taking anti-HTN medications to control BP (92% vs. 84%; p=0.05), even after controlling for group differences in BMI. Fasting glucose and HDL-C were similar between BQ OSA risk groups and TG level, though higher in the BQ High-risk compared to the BQ Low-risk group, significance did not remain after controlling for BMI; however, a higher proportion of the BQ High-risk group was taking a fibrate medications to reduce TGs (10% vs. 0%; p=0.02). Other medication classes that may influence the components of MetSyn, using the NCEP ATP III definition, including anti-lipemics and diabetic medications, were similar between BQ OSA risk groups.

Table 4 also highlights additional cardio-metabolic variables of interest related to MetSyn and OSA risk. Due to the influence and associations with BMI, HC and W/H ratio were higher among the BQ High-risk compared to the BQ Low-risk group. Fasting insulin was elevated in the BQ High-risk group compared to the BQ Low-risk group, but this difference did not remain significant after controlling for BMI. TC and LDL-C were similar between BQ OSA risk groups.

Table 5 and Figure 2 demonstrates the prevalence of MetSyn and the individual components of the disorder, as defined by the NCEP ATP III criteria, among the subject sample by OSA-risk according to the clinical interpretation of the BQ. Prevalence of MetSyn was similar between BQ High- and Low-risk groups (45% vs. 35%), respectively. The BQ High-Risk group had a higher prevalence of increased WC (51% vs. 38%) and elevated HDL/Rx niacin (59% vs. 44%) compared to their Low-risk counterparts, respectively, though these differences were not significant after controlling for BMI. BQ High- and Low-risk groups did not differ on any other component of the MetSyn, including BP (95% vs. 94%), fasting glucose (58% vs. 52%), or TGs (12% vs. 13%), respectively.

Table 6 displays the cardiovascular and metabolic biomarkers of the subject sample by BRS. Few subjects were classified in the BRS 0 group (6%), while a moderate proportion of subjects had a BRS of 1 or 2 (37% and 41%), respectively. Approximately 17% of subjects were classified in the BRS 3 group. Age was similar between the four BRS groups; BMI increased linearly with BRS and was controlled for in the analyses ($p<0.01$). Regarding constituent markers of MetSyn using the NCEP ATP III criteria, WC, was higher among the BRS group 3 compared to BRS 0 and 1 groups, but not significant after controlling for BMI. Resting BP was similar across BRS groups; however anti-HTN medication use was less prevalent among BRS group 0 vs. all other BRS groups ($p<0.01$), even after controlling for group differences in BMI. Fasting glucose and use of diabetic medications were similar across BRS groups after controlling for differences in BMI, as were HDL-C, TGs, and use of anti-lipemic medications. Table 6 also highlights additional cardio-metabolic variables of interest related to MetSyn and OSA risk. HC and W/H ratio were similar across groups after controlling for group differences in BMI, as was fasting insulin. TC and LDL-C were also similar across BRS groups.

Table 7 and Figure 3 demonstrate the prevalence of MetSyn and the individual components of the disorder, as defined by the NCEP ATP III criteria, among the subject sample by BRS. There was an increased prevalence of MetSyn among the BRS 3 group compared to the BRS 0, 1, and 2 groups (65% vs. 11%, 13%, and 37%; $p<0.01$), respectively, after controlling for group differences in BMI. MetSyn components including increased WC ($p=0.01$) and reduced HDL/Rx niacin ($p=0.04$) were also more prevalent among the BRS 3 group compared to the lower-risk groups after controlling for BMI. Elevated fasting glucose while more prevalent among the BRS 3 group, though this difference did not remain significant after controlling for BMI. MetSyn components including elevated BP or use of anti-HTN medications and elevated TG or use of fibrate medications did not differ between BRS groups, and these components were the most and least prevalent MetSyn components among the groups, respectively.

DISCUSSION

Prevalence of MetSyn and MetSyn Components among Elderly AAA Patients

Findings from this study indicate that the prevalence of MetSyn among our subject sample of elderly patients with newly diagnosed AAA disease is 41%. HTN was the most prevalent MetSyn component among our subject sample, with 95% of participants having an elevated BP by the NCEP ATP III criteria or those taking a prescribed anti-HTN medication. Prevalence of the remaining MetSyn biomarkers, including elevated fasting glucose, low HDL-C, increased WC, and high TG was 55%, 52%, 45%, and 13%, respectively. Regarding additional cardio-metabolic risk factors for MetSyn, fasting insulin level of our population was in normal range, though HOMA-IR was elevated compared to the normal upper value of 2.60 [51]. Fasting lipid values for TC, HDL-C, LDL-C, and TGs were all within clinically normal ranges, though a significant proportion of subjects (79%) were taking prescription anti-lipemic medications. Additionally, about one-fifth of the subject sample was taking one or more prescription medications to control diabetes and 83% were taking other prescription medications.

These findings regarding the prevalence of MetSyn among an elderly subject sample with AAA disease are consistent with the literature on similar sub-populations. Gorter and colleagues determined the overall and gender-specific prevalence of MetSyn and its components among 100 patients with AAA disease and found 47% of their subject sample met the NCEP ATP III criteria for having MetSyn [52]. High BP was the most prevalent risk factor among their subject sample (80%), followed by low HDL-C (44%) and high TGs (44%), high fasting glucose (38%), and abdominal obesity (37%). Olijhoek and colleagues conducted a cross-sectional study to investigate the relationship between MetSyn and vascular disease among 502 patients with recently diagnosed coronary heart disease [30]. Among their subject sample of 89 patients with AAA disease, the prevalence of MetSyn was 45%.

The prevalence of MetSyn among this elderly subject sample with AAA disease was slightly lower than those reported by Ervin and colleagues who examined the prevalence of MetSyn among a sample 3,423 adults, of which 1240 subjects were 60 years and older, from the NHANES 2003-2006 data [28]. They determined that the prevalence of MetSyn increased with each succeeding age group for both sexes and that 52% of males and 54% of females age 60 years and over met the NCEP ATP III criteria for MetSyn. However, similar to this study, HTN was the most prevalent MetSyn component for their population of older adults in the Ervin study, followed by elevated fasting glucose, while abdominal obesity and dyslipidemia were less prevalent MetSyn components. Mean age of the elderly group in the Ervin paper is not reported and our study did not report on race or ethnicity among the subject sample, all of which have been shown to influence MetSyn [28]; therefore, we cannot speculate if these factors may attribute to the difference in MetSyn prevalence reported by us vs Ervin *et al*. Additional comparisons can be made between this study and the Ervin paper regarding prevalence of MetSyn and MetSyn components by age. Ervin found that the prevalence of MetSyn among persons age 20-39 years was 15.6%-20.3% and the most prevalent MetSyn component among this age group for males was abdominal obesity, followed by elevated TGs, high fasting glucose, HTN, and low HDL-C for males [28]. For females, abdominal obesity was also the most prevalent MetSyn component, followed by low HDL-C, high TGs, elevated fasting glucose, and HTN. An interesting observation is that in younger populations, abdominal obesity it the most prevalent MetSyn component; however, in our study of older AAA patients, HTN, elevated fasting glucose, and reduced HDL-C were more prevalent than abdominal obesity. Additionally, while HTN was the most prevalent MetSyn component among subjects in this study, it was the least prevalent component among younger women and was of low prevalence among younger men. These findings indicate that while MetSyn increases with age, the cardio-metabolic profile related to MetSyn adjusts, and constituent markers such as abdominal obesity become less prevalent in older adults, while other risk factors such as HTN and elevated fasting glucose become more prevalent with age. This study support the notion that a better understanding of the progression of MetSyn and the clinical implications from young to old age is crucial for proper clinical management of all MetSyn patients and stage of life should be a consideration in how they are managed.

An interesting finding by Olijhoek and colleagues was that MetSyn in their elderly patients with AAA disease was associated with a high prevalence of microalbuminuria, or excess protein in the urine, an indication of kidney dysfunction [30]. The authors concluded that in patients with vascular disease, including AAA disease, MetSyn is associated with more advanced vascular damage, as measured by indicators for increased cardiovascular risk, including microalbuminuria [30]. Watanabe and colleagues also demonstrated significant associations between MetSyn and microalbuminuria among older adults [53]. Microalbuminuria was not evaluated in this study and is not a component of the MetSyn according to the NCEP ATP III criteria; however it is a risk factor for the World Health Organization (WHO) definition of MetSyn and has been shown to be strongly related with the components of the MetSyn [54]. The MetSyn profile among patients with vascular diseases, including AAA disease, may vary by different MetSyn criteria and definitions, including that of the WHO. The most commonly used definitions of MetSyn are those by the WHO and the NCEP ATP III, which share many similarities but offer several differences as well. Prevalence of MetSyn among various subpopulations and racial/ethnic groups may vary depending on the MetSyn definition and criteria used [55]. These differences may extend to specific subpopulations with known diseases but have yet to be determined. Further research to examine the clinical manifestation of MetSyn in elderly populations with vascular disease is warranted.

Associations between MetSyn and OSA Risk

Findings from this study indicate that approximately 57% of our subject sample of older adults with AAA disease is at high-risk for OSA according to the clinical interpretation of the BQ; among the BQ High-risk group, 45% had MetSyn according to the NCEP ATP III criteria [1]. OSA risk was not significantly associated with prevalence of MetSyn nor the prevalence of MetSyn components including elevated BP, elevated fasting glucose, or elevated TG. After controlling for BMI, prevalence of increased WC was also not associated with OSA risk. Reduced HDL-C was the only MetSyn component that was associated with BQ OSA-risk, independent of BMI. Additionally, no other cardio-metabolic risk factors of interest were associated with risk for OSA, including fasting insulin, TC, or LDL-C. The BQ and BRS High-risk OSA groups had an increased prevalence of anti-HTN medication use, suggesting that that OSA may be associated with HTN; however this component of the MetSyn was similar between groups when considering both BP level and anti-HTN medication use.

A novel finding of this study is that when OSA-risk was stratified by BRS, prevalence of MetSyn and prevalence of MetSyn components, including increased WC and reduced HDL-C, were significantly associated with OSA risk, independent of BMI. Although associations were not observed between OSA-risk and MetSyn and its constituent markers, as determined from the clinical interpretation of the BQ, when OSA-risk was further stratified to evaluate more detailed categorical responses from the BQ, associations were observed between OSA-risk, MetSyn and MetSyn components, independent of obesity. These findings suggest an association exists between OSA risk and MetSyn among subjects considered at highest-risk for OSA. To our knowledge, this study is the first to examine associations between MetSyn and biomarkers of MetSyn with risk for OSA in an elderly population with AAA disease.

Literature on the association between MetSyn and OSA in younger and middle-age cohorts is mixed and inconclusive. Several groups have demonstrated that OSA and MetSyn are highly associated, independent of obesity, and conclude that OSA is a manifestation of the MetSyn. Coughlin and colleagues examined the prevalence of MetSyn and its components in a group of middle-age males and found that MetSyn prevalence was more than twice as high among the OSA group vs. similar controls (87% vs. 35%) [33]. This group also found that independent of obesity, OSA was associated with increased BP, higher insulin and TG concentrations, decreased HDL-C, and a trend toward higher HOMA IR values. Ip and colleagues confirmed that OSA is independently associated with insulin resistance in a large group of middle-age adults, as demonstrated by higher levels of fasting insulin and HOMA-IR among subjects with OSA vs. similar controls [56, 57]. Stagnitti and colleagues also reported that middle-age subjects with OSA demonstrate a distinct profile with clustering of vascular risk factors related to MetSyn, including higher TGs, diastolic BP, and insulin levels, compared to similar controls [58]. Gruber and colleagues evaluated the associations between MetSyn, insulin resistance, and albuminuria with OSA in middle-aged adults and found that the prevalence of MetSyn was higher in OSA vs. non-OSA subjects (74% vs. 24%) [59]. Additionally, independent of obesity, TG and glucose were higher in participants with OSA compared to similar controls, while insulin levels and prevalence of microalbuminuria were similar between groups.

Conversely, conflicting literature suggests that obesity is the primary driving factor of metabolic abnormalities in OSA patients, rather than the presence of OSA. Sharma *et al.* conducted a two-year case-control study to assess the metabolic profile in middle-age subjects with OSA [60]. This group concluded that obesity was the major determinant of metabolic abnormalities in their cohort, as OSA had no independent association with components of the MetSyn, including dyslipidemia, insulin resistance, or elevated glucose. Stoohs and colleagues screened middle-aged adults for OSA and found that those with OSA had significantly more insulin resistance; however, when their model was corrected for multiple variables, BMI was the sole determinant of the observed elevated insulin resistance [61]. Barcelo and colleagues evaluated metabolic biomarkers among a group of middle-age men, including obese and non-obese patients with OSA, as well as a group of non-obese healthy subjects [62]. Their findings agree with those of Sharma and Stoohs, that metabolic abnormalities in OSA are associated with obesity rather than OSA [60, 61]. The group of obese OSA patients had higher BP, insulin and glucose levels, and HOMA-IR values than both healthy controls and non-obese OSA patients, who demonstrated similar values for metabolic risk indices.

Few studies have examined metabolic abnormalities associated with OSA in an elderly population. Stoohs and colleagues investigated the relationship between SDB and HTN in a population of older men and found that SDB is prevalent and undiagnosed in this population, as SDB was diagnosed in 80% of their cohort [63]. Additionally, no differences in BP values were observed in subjects with vs. without SDB; however, a considerable number of subjects were taking anti-HTN medications to control BP, despite presenting with hypertensive BP levels, suggesting that SDB may adversely affect the efficacy of anti-HTN treatment in patients with HTN and SDB. Nieto and colleagues assessed the association between SDB and HTN in a large cohort of middle-age and older adults from the Sleep Heart Health Study, finding that SDB is associated with HTN in both middle-age and older adults; however, the association was weaker among the older participants [7]. Resnick and colleagues also examined data from the Sleep Heart Health Study to determine associations between SDB and diabetes among older adults [64]. After adjusting for BMI and other confounding variables, there was not a significant association between diabetes and OSA severity, or differences seen in obstructive events between older diabetic and non-diabetic participants. Our findings are consistent with the very few studies that have evaluated the associations between OSA and components of the MetSyn among an elderly population, suggesting that the metabolic abnormalities that are often associated with MetSyn in pre-elderly populations, such as HTN, diabetes, and insulin resistance are not as notable in the elderly; however, a novel finding of this study is that those at highest risk for OSA may have greater a prevalence of MetSyn, independent of obesity. The clinical manifestations and associations of OSA among the elderly have been demonstrated to differ from those of younger and middle-age cohorts and some data suggest that OSA in older age may be a condition distinct from that of middle age. [19, 37-39, 41, 42, 65]. Our findings support these observations and the notion that a better understanding of OSA in the elderly and how it differs from the typical OSA patient of middle-age is crucial for proper clinical management of older patients.

A limitation of this study is that OSA was not clinically diagnosed but rather risk of the disorder was determined by interview and self-report using the BQ, the most widely used questionnaire for assessing OSA risk. A second limitation is that the BQ may not provide a high level of diagnostic specificity to discriminate OSA in an elderly population, as indicated by recent findings [66]. Despite these limitations, a strength of the methodology utilized in this study is that study staff administered the BQ to participants via interview rather than the participants completing them alone. This allowed participants to ask questions or clarify statements with research staff, if needed, and reduced individual interpretation that can be a limitation with self-report assessments.

Because subjects included in this sample were participants with AAA disease, results regarding MetSyn prevalence may not be generalizable to an elderly population; however, due to the high prevalence of undiagnosed AAA disease in the elderly observed by Singh and colleagues [67], the findings of this study may be more generalizable to the elderly population than originally thought. Additionally, race and ethnicity were not reported for these subjects, which has been shown to influence MetSyn and its constituent markers [28].

A final limitation of this study is that parametric statistical methods were utilized for all analyses of group comparisons. Non-parametric statistical tests may have been more appropriate for some dependent variables of interest that included outliers and non-normal distributions, including fasting glucose and insulin, HOMA-IR, LDL-C, and HDL-C (Shapiro-Wilk test of normality, $p<0.01$). However, controlling analyses for covariates, such as BMI, is a limitation of these non-parametric hypotheses tests and therefore, were not utilized in these analyses.

In conclusion, findings from this study indicate that the prevalence of MetSyn in this subject sample of elderly patients with AAA disease was 41%. Hypertension was the most prevalent of the MetSyn components, followed by elevated fasting glucose, low HDL-C, increased waist circumference, and elevated serum triglycerides. These findings are consistent with literature on the prevalence of MetSyn in patients with AAA disease. Evaluating the prevalence of MetSyn utilizing different MetSyn definitions, such as that of the WHO, may be considered for AAA patients to consider additional components indicative of cardio-metabolic dysfunction.

Of the 57% of subjects at High-risk for OSA included in this study, 45% also had MetSyn according to the NCEP ATP III criteria [1]. OSA risk from the BQ was not associated with prevalence of MetSyn, nor any of its components, except for HDL-C; however, subjects with the highest BRS did have a greater prevalence of MetSyn and two of its components, reduced HDL-C and increased WC, independent of obesity. Findings from this study also suggest that OSA may be associated with use of anti-HTN medications to control BP; we did not observe associations between OSA risk and any other cardio-metabolic risk factor of interest, suggesting that there is not a significant association between OSA and cardio-metabolic risk factors among our elderly subject sample of AAA patients. This study is the first to examine associations between MetSyn and biomarkers of MetSyn with risk for OSA in an elderly population with AAA disease. These findings support the notion that the clinical manifestations and associations of OSA related to cardio-metabolic disease risk among the elderly differ from those of younger and middle-age cohorts, suggesting that OSA in older age may be a condition distinct from that of middle age. Further research to examine the clinical manifestation of MetSyn across the lifespan and in populations with vascular disease is warranted for proper clinical management of older patients.

Finally, the BRS may prove a useful interpretation of the BQ for clinical purposes, as additional information regarding MetSyn risk was observed when subjects were stratified by BRS that was not observed when subjects were classified by the clinical interpretation of the BQ. The BRS may provide additional information by identifying subjects at increased risk for OSA and at risk for associated comorbid chronic diseases.

TABLES

Table 1. NCEP ATP III Clinical Identification of the Metabolic Syndrome

Risk Factor/MetSyn Component	Defining Level
Fasting Plasma Glucose (mg/dL)	≥110
WC (cm) Male; Female	>102; >88
BP (mmHg)	≥130/85
TG (mg/dL)	≥150
HDL-C (mg/dL) Male; Female	<40; <50
# of components for MetSyn diagnosis	≥3

Derived from Grundy *et al.* [1] Abbreviations: WC-waist circumference; BP-blood pressure; TG-triglycerides; HDL-C-high density lipoprotein cholesterol.

Table 2. Subject Characteristics and Cardio-metabolic Risk Factors

Characteristic	**Subject Sample, *n*=326**
Age (yr)	73.3 (8.5)
Gender (% M/F)	83% / 17%
AAA size (cm)	3.5 (0.8)
BMI (kg/m^2)	29.3 (6.1)
WC (cm)	100.7 (15.2)
SBP rest (mmHg)	142.3 (17.5)
DBP rest (mmHg)	76.6 (10.4)
Anti-HTN Med (%)	89
Fasting Glucose (mg/dL)	113.3 (27.0)
Fasting Insulin (mU/L)	13.6 (14.4)
HOMA IR	4.2 (6.2)
Diabetic Med (%)	21
TC (mg/dL)	161.8 (42.9)
HDL-C (mg/dL)	44.2 (14.2)
LDL-C (mg/dL)	93.6 (33.6)
TG (mg/dL)	98.4 (47.7)
Anti-lipemic Med (%)	79

Data are expressed as subject sample Means ± Standard Deviations (SD). Medication data is presented as a group percentage (%) taking each class of medication. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication; HOMA IR- homeostatic model assessment for insulin resistance; TC-total cholesterol; HDL-C-high density lipoprotein-cholesterol; LDL-C-low density lipoprotein-cholesterol; TG-triglycerides.

Table 3. Prevalence of Metsyn Components and MetSyn Among SubjectS

MetSyn Component (NCEP ATP III)	**Subject Sample Prevalence, *n*=326**
Increased WC (%)	45
Elevated BP or anti-HTN medication (%)	95
Elevated Fasting Glucose or diabetic Med (%)	55
Elevated TG or Rx Med (%)	13
Reduced HDL or Rx Med (%)	52
MetSyn (≥3 components; %)	41

Data are expressed as prevalence of each MetSyn component and MetSyn, as defined by the NCEP ATP III, among the subject sample. Abbreviations: WC-waist circumference; BP-blood pressure; HTN-hypertension; Rx-prescription; Med-medication; TG-triglycerides; HDL-C-high density lipoprotein cholesterol.

Table 4. Subject Characteristics and Cardiovascular and Metabolic Biomarkers by BQ OSA-Risk

Characteristic	**BQ Low-Risk, *n*=139**	**BQ High-Risk, *n*=187**	***t* statistic/F ratio**	**Pearson Chi Square**	***p* value**
Proportion (%)	43	57	_	7.07	<0.01
Age (yrs)	74.5 (8.6)	72.3 (8.3)	2.30	_	0.02
AAA size (cm)	3.5 (0.7)	3.5 (0.8)	-0.69	_	0.49
BMI (kg/m^2)	27.6 (5.1)	30.5 (6.5)	-4.35	_	<0.01
WC (cm)	97.0 (14.2)	103.4 (15.2)	-3.69 / 2.31	_	<0.01/ 0.63
HC (cm)	102.8 (10.2)	107.2 (13.1)	-3.13 / 18.3	_	<0.01 / 0.52
W/H ratio	0.94 (0.07)	0.96 (0.08)	-2.68 / 1.83	_	<0.01 / 0.18
SBP rest (mmHg)	143.3 (17.5)	141.6 (17.6)	0.83	_	0.41

DBP rest (mmHg)	76.3 (9.8)	76.8 (10.8)	-0.39	_	0.69
Anti-HTN Med (%)	84	92	-2.30 /3.1	5.2	0.02/0.05
Fasting Glucose (mg/dL)	112.3 (31.8)	114.1 (22.9)	-0.56	_	0.57
Fasting Insulin (mU/L)	11.1 (10.6)	15.4 (16.5)	-2.64 / 0.89	_	0.01/ 0.35
HOMA IR	3.5 (6.1)	4.7 (6.2)	-1.66	_	0.10
Diabetic Med (%)	17	24	-1.43	2.03	0.15
TC (mg/dL)	160.1 (44.5)	162.4 (41.8)	-0.29	_	0.77
TG (mg/dL)	91.6 (45.1)	103.3 (49.0)	-2.03 / 1.80	_	0.04 / 0.18
HDL (mg/dL)	45.6 (13.7)	43.1 (14.5)	1.49	_	0.14
LDL (mg/dL)	92.3 (32.8)	94.6 (34.3)	-0.59	_	0.56

Anti-lipemic Med (%)	79	80	-3.32	0.11	0.74

Data are expressed as group Mean and Standard Deviation (SD). BMI was controlled for in the analyses; *p* values and *F* ratios for statistical difference between groups are expressed as without the covariate / with the covariate, where appropriate. Medication data is presented as a group percentage (%) taking each class of medication. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication; HOMA IR-homeostatic model assessment for insulin resistance; TC-total cholesterol; HDL-C-high density lipoprotein-cholesterol; LDL-C-low density lipoprotein-cholesterol; TG-triglycerides.

Table 5. MetSyn Components and Status by BQ OSA-Risk

MetSyn Component (NCEP ATP III)	**BQ Low-Risk, *n*=139**	**BQ High-Risk, *n*=187**	***t* statistic/ F ratio**	**Pearson Chi-Square**	***p* value**
Increased WC (%)	38	51	-2.39 / <0.01	5.57	0.02 / 0.99
Elevated BP or anti-HTN medication (%)	94	95	-0.46	0.21	0.64
Elevated Fasting Glucose or diabetic Med (%)	52	58	-0.99	0.97	0.32
Elevated TG or Rx Med (%)	13	12	0.11	0.01	0.91
Reduced HDL or Rx Med (%)	44	59	-2.58 / 3.96	6.54	0.01 / 0.05
MetSyn (≥3 components; %)	35	45	-1.93	3.66	0.06

Data are expressed as prevalence of individual MetSyn components, and MetSyn as a disorder, by BQ Low- vs. High-risk groups. BMI was controlled for in the analyses; *p* values and *F* ratios for statistical difference between groups are expressed as without the covariate / with the covariate, where appropriate. Abbreviations: WC-waist circumference; BP-blood pressure; HTN-hypertension; Rx-prescription; Med-medication; TG-triglycerides; HDL-C-high density lipoprotein cholesterol.

Table 6. Cardiovascular and Metabolic Biomarkers by Berlin Risk Score

Characteristic	**BRS 0, *n*=18**	**BRS 1, *n*=121**	**BRS 2, *n*=133**	**BRS 3, *n*=54**	***F* ratio**	**Pearson Chi-Square**	***p* value**
Proportion (%)	6	37	41	17	_	110.4	<0.01
Age (yr)	72.6 (9.5)	74.8 (8.5)	72.3 (7.9)	72.4 (9.4)	2.10	_	0.10
BMI (kg/m^2)	24.4 (3.2) [b]	28.1 (5.2) [b]	29.8 (6.3) [ab]	32.5 (6.6)	11.45	_	<0.01
WC (cm)	89.6 (12.1) [b]	98.2 (14.2) [b]	101.8 (15.8) [a]	107.2 (13.2)	8.05 / 0.17	_	<0.01 / 0.92
HC (cm)	97.8 (9.8)	103.7 (10.1)	106.5 (13.6) [a]	109.0 (11.5) [a]	5.10 / 0.97	_	<0.01 / 0.41
W/H ratio	0.91 (0.06) [b]	0.95 (0.08) [b]	0.96 (0.07)	0.99 (0.09)	5.00 / 1.59	_	<0.01 / 0.19

SBP rest (mmHg)	144.7 (17.4)	143.1 (17.6)	140.5 (15.7)	144.3 (21.4)	0.82	_	0.48
DBP rest (mmHg)	77.8 (11.8)	76.1 (9.4)	76.6 (11.0)	77.2 (10.4)	0.23	_	0.88
Fasting Glucose (mg/dL)	96.4 (9.8) [b]	114.7 (33.3)	112.0 (20.2)	119.6 (28.3)	3.19 / 1.76	_	0.02 / 0.16
Fasting Insulin (mU/L)	8.3 (5.7)	11.5 (11.1) [b]	14.2 (17.0)	18.5 (14.8)	3.28/0.70	_	0.02 / 0.56
HOMA IR	2.0 (1.3)	3.7 (6.5)	4.3 (6.3)	5.8 (5.8)	1.90	_	0.13
TC (mg/dL)	158.6 (30.9)	161.4 (46.4)	165.8 (44.1)	154.0 (34.3)	0.94	_	0.42
TG (mg/dL)	81.3 (33.3)	93.3 (46.8)	100.4 (46.6)	110.6 (54.3)	2.34	_	0.07

HDL (mg/dL)	48.6 (14.3)	45.1 (13.6)	43.5 (15.2)	42.2 (12.7)	1.13	_	0.34
LDL (mg/dL)	90.4 (27.4)	92.7 (22.7)	98.4 (36.8)	85.0 (24.3)	2.0	_	0.11
Anti-HTN Med (%)	50	90 [a]	92 [a]	94 [a]	3.0 / 8.54	31.1	<0.01 / <0.01
Anti-lipemic Med (%)	72	80	77	88	0.95	2.88	0.41
Diabetic Med (%)	11	18 [b]	18 [b]	38	3.47 / 2.23	10.2	0.02 / 0.09

Data are expressed as group Mean and Standard Deviation (SD). BMI was controlled for in the analyses; *p* values and *F* ratios for statistical difference between groups are expressed as without the covariate / with the covariate, where appropriate. Bonferroni post-hoc comparisons were used to investigate differences between BRS groups. [a] =different from BRS 0, and [b] =different from BRS 3. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication; HOMA IR-homeostatic model assessment for insulin resistance; TC-total cholesterol; HDL-C-high density lipoprotein-cholesterol; LDL-C-low density lipoprotein-cholesterol; TG-triglycerides.

Table 7. MetSyn Components and Status by Berlin Risk Score

MetSyn Component (NCEP ATP III)	**BRS 0, n=18**	**BRS 1, n=121**	**BRS 2, n=133**	**BRS 3, n=54**	***F* ratio**	**Pearson Chi-Square**	***p* value**
Increased WC (%)	11 [b]	42 [b]	42 [b]	75	3.93	27.2	<0.01 / <0.01
Elevated BP or anti-HTN medication (%)	83	95	95	96	1.58	4.73	0.19
Elevated Fasting Glucose or Rx Med (%)	38 [b]	54	51	73	2.25	8.94	0.03 / 0.08
Elevated TG or Rx Med (%)	6	14	12	14	0.41	1.25	0.74

Reduced HDL or Rx Med (%)	17	48	58 [a]	61 [a]	2.87	12.9	<0.01 / 0.04
MetSyn (≥3 components; %)	11 [b]	13 [b]	37 [b]	65	3.34	20.6	<0.01 / 0.02

Data are expressed as prevalence of individual MetSyn components, and MetSyn as a disorder, by BRS OSA-risk groups. BMI was controlled for in the analyses; *p* values and *F* ratios for statistical difference between groups are expressed as without the covariate / with the covariate, where appropriate. Abbreviations: WC-waist circumference; BP-blood pressure; HTN-hypertension; Med-medication; Rx-prescription; TG-triglycerides; HDL-C-high density lipoprotein cholesterol.

FIGURES

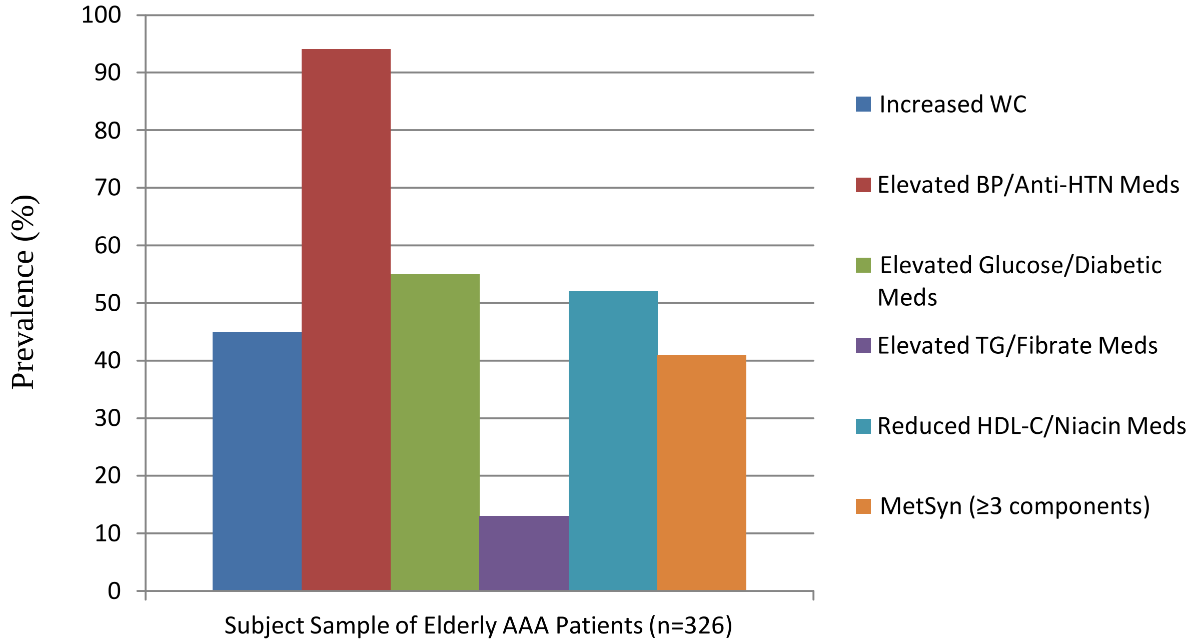

Figure 1. Prevalence of MetSyn Components and MetSyn among the Subject Sample.

Abbreviations: WC-waist circumference; BP- blood pressure; HTN-hypertension; Med-medication; TG-triglycerides; HDL-C-high density lipoprotein cholesterol; AAA-abdominal aortic aneurysm.

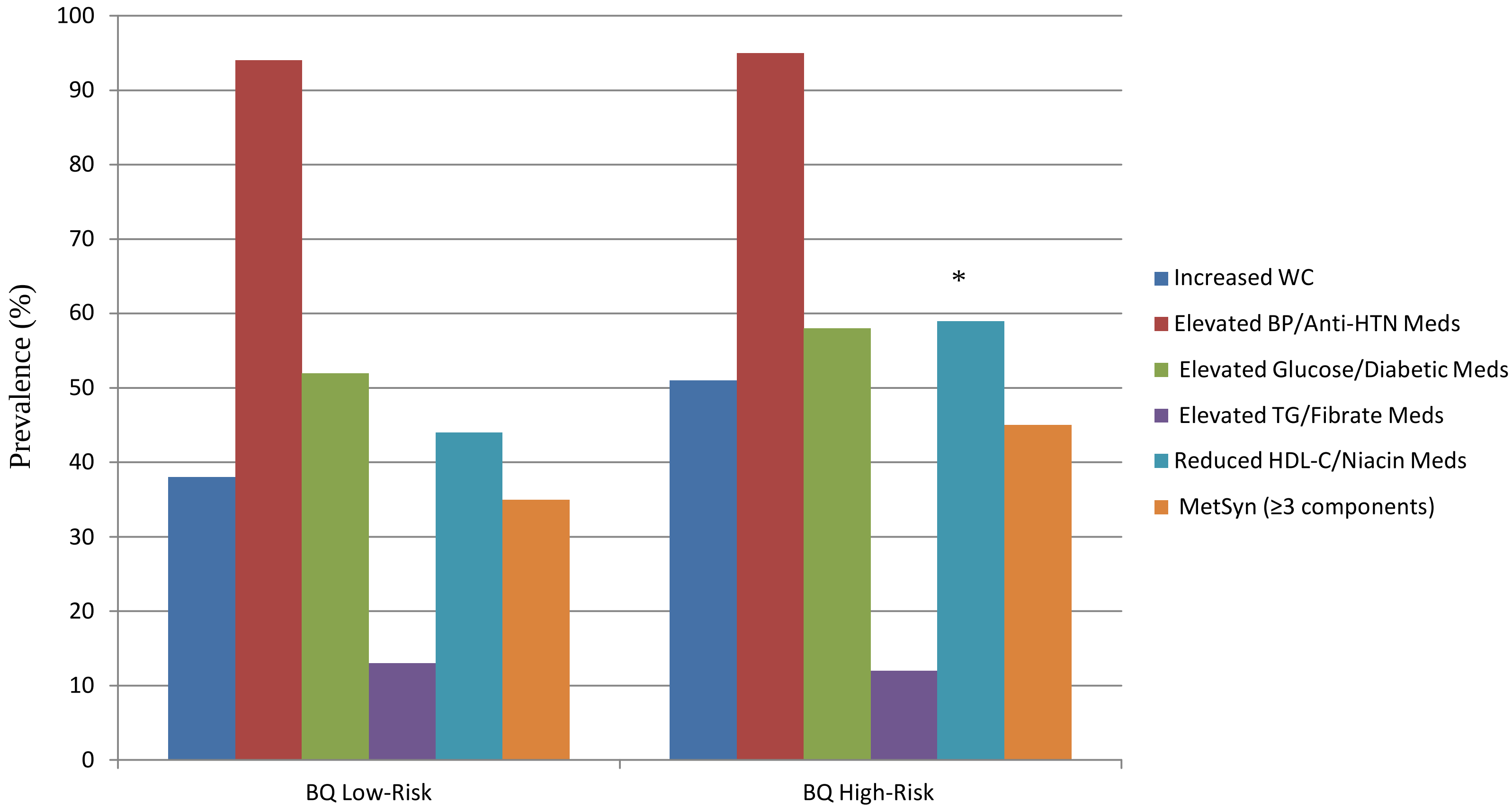

Figure 2. MetSyn Components and Status by BQ OSA-Risk.

Data are expressed as prevalence of individual MetSyn components, and MetSyn as a disorder, by BQ Low- vs. High-risk groups. BMI was controlled for in the analyses and * indicates statistical significance, which was set at $p<0.05$. Abbreviations: WC-waist circumference; BP-blood pressure; HTN-hypertension; Med- medication; TG-triglycerides; HDL-C-high density lipoprotein cholesterol; BQ-Berlin Questionnaire.

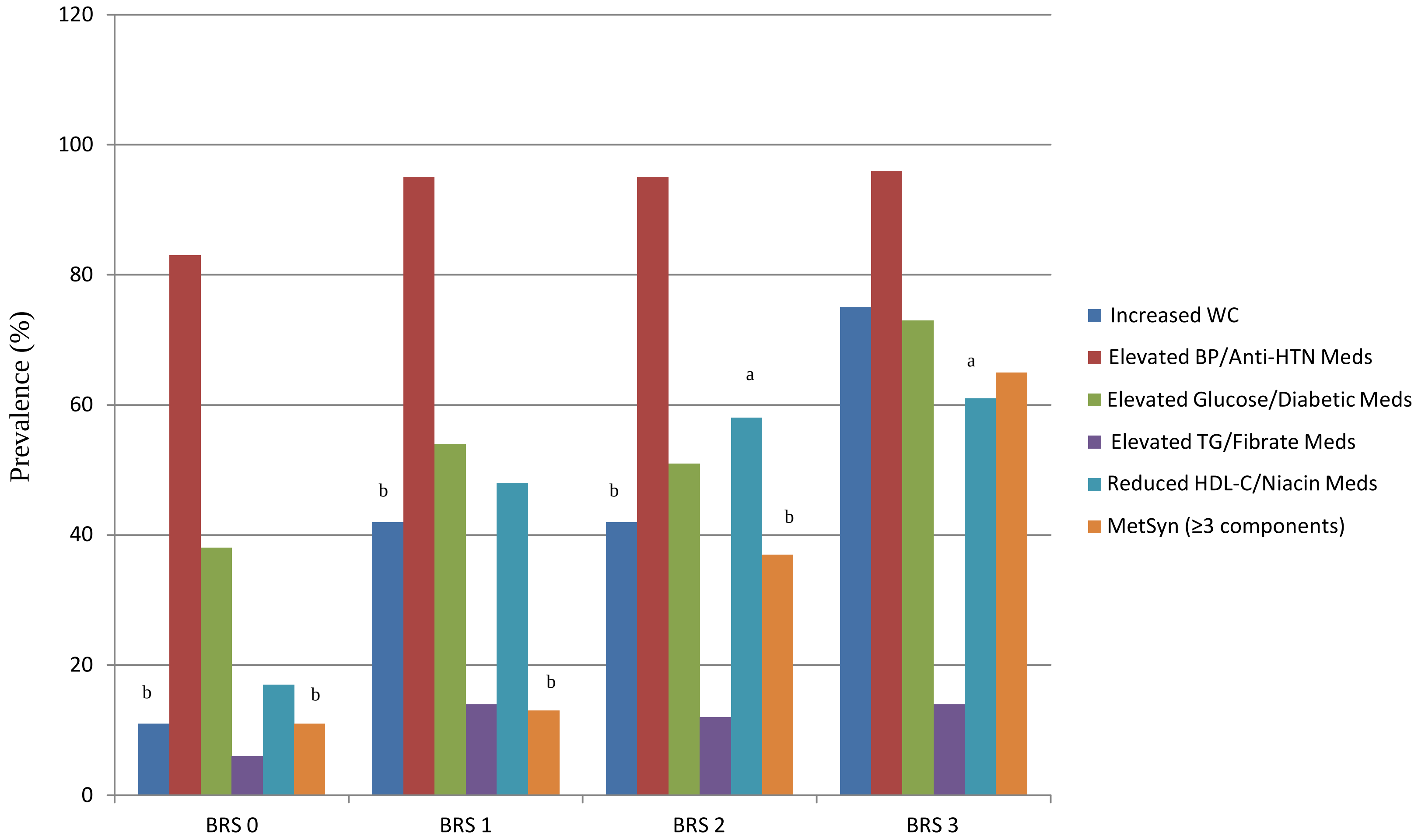

Figure 3. MetSyn Components and Status by Berlin Risk Score.

Data are expressed as group Mean (Standard Deviation-SD). BMI was controlled for in the analyses. Bonferroni post-hoc comparisons were used to investigate differences between BRS groups. [a]=different from BRS 0, and [b] =different from BRS 3. Statistical significance was set at $p<0.05$. Abbreviations: WC-waist circumference; BP-blood pressure; HTN-hypertension; Med-

medication; TG-triglycerides; HDL-C-high density lipoprotein cholesterol; BRS-Berlin Risk Score.

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CHAPTER FOUR

OBSTRUCTIVE SLEEP APNEA RISK IN ABDOMINAL AORTIC ANUERYSM DISEASE PATIENTS: ASSOCIATIONS WITH EXERCISE CAPACITY AND TOLERANCE

ABSTRACT

Purpose: Compare and contrast exercise capacity and physiological responses to Cardiopulmonary exercise testing (CPET) in elderly patients with abdominal aortic aneurysm (AAA) disease relative to risk for obstructive sleep apnea (OSA). **Methods:** 114 elderly volunteer subjects with newly diagnosed small AAAs participated. Study methods for all participants included extraction of medical history and drug information from medical records; completion of a physical examination with study personnel to assess measures of body habitus including body mass index (BMI) calculation; completion of a symptom-limited CPET with gas exchange using an individualized treadmill protocol to assess exercise capacity and responses during CPET; and completion of the Berlin Questionnaire (BQ), with verification of responses completed by interviews with study staff, to assess OSA risk. Subjects were classified as High-Risk or Low-Risk for OSA, using the BQ; to further examine gradations in OSA risk, subjects were also classified by their Berlin Risk Score (BRS), as determined by summing the three categorical scores from the BQ (BRS 0, 1, 2, or 3). **Results:** Exercise capacity and responses at rest, the VT, peak exercise, and during active recovery, including HR, BP, VE, VO2, VE/VCO_2 slope, and RER were not different between BQ High- and Low-risk groups. After controlling for group differences in BMI, exercise capacity and responses at rest, the VT, peak exercise, and during active recovery were also similar between BRS groups. **Conclusion:** OSA risk, in this study of elderly AAA disease patients, did not influence exercise capacity or physiological responses to cardiopulmonary exercise testing. Further research is needed to better understand the clinical implications OSA may have on the elderly with AAA disease.

INTRODUCTION

Obstructive sleep apnea (OSA) is the most common sleep related breathing disorder, affecting an estimated 20% of the U.S. adult population [1]; Prevalence of OSA is difficult to report, as up to 90% of people with the disorder remain undiagnosed [2], though it is anticipated to rise as an increasing proportion of Americans are obese and elderly, both of which are risk factors for OSA. OSA is characterized by repetitive bouts of upper airway occlusion or collapse during sleep, resulting in intermittent periods of hypoxia, hypercapnia, and fragmented sleep [3]. Obesity is the primary risk factor for OSA and is reported in more than 40% of OSA cases; furthermore, more than 80% of individuals with OSA are also obese [4].

Untreated OSA can increase risk for several chronic diseases and disorders including obesity, HTN and CVD, metabolic disorders, depression, and aortic disease [5-13]; however, the mechanism(s) linking OSA to HTN and CVD remains undetermined. Repetitive nighttime apneas and hypopneas (cessations and pauses in breathing) result in activation of the sympathetic nervous system (SNS) and stressful arousals to reestablish breathing. It has been determined that OSA patients demonstrate an exaggerated activation of the SNS that persists into waking hours that can lead to elevations in HR and BP [14]. Over time, activation of the baroreceptors, which respond to normalize these HR and BP oscillations, become altered and depressed in OSA patients [15], suggesting an impairment of the cardiovascular autonomic system, thereby increasing risk for HTN and CVD.

The “gold standard” for diagnosing OSA is laboratory polysomnography (PSG); however, sleep health questionnaires that stratify patients based on clinical symptoms, physical examinations, and risk factors, are often employed as a first step assessment to screen for OSA. Questionnaires that are commonly used to screen for OSA and have been validated against PSG, include the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Berlin

Questionnaire (BQ), and most recently, the STOP-Bang questionnaire. Sleep screening questionnaires do not require complicated calculations to identify high risk patients, and they are relatively easy and cost-effective to apply clinically; however, there are also limitations. Sleep questionnaires rely on self-report and disclosure of signs and symptoms, as well as the patient's memory and ability and willingness to follow instructions. Additionally, many of the signs and symptoms of OSA may be difficult for the patient to self-identify, such as snoring and choking during sleep, and can be misinterpreted as other conditions; however, the BQ is regarded for its high specificity and sensitivity for predicting moderate to severe OSA [16]. The BQ is also among the most accurate screening questionnaires for OSA [17].

Sleep disorders, specifically OSA, are highly prevalent in older adults; the Sleep Heart Health Study found that among 6,400 older adults, sleep disordered breathing (SDB) prevalence rates for mild to severe SDB ranged from 19-36% for adults 60-98 years old [18]. These rates far outpace those for middle aged adults, age 30-60 years old, whose SDB rates were 2-4% for women and men [19]. One cohort study found that for adults 71-100 years, the prevalence of mild OSA was 80% and moderate OSA was 49% for women and 57% for men [20, 21]. Despite these high prevalence rates, studies have suggested that most of the age-related increase in prevalence of OSA occurs before age 65 and plateaus at some point after age 65 [22, 23].

Recently, OSA was determined to be highly prevalent among patients with AAA disease, a disease of the elderly in which the lower part of the aorta is weakened and bulging. Moderate or severe OSA was present in 42% of their subjects with AAA disease [24]. One very recent report suggested that OSA may not only be a risk for factor for aortic disease [10], but a causal factor for faster AAA expansion [24]. AAA disease is prevalent in the elderly, most often occurring in people age 60 years and older, and AAA presence is associated with overweight and obesity [25]. Risk factors for AAA include advancing age, history of cigarette smoking, male gender and family history.

Increases in chronic diseases and disabilities that often accompany aging, in addition to AAA disease, may limit the daily activities of older adults and reduce health-related quality of life. Approximately 80% of older Americans have at least one and 50% have at least two chronic conditions, such as cardiovascular disease (CVD), type II diabetes, or cancer [26]. Chronic illness also may contribute to the reductions in physical activity (PA) and exercise capacity in older adults. Unfortunately, few older adults achieve the minimum recommendation for PA; up to 34% of adults age 65-74 years and up to 44% of adults ages 75 years and older are inactive [27]. This, despite the recommendations that older adults without specific health limitations should engage in 150 minutes of moderate intensity aerobic activity each week, or 75 minutes of vigorous intensity aerobic activity, in addition to two days each week of muscle-strengthening activities [28].

Conversely, physical inactivity and a sedentary lifestyle contribute to and exacerbate many chronic diseases that are the leading causes of death in the U.S, including cardiovascular and metabolic diseases [29]. In 2002, the primary causes of death for older adults in the U.S. were heart disease, cancer, and stroke, together accounting for 61% of all deaths in America, among those age 65 years and older [30]. Three studies from the last two decades clearly point to poor health behaviors, including diet, physical inactivity, and smoking, as accountable for somewhere between 14-35% of the deaths each year that are attributable chronic diseases [31-33].

Regular PA is important for improving the health and wellbeing of people of all ages. PA increases cardiovascular functional capacity and decreases myocardial oxygen demand at any level of exertion by increasing both maximum cardiac output and the ability of muscles to extract and utilize oxygen from the blood [34]. Beneficial changes in hemodynamic, hormonal, metabolic, neurological, and respiratory function also occur with increased exercise capacity [35-38]. Developing and maintaining aerobic endurance, joint flexibility, and muscle strength is especially important for aging individuals [39] to improve mobility and physical functioning and ability to complete activities of daily living (ADLs), in addition to the mental health and quality of life benefits. A fundamental requirement for many ADLs is the ability to perform aerobic work, requiring the efforts of the heart, lungs, and circulation to deliver oxygen to metabolically active muscles. Exercise capacity is affected by age, sex, conditioning status, presence of diseases, or medications that can influence peak oxygen consumption (VO_{2peak}) [40].

Previous studies have shown that elderly individuals experience changes in the cardiac autonomic control, due to aging, demonstrating a marked reduction in parasympathetic modulation [41]; therefore, this population demonstrates a reduction in cardiac output (CO), peripheral blood flow, and muscle metabolism, which can promote changes related to the transport and use of oxygen in the body [42]. During cardio-pulmonary exercise testing (CPET), elderly persons demonstrate lower values for maximal power (cycle ergometry), and peak HR, as well as ventilatory and metabolic variables, compared to younger populations; this is primarily due to muscular and cardiorespiratory changes caused by aging [42].

The assessment of exercise capacity and physiological responses during CPET provides important diagnostic and prognostic information in a clinical setting [40] and is an effective tool for identifying those at high risk for CVD [43]. Exercise capacity and PA status are well-established predictors of cardiovascular and overall mortality [44-46], supporting the value of CPET as a clinical tool that provides relevant diagnostic and prognostic information in both healthy persons and those with cardiovascular conditions [46]. CPET is frequently used to assess integrated response of cardiovascular, respiratory, and muscular systems to graded physical exercise. In addition to exercise capacity, other physiological responses during CPET are of clinical utility, including responses at the ventilatory threshold (VT) and during exercise recovery. The VT, defined by the exercise level at which ventilation begins to increase exponentially for a given increment in oxygen consumption ($V0_2$), can predict exercise performance and intensity. Researchers have identified oxygen consumption at the VT as a parameter of comparable importance to VO_2 at peak exercise for identifying patients at increased mortality risk [47]. Additionally, recovery responses post exercises reflect impairment in autonomic regulation and may have prognostic value for those at risk for cardiovascular complications; abnormal HR or BP responses during exercise recovery have been shown to predict future CVD [48] and mortality [49, 50]. CPET has also been safe and effective for evaluating AAA patients; Myers and colleagues evaluated exercise capacity and responses to CPET in elderly patients with small AAAs and found that although they demonstrated similar exercise capacities, AAA patients had a slightly higher incidence of hyper- and hypotensive responses to exercise than the age-matched referral group, suggestive of potential autonomic imbalance [51].

Patients with OSA are also characterized by excessive daytime sleepiness (EDS), fatigue, and decreased daily PA which may also impair muscle energy metabolism and decrease exercise tolerance [52]. Obesity is often a co-morbid condition in individuals with OSA and may also influence exercise capacity through abnormalities in lung function and increases in ventilatory stress [53]. Decreased exercise capacity, an independent predictor for all-cause mortality in older men [46], has been demonstrated in middle-aged adults with OSA [54-56]; however, the mechanisms by which have not been thoroughly determined. Possible causes include cardiovascular [57], respiratory [58], and peripheral muscular abnormalities [52]. Autonomic nervous system dysfunction has been hypothesized to link OSA to CVDs such as HTN, heart failure, myocardial infarction, and stroke [59]. In patients with OSA, sympathetic drive is increased during nighttime apneic events as well as during daytime awake periods [14]. Recovery responses following maximal exercise reflect primarily parasympathetic reactivation and have been shown to be of prognostic importance in the general population [60]. The influence of OSA risk on exercise capacity and physiological responses during exercise and recovery has been examined in pre-elderly populations with OSA [53, 56, 61, 62] but not systematically examined in an elderly population at risk for OSA with newly diagnosed AAAs.

RESEARCH AIM AND HYPOTHESIS

The aim of this study is to compare and contrast exercise capacity and physiological responses to CPET in elderly patients with AAA disease according to risk for OSA, as assessed by the BQ. The working hypothesis is that OSA risk is associated with reduced exercise capacity and with physiological responses to exercise suggestive of autonomic imbalance and ventilatory inefficiency.

METHODS

A total of 114 subjects with newly diagnosed small AAAs (aortic diameter ≥2.5 and < 5.5 cm) were recruited from Stanford University Medical Center, the Veterans Affairs Palo Alto Health Care System (VAPAHCS) and Kaiser Permanente of Northern California. Subjects were 50 years of age or older, agreed to comply with study protocols and procedures, and provided voluntary consent to participate. Additional exclusion criteria is discussed in Appendix A. Recruitment procedures and all study-related activities were reviewed and approved in advance by Institutional Review Boards (IRBs) at Stanford University (including VAPAHCS) as well as the Kaiser Permanente Division of Research and an independent Data Safety Monitoring Board (DSMB) organized by the NHLBI. Additional details on recruitment procedures can be found in Appendix A. Study methods for all participants included extraction of medical history and drug information from medical records and subject completion of a health history questionnaire which included self-report medication use; completion of a physical examination with study personnel to assess resting systolic and diastolic BP, as well as measures of body habitus including height and weight for body mass index (BMI) calculation and waist (WC) and hip (HC) circumference measurements; completion of the BQ, with verification of responses completed by interviews with study staff, to assess OSA risk; and completion of a symptom-limited CPET with gas exchange using an individualized treadmill protocol according to recommended procedures to assess exercise capacity and physiological responses during CPET [43].

Physical Examination and Health History

Subjects underwent a physical examination with study personnel to assess resting systolic and diastolic BP, as well as measures of body habitus, including height and weight for BMI calculation and waist (WC) and hip circumference (HC) measurements, which were also used to calculate waist/hip (W/H) ratio. Detailed assessment protocols for these measures are included in Appendix A. Subjects also provided information on prescriptive medications they were receiving to determine the extent of medically managed HTN, dyslipidemia, type II diabetes, and other diseases and disorders in the sample.

Berlin Questionnaire

The modified Berlin Questionnaire (BQ) is a 12-item self-report questionnaire that includes questions about risk factors for OSA that can be identified with three discrete sign/symptom categories of 1.) snoring behavior, 2.) wake time sleepiness and fatigue, and 3.) obesity and HTN. The modified BQ, an extension of the original BQ, includes three additional questions regarding choking behavior and wake-time sleepiness. The modified BQ is a validated instrument used to identify individuals who are at risk for OSA with a sensitivity (86%) and specificity (95%) comparable to the original BQ [63-66]; positive and negative predictive values of 96% and 82%, respectively, were reported for the modified BQ [66]. Subjects completed the BQ and responses were confirmed and clarified by one-on-one interview between subject and study personnel.

Patients were classified as Low- or High-Risk for OSA based on their responses to the individual items and their overall scores in the three symptom categories, according to the scoring instructions detailed by Netzer and colleagues [64]. To further examine gradations in OSA risk, subjects also were classified by their Berlin Risk Score (BRS) which, for this study, was defined as the sum of the three categorical scores from the BQ. Subjects were grouped into one of four BRS groups which equated to the number of categories that were scored positive from their BQ (BRS 0, 1, 2, or 3). It should be noted that this is not a validated interpretation of the BQ, but simply an approach to examine a more detailed analysis of risk for OSA from patient responses to the individual questions and risk factor categories that comprise the BQ.

Cardiopulmonary Exercise Testing

Participants completed a symptom-limited CPET with gas exchange using an individualized ramp treadmill protocol, as previously described by Myers *et al*. [67] and according to standard protocols and recommended procedures to assess exercise capacity and physiological responses during CPET [43]. Standardized medical examinations were performed prior to testing and medication use was continued as prescribed. Protocols were individualized to fall within the recommended 8 to 12 minute range. Electrocardiograms (ECGs) for HR and rhythm were obtained at rest, each minute during exercise, and during recovery. BP was measured at rest, every 2 minutes during exercise, and during recovery or until symptoms, ECG changes, and BP stabilized. For individual patients, a supervising physician was present who determined if CPET's should be terminated before pre-determined endpoints, whenever untoward signs, symptoms, or responses occurred. In the absence of indications to stop the test, participants were encouraged to exercise until volitional fatigue. The Borg scale for perceived exertion was used to quantify effort [68]. Exercise capacity was estimated from peak treadmill speed and grade [43]. CPET responses were obtained using a CosMed Quark CPET metabolic system (CosMed Inc, Rome, Italy). Minute ventilation (V_E), oxygen uptake (VO_2), carbon dioxide production (VCO_2), and other cardiopulmonary exercise test variables were acquired breath by breath, reported at 10-second intervals, and averaged over 30 seconds. The VT was determined using the V-slope method. The V_E/VCO_2 slope was calculated using measured VE and VCO2 responses during exercise. Detailed protocols and procedures for these measures are discussed by Myers *et. al* in a previous publication that evaluated exercise training in patients with AAA disease [69].

Statistical Analyses

Data were stored electronically in a SPSS® (SPSS, Inc., Chicago, IL) database (Version 20.0). Statistical significance was determined *a priori* for all experimental analyses as a p value < 0.05. Descriptive statistics were assessed for each group to observe means, standard deviations (S.D), and ranges for variables of interest related to exercise capacity and physiological responses at rest, during exercise, at peak exercise, and during recovery. To compare means between groups, independent student t-tests and ANOVA were performed, for two- and four-group comparisons, respectively; Bonferroni post hoc analysis were used to further examine differences between four-group comparisons for all dependent variables of interest. Although the subject sample was similar, group differences existed for BMI that may affect relationships between dependent variables of interest related to exercise capacity and physiological responses to CPET; therefore, when statistically significant differences between groups were observed for variables of interest, a general linear model univariate procedure was performed to control for BMI.

RESULTS

Characteristics of Study Participants by OSA Risk

Characteristics of individual subjects are presented in Appendix D. Men comprised 94% of the subject sample. Means ±SD values for characteristics of the study groups, identified at Low- and High- risk for OSA according to subject BQ clinical risk scores are presented in Table 1. Approximately half of the overall sample (48%) was classified as High-risk for OSA by this method. The BQ High-risk group was, on average, 3.5 years younger (t=2.21; p=0.03) and had a greater BMI (t=-2.29; p=0.02) than the Low-risk group. Given the significant relationship between age and BMI (F=11.6; p<0.01), analyses were controlled for the influences of BMI. AAA size was similar between OSA-risk groups, as was resting BP. Measures of body habitus, including WC and W/H ratio were higher among the BQ High- vs. Low-risk group ($p<0.01$). Self-reported use of anti-HTN and anti-lipemic medications were relatively high in both groups, while twice the percentage of patients in the BQ High-risk group reported higher use of anti-diabetic medications.

Table 1. Subject Characteristics by OSA-Risk

Characteristic	**BQ Low-Risk, *n*=60**	**BQ High-Risk, *n*=54**	***t* statistic**	**Pearson Chi-Square**	***p* value**
Proportion (%)	52	48	_	0.32	0.57
Age (yrs)	73.2 (8.2)	69.7 (8.3)	2.21	_	0.03
AAA size (cm)	3.5 (0.8)	3.4 (0.9)	0.60	_	0.55
BMI (kg/m^2)	27.4 (5)	29.9 (6.8)	-2.29	_	0.02
WC (cm)	96.5 (12.1)	103.8 (14.4)	-2.92	_	<0.01
HC (cm)	103.0 (10.6)	105.6 (9.9)	-1.37	_	0.17
Waist/Hip Ratio	0.94 (0.07)	0.99 (0.07)	-4.13	_	<0.01
SBP rest (mmHg)	134.0 (14.8)	136.5 (14.8)	-0.91	_	0.37
DBP rest (mmHg)	76.1 (7.9)	79.1 (9.7)	-1.85	_	0.07

Anti-HTN Med (%)	68	76	_	0.76	0.38
Anti-lipemic Med (%)	65	64	_	0.10	0.92
Diabetic Med (%)	11	24	_	3.31	0.07

Data are expressed as group Mean and SD. Medication data is presented as a group percentage (%) taking each class of medication. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H-waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

Subject characteristics for groups defined by BRS risk score (stratification according to four risk levels) are presented in Table 2. This stratification resulted in the majority of subjects being classified as either BRS 1 and 2 groups, 44% and 37%, respectively, and substantially fewer categorized in the lowest and highest OSA risk classifications ($X2=45.0$; $p<0.01$). Age and AAA size were similar across groups. BMI and measures of body habitus including WC and W/H ratio significantly increased linearly across BRS groups; therefore, BMI was controlled for in the analyses, where appropriate. HC and SBP were similar across groups, as was use of medications to control HTN and anti-lipemic medications. Use of medications to control diabetes was significantly higher in the BRS 3 group compared to BRS 0 and 1 groups.

Table 2. Subject Characteristics by Berlin Risk Score

Characteristic	BRS 0, *n*=9	BRS 1, *n*=51	BRS 2, *n*=41	BRS 3, *n*=13	*F* ratio	Pearson Chi-Square	*p* value
Proportion (%)	8	44	37	11	_	45.0	<0.01
Age (yrs)	72.4 (6.7)	73.3 (8.5)	69.8 (8.4)	69.6 (8.5)	1.63	_	0.19
AAA size (cm)	3.1 (1.0)	3.6 (0.7)	3.5 (0.7)	3.4 (1.2)	0.97	_	0.41
BMI (kg/m^2)	24.4 (3.4) [a]	27.9 (5.1)	29.8 (7.4)	30.5 (4.8)	2.71	_	0.05
WC (cm)	88.1 (10.6) [b]	98.0 (11.8)	102.8 (15.3)	106.8 (11.1)	4.73	_	<0.01
HC (cm)	96.7 (7.9)	104.1 (10.6)	105.4 (10.3)	106.3 (8.8)	2.02	_	0.12
Waist/Hip Ratio	0.92 (0.06) [b]	0.94 (0.07) [b]	0.99 (0.07)	1.0 (0.05)	6.53	_	<0.01
SBP rest (mmHg)	129.9 (10.5)	134.7 (15.5)	135.7 (15.3)	139.2 (13.3)	0.72	_	0.54

DBP rest (mmHg)	75.4 (6.5)	76.2 (8.2)	78.4 (9.9)	81.6 (9.1)	0.19	_	1.60
Anti-HTN Med (%)	67	69	70	92	1.02	3.09	0.38
Anti-lipemic Med (%)	56	67	62	69	0.20	0.63	0.89
Diabetic Med (%)	0 [a]	13 [a]	16	46	3.66	10.3	0.02

Data are expressed as group Mean and Standard Deviation (SD). Medication data is presented as a group percentage (%) taking each class of medication. Bonferroni post-hoc comparisons were used to investigate differences between groups. [a] = different from BQ+ Class 3, [b] = different from BQ+ Class 2 and 3. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H-waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

Table 3 highlights the cardiopulmonary variables of interest from the CPET and recreational PA by BQ OSA risk-group. For exercise capacity and variables assessed at rest, at the VT, and peak exercise, including HR, BP, VE, VO_2, RER, and VE/VCO_2 slope, no differences were found between groups classified as Low- vs. High--risk for OSA. Figures 1 and 2 graphically demonstrate HR and BP response during post-exercise active recovery, respectively, neither of which differed between groups.

Table 3. CPET Variables by Clinical Berlin OSA-Risk

Characteristic	**BQ Low-Risk, *n*=60**	**BQ High-Risk, *n*=54**	***t* statistic**	***p* value**
HR at rest-supine (bt/min)	64 (11)	64 (11)	0.15	0.88
SBP at rest-supine (mmHg)	131.1 (14.6)	134.4 (14.9)	-1.20	0.23
DBP at rest-supine (mmHg)	76.0 (8.4)	78.8 (8.6)	-1.76	0.08
HR at rest-standing (bt/min)	69.6 (13.7)	67.9 (13.6)	0.65	0.52
SBP at rest-standing (mmHg)	130.0 (17.2)	134.7 (18.3)	-1.40	0.17
DBP at rest-standing (mmHg)	76.4 (8.9)	77.7 (10.9)	-0.69	0.49
HR at VT (bt/min)	102 (24)	100 (19)	0.97	0.73

Time at VT (% Max Exercise Time)	41	47	-1.11	0.27
VE at VT (L/min)	36.0 (12.0)	36.9 (11.3)	-0.11	0.69
VO_2 at VT (ml/kg/min)	14.9 (4.1)	14.7 (4.2)	0.24	0.81
RER at VT	0.9 (0.3)	0.8 (0.2)	1.14	0.26
VE/VCO_2 slope at VT	0.30 (0.04)	0.29 (0.06)	0.80	0.43
HR peak (bt/min)	131.7 (23.7)	126.8 (21.9)	1.15	0.26
SBP peak (mmHg)	180.6 (25.4)	189.4 (29.6	-1.69	0.09
DBP peak (mmHg)	78.0 (12.4)	82.5 (14.2)	-1.80	0.08
VE peak (L/min)	62.7 (20.7)	69.2 (19.9)	-1.70	0.09
VO_2 peak (ml/kg/min)	20.8 (7.3)	20.9 (6.3)	-0.12	0.91
RER peak	1.1 (0.2)	1.5 (2.6)	-0.24	0.29

Data are expressed as group Mean and SD. BMI was controlled for in the analyses; *p* values and *F* ratios are expressed as without the covariate / with the covariate where appropriate.

Abbreviations: HR-heart rate; SBP-systolic blood pressure; DBP-diastolic blood pressure; VT-ventilatory threshold; VO^2-oxygen consumption; RER-respiratory exchange ratio.

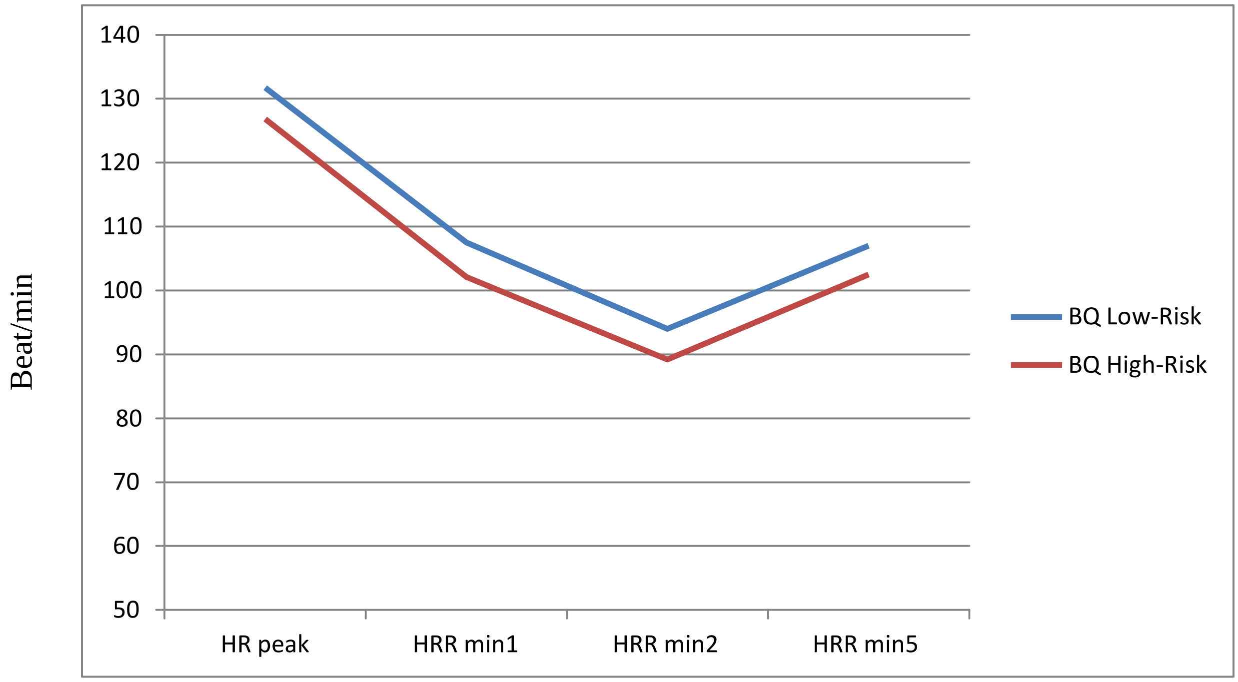

Figure 1. HR Slope During Post-Exercise Recovery by Clinical Berlin OSA-Risk.

BMI was controlled for in the analyses. Abbreviations: BQ-Berlin Questionnaire; HR-heart rate; HRR- heart rate recovery.

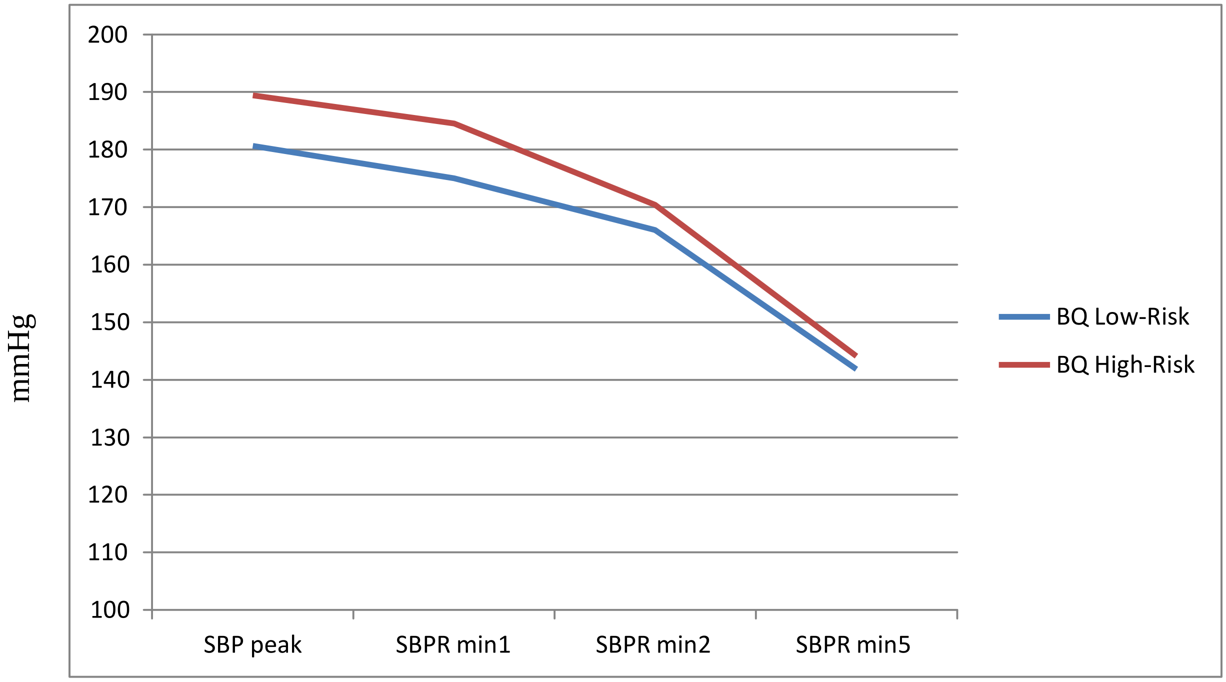

Figure 2. SBP Slope During Post-Exercise Recovery by Clinical Berlin OSA-Risk.

BMI was controlled for in the analyses. Abbreviations: BQ-Berlin Questionnaire; SBP-systolic blood pressure; SBPR- systolic blood pressure recovery.

Table 4 highlights the cardiopulmonary variables of interest from the CPET by BRS group. Exercise capacity and physiological responses at rest and the VT including HR, BP, VE, VO_2, RER, and VE/VCO_2 slope were similar across BRS groups at the VT. Physiological responses recorded at peak exercise were also similar between groups, including BP, VE, VO_{2max}, and RER_{peak}, though HR at peak exercise was higher among the BRS 0 group compared to BRS groups 1, 2, and 3 (F=2.81; p=0.04). SBP during the first minute of active recovery was higher among the BRS 0 group compared to the BRS 1 group but no longer remained significant after controlling for group differences in BMI. No other measurement of HR or BP differed between groups during active recovery between BRS groups. Figures 3 and 4 graphically demonstrate HR and BP response during post-exercise active recovery, respectively, across BRS groups.

Table 4. CPET Variables by Berlin Risk Score

Characteristic	Berlin Risk Score=0, n=9	Berlin Risk Score=1, n=51	Berlin Risk Score=2, n=41	Berlin Risk Score=3, n=13	*F* ratio	*p* value
HR at rest-supine (bt/min)	64.2 (13.6)	64.2 (10.9)	64.6 (10.5)	61.7 (11.7)	0.23	0.87
SBP at rest-supine (mmHg)	125.3 (13.7)	132.1 (14.6)	134.0 (13.9)	135.8 (18.5)	1.06	0.40
DBP at rest-supine (mmHg)	78.2 (6.4)	75.6 (8.7)	78.2 (7.5)	81.0 (11.6)	1.60	0.19
HR at rest-standing (bt/min)	70.2 (13.8)	69.4 (13.8)	69.6 (14.2)	62.8 (10.3)	0.94	0.42
SBP at rest-standing (mmHg)	125.1 (14.3)	130.9 (17.6)	134.2 (18.8)	136.2 (17.6)	0.95	0.42
DBP at rest-standing	76.9 (9.5)	76.4 (8.9)	76.8 (10.5)	80.6 (12.2)	0.66	0.58

(mmHg)						
HR at VT (bt/min)	118.0 (17.6)	102.6 (18.3)	99.8 (17.4)	102.0 (23.1)	1.36	0.26
Time at VT (% Max Exercise Time)	61	38	45	52	2.57	0.06
VE at VT (L/min)	44.7 (8.0)	35.5 (10.5)	36.7 (11.8)	37.5 (9.9)	1.49	0.22
VO_2 at VT (ml/kg/min)	17.2 (2.5)	14.5 (4.2)	14.5 (4.5)	15.1 (3.5)	0.90	0.44
RER at VT	0.93 (0.07)	0.86 (0.10)	0.84 (0.11)	0.86 (0.10)	1.66	0.18
VE/VCO_2 slope at VT	0.28 (0.02)	0.30 (0.04)	0.29 (0.06)	0.29 (0.06)	0.52	0.67
HR peak (bt/min)	149.9 (22.2) [c]	128.4 (22.6)	126.8 (20.7)	126.5 (26.0)	3.05 / 2.81	0.03 / 0.04

SBP peak (mmHg)	186.9 (35.6)	179.4 (23.4)	188.2 (30.0)	193.1 (29.2)	1.23	0.30
DBP peak (mmHg)	82.1 (11.2)	77.2 (12.5)	82.4 (15.1)	82.8 (11.4)	1.41	0.24
VE peak (L/min)	69.8 (10.3)	61.3 (21.9)	68.7 (19.3)	70.7 (22.7)	1.43	0.24
VO_2 peak (ml/kg/min)	21.6 (10.3)	20.2 (7.3)	20.6 (7.0)	20.3 (6.5)	0.09	0.96
RER peak	1.1 (0.1)	1.1 (0.2)	1.1 (0.1)	1.1 (0.1)	0.08	0.97

Data are expressed as group Means and SD. BMI was controlled for in the analyses; *p* values and *F* ratios are expressed as without the covariate / with the covariate where appropriate. Bonferroni post-hoc comparisons were used to investigate differences between groups. [a] = different from BQ+ Class 3; [c] = different from BQ+ Class 1,2, and 3; and [d] = different from BQ+ Class 0. Abbreviations: HR-heart rate; SBP-systolic blood pressure; DBP-diastolic blood pressure; VT-ventilatory threshold; VO^2-oxygen consumption; RER-respiratory exchange ratio.

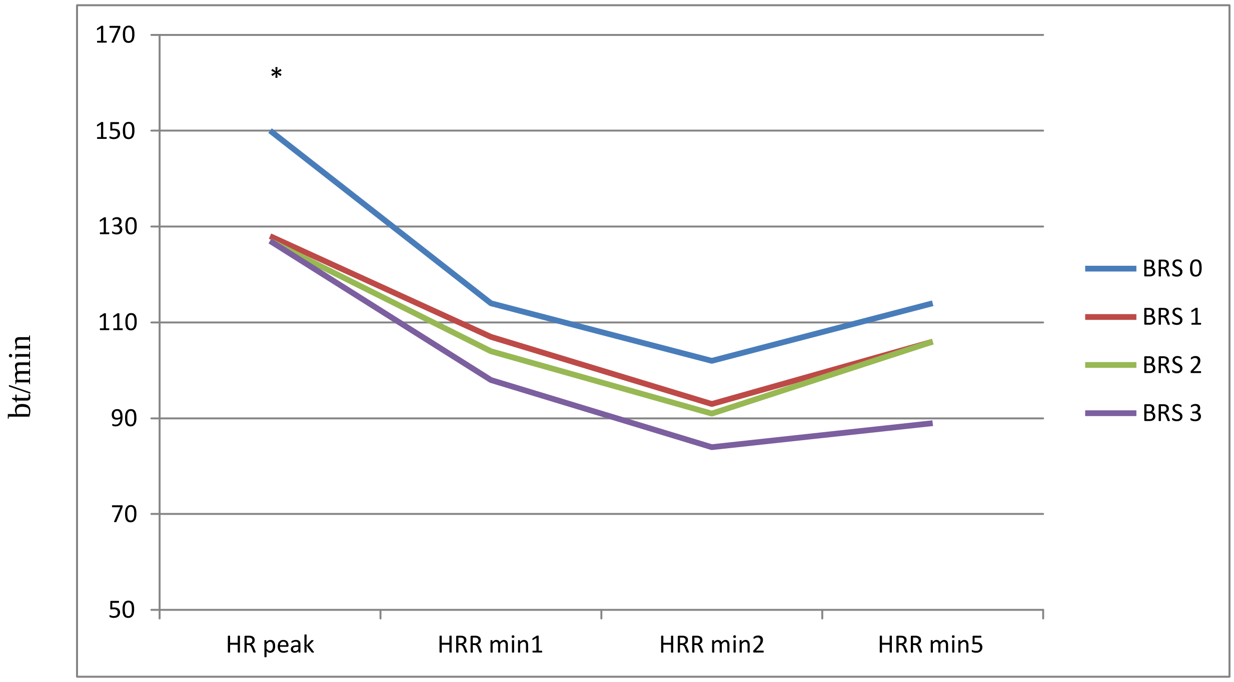

Figure 3. HR Slope During Post-Exercise Recovery by Berlin Risk Score.

BMI was controlled for in the analyses. Bonferroni post-hoc comparisons were used to investigate differences between BRS groups. * indicates BRS 0 ≠ BRS 1, 2 and 3. Statistical significance was set at $p<0.05$. Abbreviations: BRS-Berlin Risk Score; HR-heart rate; HRR-heart rate recovery.

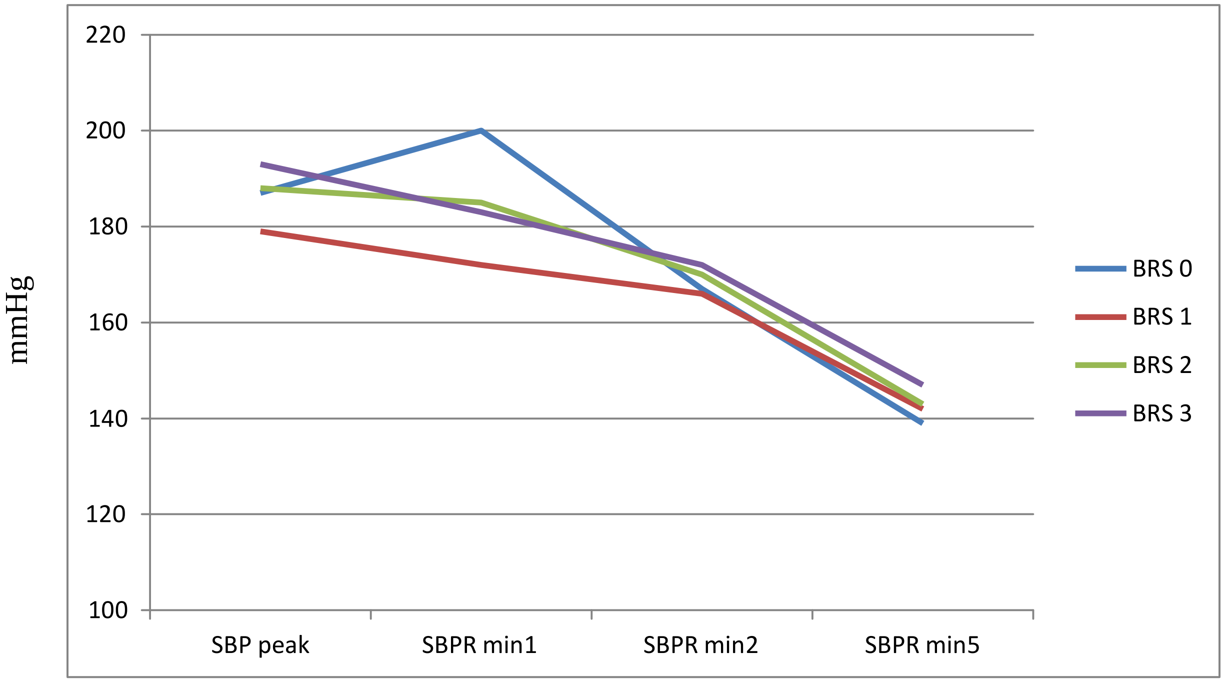

Figure 4. SBP Slope During Post-Exercise Recovery by Berlin Risk Score.

BMI was controlled for in the analyses. Bonferroni post-hoc comparisons were used to investigate differences between BRS groups. Statistical significance was set at $p<0.05$. No differences found between groups. Abbreviations: BRS-Berlin Risk Score; SBP-systolic blood pressure; SBPR- systolic blood pressure recovery.

DISCUSSION

Findings indicate that the group of elderly AAA patients at High-risk for OSA, as indicated from the BQ, demonstrate similar exercise capacity and physiological responses to CPET compared to their Low-risk counterparts, suggesting that exercise tolerance was not impacted by presence of OSA risk in elderly AAA patients. Stratifying the subject sample by BRS revealed group differences for peak HR, which was higher among the lowest risk BRS group compared to BRS 1, 2, and 3 groups. Group differences in HR at peak exercise were not due to the influences of medication known to affect physiological responses to exercise, as use of anti-HTN medications was similar across OSA-risk groups. To investigate this further, a non-parametric Kruskal Wallis test to account for the non-normal distribution of the mean HR_{peak} revealed that group differences for HR_{peak} were not significant (p=0.06). All OSA-risk groups (BQ High- vs. Low-risk and BRS groups) were able to achieve at least 80% of their age-predicted maximal HR, which was not influenced by OSA-risk, further supporting the findings exercise capacity and responses are not associated with OSA risk in elderly AAA patients.

This is the first study to evaluate the associations between OSA risk and exercise capacity and responses in an elderly group of AAA patients; interestingly, these findings contrast with those that have evaluated influences of OSA and exercise tolerance in middle-age and young adult populations. Przybylowski and colleagues found that exercise capacity can be limited due to hypertensive responses during exercise in middle-age OSA patients; they also found that those with severe OSA have exaggerated hemodynamic response to exercise and delayed post-exercise BP recovery [53]. Nanas et al. evaluated the CPET responses among middle-age men with and without moderate to severe OSA, as diagnosed from overnight PSG, and determined that OSA patients demonstrated reduced exercise capacity and delayed heart rate recovery (HRR) compared to men without OSA [54]. Kaleth and colleagues found a distinctive response to CPET in middle-age OSA patients, characterized by a blunted HR response during exercise, delayed systolic BP response in early recovery, and elevated diastolic BP in both exercise and early recovery [61]. Tryfon and colleagues investigated BP responses during CPET in a group of young to middle age men (range 22-54 years) and found that normotensive OSA patients develop diastolic BP elevation earlier during exercise and at peak exercise compared to normotensive men without OSA [70]. These findings are of clinical importance, as diastolic HTN during exercise is a risk factor for developing future HTN and can be a limiting factor of physical performance [71]. Hargens and colleagues observed the influences of OSA on exercise responses in young, college-age men and determined that OSA elicits an attenuated HR recovery post-exercise, indicative of potential autonomic regulation imbalance, as well as increased ventilatory responses to exercise suggestive of increased sympathetic drive [62, 72]. Aron *et al.* [56] published a review of the literature examining exercise testing in OSA patients, citing that several studies found that patients with OSA have a reduced exercise capacity, blunted HR response during exercise, and atypical BP response during exercise and recovery. Aron highlighted possible explanations for these responses, including cardiac dysfunction, impaired muscle metabolism, chronic sympathetic over-activation, and endothelial dysfunction [56]. The age of subjects included in Aron's review ranged from 22 to 52 years of age, confirming the lack of literature regarding OSA and exercise capacity and responses in older adults.

Research suggests that OSA in older age may be a condition distinct from that of middle age. Many of the cardiovascular and metabolic abnormalities that are highly associated with OSA in middle-age adults are less associated in older adults with OSA. Both HTN and obesity, which are highly associated and influenced by OSA risk in middle-age populations, are less related in older adults [6, 73, 74]. Additionally, comorbidities that worsen with OSA severity and time untreated in middle-aged cohorts may not be linked to severity of OSA in the elderly and may actually decrease with age [75]. This unique clinical manifestation of OSA in the elderly may also influence exercise capacity and tolerance in these AAA patients. Although OSA prevalence increases with age, several studies have demonstrated that this steady increase in prevalence with each decade plateaus or decreases after age 65 [22, 23, 76] and OSA in older patients may be less severe than OSA in younger populations [23]. It may be that a remission of OSA or physiological adaptations to OSA exists with aging and the disorder has less of an influence on exercise capacity and tolerance in older adults than is seen in younger populations. Further research is needed to better understand the long term impact of untreated OSA and the clinical implications for the elderly with OSA.

A limitation of this study is that OSA was not clinically diagnosed but rather risk of the disorder was determined by interview and self-reports, using the BQ, the most widely used questionnaire for assessing OSA risk. A second limitation is that the BQ may not provide a high level of diagnostic specificity to discriminate OSA in an elderly population, as indicated by recent findings [77]. Despite these limitations, a strength of the methodology utilized in this study is that study staff administered the BQ to participants via interview rather than the participants completing them independently. This allowed participants to ask questions or clarify statements with research staff, if needed, and reduced individual interpretation that can be a limitation with self-report assessments.

A final limitation of this study is that because subjects were a convenience sample of patients with AAA disease, results may not be generalizable to an elderly population; however, due to the high prevalence of undiagnosed AAA disease in the elderly [78], the findings of this study may be more generalizable to the elderly population than originally thought. Furthermore, Myers and colleagues demonstrated that AAA patients are capable of achieving exercise capacities and CPET results and risk scores similar to age-matched referral subjects [51].

In conclusion, the working hypothesis was proved incorrect, as findings indicate that OSA risk does not influence exercise capacity or physiological responses to exercise during CPET among an elderly group of AAA patients. This is the first study to evaluate the associations between OSA risk and exercise capacity and responses in an elderly sub-population. Our findings contrast with those that have demonstrated associations between OSA and reduced exercise capacity, chronotropic incompetence, and autonomic imbalance in middle-age and young adult populations [53, 54, 56, 61, 62, 70]. Research suggests that OSA in older age may be a condition distinct from that of middle age; this unique clinical manifestation of OSA in the elderly may also influence exercise capacity and tolerance in these AAA patients due to physiological adaptations to OSA that may develop with aging. Further research is needed to better understand the long term impact of untreated OSA and the clinical implications for the elderly with OSA.

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CHAPTER FIVE

SUMMARY AND RECOMMENDATIONS

Obstructive sleep apnea, the most common sleep related breathing disorder, is highly prevalent among older adults. At least 1 in 10 people older than 65 years of age have diagnosed OSA (compared to 1 in 20 adults in the general population) and prevalence is anticipated to rise as an increasing proportion of Americans are obese and elderly, both of which are risk factors for OSA [1, 2]; however under diagnosis remains a significant concern. It is estimated that up to 90% of people with OSA remain undiagnosed, likely due to poor awareness of the disorder, lack of routine screening, and limited diagnostic sleep study facilities. Additionally, among elderly adults, OSA is weakly associated with common signs and symptoms and may be difficult to detect in this population [3]. Another concern is limited research on the clinical manifestations of OSA in older adults. OSA in older adults is complex and some data suggest that in older age, OSA may be a condition distinct from that of middle age [3-11].

The subject sample included in this dissertation represents a unique group of elderly AAA patients who may be at increased risk for OSA. Recently, OSA was determined to be highly prevalent among patients with AAA disease [12] and may not only be a risk for factor for aortic disease [13], but a causal factor for faster AAA expansion [12]. Due to the limited literature regarding the influences of OSA risk on health status and disease risk among this unique population, the primary aims of this dissertation were to:

- Evaluate the risk of OSA among elderly patients with newly diagnosed AAA disease and examine associations between OSA risk and self-report PA behavior in the subject sample (Study 1);
- Examine the cardio-metabolic profile related to MetSyn and the constituent markers of MetSyn among elderly patients with newly diagnosed AAA disease

and assess how risk for OSA may be associated with biomarkers of MetSyn and MetSyn status among this group (Study 2); and

- Examine and compare and contrast exercise capacity and physiological responses to CPET in elderly patients with AAA disease relative to OSA risk

Study 1

Findings from this study indicate that approximately 57% of subjects were indicated at high-risk for OSA, and approximately 17% of the subject sample was indicated at “highest” risk by a positive score for all three of the BQ risk categories, including snoring behavior, EDS, and presence of obesity or HTN. These findings appear to be consistent with the literature, demonstrating that OSA prevalence increases with age and is higher among people older than 65 years [14-16], and is prevalent in patients with AAA disease [12].

Some data suggest that OSA in older individuals may be a distinctly different disorder than that suffered by those of middle age, including markers that are strong predictors of OSA in middle-aged adults, such as increased body mass and central fat accumulation, are less strongly associated with OSA in the elderly [11, 17, 18]; however, findings of this study indicated that elderly participants at High-risk for OSA have greater BMIs, and indices of central fat and body habitus, WC, HC, and W/H ratios compared to their Low-risk counterparts. This study concluded that indices of body habitus of the subject sample are consistent with the clinical signature of OSA among the general population. An interesting finding was that only the BRS 3 group was higher on measures of body habitus, suggesting that this subset of subjects at High-risk for OSA (17%) contributes to the majority of the difference observed in body habitus between High- and Low-risk groups. There was a greater incidence of diagnosed HTN and diabetes in the High-risk OSA groups, reflected by use of anti-HTN and diabetic controlling medications. Although previous studies of OSA in older populations report little association between OSA and HTN or diabetes [19, 20], results of this study are more consistent with OSA symptomology in the general population, in which OSA is associated with HTN are glucose dysregulation [21-23].

These findings indicate that subjects at High-risk for OSA report engaging in less daily moderate and vigorous PA, including block walking and stair climbing, and expend less energy engaging in these activities compared to their Low-risk counterparts, even after controlling for differences in body habitus. Interestingly, when stratified by BRS, only the BRS 3 group was less active, suggesting again, that this small group of High-risk subjects (17%) contributes to the majority of the differences observed in PA habits between High- and Low-risk groups. These findings have important implications for older adults, as stair climbing is a precise indication of overall cardiovascular fitness [24] and a reliable surrogate of peak oxygen consumption, a powerful predictor of cardiovascular morbidity and premature cardiovascular mortality [25]. The inability to climb stairs has also been associated with higher all-cause and CVD mortality [24]. Results are consistent with the literature among young and middle-age populations, which demonstrate that OSA is associated with decreased subjective and objective measures of PA [26-29]. It is unclear whether the reduced daily PA observed in our subject sample at High-risk for OSA is a result of their OSA risk or a contributing factor to it. It may be that patients with OSA are neither psychologically motivated nor physically able to engage in regular PA due in part to fatigue and EDS. Or perhaps this groups' sedentary behavior has over time contributed to their OSA risk, in part through influences on obesity.

Finally, the BRS may prove a useful interpretation of the BQ for clinical purposes, as additional information was teased out when subjects were stratified by BRS that was not observed when subjects were classified by the clinical interpretation of the BQ. The BRS may provide additional information by identifying subjects at increased risk for OSA and at risk for associated comorbid chronic diseases.

Study 2

Findings from this study indicate that the prevalence of MetSyn, as defined by the NCEP ATP III, among our subject sample of elderly patients with newly diagnosed AAA disease was 41%, with HTN being the most prevalent MetSyn component at 94%, followed by elevated fasting glucose (55%), low HDL-C (52%), increased WC (45%), and elevated TGs (13%). While prevalence of MetSyn increases with age, our findings indicate that the cardio-metabolic profile related to MetSyn adjusts in later life, and constituent markers, such as abdominal obesity that are highly prevalent among younger groups with MetSyn, become less prevalent in older adults; additionally, risk factors such as HTN and elevated fasting glucose become more prevalent with age, while seemingly less prevalent in younger populations [30]. Results are consistent with literature on MetSyn prevalence among similar sub-populations of patients with AAA disease; however, are slightly lower than those reported in a large cohort of apparently healthy older adults [30]. One speculation that warrants further investigation is that MetSyn in patients with vascular disease, including AAA disease, may be associated with more advanced vascular damage, as measured by indicators for increased cardiovascular risk, including microalbuminuria [31, 32]. Evaluating the prevalence of MetSyn in this specific population utilizing different criteria that considers additional components indicative of cardio-metabolic dysfunction, such as that of the WHO, may be warranted.

MetSyn was prevalent in 45% of our subject sample of older adults with AAA disease at High-risk for OSA. Independent of BMI, OSA risk from the BQ was not associated with prevalence of MetSyn, nor any of its components, except for HDL-C; however, an interesting finding was that subjects considered at highest risk for OSA from the BRS did have a greater prevalence of MetSyn and two of its components, reduced HDL-C and increased WC, independent of obesity, suggesting that there may be an association between OSA risk and MetSyn among those considered at highest risk for MetSyn. High-risk OSA groups had an increased prevalence of anti-HTN medication use, suggesting that that OSA may be associated with HTN; however this component of the MetSyn was similar between groups when considering both BP level and anti-HTN medication use. Additionally, associations were not observed between OSA risk and any other cardio-metabolic risk factor of interest, suggesting that there is not a significant association between OSA and cardio-metabolic risk factors among our elderly subject sample of AAA patients.

The literature on associations between MetSyn and OSA in younger and middle-age cohorts is mixed and inconclusive. Several groups have demonstrated that OSA is highly associated with MetSyn and the individual components that comprise the disorder, and these relationships exist independent of obesity [23, 33, 34]. It has also been suggested that OSA is a manifestation of the MetSyn. Conflicting literature, however, suggests that obesity is the primary driving factor of metabolic abnormalities in OSA patients, rather than the presence of OSA [20, 35, 36]. Findings from this study are consistent with the limited literature that has evaluated the associations between OSA and components of the MetSyn among an elderly population, suggesting that the metabolic abnormalities that are often associated with MetSyn in pre-elderly populations, such as HTN, diabetes, and insulin resistance are not as notable in the elderly [21,36, 37]. This study is the first to examine associations between MetSyn and biomarkers of MetSyn with risk for OSA in an elderly population with AAA disease. These findings support the notion that the clinical manifestations and associations of

OSA among the elderly differ from those of younger and middle-age cohorts, suggesting that OSA in older age may be a condition distinct from that of middle age. Further research to better understand the manifestation of OSA in the elderly is crucial for proper clinical management of older patients. Additionally, the BRS may prove a useful interpretation of the BQ for clinical purposes, as additional information regarding MetSyn risk was observed when subjects were stratified by BRS that was not observed when subjects were classified by the clinical interpretation of the BQ. The BRS may provide additional information by identifying subjects at increased risk for OSA and at risk for associated comorbid chronic diseases.

Study 3

Findings from Study 3 indicate that OSA risk does not influence exercise capacity, or physiological responses to exercise during CPET among an elderly group of AAA patients. After controlling for BMI and accounting for non-normal distribution of data, OSA High- and Low- risk groups demonstrated similar values for physiological measures of interest at rest, the VT, peak exercise, and during active recovery. Additionally, the proportion of the subject sample taking anti-HTN medications known to affect physiological responses to exercise, including HR and BP, was similar across OSA-risk groups.

Results from this study contrast with those in middle-age and young adult populations that have demonstrated associations between OSA and reduced exercise capacity, chronotropic incompetence, and autonomic imbalance [38-43], supporting the notion that OSA in older age may be a condition distinct from that of younger cohorts. Research has shown that middle-age patients with OSA demonstrate reduced exercise capacity, blunted HR and hypertensive responses during exercise, and delayed post-exercise HR and BP recovery [40-42]. Regarding younger groups, research has demonstrated that in comparison to similar controls without OSA, young adult OSA patients develop diastolic BP elevation earlier during exercise and at peak exercise, in addition to increased ventilatory responses to exercise and an attenuated HR recovery post-exercise indicative of sympathetic drive and autonomic imbalance [39, 43, 44]. Aron *et al.* [38] discusses possible explanations for these unique responses in a review of the literature examining CPET in OSA patients, including cardiac dysfunction, impaired muscle metabolism, chronic sympathetic over-activation, and endothelial dysfunction [38]. The age of subjects included in Aron's review ranged from 22 to 52 years of age, confirming the lack of literature regarding OSA and exercise capacity and responses in older adults. Findings from this study support research that suggests OSA in older patients may be a condition distinct from that of middle age and less severe than OSA in younger populations [18]. It may be that a remission of OSA or physiological adaptations to OSA exists with aging and the disorder has less of an influence on exercise capacity and tolerance in older adults than is seen in younger and middle- age cohorts. Further research is needed to better understand the long term impact of untreated OSA and the clinical implications for the elderly with OSA.

Finally, the BRS may prove a useful interpretation of the BQ for clinical purposes, as additional information was observed regarding exercise responses during CPET and recreational PA behavior when subjects were stratified by BRS that was not observed by the clinical interpretation of the BQ (High vs. Low-risk for OSA). The BRS may provide additional information by identifying subjects at increased risk for OSA and at risk for associated comorbid chronic diseases.

CLINICAL IMPLICATIONS

Results from the studies included in this dissertation have important practical applications for clinicians working with elderly patients at risk for OSA. Elderly AAA patients at High-risk for OSA report engaging in less daily moderate and vigorous PA compared to their Low-risk counterparts, which could have implications for not only cardiovascular fitness, but also all- cause and CVD mortality. The importance of daily moderate to vigorous PA should be stressed to elderly patients at risk for OSA and they should strive to meet the PA levels recommended by the Centers for Disease Control and Prevention (CDC) [45] for older adults, which includes 150 minutes of moderate intensity aerobic activity each week, or 75 minutes of vigorous intensity aerobic activity, in addition to two days each week of muscle-strengthening activities that work all major muscle groups [46]. Additionally, regular exercise may limit progression of early AAA disease in these patients. [47].

Findings from these studies also support the notion that OSA in older adults is a distinct condition from that of younger cohorts and should be considered when evaluating and treating OSA in the elderly. MetSyn was prevalent in 45% of our subject sample of older adults with AAA disease at High-risk for OSA; however, there was an association observed between OSA risk and MetSyn among only subjects considered at highest-risk for OSA from the BRS, suggesting that the BRS may prove a useful interpretation of the BQ for clinical purposes, by further stratifying patients beyond a dichotomous High- vs. Low-risk. Additionally, associations were not observed between OSA risk and other cardio-metabolic risk factor of interest, except for HTN as indicated by use of anti-HTN medications, suggesting that unlike middle-age cohorts, there is not a significant association between OSA and cardio-metabolic risk factors among elderly AAA patients.

Indications from this study that OSA risk did not influence exercise capacity, nor physiological responses to exercise during CPET among elderly AAA patients further supports the notion that OSA in older patients may be a condition distinct from that of middle age and less severe than OSA in younger populations. It may be that a remission of OSA or physiological adaptations to the disorder exists with aging and OSA has less of an influence on exercise capacity and tolerance in older adults than is observed in younger groups. It is encouraging to demonstrate that elderly AAA patients at risk for OSA are equally tolerant of vigorous exercise and capable of achieving adequate and age-appropriate levels for exercise capacity.

RECOMMENDATIONS FOR FUTURE RESEARCH

Based on the findings of the current studies and the available research pertaining to PA, MetSyn risk, and CPET responses to exercise and recovery in elderly AAA patients at risk for OSA, the following recommendations are suggested for future research:

1. Elderly AAA patients at High-risk for OSA reported engaging in less daily moderate and vigorous PA compared to their Low-risk counterparts, which could have implications for cardiovascular fitness and all-cause and CVD mortality. It may be that patients with OSA are neither psychologically motivated nor physically able to engage in regular PA due in part to fatigue and EDS, or perhaps this groups' sedentary behavior has over time contributed to their OSA risk, in part through influences on obesity. Further studies are warranted to examine the potential causal relationship between OSA and reduced PA, as it is unclear whether the reduced daily PA observed in our subject sample at High-risk for OSA is a result of their OSA risk or a contributing factor to it.
2. In contrast to middle-age cohorts, associations between OSA risk, MetSyn, and cardio-metabolic risk factors were not observed among this sample of elderly AAA patients;

however, there may be an association between OSA risk and MetSyn among those considered at highest risk for MetSyn. Future research is warranted to better understand the unique clinical manifestation of OSA demonstrated in older age.

3. In contrast to young adult and middle-age cohorts, our findings that OSA risk does not influence exercise capacity, nor physiological responses to exercise during CPET among elderly AAA patients further supports the idea that OSA in older patients may be a condition distinct from that of middle age and potentially less severe than OSA in younger populations. Research is warranted to examine if a remission of OSA or physiological adaptations to the disorder exists with aging.
4. This study was the first to further examine gradations in OSA risk by classifying participants by their Berlin Risk Score, a sum of the three categorical scores from the Berlin Questionnaire. Although this is not a validated interpretation of the BQ, but simply an approach to examine a more detailed analysis of risk for OSA from patient responses to the individual questions and risk factor categories that comprise the BQ, findings from these studies suggest that the BRS may prove a useful interpretation of the BQ for clinical purposes, as additional information and group differences were observed by further stratifying patients beyond a dichotomous High- vs. Low-risk. Future studies to examine the utility of this BRS classification for examining OSA-risk are recommended.

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APPENDIX A

DETAILED METHODOLOGY

Subject Recruitment

Existing patients with newly diagnosed small AAAs (aortic diameter ≥2.5 and < 5.5 cm) from Stanford University Medical Center, the Veterans Affairs Palo Alto Health Care System (VAPAHCS) and Kaiser Permanente of Northern California were recruited to voluntarily participate in this research. Recruitment efforts included development of a study website to inform potential subjects and referring physicians about the study, study brochures targeted to both potential subjects and referring physicians, newspaper and newsletter advertisements, and study posters displayed at participating study sites to provide patients information about the study. For the purpose of this dissertation research, subjects with data collection records for key measurements and analyses were included (*n*=326 for Studies 1 and 2; *n*=114 for Study 3). Recruitment procedures and all study-related activities were reviewed and approved in advance by Institutional Review Boards (IRBs) at Stanford University (including VAPAHCS) as well as the Kaiser Permanente Division of Research and an independent Data Safety Monitoring Board (DSMB) organized by the NHLBI. The ancillary study for the analyses pertaining to this dissertation was approved by the IRB at Virginia Tech (Appendix B).

Experimental Design

Ambulatory volunteer patients from the three participating medical centers (Stanford, VA Palo Alto, and Kaiser Santa Clara) were identified for study recruitment and asked to participate in the study if they met the following inclusion criteria, applicable to all subjects for all studies:

- Age ≥50 years;
- AAA aortic diameter ≥2.5 and < 5.5 cm indicated from abdominal imaging studies; and
- Provided voluntary consent to participate and is able to comply with study protocol procedures

For Study 3, specifically, volunteers were *excluded* if they met any of the following criteria:

- Unstable angina
- Uncontrolled atrial fibrillation or ventricular arrhythmias
- Critical aortic stenosis
- Class III/IV heart failure and/or ejection fraction <20%
- Active pericarditis or myocarditis
- Embolism within previous 6 months
- Thrombophlebitis
- Hospitalized due to an infectious disease within the past three months
- Pulmonary disease with a drop in O_2 saturation with exercise to 90%
- Evidence of significant coronary artery disease as determined by profound ischemic markers, ominous arrhythmias, and resting electrocardiograms (ECGs) that confound the recognition of ischemia (bundle branch block, > 1 mm ST depression, paced rhythm);
- Inability to complete exercise training for 3 years or a life expectancy ≤ 5 years;
- Inability to participate in an exercise stress test
- Morbid obesity (BMI>39 kg/m^2)
- Weight gain/loss of 20 lbs. over previous three months
- Claustrophobia
- Hemodynamic instability with exercise
- Contraindication to MRI per standard screening form (e.g. pacemaker, metal injury, etc.);
- Severe renal insufficiency (serum creatinine level > 3.0 mg%);
- Heavy alcohol use;
- History of severe liver disease.

Medical history and drug information was extracted from existing patient medical records for all participants. Study personnel conducted a physical examination with participants to assess vital signs, including heart rate (HR)and systolic and diastolic blood pressure (BP), as well as anthropometric measurements including height and weight for body mass index (BMI) calculation and waist and hip circumference (WC; HC) measurements to also calculate waist/hip (W/H) ratio. Subjects then completed interview-style questionnaires with research personnel regarding health history, physical activity (PA) behavior and habits (Veterans Affairs Physical Activity Questionnaire-VAPAQ), and risk for OSA (modified Berlin Questionnaire-BQ). Abdominal ultrasound imaging was performed on all patients to confirm AAA size. A fasting blood draw for analysis of complete lipid panel [total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG)], and serum insulin and glucose levels was also completed by all subjects. In addition, subjects included in Study 3 completed a symptom-limited CPET with gas exchange using an individualized ramp treadmill protocol, as previously described by Myers *et al*. [1] and according to standard protocols and recommended procedures as outlined by the *American College of Sports Medicine's Guidelines for Exercise Testing and Prescription* to assess exercise capacity and physiological responses during CPET [2].

Measurements

Berlin Questionnaire

The modified Berlin Questionnaire (BQ) is a 12-item self-report questionnaire that includes questions about risk factors for OSA that can be identified with three discrete sign/symptom categories of 1.) snoring behavior, 2.) wake time sleepiness and fatigue, and 3.) obesity and HTN. The modified BQ, an extension of the original BQ, includes three additional questions regarding choking behavior and wake-time sleepiness. The modified BQ is a validated instrument used to identify individuals who are at risk for OSA with a sensitivity (86%) and specificity (95%) comparable to the original BQ [3-6]; positive and negative predictive values of 96% and 82%, respectively, were reported for the modified BQ [6]. Subjects completed the BQ and responses were confirmed and clarified by one-on-one interview between subject and study personnel.

Subjects were grouped into High-risk and Low-risk categories for obstructive sleep apnea (OSA) using the modified BQ risk categorization as described previously by Netzer *et al* [4]. A 4-point frequency scale [0- never, 1- rarely (1-2/month), 2-sometimes (1-2/wk), 3-frequently (3-4/wk), 4-always (>4/wk)] was used for defining various indices like snoring, choking, and sleepiness. Determination of High-risk and Low-risk for OSA was based on responses in three symptom categories. In category 1, High-risk was defined as persistent symptoms (>3 to 4 times/wk) in two or more questions about their snoring. In category 2, High-risk was defined as persistent symptoms (>3 to 4 times/wk) in two or more questions about their wake time sleepiness. In category 3, High-risk was defined as a history of high blood pressure as per the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) [7] or a body mass index (BMI) >30 kg/m^2. To be considered High-risk for OSA, patients had to have a positive score for at least two symptom categories.

To further examine gradations in OSA risk, subjects were also classified by their Berlin Risk Score (BRS), the sum of the three categorical scores from the BQ. Subjects were grouped into one of four BRS groups which equated to the number of categories that were scored positive from their BQ (BRS 0 – no categories scored positive from the BQ; BRS 1 – 1 category scored positive from the BQ; BRS 2 – 2 categories scored positive from the BQ; and BRS 3 – 3 categories scored positive from the BQ). It should be noted that this is not a validated interpretation of the BQ, but simply an approach to examine a more detailed analysis of risk for OSA from patient responses to the individual questions and risk factor categories that comprise the BQ.

Veterans Affairs Physical Activity Questionnaire

The quantification of PA was recorded by use of the VAPAQ, modeled after the Harvard Alumni studies of Paffenbarger and colleagues [8]. Respondents were asked to report the number of city blocks they walk and the number of flights of stairs they climb on a typical day, as well as the occupational and recreational activities they regularly participate in and responses were confirmed and clarified by one-on-one interview between subject and study personnel. Energy costs of activities were estimated from the compendium of activities developed by Ainsworth and associates [9]. Energy cost of stairs climbed per week was calculated using the estimation of Basset and associates [10]. One flight of stairs equals 10 steps, and 12 blocks is considered 1 mile. Energy expenditure was expressed in terms of lifetime adulthood recreational and occupational PA. Recreational PA was also expressed separately as energy expended during the previous year (recent activity). The VAPAQ has been validated and successfully used in large numbers of veteran patients and others as reported in previous publications and has been useful in predicting all-cause mortality [11, 12].

Physical Examination

Subjects underwent a physical examination with study personnel to assess vital signs, including HR and systolic and diastolic BP, as well as measures of body habitus, including height and weight for BMI calculation, and WC and HC measurements to also calculate W/H ratio. Subjects also completed a health history questionnaire which included self-reported medication use to assess medically controlled HTN, dyslipidemia, diabetes, and other diseases and disorders.

Metabolic and Cardiovascular Biomarkers

Fasting serum blood was collected from participants and evaluated for biomarkers of metabolic and cardiovascular diseases, including serum insulin and glucose, lipid profile, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). Following an overnight fast, whole blood samples were collected in vacutainers from each subject. After allowing 60 minutes for coagulation, serum was separated from samples and transferred to sterile glass tubes for later biochemical analyses. Each serum sample was coded with the specimen procurement date and patient identification number assigned on entry to the trial, both to maintain patient confidentiality and to blind samples during biochemical analysis.

Metabolic Syndrome

Presence of MetSyn among the subject sample was determined based on the NCEP ATP III guidelines [13], characterized by presence of at least three of the five risk factors outlined in Table 1 below. Prescription medication use was also taken into consideration when identifying the presence or absence of each of the MetSyn risk factors. Subjects taking an anti-HTN medication to control BP were identified as positive for having an elevated BP, according to the ATP III MetSyn criteria. Similarly, patients taking an anti-diabetic medication were identified as positive for having an elevated fasting glucose, and subjects taking a fibrate or niacin medication to control elevated TGs and HDL-C, respectively, were considered positive for each of the

MetSyn components.

Table 1. NCEP ATP III Clinical Identification of the Metabolic Syndrome

Risk Factor/MetSyn Component	Defining Level
Fasting Plasma Glucose (mg/dL)	≥110
WC (cm) Male; Female	>102; >88
BP (mmHg)	≥130/85
TG (mg/dL)	≥150
HDL-C (mg/dL) Male; Female	<40; <50
# of components for MetSyn diagnosis	≥3

Derived from Grundy *et al.* [13] Abbreviations: WC-waist circumference; BP-blood pressure; TG-triglycerides; HDL-C-high density lipoprotein cholesterol.

Cardiopulmonary Exercise Testing

Participants completed a symptom-limited CPET with gas exchange using an individualized ramp treadmill protocol, as previously described by Myers *et al*. [1] and according to standard protocols and recommended procedures as outlined by the *American College of Sports Medicine's Guidelines for Exercise Testing and Prescription* to assess exercise capacity and physiological responses during CPET [2]. Standardized medical examinations were performed prior to testing and medication use was continued as prescribed. Protocols were individualized to fall within the recommended 8 to 12 minute range. Subjects were discouraged from using handrails for support. ECG for HR and rhythm were obtained at rest, each minute during exercise, and during recovery. BP was measured manually at rest, every 2 minutes during exercise, and during recovery or until symptoms, ECG changes, and BP stabilized. CPET was aborted following the recommendations of the *American College of*

Sports Medicine's Guidelines for Exercise Testing and Prescription [2]. In the absence of indications to stop the test, participants were encouraged to exercise until volitional fatigue. The Borg scale for perceived exertion was used to quantify effort [14]. Exercise capacity in METs was estimated from peak treadmill speed and grade [2]. CPET responses were obtained using a CosMed Quark CPET metabolic system (CosMed Inc, Rome, Italy). Minute ventilation (V_E), oxygen uptake (VO_2), carbon dioxide production (VCO_2), and other cardiopulmonary exercise test variables were acquired breath by breath, reported at 10-second intervals, and averaged over 30 seconds. The VT was determined using the V-slope method. Measured VE and VCO2 responses during exercise were used to calculate the V_E/VCO_2 slope via least-squares linear regression ($y = mx + b$, m=slope) [15]. CPETs were performed, analyzed, and reported according to a standardized protocol and utilizing a computerized database [16].

APPENDIX B

INSTITUTIONAL REVIEW BOARD APPROVAL

W VirginiaTech

Office of Research Compliance
InstlbJtjonal Revaew So.:trd
2000 J<:r.fl Drive. Suite 2000 (0497)
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MEMORANDUM

DATE: February 8, 2011

TO: William G. Herbert, Jessica Mabry, Laura Newsome

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires October 26,

2013) PROTOCOL TITLE: Evaluation of Exercise Therapy lor Small AAA

IRB NUMBER: 11-115

Effective February 8, 2011, the Virginia Tech IRB Chair, Or. David M. Moore, approved the new protocol lor the above-mentioned research protocol.

This approval provides pem1ission to begin the human subject activities outlined in the IRS-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or support ng documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or hanns to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at http://Www.irb.vt.edu/pages/resoonsibilities.htm (please review before the commencement of your research).

PROTOCOL INFORMATION:
Approved as: Exempt, under 45 CFR 46.101(b) category(ies) 4
Protocol Approval Date: 2/8/2011
Protocol Expiration Date: NA
Continuing Review Due Date•:
NA
•oate a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEOERALLY FUNDED RESEARCH REQUIREMENTS:
Per federally regulations, 45 CFR 46.103(1), the IRB is required to compare all federally funded grant proposals / work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates Whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

			Comparison

•Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

cc: File

APPENDIX C

DATA COLLECTION QUESTIONNAIRES

Modified Berlin Questionnaire

Veterans Affairs Physical Activity Questionnaire

MODIFIED BERLIN QUESTIONNAIRE [6]

Height (m) ________ Weight (kg)________ Age______ Male / Female

Please choose the correct response to each question.

CATEGORY 1

1. **Do you snore?**
□ a. Yes
□ b. No
□ c. Don't know

If you snore:

2. **Your snoring is:**
□ a. Slightly louder than breathing
□ b. As loud as talking
□ c. Louder than talking
□ d. Very loud – can be heard in adjacent rooms

3. **How often do you snore?**
□ a. Nearly every day
□ b. 3-4 times a week
□ c. 1-2 times a week
□ d. 1-2 times a month
□ e. Never or nearly never

4. **Has your snoring ever bothered other people?**
□ a. Yes
□ b. No

5. **Has anyone noticed that you quit breathing during your sleep?**
□ a. Nearly every day
□ b. 3-4 times a week
□ c. 1-2 times a week
□ d. 1-2 times a month
□ e. Never or nearly never

6. **Do you choke while you are sleeping?**
□ a. Nearly every day
□ b. 3-4 times a week
□ c. 1-2 times a week
□ d. 1-2 times a month
□ e. Never or nearly never

CATEGORY 2

7. **How often do you feel tired or fatigued after your sleep?**
□ a. Nearly every day
□ b. 3-4 times a week
□ c. 1-2 times a week
□ d. 1-2 times a month
□ e. Never or nearly never

8. **During your waking time, do you feel tired, fatigued or not up to par?**
□ a. Nearly every day
□ b. 3-4 times a week
□ c. 1-2 times a week
□ d. 1-2 times a month
□ e. Never or nearly never

9. **Have you ever fallen asleep while waiting in a line to meet your doctor?**
□ a. Nearly in every visit
□ b. In 3-4 visits
□ c. In 1-2 visits
□ d. Never or nearly never

10. **Have you ever fallen asleep while watching television at your home during the daytime? If yes, how frequently?**
□ a. Nearly every day
□ b. 3-4 times a week
□ c. 1-2 times a week
□ d. 1-2 times a month
□ e. Never or nearly never

11. **Have you ever fallen asleep while waiting in a line to pay your electricity or telephone bills?**
□ a. Nearly in every visit
□ b. In 3-4 visits
□ c. In 1-2 visits
□ d. Never or nearly never

CATEGORY 3

12. **Do you have high blood pressure?**
□ Yes
□ No
□ Don't know

Berlin Questionnaire (for sleep apnea)

Scoring Berlin Questionnaire

Adapted from: Table 2 from [4]
(Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999 Oct 5;131(7):485 91).

The questionnaire consists of 3 categories related to the risk of having sleep apnea. Patients can be classified into High Risk or Low Risk based on their responses to the individual items and their overall scores in the symptom categories.

Categories and scoring:

Category 1: items 1, 2, 3, 4, 5.

Item 1: if '**Yes**', assign **1 point**
Item 2: if '**c**' or '**d**' is the response, assign **1 point**
Item 3: if '**a**' or '**b**' is the response, assign **1 point**
Item 4: if '**a**' is the response, assign **1 point**
Item 5: if '**a**' or '**b**' is the response, assign **2 points**
Item 6: if '**a**' or '**b**' is the response, assign **1 point**

Add points. Category 1 is positive if the total score is 2 or more points

Category 2: items 7, 8, 9, 10, 11
Item 6: if '**a**' or '**b**' is the response, assign **1 point**
Item 7: if '**a**' or '**b**' is the response, assign **1 point**
Item 8: if '**a**' or '**b**' is the response, assign **1 point**
Item 9: if '**a**' or '**b**' is the response, assign **1 point**
Item 10: if '**a**' or '**b**' is the response, assign **1 point**
Item 11: if '**a**' or '**b**' is the response, assign **1 point**

Add points. Category 2 is positive if the total score is 2 or more points

Category 3 is positive if the answer to item 10 is 'Yes' OR if the BMI of the patient is greater than 30 kg/m^2.

(BMI must be calculated. BMI is defined as weight (kg) divided by height (m) squared, i.e., kg/m2).

High Risk: if there are 2 or more Categories where the score is positive
Low Risk: if there is only 1 or no Categories where the score is positive

Physical Activity Questionnaire

Initials (L-M-F):	__-__-__	**Test Date** (mm/dd/yyyy):	_ _ / _ _ / _ _ _ _
Study ID :	______________	**DOB** (mm/dd/yyyy) :	_ _ / _ _ / _ _ _ _
		Age : _____ years	**Age-25** = _____ years

Below are a few questions regarding your current and past patterns of physical activity. **Please take a moment to answer these questions thoroughly.** It is very important that you be as specific as possible when filling out this questionnaire, so please do not hesitate to ask questions if any part of it is unclear.

LAST YEAR PHYSICAL ACTIVITIES

1. How many city blocks or their equivalent do you walk on a typical day? *(One mile walked is about 12 blocks).* ______ **Blocks/Day**

2. What is your usual **pace of walking**? *(Please check one).*
   - ☐ Casual or strolling (less than 2 mph)
   - ☐ Fairly brisk (3 to 4 mph)
   - ☐ Steady, light pace (2 to 3 mph)
   - ☐ Brisk or striding (4 mph or faster)

3. How many flights of stairs do you climb each day? *(Ten steps are about one flight).* ______ **Flights/Day**

4. Which of the statements below best expresses your view? *Please check one:*
   - ☐ I participate in enough exercise to keep healthy.
   - ☐ I ought to participate in more exercise.
   - ☐ I don't know.

5. At least once a week, do you engage in some form of regular activity such as brisk walking, jogging, bicycling, or swimming, long enough to work up a sweat, get your heart thumping, or become short of breath? ☐ No ☐Yes
   If yes, how many times per week? ___**Times per week** **Activity**________________

6. On a usual weekday and weekend day, how much time do you spend on the following activities?

Please fill in the table below and account for the entire 24 hours of each day.	**Usual Day** (hours per day)	
	Week	**Weekend**
A. Vigorous activity (strenuous sports, jogging, aerobic dancing, swimming, brisk walking, heavy carpentry, bicycling on hills, etc.)		
B. Moderate activity (housework, light sports, walking, golf, yard work, lawn mowing, painting, repairing, light carpentry, etc.)		
C. Light activity (office work, driving a car, strolling, personal care, standing with little motion, etc.)		
D. Sitting activity (eating, reading, desk work, watching TV, listening to radio, etc)		
E. Sleeping or reclining		
Total hours	**24**	**24**

LAST YEAR RECREATIONAL ACTIVITY

From the list below, select all sports or recreational activities you have actively participated in at any time during the past year. Please remember seasonal sports or events, such as skiing or swimming. If the activity is not included in the list, please list it under "Other".

- □ Bicycling
- □ Fishing & hunting
- □ Carpentry (outside house)
- □ Lawn & garden
- □ Music playing
- □ Weight lifting
- □ Health club exercise (aerobic or other)
- □ Dancing
- □ Walking, leisurely (2-3 mph)
- □ Walking briskly
- □ Jogging (slowly 4-5 mph)
- □ Jogging briskly (6-7 mph)
- □ Swimming
- □ Golf (carrying clubs)
- □ Golf, using power cart
- □ Gymnastics
- □ Shuffle board, lawn bowling, or bowling
- □ Soccer
- □ Softball
- □ Table tennis
- □ Tennis, singles
- □ Tennis, doubles
- □ Other (List) ____________
- □ Other (List) ____________
- □ Other (List) ____________
- □ Other (List) ____________
- □ Other (List) ____________

In the table below, please list all the activities selected above. In the next step, record the **number of months per year, number of times per week** and **the average number of minutes spent EACH TIME you participated in each activity**.

Last Year Activities *(Please list all activities selected from the list above)*	**Months per Year (number)** [MSeas]	**Frequency (times per week)** [Fweek]	**Duration per session (minutes)** [Dmin]	Office Use Only Freq. (per year) [MSeas*Fweek*4]	Office Use Only Duration (hours) [Dmin/60]	Office Use Only METs (from PA Compend.)
Comments:						

7. When you are exercising in your usual fashion, for all the activities performed during the last year, how would you rate your level of exertion (degree of effort)? **Please circle one number:**

0	.5	1	2	3	4	5	6	7	8	9	10
Nothing		Very Weak	Weak	Moderate	Somewhat strong	Strong		Very strong			Very, very strong (almost max)

LIFETIME RECREATIONAL ACTIVITY

From the list below, select all **sports or recreational activities** you have actively **participated in** at any time your adult life **after the age of 25**. Please note that these activities are separate from your occupational activities. **Check all the relevant activities** below and be as specific as possible. Please give careful consideration to the "**other**" category at the end.

- ☐ Bicycling
- ☐ Fishing & hunting
- ☐ Carpentry (outside house)
- ☐ Lawn & garden
- ☐ Music playing
- ☐ Weight lifting
- ☐ Health club exercise (aerobic or other)
- ☐ Dancing
- ☐ Walking, leisurely (2-3 mph)
- ☐ Walking briskly
- ☐ Jogging (slowly 4-5 mph)
- ☐ Jogging briskly (6-7 mph)
- ☐ Swimming
- ☐ Golf (carrying clubs)
- ☐ Golf, using power cart
- ☐ Gymnastics
- ☐ Shuffle board, lawn bowling, or bowling
- ☐ Soccer
- ☐ Softball
- ☐ Table tennis
- ☐ Tennis, singles
- ☐ Tennis, doubles
- ☐ Other (List) ______________
- ☐ Other (List) ______________
- ☐ Other (List) ______________
- ☐ Other (List) ______________
- ☐ Other (List) ______________

☐ Generally, I have not participated in recreational activities on a regular basis.

In the table below, please list all the activities selected above. In the next step, record the **number of years, average number of months per year, number of times per week** and the **average number of minutes spent** EACH TIME you participated in each activity.

Lifetime Recreational Activities *(Please list all activities selected from the list above)*	**Number of Years (after age 25)** [Years]	**Months per Year** [MSeas]	**Frequency (times per week)** [Fweek]	**Duration per session (minutes)** [Dmin]	Office Use Only: Freq. per month [(MSeas*Fweek*4)/12]	Office Use Only: Duration (hours) [Dmin/60]	Office Use Only: METs (from PA Comp.)

Comments:

Physical Activity Questionnaire

LIFETIME OCCUPATIONAL ACTIVITY

In the table below, please list all the occupations that you have held as an adult **since the age of 25**. For examples, please refer to the list of occupations indicated at the bottom of the page. If none of the occupations listed below apply to you, use the "**other**" option at the end of the list to describe your occupation(s). Include all that apply.

In the next step, record the **number of years** and **age range** during which you held each occupation.

Lifetime Occupational Activities *(Please list and describe your occupations)*	Number of Years (after age 25) [Years]	Age Range (example: from 25 to 35 years of age)	Office Use Only METs (from PA Compend.)
Example: Construction (outdoor)	*10*	*Age 25 to 35*	
Comments:			

Examples of occupations:

- ☐ Heavy or major cleaning (e.g. Wash car, wash windows, mop, clean garage)
- ☐ Cooking or food preparation-standing
- ☐ Serving food-standing and walking
- ☐ Automobile repair
- ☐ Carpentry, outside house
- ☐ Indoor painting, papering, plastering, scraping, remodeling
- ☐ Plumbing or Electrician
- ☐ Sitting-writing, talking on the phone, typing, computer or, similar desk work
- ☐ Carrying heavy loads, such as bricks
- ☐ Carrying moderate loads up stairs, moving
- ☐ Construction (outdoor)
- ☐ Construction (indoor, i.e. Cabinetry, etc.)
- ☐ Farming
- ☐ Fire fighter
- ☐ Forestry
- ☐ Locksmith
- ☐ Masonry or concrete work
- ☐ Police
- ☐ Bartending, store clerk
- ☐ Using heavy machinery
- ☐ Other (List) ____________________
- ☐ Other (List) ____________________
- ☐ Other (List) ____________________
- ☐ Other (List) ____________________

APPENDIX D

ADDITIONAL DATA TABLES

Chapters 2 and 3 Additional Data Tables

Table 1. Subject Characteristics and by Gender

Characteristic	Men (n=271)	Women (n=55)	*t* statistic	*Pearson Chi-Square*	*p* value
Age (yrs)	73.1 (8.4)	74.2 (9.1)	-0.94	-	0.35
AAA (cm)	3.5 (0.7)	3.4 (0.8)	1.08	-	0.28
Weight (kg)	90.4 (19.5)	73.3 (18.5)	5.96	-	<0.01
Height (m)	1.7 (0.08)	1.6 (0.07)	12.2	-	<0.01
BMI (kg/m^2)	29.5 (5.9)	28.3 (7.0)	1.38	-	0.22
WC (cm)	102.1 (13.9)	93.6 (18.6)	3.77	-	<0.01
HC (cm)	105.2 (11.2)	106.4 (16.3)	-0.72	-	0.58
W/H Ratio	0.97 (0.07)	0.88 (0.08)	8.92	-	<0.01
SBP rest (mmHg)	142.6 (17.2)	141.1 (19.4)	0.56	-	0.57
DBP rest (mmHg)	77.7 (10.0)	71.2 (10.9)	4.14	-	<0.01
Anti-HTN Med (%)	89	91	-0.55	0.31	0.58
Anti-lipemic Med (%)	81	70	1.72	2.93	0.09
Diabetic Med (%)	21	19	0.31	0.10	0.75

Data are expressed as group Mean and Standard Deviation (SD). Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H- waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

Table 2. OSA Risk Classification by Gender

OSA-Risk	Men (n=271)	Women (n=55)	Pearson Chi-Square	*p* value		Men (n=271)	Women (n=55)	Pearson Chi-Square	*p* value
BQ OSA Low-Risk	43	40	0.19	0.67	BRS 0	6	4	1.65	0.65
BQ OSA High-Risk	57	60			BRS 1	37	36		
					BRS 2	41	38		
					BRS 3	15	22		

Data are expressed as subject sample proportions. Abbreviations: OSA-obstructive sleep apnea; BQ-Berlin Questionnaire; BRS-Berlin Risk Score.

Table 3. Additional Cardio-metabolic Risk Factors by Gender

Characteristic	Men, n=271	Women, n=55	*t* statistic	*p* value
Fasting Glucose (mg/dL)	114.3 (27.1)	108.7 (26.3)	1.3	0.19
Fasting Insulin (mU/L)	13.7 (14.8)	12.9 (12.5)	0.35	0.73
HOMA IR	4.2 (6.4)	4.0 (5.2)	0.24	0.81
TC (mg/dL)	159.0 (40.3)	175.5 (52.4)	-2.53	0.01
HDL-C (mg/dL)	42.4 (13.2)	53.2 (15.6)	-5.17	<0.01
LDL-C (mg/dL)	92.6 (30.9)	98.9 (44.6)	-1.23	0.22
TG (mg/dL)	96.6 (46.8)	106.6 (51.2)	-1.36	0.18

Data are expressed as group Mean and Standard Deviation (SD). Abbreviations: HOMA IR-homeostatic model assessment for insulin resistance; TC-total cholesterol; HDL-C-high density lipoprotein-cholesterol; LDL-C-low density lipoprotein-cholesterol; TG-triglycerides.

Table 4. Prevalence of MetSyn Components and MetSyn Among Subjects and by Gender

MetSyn Component (NCEP ATP III)	Males, *n*=271	Females, *n*=55	Pearson Chi-Square	p value
Increased WC (%)	44	51	0.76	0.38
Elevated BP or anti-HTN Med (%)	94	96	0.31	0.58
Elevated Fasting Glucose or Rx Med (%)	57	44	2.97	0.09
Elevated TG or Rx Med (%)	13	12	0.03	0.85
Reduced HDL-C or Rx Med (%)	53	49	0.27	0.61
MetSyn (≥3 components; %)	42	35	1.04	0.31

Data are expressed as prevalence of individual MetSyn components, and MetSyn as a disorder. Abbreviations: MetSyn-metabolic syndrome; WC-waist circumference; BP-blood pressure; HTN-hypertension; TG-triglycerides; Rx Med-prescription medication; HDL-C-high density lipoprotein cholesterol.

Chapter 4 Additional Data Table

Table 5. Subject Characteristics and by Gender

Characteristic	Subject Sample, *n*=114	Men, *n*=107	Women, *n*=7	*t* statistic	Pearson Chi-Square	*p* value
Age (yrs)	71.5 (8.4)	71.1 (8.3)	77.6 (7.8)	-1.99	-	0.05
AAA (cm)	3.5 (0.82)	3.5 (0.84)	3.6 (0.45)	-0.31	-	0.76
Weight (kg)	88.9 (20.5)	89.7 (19.8)	76.8 (28.1)	1.62	-	0.12
Height (m)	1.75 (0.18)	1.75 (0.18)	1.66 (0.07)	1.37	-	0.18
BMI (kg/m^2)	28.7 (6.09)	28.7 (5.8)	28.1 (10.5)	0.23	-	0.82
WC (cm)	100.1 (13.7)	100.7 (13.2)	91.1 (19.2)	1.81	-	0.07
HC (cm)	104.3 (10.3)	104.0 (9.3)	108.3 (21.7)	-1.07	-	0.29
W/H Ratio	0.97 (0.07)	0.97 (0.07)	0.84 (0.05)	5.03	-	<0.01
SBP rest (mmHg)	135.2 (14.9)	135.4 (14.9)	132.4 (15.3)	0.52	-	0.61
DBP rest (mmHg)	77.5 (8.9)	78.0 (8.9)	70.9 (6.4)	2.06	-	0.04
Anti-HTN Med (%)	72	70	100	-1.72	2.92	0.09
Anti-lipemic Med (%)	65	66	43	1.23	1.53	0.22
Diabetic Med (%)	17	18	0	1.23	1.53	0.22

Data are expressed as group Mean and Standard Deviation (SD). Medication data is presented as a group percentage (%) taking each class of medication. Abbreviations: AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H-waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

APPENDIX E

RAW DATA

Chapter 2 and 3 Raw Data

Table 1. Subject Characteristics

Subject	BQ OSA-risk	BRS	Age (yr)	AAA (cm)	BMI (kg/m2)	WC (cm)	HC (cm_	W/H ratio	SBP (mmHg)	DBP (mmHg)	Anti-HTN Med	Anti-lipemic Med	Diabetic Med
1	Low	1	82	3.6	25.2	99.1	99.1	1	129	72	Y	Y	N
2	Low	1	77	3.8	29.0	104.1	109.2	0.95	150	68	Y	Y	N
3	High	3	77	3.7	29.2	109.2	102.9	1.06	142	74	N	Y	Y
4	High	2	68	3.4	26.4	97.8	105.4	0.93	128	80	Y	Y	N
5	Low	1	75	4.53	22.2	76.2	83.8	0.91	106	59	Y	Y	N
6	High	2	66	3.57	32.1	109.2	105.4	1.04	126	64	Y	Y	N
7	Low	1	63	3.69	30.5	97.8	113.8	0.86	153	79	Y	Y	N
8	High	2	76	3.91	32.1	115.6	106.7	1.08	115	58	Y	Y	N
9	High	2	75	3	28.3	96.5	96.5	1	132	78	Y	N	N
10	High	2	69	3.81	25.0	86.4	102.9	0.84	140	80	Y	N	N
11	High	2	70	3.57	33.9	110.5	110.5	1	151	90	Y	Y	N
12	High	2	70	3.73	31.5	101.6	108.0	0.94	120	68	Y	Y	N
13	Low	1	83	4.09	25.7	88.9	98.6	0.9	154	70	Y	Y	N
14	High	2	67	4.74	30.5	94.0	104.1	0.9	118	86	Y	N	N
15	High	2	79	3.25	35.7	111.8	116.8	0.96	140	90	Y	Y	N
16	High	3	83	3.2	31.8	110.5	106.7	1.04	158	76	Y	Y	N
17	Low	1	86	3.34	23.3	87.6	95.3	0.92	160	90	Y	Y	N
18	High	2	82	3.03	37.0	114.3	123.2	0.93	130	84	Y	Y	N
19	Low	1	83	3.2	32.0	106.7	108.7	0.98	136	72	Y	Y	N
20	High	2	68	4.52	25.5	90.2	95.3	0.95	132	70	Y	Y	N
21	High	2	77	4.92	26.7	119.4	113.0	1.06	140	68	Y	Y	Y
22	High	3	84	4.2	32.3	114.3	106.7	1.07	145	84	Y	Y	N
23	High	2	83		29.5	96.5	94.0	1.03	130	60	Y	Y	Y
24	High	2	74	3.01	29.0	99.1	108.0	0.92	145	76	Y	Y	N
25	Low	1	50	4.12	36.4	116.8	111.8	1.05	126	75	Y	N	Y
26	High	2	74	3.03	26.9	91.4	102.9	0.89	128	68	Y	N	N
27	Low	1	80	3.5		106.7	106.7	1	146	64	Y	Y	N
28	High	2	66	4.89	27.1	99.1	106.7	0.93	146	89	Y	Y	N

29	High	2	81	3.81	28.5	91.4	99.1	0.92	142	82	Y	Y	N
30	Low	1	66	2.87	21.0	78.7	90.2	0.87	145	79	N	Y	N
31	Low	1	74	3.75	33.0	121.9	114.3	1.07	147	72	Y	Y	Y
32	Low	0	59	3.55	26.8	101.6	108.0	0.94	173	96	N	N	N
33	Low	1	84	3.34	23.3	96.5	101.6	0.95	167	72	Y	N	Y
34	Low	1	76	4.32	25.0	92.7	102.9	0.9	159	77	Y	N	N
35	Low	1	82	3.8	30.0	105.4	102.9	1.02	167	93	Y	Y	N
36	High	2	58	3.7	44.0	129.5	134.6	0.96	146	77	Y	Y	Y
37	Low	1	71	3.55	30.3	99.1	104.1	0.95	130	76	Y	N	N
38	Low	0	69	4.02	23.5	91.4	97.8	0.94	143	87	Y	Y	N
39	High	3	83	2.54	25.5	83.8	94.0	0.89	146	76	Y	Y	Y
40	Low	0	71	3.42	30.0	111.8	110.5	1.01	162	76	Y	Y	N
41	Low	1	66	4.88	28.2	101.6	99.1	1.03	210	104	Y	Y	N
42	Low	1	65	4.02	28.0	106.7	100.3	1.06	154	84	Y	Y	Y
43	Low	1	75	4.02	27.1	87.6	91.4	0.96	128	71	Y	Y	N
44	Low	1	62	5.39	20.2	72.4	86.4	0.84	148	78	Y	Y	N
45	High	2	66	3.3	34.1	97.8	101.6	0.96	138	77	Y	Y	N
46	Low	1	72	4.56	34.4	115.6	113.0	1.02	119	63	Y	Y	N
47	High	2	68	4.15	24.9	83.8	96.5	0.87	146	92	Y	Y	Y
48	High	2	67	5.01	30.8	104.1	108.0	0.96	129	85	N	Y	N
49	Low	1	85	3.53	30.3	102.9	106.7	0.96	165	79	Y	Y	Y
50	Low	1	72	3.68	26.6	101.6	106.7	0.95	157	87	Y	N	N
51	High	2	75	4.56	27.0	92.7	94.0	0.99	134	72	Y	Y	N
52	High	2	69	4.02	24.1	92.7	99.1	0.94	153	83	Y	Y	N
53	High	2	79	3.18	22.7	90.2	97.8	0.92	156	65	Y	Y	Y
54	Low	1	76	4.21	31.6	114.3	116.8	0.98	162	90	Y	N	N
55	High	2	70	2.76	24.1	94.0	99.1	0.95	164	80	Y	Y	N
56	Low	1	76	3.03	26.7	99.1	96.5	1.03	125	64	Y	Y	N
57	Low	0	65	4.36	24.6	88.9	96.5	0.92	116	60	N	Y	N
58	High	2	74	3.41	26.5	99.1	104.1	0.95	131	66	Y	Y	N
59	High	2	79	3.29	28.8	111.8	111.8	1	118	64	Y	Y	N
60	Low	1	77	3.36	41.2	134.6	128.3	1.05	154	76	Y	Y	N
61	Low	0	91	3.01	27.8	97.8	105.4	0.93	136	69	Y	Y	Y

62	High	2	68	3	25.5	94.0	96.5	0.97	142	60	Y	Y	Y
63	Low	1	85	2.34	28.9	102.9	111.8	0.92	166	92	Y	Y	N
64	Low	1	83	3.19	29.9	106.7	104.1	1.02	171	66	Y	Y	N
65	Low	1	86	3	23.6	88.9	101.6	0.88	160	71	Y	N	N
66	High	2	74	4	29.5	111.8	110.5	1.01	122	64	Y	Y	N
67	Low	1	76	3.5	38.9	119.4	124.5	0.96	150	82	Y	Y	N
68	Low	1	80	3.9	29.8	101.6	101.6	1	162	73	Y	Y	N
69	Low	1	78	3.05	29.0	99.1	104.1	0.95	172	96	Y	N	N
70	High	3	70	2.67	25.9	87.6	102.9	0.85	149	78	Y	Y	N
71	Low	1	87	3.3	31.5	114.3	114.3	1.01	156	79	Y	Y	Y
72	Low	1	83	3.03	27.0	97.8	111.8	0.88	160	90	Y	Y	N
73	High	2	70	3.5	38.1	127.0	119.4	1.06	135	75	Y	Y	N
74	Low	1	82	4.4	35.6	130.8	133.4	0.98	137	69	Y	Y	N
75	High	3	79	4.3	33.1	104.1	104.1	1	132	71	Y	Y	N
76	High	2	78	3.02	32.9	108.0	109.2	0.99	158	85	Y	Y	Y
77	Low	1	74	4.2	33.1	116.8	115.6	1.01	160	90	Y	Y	N
78	Low	1	81	3.1	31.1	120.7	115.6	1.04	152	90	Y	N	N
79	High	3	81	3.6	32.2	106.7	108.0	0.99	129	63	Y	N	N
80	High	2	75	3.08	25.2	95.3	99.1	0.96	119	67	Y	Y	N
81	Low	1	75	4.3	26.5	91.4	101.6	0.9	118	75	Y	N	N
82	High	3	91	3.01	22.0	80.0	100.3	0.8	181	87	Y	Y	N
83	High	2	70	4.1	41.0	129.5	133.4	0.97	117	64	Y	Y	N
84	Low	1	64	3.5	31.5	105.4	108.0	0.98	161	86	Y	Y	N
85	High	3	87	3.3	28.4	96.5	104.1	0.93	178	63	Y	Y	N
86	High	3	52	2.88	31.7	106.7	109.2	0.98	146	87	N	Y	N
87	Low	0	80	2.7	25.2	85.1	95.3	0.89	131	81	Y	Y	N
88	Low	0	85	2.6	24.6	95.3	102.9	0.93	149	80	N	N	N
89	High	2	76	3.3	23.8	99.1	99.1	1	150	88	Y	Y	N
90	High	3	72	3	35.4	106.7	106.7	1	165	97	Y	Y	N
91	High	3	80	3.5	25.5	97.8	100.3	0.97	120	65	Y	Y	Y
92	High	3	78		31.5	110.5	106.7	1.04	128	80	Y	N	N
93	Low	0	69	4.4	24.4	97.8	111.8	0.88	159	97	N	Y	N
94	Low	1	64	3.7	27.5	97.8	99.1	0.99	141	90	N	Y	N

95	Low	0	77	2.6	25.3	96.5	101.6	0.95	146	68	Y	Y	N
96	Low	1	89	3.7	21.0	86.4	100.3	0.86	175	86	Y	Y	N
97	High	2	73	3.1	29.6	96.5	99.1	0.97	115	66	Y	Y	N
98	High	2	59	3.1	31.2	96.5	114.3	0.84	133	78	Y	Y	N
99	Low	1	68	3.2	24.1	104.1	109.2	0.95	126	74	N	Y	N
100	High	2	72	4.9	25.7	99.1	106.7	0.93	154	86	Y	Y	N
101	High	2	91	3.2	24.2	99.1	97.8	1.01	131	67	Y	N	N
102	High	3	62	-	26.6	94.0	100.3	0.94	130	60	Y	Y	N
103	Low	1	87	4.1	23.6	95.3	95.3	1	151	81	Y	Y	N
104	High	3	63	3.1	25.8	91.4	94.0	0.97	198	82	Y	Y	Y
105	High	2	70	3.6	33.7	111.8	114.3	0.98	167	97	Y	N	N
106	High	2	57	3.8	24.3	94.0	99.1	0.95	130	66	Y	Y	N
107	Low	1	83	4.5	23.1	88.9	101.6	0.88	133	78	N	Y	N
108	High	2	58	3.3	46.3	134.6	127.0	1.06	162	94	Y	N	N
109	Low	1	79	4	23.3	88.9	97.8	0.91	148	84	N	Y	N
110	High	2	65	3.6	28.8	101.6	104.1	0.98	160	100	-	N	N
111	Low	1	79	2.9	22.6	91.4	99.1	0.92	143	80	Y	Y	N
112	High	3	73	3.5	37.4	128.3	115.6	1.11	155	79	Y	Y	N
113	High	2	72	3.9	23.9	85.1	94.0	0.91	166	95	Y	N	N
114	High	2	70	3.6	29.0	96.5	109.2	0.88	179	94	Y	Y	N
115	High	2	75	2.9	38.2	106.7	109.2	0.98	134	72	Y	Y	N
116	Low	1	69	3	22.6	80.0	90.2	0.89	144	89	Y	Y	N
117	High	3	58	4	30.8	110.5	109.2	1.01	128	78	Y	Y	Y
118	High	3	76	3.8	32.0	109.2	101.6	1.08	115	78	Y	Y	Y
119	High	3	74	4.1	41.0	137.2	115.6	1.19	153	77	Y	Y	Y
120	Low	0	57	3.3	22.5	94.0	96.5	0.97	146	90	N	Y	N
121	Low	1	84	2.7	25.8	97.8	94.0	1.04	137	58	Y	Y	Y
122	Low	1	71	3.7	28.7	108.0	104.1	1.04	129	75	N	N	N
123	Low	1	69	4.5	38.7	120.7	123.2	0.98	142	75	Y	Y	Y
124	Low	1	83	5	26.9	96.5	99.1	0.97	136	72	Y	Y	N
125	High	3	70	3.1	30.3	99.1	101.6	0.98	128	75	Y	Y	Y
126	High	2	80	3.8	23.4	86.4	88.9	0.97	161	73	Y	Y	N
127	High	3	78	3.3	30.2	110.5	108.0	1.02	149	94	Y	Y	N

128	High	2	70	3.8	40.3	120.7	135.9	0.89	149	63	Y	Y	N
129	High	2	93	4.7	19.0	83.8	94.0	0.89	126	74	Y	Y	N
130	Low	1	76	4	33.5	119.4	109.2	1.09	137	80	N	Y	N
131	High	2	60	3.3	23.6	81.3	95.3	0.85	128	80	Y	Y	Y
132	High	2	75	3.4	27.2	96.5	101.6	0.95	143	83	Y	Y	N
133	Low	1	60	2.4	23.8	88.9	99.1	0.9	138	75	Y	Y	N
134	High	2	72	3.3	31.5	109.2	105.4	1.04	155	94	Y	Y	Y
135	High	2	66	3	29.4	110.5	111.8	0.99	149	76	N	N	N
136	High	2	59	2.9	23.1	97.5	95.3	1.02	126	66	Y	Y	N
137	High	3	70	3	30.4	114.3	101.6	1.12	163	81	Y	Y	N
138	Low	1	65	3.2	29.6	99.1	99.1	1	132	80	Y	Y	N
139	High	2	80	2.7	31.1	102.9	111.8	0.92	143	74	Y	Y	N
140	High	2	72	3.5	32.2	105.4	109.2	0.97	162	80	Y	Y	N
141	High	2	82	3	39.3	133.4	132.1	1.01	142	71	Y	Y	N
142	High	3	71	3.4	32.5	110.5	104.1	1.06	198	98	Y	Y	N
143	Low	1	71	2.9	34.5	111.8	113.0	0.99	126	74	Y	Y	N
144	High	2	62	5.2	29.4	97.8	102.9	0.95	174	89	Y	Y	N
145	High	2	78	3.5	29.3	101.6	99.1	1.03	144	78	Y	Y	N
146	Low	1	82	4	27.2	111.8	104.1	1.07	115	51	Y	Y	N
147	High	2	66	3.2	19.7	76.2	83.8	0.91	142	60	Y	N	N
148	High	2	75	3.1	30.8	105.4	101.6	1.04	130	77	Y	Y	N
149	High	2	77	3.8	27.2	99.1	99.8	0.99	155	92	Y	Y	N
150	High	3	68	3.4	30.1	102.9	108.0	0.95	143	73	Y	Y	N
151	High	2	88	3	31.9	106.7	100.3	1.06	144	76	Y	Y	N
152	Low	1	79	2.5	31.1	101.6	94.0	1.03	133	74	Y	Y	N
153	High	2	69	4.6	40.4	116.8	119.4	0.98	145	96	Y	N	N
154	High	2	77	4.6	27.1	92.7	99.1	0.94	142	76	Y	Y	N
155	High	2	70	-	28.7	-	-	-	-	-	Y	N	N
156	High	2	65	2.5	31.8	101.6	105.4	0.96	140	83	Y	Y	N
157	Low	1	82	4.33	29.8	109.2	108.0	1.01	155	85	Y	Y	N
158	High	2	72	3.4	31.9	100.3	102.9	0.98	162	72	Y	Y	N
159	Low	1	67	2.58	27.4	88.9	101.6	0.88	133	82	Y	Y	N
160	High	2	70	3.8	57.3	165.1	188.0	0.88	140	92	N	N	N

161	Low	1	78	3.4	33.3	108.0	114.3	0.94	136	83	Y	Y	Y
162	High	2	85	3.7	24.0	91.4	94.0	0.97	152	68	Y	N	N
163	High	3	74	3.4	28.3	109.2	98.6	1.11	140	69	Y	Y	N
164	High	2	64	4.02	28.4	100.3	108.0	0.93	118	64	Y	Y	N
165	Low	1	82	2.73	23.8	88.9	97.8	0.91	153	81	Y	Y	N
166	Low	1	87	3.88	33.7	91.4	102.9	0.89	136	71	Y	Y	N
167	High	2	85	4.22	26.3	97.8	99.1	0.99	143	89	Y	Y	N
168	Low	1	74	3	26.6	102.9	102.9	1	126	65	Y	Y	N
169	High	2	74	3.4	25.2	91.4	100.3	0.91	138	46	Y	Y	N
170	Low	0	79	3.9	19.2	67.3	73.7	0.91	108	60	N	N	N
171	Low	1	58	3.1	32.4	114.3	106.7	1.07	129	80	Y	N	N
172	Low	1	81	3.29	28.6	108.0	108.0	1	121	69	Y	Y	N
173	Low	1	76	3.5	26.2	85.1	99.1	0.86	127	69	Y	Y	N
174	Low	1	81	4.5	33.7	111.8	118.1	0.95	165	67	Y	N	Y
175	High	2	71	3	27.2	101.6	99.1	1.03	140	76	Y	Y	N
176	High	3	80	4.3	30.6	114.3	114.3	1	149	75	Y	Y	N
177	Low	1	87	-	26.4	-	-	-	180	82	N	Y	N
178	High	2	80	4.8	36.9	114.3	111.8	1.02	144	70	Y	N	N
179	High	3	79	3.3	41.3	127.0	121.9	1.04	146	85	Y	Y	Y
180	Low	0	75		25.9	104.1	105.4	0.99	143	82	Y	N	N
181	Low	1	72	3.8	21.6	82.6	92.7	0.89	144	75	Y	Y	N
182	High	2	79	4	25.8	101.6	105.4	0.96	121	67	Y	N	N
183	High	2	80	4	23.1	88.9	91.4	0.97	180	86	Y	Y	Y
184	Low	0	73	3.5	26.8	88.9	96.5	0.92	170	86	N	Y	Y
185	High	2	80	3	25.7	91.4	94.0	0.97	158	76	Y	Y	N
186	Low	1	82	3.05	22.6	96.5	102.9	0.94	173	83	Y	Y	N
187	High	3	77	3.61	34.0	106.7	111.8	0.95	120	80	Y	Y	N
188	High	2	64	4.5	36.6	135.9	120.7	1.13	139	77	Y	Y	Y
189	High	2	68	4	27.7	101.6	102.9	0.99	149	83	Y	Y	N
190	High	2	72	5	28.2	96.5	99.1	0.97	130	65	Y	Y	N
191	High	2	66	4.2	34.0	118.1	121.9	0.97	171	94	N	Y	Y
192	High	2	65	3.7	27.7	99.1	104.1	0.95	126	74	Y	Y	N
193	High	2	73	4	24.8	95.3	95.3	1	149	85	Y	Y	N

194	High	3	82	4.4	38.3	124.5	113.0	1.1	130	65	Y	N	N
195	High	3	71	4.7	32.4	105.4	106.7	0.99	160	79	Y	Y	N
196	High	3	80	3	26.0	92.7	99.1	0.94	158	79	Y	Y	Y
197	High	2	71	3	33.3	116.8	105.4	1.11	148	90	Y	Y	Y
198	Low	1	87	4.5	25.5	94.0	99.1	0.95	124	61	N	Y	N
199	Low	1	66	3.8	34.4	106.7	116.8	0.91	135	71	Y	Y	Y
200	High	3	71	5.3	28.2	102.9	99.1	1.04	152	82	Y	Y	Y
201	High	3	60	-	32.4	-	-	-	-	-	-	-	-
202	High	2	92	3.6	27.2	90.2	100.3	0.9	133	68	Y	Y	N
203	Low	1	73	4	41.2	129.5	124.5	1.04	130	75	Y	N	N
204	Low	1	79	2.5	31.1	101.6	99.1	1.03	137	79	Y	Y	N
205	Low	1	72	3.1	33.7	115.6	120.7	0.96	122	67	Y	Y	Y
206	High	2	53	2.25	51.9	182.9	148.6	1.23	156	98	Y	Y	Y
207	High	2	62	2.18	33.8	109.2	102.9	1.06	118	68	Y	N	Y
208	Low	1	51	2.83	34.3	104.1	94.0	1.11	134	88	Y	N	Y
209	High	2	74	2.37	28.8	102.9	109.2	0.94	150	66	Y	Y	N
210	Low	1	59	2.29	29.1	92.7	101.6	0.91	126	80	N	Y	N
211	High	3	58	2.31	39.8	121.9	124.5	0.98	138	84	Y	N	N
212	High	2	59	2.17	30.7	100.3	105.4	0.95	122	84	N	N	N
213	Low	1	76	2.55	26.7	96.5	101.6	0.95	132	72	Y	Y	N
214	Low	1	62	1.94	24.7	88.9	104.1	0.85	144	90	Y	Y	N
215	High	3	83	1.89	27.6	97.8	101.6	0.96	158	84	Y	Y	Y
216	Low	1	68	2.02	33.6	109.2	113.0	0.97	122	76	Y	Y	Y
217	High	3	61	2.14	35.0	124.5	115.6	1.08	130	90	Y	Y	Y
218	High	2	61	1.86	30.0	94.0	96.5	0.97	128	78	Y	Y	Y
219	High	2	60	2.03	37.5	116.8	116.8	1	134	80	Y	Y	Y
220	Low	1	71	2.22	27.0	100.3	108.0	0.93	144	86	Y	Y	Y
221	High	3	60	6.06	31.2	109.2	101.6	1.08	160	98	Y	N	N
222	High	3	62	1.87	29.4	96.5	96.5	1	132	78	Y	Y	N
223	Low	1	79	2.38	27.0	86.4	95.3	0.91	138	80	Y	Y	N
224	Low	1	52	2.55	31.6	95.3	106.7	0.89	140	82	Y	N	Y
225	High	2	64	1.89	26.1	94.0	101.6	0.92	130	78	Y	Y	N
226	Low	0	65	1.85	20.1	81.3	86.4	0.94	138	84	Y	N	N

227	Low	0	64	2.27	29.4	91.4	104.1	0.88	130	78	N	Y	N
228	Low	0	64	2.18	21.1	73.7	88.9	0.83	140	80	N	Y	N
229	High	2	72	3.43	24.7	92.7	99.1	0.94	130	80	-	-	-
230	High	2	70	4.42	24.7	102.9	96.5	1.07	140	68	-	-	-
231	Low	1	63	3.01	28.6	101.6	105.4	0.96	139	73	Y	Y	N
232	Low	1	76	4.25	30.6	113.0	110.5	1.02	134	78	Y	Y	Y
233	High	2	86	3.7	32.6	114.3	120.7	0.96	118	74	-	-	-
234	High	2	71	3.1	27.6	94.0	97.8	0.96	124	65	Y	Y	N
235	High	2	79	3.57	26.1	88.9	100.3	0.89	162	85	Y	Y	N
236	Low	1	80	3.5	31.5	114.3	118.1	0.97	168	89	-	-	-
237	High	2	73	4.7	25.5	100.3	101.6	0.99	150	93	Y	Y	N
238	High	2	75	3.7	30.9	109.2	111.8	0.98	116	62	Y	N	Y
239	High	2	73	3	23.8	83.8	95.3	0.88	130	79	-	-	-
240	Low	1	76	3.74	26.7	91.4	94.0	0.97	145	78	-	-	-
241	Low	1	67	3.7	23.2	82.6	91.4	0.9	109	68	Y	Y	N
242	Low	1	64	4.6	28.3	102.9	102.9	1	118	72			
243	Low	1	71	-	33.7	-	-	-	-	-	-	-	-
244	High	2	80	-	25.0	-	-	-	-	-	-	-	-
245	High	2	67	-	38.1	-	-	-	-	-	-	-	-
246	Low	1	70	-	46.5	-	-	-	-	-	-	-	-
247	High	3	73	-	42.3	-	-	-	-	-	-	-	-
248	Low	1	72	-	21.9	-	-	-	-	-	-	-	-
249	Low	1	61	-	32.1	-	-	-	-	-	-	-	-
250	High	2	64	-	28.3	-	-	-	-	-	-	-	-
251	Low	1	72	-	24.3	-	-	-	-	-	-	-	-
252	High	3	72	4.02	65.0	94.0	127.0	0.74	179	80	-	-	-
253	High	3	65	-	40.0	-	-	-	-	-	-	-	-
254	High	2	69	-	32.4	104.1	109.2	0.95	149	91	-	-	-
255	Low	1	80	-	28.2	91.4	101.6	0.9	136	69	-	-	-
256	High	3	66	-	26.4	108.0	108.0	1	136	93	-	-	-
257	Low	1	63	-	-	-	-	-	-	-	-	-	-
258	Low	1	77	-	-	-	-	-	-	-	-	-	-
259	High	2	74		23.9	86.4	96.5	0.89	133	66	-	-	-

260	High	2	76	4.1	24.8	95.3	91.4	1.04	128	83	-	-	-
261	Low	1	79	3.2	28.9	99.1	99.1	1	-	-	-	-	-
262	Low	1	73	3.34	29.1	96.5	99.1	0.97	134	71	-	-	-
263	High	2	75	4.4	32.1	116.8	101.6	1.15	-	75	-	-	-
264	High	2	78	-	-	-	-	-	-	-	-	-	-
265	Low	1	76	4.2	28.4	91.4	108.0	0.85	145	80	-	-	-
266	High	3	79	4.3	36.1	114.3	132.1	0.87	128	68	-	-	-
267	Low	1	61	4.94	26.0	86.4	100.3	0.86	130	70	Y	Y	N
268	High	3	82	3.12	39.3	133.4	123.2	1.08	118	78	Y	Y	N
269	High	2	74	3.34	23.1	81.3	92.5	0.88	146	64	Y	Y	N
270	Low	1	90	3.79	26.1	86.4	88.9	0.97	138	70	Y	Y	N
271	Low	1	80	4.42	22.5	71.1	88.9	0.79	128	64	Y	N	N
272	High	3	76	3.2	31.3	113.0	111.8	1.01	118	82	Y	Y	N
273	High	2	63	3.63	48.8	134.6	149.9	0.9	165	74	Y	Y	N
274	High	2	64	3.94	26.1	87.6	100.3	0.87	160	94	Y	N	N
275	Low	1	64	2.79	24.0	80.0	96.5	0.83	123	61	Y	N	N
276	High	2	74	4.31	31.3	102.9	128.3	0.8	138	88	Y	Y	N
277	High	3	74	3.7	35.5	96.5	124.5	0.78	134	63	Y	Y	N
278	High	2	77	3	30.7	91.4	102.9	0.89	140	74	N	N	Y
279	Low	1	86	2.87	21.6	57.2	81.3	0.7	168	68	Y	Y	N
280	High	2	80	4.04	26.5	87.6	101.6	0.86	155	77	Y	Y	N
281	Low	0	79	3.77	23.0	73.7	94.0	0.78	149	57	Y	Y	N
282	High	2	65	4.42	40.5	114.3	127.0	0.9	117	69	Y	Y	N
283	Low	1	85	3.17	22.7	78.7	96.5	0.82	136	67	Y	N	N
284	High	2	82	3.63	28.7	100.3	114.3	0.88	151	66	Y	N	N
285	Low	1	80	3	25.5	86.4	102.9	0.84	170	80	Y	Y	N
286	Low	1	81	2.84	24.6	83.8	94.0	0.89	129	60	Y	Y	N
287	High	3	57	0	35.8	114.3	127.0	0.9	126	66	Y	Y	Y
288	High	2	72	3.5	28.0	87.6	113.0	0.78	165	72	Y	Y	N
289	High	2	88	2.82	30.7	102.9	114.3	0.9	154	52	Y	N	N
290	Low	1	74	3	40.3	120.7	134.6	0.9	111	46	Y	Y	N
291	High	2	79	4.9	24.3	78.7	86.4	0.91	117	62	Y	N	N
292	Low	1	78	2.5	27.0	92.7	104.1	0.89	153	70	Y	Y	N

293	High	2	61	3.3	32.7	97.8	110.5	0.89	129	71	Y	Y	Y
294	Low	1	77	4.6	18.2	74.9	87.6	0.86	140	78	Y	Y	N
295	High	2	67	2.6	23.7	83.8	101.6	0.82	150	76	Y	N	N
296	High	3	57	3.2	39.9	127.0	139.7	0.91	130	62	Y	Y	Y
297	High	3	74	2.9	30.7	109.2	106.7	1.02	180	60	Y	Y	Y
298	High	3	88	3.6	24.2	91.4	96.5	0.95	170	85	Y	Y	N
299	High	3	55	3	28.0	104.1	99.1	1.05	107	56	Y	Y	Y
300	High	2	75	2.7	25.6	88.9	101.6	0.88	135	78	Y	Y	N
301	High	2	66	2.7	40.0	123.2	125.7	0.98	140	76	Y	Y	Y
302	High	2	65	2.69	29.2	99.1	108.0	0.92	131	76	-	-	-
303	High	2	68	4.4	26.5	83.8	104.1	0.8	182	106	N	N	N
304	Low	1	74	2.33	21.0	75.6	96.0	0.79	122	68	Y	N	N
305	High	2	58	3.1	21.8	68.6	94.0	0.73	129	86	N	N	N
306	High	2	83	4	34.4	119.4	114.3	1.04	109	55	Y	Y	N
307	High	2	84	2.56	19.2	86.4	95.3	0.91	166	70	Y	Y	N
308	High	3	62	3.9	32.0	96.5	109.2	0.88	113	60	N	N	Y
309	High	3	68	4.3	24.2	78.7	91.4	0.86	119	74	Y	Y	N
310	Low	1	75	2.8	23.6	81.3	99.1	0.82	151	80	Y	Y	N
311	High	3	81	3.8	36.7	129.5	144.8	0.89	148	84	Y	Y	N
312	Low	0	85	3.1	18.8	72.4	85.1	0.85	166	70	Y	Y	N
313	Low	1	81	3.3	16.1	68.6	87.6	0.78	150	70	-	-	-
314	Low	1	83	3.6	23.5	94.0	106.7	0.88	165	80	Y	N	Y
315	Low	1	73	-	21.7	-	-	-	-	-	-	-	-
316	Low	1	70	-	28.4	-	-	-	-	-	-	-	-
317	High	2	88	-	41.0	-	-	-	-	-	-	-	-
318	Low	1	64	-	29.7	-	-	-	-	-	-	-	-
319	High	2	72	3.43	24.7	92.7	99.1	0.94	130	80	Y	Y	N
320	High	2	70	4.42	24.7	102.9	96.5	1.07	140	68	N	Y	N
321	Low	1	81	3.3	16.1	68.6	87.6	0.8	150	70	Y	Y	N
322	High	2	86	3.7	32.6	114.3	120.7	1	118	74	Y	Y	N
323	Low	1	80	3.5	31.5	114.3	118.1	1	168	89	Y	Y	N
324	High	2	73	3	23.8	83.8	95.3	0.9	130	79	Y	Y	N
325	Low	1	76	3.74	26.7	91.4	94.0	1	145	78	Y	Y	N

326	Low	1	64	4.6	28.3	102.9	102.9	1	118	72	Y	Y	N

Abbreviations: OSA-obstructive sleep apnea; BQ-Berlin Questionnaire; BRS-Berlin Risk Score; AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H-waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

Table 2. Indices of Physical Activity from Veterans Affairs Physical Activity Questionnaire

Subject	Blocks Walked/Day	Stair Flights Climbed/Day	Blocks and Stairs/Day (kcals)	Last Year Recreational PA (kcals/week)	Lifetime Recreational PA (kcals/week)
1	2	0	17	285	115
2	1	5	18	73	228
3	2	0	17	-	-
4	0	0	0	-	-
5	-	-	-	1991	2192
6	-	-	-	473	170
7	-	-	-	487	515
8	12	0	100	911	678
9	8	0	67	2967	1945
10	-	-	-	-	-
11	-	-	-	-	-
12	2	0	17	-	-
13	1	2	12	1913	1354
14	0	5	10	994	1243
15	9	0	75	182	27
16	-	-	-	-	30
17	-	-	-	-	-
18	0	0	0	290	390
19	-	-	-	1197	82
20	0	0	0	-	616
21	-	-	-	-	153
22	0	3	6	990	1424
23	-	-	-	360	484
24	12	0	100	1905	630
25	-	-	-	77	41
26	36	0	300	3077	1574
27	0	0	0	21	172
28	-	-	-	2913	2722
29	18	0	150	1125	2143

30	42	0	350	3673	834
31	-	-	-	15	184
32	9	0	75	929	1185
33	-	-	-	884	349
34	-	-	-	681	316
35	0	0	0	524	2094
36	0	0	0	-	-
37	30	0	250	2922	1894
38	0	4	8	608	210
39	4	0	33	1607	1892
40	15	0	125	994	484
41	6	0	50	612	2806
42	0	0	0	1979	1431
43	7	0	58	945	1803
44	28	6	245	1980	769
45	15	0	125	1181	1043
46	-	-	-	484	868
47	-	-	-	608	1080
48	0	0	0	1755	875
49	-	-	-	1069	1290
50	-	-	-	5935	1842
51	-	-	-	1080	385
52	24	0	200	4071	2754
53	0	15	30	540	313
54	12	14	128	2093	3978
55	0	0	0	540	54
56	0	0	0	405	144
57	13	0	108	1103	236
58	0	0	0	-	100
59	0	0	0	56	88
60	12	0	100	656	260
61	6	0	50	1303	948
62	3	3	31	979	333

63	0	0	0	820	411
64	12	0	100	1485	1563
65	0	0	0	1952	2259
66	0	0	0	-	129
67	6	0	50	249	235
68	31	4	266	2228	801
69	0	0	0	2818	637
70	20	3	173	4253	2400
71	4	0	33	769	542
72	24	0	200	769	542
73	0	0	0	1080	1040
74	0	0	0	-	912
75	6	0	50	872	335
76	20	12	191	1701	920
77	15	0	125	1283	1699
78	0	0	0	-	148
79	10	0	83	703	2658
80	6	0	50	608	656
81	12	0	100	654	100
82	9	0	75	338	2304
83	48	5	410	3173	3255
84	2	10	37	2115	1765
85	6	0	50	540	1215
86	2	4	25	929	1207
87	0	6	12	3038	1139
88	8	10	87	945	154
89	12	10	120	2559	1298
90	3	0	25	857	1617
91	6	0	50	1154	611
92	0	0	0	125	1319
93	8	0	67	1514	696
94	0	0	0	720	1605
95	0	0	0	-	-

96	12	5	109	1772	1970
97	7	5	68	1044	1188
98	0	0	0	1436	6994
99	30	2	254	3359	1761
100	5	0	42	665	366
101	4	0	33	328	126
102	0	1	2	-	-
103	34	0	283	1647	958
104	8	5	76	799	723
105	0	10	20	-	432
106	0	0	0	617	626
107	0	0	0	1463	1044
108	0	5	10	342	448
109	0	0	0	-	145
110	0	10	20	1828	3619
111	22	0	183	1800	618
112	0	0	0	-	-
113	7	0	58	1071	476
114	0	3	6	2027	481
115	12	0	100	1468	1631
116	36	1	302	2158	680
117	0	1	2	620	881
118	0	0	0	1069	2112
119	0	0	0	74	108
120	24	0	200	135	97
121	0	0	0	1258	833
122	0	3	6	1890	3845
123	50	8	433	1700	1799
124	0	8	16	810	538
125	0	0	0	43	795
126	0	0	0	135	45
127	0	0	0	731	58
128	0	0	0	-	882

129	0	0	0	-	235
130	2	2	21	10	0
131	0	0	0	-	205
132	0	0	0	52	332
133	6	2	54	818	160
134	0	0	0	-	-
135	0	0	0	2160	1940
136	0	0	0	85	590
137	6	0	50	-	-
138	4	4	41	236	759
139	3	0	25	1322	1008
140	0	3	6	-	1038
141	0	0	0	-	669
142	12	0	100	180	407
143	0	0	0	93	36
144	0	0	0	6856	4581
145	0	4	8	-	177
146	4	3	39	586	241
147	0	3	6	51	1098
148	6	0	50	1499	875
149	0	4	8	-	1694
150	0	0	0	-	-
151	12	0	100	2354	3369
152	-	-	-	-	-
153	12	0	100	-	-
154	6	1	52	2473	1191
155	0	0	0	-	-
156	9	0	72	-	-
157	0	0	0	-	-
158	12	8	116	-	-
159	0	0	0	-	-
160	2	0	17	-	1187
161	6	0	50	4	338

162	0	1	2	1634	1599
163	0	0	0	-	250
164	0	6	12	1412	262
165	0	10	20	3240	919
166	-	-	-	-	427
167	0	0	0	1118	3207
168	-	-	-	643	564
169	0	0	0	1080	674
170	6	0	50	251	45
171	12	6	112	-	-
172	0	1	2	338	1535
173	12	0	100	1530	1369
174	0	0	0	-	885
175	24	0	200	433	0
176	4	0	33	2055	1131
177	2	6	29	678	310
178	1	6	20	62	412
179	2	0	17	809	2317
180	1	0	8	188	-
181	12	0	100	1789	1791
182	18	1	152	0	13
183	1	0	8	779	0
184	36	0	300	35	177
185	5	0	42	604	-
186	20	0	167	1029	308
187	12	0	100	2125	1171
188	3	5	35	2125	1171
189	3	6	37	2313	757
190	12	6	112	-	-
191	0	0	0	-	-
192	0	0	0	-	920
193	0	0	0	57	31
194	0	0	0	-	-

195	13	0	108	833	257
196	0	0	0	91	192
197	7	0	57	389	420
198	6	0	50	-	-
199	0	3	6	-	-
200	0	0	0	-	-
201	10	0	83	-	-
202	0	0	0	-	-
203	0	0	0	292	348
204	0	3	6	-	-
205	0	2	4	-	-
206	0	0	0	-	2187
207	7	0	57	406	583
208	24	0	-	-	414
209	4	0	33	149	1464
210	12	30	-	2911	3375
211	12	2	104	717	541
212	0	0	0	360	323
213	10	0	83	675	198
214	10	10	103	1927	4771
215	-	-	-	1118	1662
216	-	-	-	512	422
217	-	-	-	1802	568
218	-	-	-	1656	940
219	-	-	-	1969	505
220	-	-	-	2700	1453
221	12	0	100	1350	35
222	5	1	44	775	97
223	-	-	-	506	383
224	0	0	0	-	117
225	-	-	-	2138	1556
226	36	0	300	2430	1389
227	24	0	200	1328	397

228	12	0	100	2445	864
229	0	0	0	1530	1360
230	8	0	67	1091	241
231	0	0	0	878	1907
232	12	7	114	606	1068
233	0	0	0	1733	98
234	0	0	0	810	249
235	28	4	241	1215	447
236	18	0	150	2076	717
237	18	0	150	1013	221
238	0	5	10	-	674
239	15	0	125	1575	1588
240	0	0	0	42	1463
241	51	10	445	2653	1366
242	5	1	44	104	1918
243	0	0	0	-	-
244	26	0	217	-	-
245	12	0	100	-	-
246	0	0	0	-	-
247	12	0	100	-	-
248	0	0	0	-	-
249	24	0	200	-	-
250	15	7	139	-	-
251	-	-	-	-	-
252	34	5	294	-	-
253	0	8	16	-	-
254	0	0	0	-	-
255	36	6	312	-	-
256	0	0	0	-	-
257	0	0	0	-	-
258	18	50	250	-	-
259	0	2	4	-	-
260	9	10	95	-	-

261	1	5	18	-	-
262	12	20	140	-	-
263	12	0	100	-	-
264	12	0	100	-	-
265	5	2	46	0	779
266	1	0	8	523	509
267	0	4	8		9
268	-	-	-	-	-
269	-	-	-	-	-
270	-	-	-	-	-
271	-	-	-	1781	1309
272	-	-	-	-	-
273	-	-	-	504	124
274	-	-	-	90	2
275	16	10	153	2100	1483
276	-	-	-	2093	617
277	0	0	0	-	-
278	30	0	250	3578	1687
279	12	1	102	1283	143
280	0	9	18	900	768
281	-	-	-	-	2
282	0	0	0	-	296
283	-	-	-	1238	501
284	5	0	42	1080	1258
285	0	12	24	106	243
286	12	0	100	2158	928
287	8	0	67	1234	437
288	0	0	0	540	420
289	0	0	0	-	186
290	0	3	6	-	290
291	0	0	0	-	-
292	0	4	8	-	-
293	8	6	79	855	438

294	1	0	8	2356	1412
295	28	4	241	450	193
296	3	0	25	68	368
297	0	0	0	-	-
298	2	0	17	122	140
299	0	3	6	208	305
300	12	0	100	-	-
301	12	4	108	-	-
302	0	2	4	-	-
303	8	0	67	-	270
304	-	-	-	-	-
305	12	0	-	1373	587
306	0	0	0	270	381
307	4	0	33	919	870
308	0	0	0		419
309	2	8	33	225	261
310	8	9	85	805	12
311	0	0	0		113
312	6	0	50	919	870
313	17	0	142	2700	521
314	14	0	117	1890	771
315	0	0	0	-	-
316	0	0	0	-	-
317	3	0	25	-	-
318	7	0	58	-	-
319	-	-	-	1530	1360
320	8	0	67	1091	241
321	-	-	-	2700	521
322	-	-	-	1733	98
323	-	-	-	2076	717
324	-	-	-	1575	1588
325	-	-	-	42	1463
326	-	-	-	104	1918

Abbreviations: kcals-kilocalories; PA-physical activity

Table 3. Cardiovascular and Metabolic Biomarkers

Subject	Glucose (mg/dL)	Insulin (mU/L)	TC (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	TG (mg/dL)	MetSyn
1	-	-	148.0	45.0	65.0	188.0	-
2	-	-	118.0	57.0	51.0	50.0	-
3	133.0	17.6	154.0	46.0	78.0	115.0	N
4	99.0	7.1	155.0	56.0	81.0	88.0	N
5	111.0	12.7	133.0	23.0	86.0	65.0	Y
6	112.0	13.6	137.0	29.0	83.0	97.0	Y
7	84.0	6.8	142.0	39.0	78.0	92.0	Y
8	112.0	19.5	140.0	37.0	85.0	90.0	Y
9	111.0	14.2	213.0	40.0	152.0	75.0	Y
10	129.0	14.5	249.0	32.0	190.0	89.0	N
11	114.0	10.9	158.0	38.0	90.0	113.0	N
12	104.0	22.3	110.0	38.0	52.0	76.0	N
13	104.0	3.3	138.0	35.0	88.0	74.0	Y
14	134.0	13.5	179.0	34.0	110.0	123.0	Y
15	102.0	5.4	189.0	78.0	101.0	50.0	Y
16	96.0	14.0	172.0	38.0	105.0	112.0	Y
17	97.0	3.7	149.0	59.0	72.0	91.0	N
18	104.0	5.6	193.0	38.0	126.0	112.0	Y
19	118.0	13.4	174.0	44.0	116.0	71.0	Y
20	106.0	3.2	135.0	32.0	78.0	85.0	Y
21	104.0	6.4	118.0	44.0	63.0	55.0	Y
22	93.0	9.8	219.0	54.0	113.0	200.0	Y
23	96.0	23.3	151.0	36.0	88.0	97.0	Y
24	97.0	12.2	111.0	31.0	62.0	89.0	Y
25	141.0	20.6	494.0	26.0	-	-	Y
26	111.0	8.3	197.0	44.0	137.0	82.0	Y
27	99.0	7.8	138.0	34.0	77.0	103.0	Y
28	105.0	9.0	127.0	41.0	74.0	60.0	Y
29	107.0	8.1	116.0	52.0	52.0	59.0	Y
30	85.0	2.0	128.0	55.0	64.0	43.0	Y

31	264.0	98.4	121.0	43.0	64.0	71.0	Y
32	87.0	2.0	242.0	45.0	162.0	132.0	Y
33	103.0	8.5	147.0	30.0	102.0	75.0	Y
34	123.0	11.9	201.0	37.0	115.0	174.0	Y
35	101.0	8.4	214.0	71.0	112.0	118.0	Y
36	143.0	147.6	133.0	30.0	73.0	119.0	N
37	122.0	9.4	228.0	31.0	163.0	125.0	Y
38	93.0	6.0	148.0	20.0	83.0	158.0	Y
39	143.0	9.2	161.0	71.0	81.0	46.0	Y
40	112.0	7.5	106.0	45.0	53.0	41.0	Y
41	104.0	13.4	144.0	33.0	87.0	88.0	Y
42	161.0	6.4	105.0	25.0	62.0	89.0	Y
43	104.0	12.7	130.0	44.0	70.0	82.0	Y
44	133.0	10.3	154.0	45.0	94.0	76.0	Y
45	100.0	15.6	147.0	37.0	93.0	85.0	Y
46	97.0	23.1	114.0	33.0	62.0	94.0	Y
47	146.0	16.1	156.0	32.0	74.0	160.0	Y
48	121.0	9.5	176.0	26.0	131.0	95.0	Y
49	161.0	13.7	101.0	33.0	44.0	90.0	Y
50	95.0	4.2	170.0	44.0	107.0	95.0	Y
51	103.0	4.0	162.0	41.0	114.0	34.0	Y
52	91.0	4.7	206.0	45.0	141.0	71.0	Y
53	121.0	5.4	110.0	37.0	56.0	87.0	Y
54	96.0	11.8	125.0	37.0	69.0	93.0	Y
55	108.0	3.6	184.0	67.0	101.0	78.0	Y
56	53.0	2.0	172.0	53.0	103.0	82.0	Y
57	96.0	9.2	121.0	35.0	67.0	96.0	Y
58	92.0	17.7	126.0	36.0	70.0	74.6	Y
59	93.0	7.0	148.0	38.0	90.0	77.4	Y
60	101.0	12.0	167.0	38.0	95.0	137.5	Y
61	84.0	2.0	166.0	72.0	87.0	34.0	Y
62	108.0	11.1	142.0	35.0	84.0	82.4	Y
63	88.0	11.5	150.0	39.0	94.0	84.0	Y

64	104.0	12.5	175.0	52.0	98.0	94.5	Y
65	117.0	8.7	134.0	36.0	84.0	72.0	Y
66	124.0	32.2	158.0	35.0	75.0	184.3	Y
67	111.0	31.5	204.0	39.0	118.0	186.0	Y
68	106.0	5.1	153.0	64.0	75.0	72.0	Y
69	96.0	6.9	208.0	57.0	141.0	52.0	Y
70	118.0	14.2	177.0	57.0	98.0	73.4	Y
71	129.0	14.0	171.0	34.0	95.0	163.6	Y
72	97.0	2.6	145.0	63.0	75.0	34.0	Y
73	119.0	33.5	173.0	38.0	108.0	106.4	Y
74	116.0	13.4	210.0	61.0	135.0	72.0	Y
75	96.0	11.4	147.0	32.0	97.0	91.0	Y
76	139.0	9.0	135.0	30.0	85.0	99.0	Y
77	99.0	4.2	150.0	40.0	100.0	51.0	Y
78	106.0	4.5	146.0	37.0	87.0	88.5	Y
79	123.0	35.1	134.0	33.0	86.0	77.0	Y
80	100.0	6.1	194.0	97.0	82.0	74.0	Y
81	102.0	32.0	174.0	32.0	122.0	71.1	Y
82	126.0	3.0	164.0	78.0	73.0	64.0	Y
83	94.0	10.8	134.0	27.0	82.0	101.2	Y
84	136.0	14.5	149.0	49.0	76.0	90.3	Y
85	130.0	3.8	113.0	44.0	56.0	65.0	Y
86	108.0	19.2	228.0	36.0	-	316.3	Y
87	96.0	5.3	147.0	41.0	90.0	81.0	Y
88	118.0	11.1	174.0	50.0	113.0	55.0	Y
89	108.0	8.6	168.0	31.0	110.0	99.7	Y
90	110.0	38.3	195.0	58.0	117.0	99.0	Y
91	131.0	69.3	180.0	36.0	92.0	189.2	Y
92	87.0	6.8	218.0	59.0	133.0	101.8	Y
93	104.0	15.1	151.0	46.0	86.0	96.0	Y
94	106.0	9.5	158.0	53.0	93.0	58.0	Y
95	89.0	23.5	126.0	45.0	58.0	83.0	N
96	113.0	3.0	150.0	51.0	91.0	38.0	Y

97	95.0	5.1	151.0	28.0	95.0	103.4	Y
98	102.0	6.4	215.0	42.0	143.0	110.0	Y
99	127.0	5.8	187.0	55.0	112.0	77.0	Y
100	93.0	8.7	213.0	49.0	118.0	169.1	Y
101	106.0	3.5	184.0	36.0	132.0	82.0	Y
102	123.0	-	140.0	25.0	81.0	123.3	N
103	108.0	10.2	148.0	31.0	72.0	161.9	Y
104	114.0	8.6	159.0	60.0	87.0	60.0	Y
105	104.0	22.4	223.0	28.0	157.0	147.1	Y
106	104.0	6.7	125.0	30.0	80.0	74.0	Y
107	81.0	1.0	206.0	58.0	138.0	52.0	Y
108	114.0	25.2	198.0	28.0	133.0	151.2	Y
109	115.0	9.3	200.0	44.0	144.0	60.0	Y
110	121.0	15.0	261.0	47.0	180.0	128.5	Y
111	117.0	3.6	148.0	51.0	88.0	44.0	Y
112	108.0	18.9	111.0	41.0	57.0	67.0	N
113	129.0	15.6	229.0	34.0	167.0	91.8	Y
114	116.0	10.0	158.0	42.0	100.0	80.0	Y
115	90.0	10.7	129.0	42.0	76.0	54.0	Y
116	89.0	4.5	126.0	52.0	54.0	60.7	Y
117	122.0	31.0	90.0	31.0	33.0	101.0	Y
118	122.0	31.5	141.0	39.0	69.0	127.6	Y
119	223.0	37.7	193.0	34.0	94.0	263.6	Y
120	102.0	5.3	155.0	34.0	103.0	88.0	Y
121	217.0	20.0	108.0	20.0	56.0	118.1	Y
122	103.0	6.8	151.0	31.0	108.0	58.0	Y
123	155.0	18.6	144.0	37.0	88.0	97.0	Y
124	94.0	5.9	187.0	57.0	99.0	112.9	Y
125	80.0	18.6	114.0	34.0	63.0	83.0	Y
126	100.0	3.6	140.0	73.0	53.0	70.0	Y
127	117.0	10.0	140.0	43.0	77.0	98.0	Y
128	121.0	32.9	168.0	28.0	111.0	-	Y
129	112.0	4.6	126.0	65.0	44.0	84.0	Y

130	140.0	29.4	137.0	38.0	58.0		N
131	102.0	6.5	252.0	52.0	180.0	98.0	Y
132	170.0	60.0	170.0	60.0	92.0	91.0	Y
133	106.0	7.8	180.0	51.0	118.0	55.0	Y
134	119.0	10.7	146.0	41.0	88.0	86.0	N
135	96.0	11.4	149.0	53.0	88.0	39.0	Y
136	102.0	6.0	127.0	73.0	75.0	43.0	Y
137	149.0	16.0	174.0	37.0	116.0	80.3	N
138	110.0	23.1	176.0	37.0	91.0	177.2	Y
139	131.0	17.6	151.0	32.0	91.0	104.4	Y
140	119.0	21.2	162.0	66.0	80.0	78.0	Y
141	108.0	13.4	114.0	31.0	67.0	80.0	Y
142	122.0	20.9	198.0	66.0	101.0	120.3	Y
143	103.0	6.3	147.0	35.0	94.0	90.0	Y
144	96.0	10.7	160.0	23.0	137.0	111.5	Y
145	95.0	4.1	196.0	64.0	109.0	85.2	Y
146	106.0	9.9	137.0	36.0	84.0	87.0	Y
147	93.0	1.6	163.0	49.0	98.0	78.0	Y
148	105.0	17.1	169.0	34.0	105.0	112.3	Y
149	107.0	11.2	161.0	45.0	93.0	84.2	Y
150	112.0	10.1	149.0	38.0	91.0	76.6	N
151	114.0	9.8	170.0	48.0	88.0	128.0	Y
152	94.0	4.4	178.0	51.0	114.0	63.0	N
153	101.0	27.0	186.0	40.0	123.0	89.4	N
154	118.0	13.3	225.0	51.0	160.0	71.0	Y
155	-	-	-	-	-	-	-
156	103.0	7.8	113.0	33.0	53.0		N
157	128.0	10.1	152.0	45.0	89.0	89.0	N
158	120.0	4.8	201.0	60.0	125.0	81.0	N
159	115.0	12.2	115.0	44.0	83.0	76.0	N
160	-	-	221.0	52.0	151.0	89.0	Y
161	-	-	174.0	70.0	93.0	56.0	Y
162	-	-	166.0	48.0	105.0	64.0	Y

163	89.0	9.7	116.0	36.0	59.0	79.1	Y
164	94.0	2.0	125.0	31.0	78.0	79.0	Y
165	136.0	3.6	153.0	56.0	86.0	57.0	Y
166	97.0	2.5	172.0	54.0	99.0	95.0	Y
167	106.0	10.4	137.0	38.0	85.0	68.0	Y
168	131.0	9.3	131.0	57.0	48.0	111.9	Y
169	107.0	6.2	141.0	37.0	84.0	99.0	Y
170	90.0	5.2	160.0	40.0	96.0	35.4	Y
171	117.0	8.9	161.0	34.0	111.0	78.0	N
172	82.0	8.9	110.0	36.0	46.0	105.6	Y
173	120.0	13.4	121.0	24.0	84.0	67.0	Y
174	153.0	-	192.0	45.0	130.0	84.0	Y
175	-	-	213.0	31.0	142.0	201.0	N
176	-	-	130.0	32.0	75.0	116.0	Y
177	-	-	127.0	51.0	66.0	52.0	Y
178	-	-	125.0	32.0	65.0	108.3	Y
179	-	-	131.0	39.0	77.0	73.0	Y
180	-	-	125.0	48.0	55.0	81.5	N
181	-	-	120.0	45.0	55.0	102.0	Y
182	-	-	173.0	28.0	129.0	82.0	Y
183	-	-	136.0	37.0	84.0	76.0	N
184	-	-	169.0	53.0	94.0	110.0	Y
185	100.0	-	107.0	35.0	48.0	84.4	N
186	105.0	5.0	120.0	39.0	71.0	49.0	Y
187	94.0	3.1	114.0	40.0	66.0	42.0	Y
188	113.0	12.4	134.0	40.0	73.0	83.4	Y
189	110.0	9.8	161.0	71.0	81.0	47.0	Y
190	114.0	13.2	119.0	39.0	58.0	81.6	N
191	107.0	27.6	174.0	41.0	99.0	133.7	N
192	101.0	18.2	212.0	31.0	60.0	356.6	Y
193	96.0	5.7	161.0	47.0	98.0	79.0	Y
194	101.0	14.9	166.0	27.0	115.0	95.5	N
195	106.0	7.0	120.0	24.0	79.0	85.0	Y

196	113.0	7.8	113.0	29.0	76.0	88.0	Y
197	135.0	10.5	171.0	24.0	92.0	217.2	Y
198	109.0	7.7	118.0	34.0	67.0	87.0	N
199	105.0	11.4	122.0	26.0	77.0	94.0	N
200	135.0	8.9	128.0	55.0	61.0	60.0	N
201	-	-	-	-	-	-	-
202	159.0	9.2	124.0	32.0	68.0	82.2	N
203	94.0	12.5	178.0	53.0	105.0	81.9	Y
204	94.0	4.4	178.0	51.0	114.0	63.0	N
205	226.0	18.5	137.0	24.0	83.0	118.0	N
206	187.0	11.9	145.0	36.0	83.0	108.4	Y
207	178.0	73.1	120.0	20.0	59.0	156.0	Y
208	94.0	6.9	244.0	32.0	297.0	338.3	Y
209	100.0	13.3	120.0	25.0	67.0	104.4	Y
210	99.0	17.3	136.0	48.0	62.0	93.8	Y
211	133.0	18.0	114.0	22.0	56.0	141.0	Y
212	93.0	8.8	209.0	30.0	133.0	171.6	Y
213	120.0	6.2	145.0	43.0	89.0	67.0	Y
214	114.0	11.5	124.0	32.0	78.0	71.0	Y
215	100.0	10.6	207.0	41.0	135.0	112.2	Y
216	99.0	32.5	181.0	48.0	118.0	77.0	Y
217	131.0	10.4	141.0	40.0	57.0	77.0	Y
218	124.0	5.6	159.0	46.0	85.0	77.0	Y
219	143.0	35.3	126.0	26.0	72.0	77.0	Y
220	202.0	21.8	125.0	34.0	75.0	82.0	Y
221	118.0	12.6	226.0	29.0	159.0	147.5	Y
222	119.0	14.6	152.0	43.0	92.0	85.0	Y
223	94.0	19.0	130.0	38.0	74.0	92.0	Y
224	94.0	19.8	228.0	96.0	122.0	48.0	Y
225	97.0	5.7	224.0	37.0	128.0	212.9	Y
226	89.0	2.0	189.0	53.0	117.0	93.0	Y
227	94.0	6.3	177.0	48.0	103.0	90.1	Y
228	107.0	9.5	179.0	52.0	119.0	41.0	Y

229	99.0	11.9	116.0	31.0	68.0	87.0	Y
230	106.0	9.8	195.0	55.0	114.0	96.1	Y
231	119.0	24.6	198.0	39.0	102.0	212.9	Y
232	143.0	13.6	162.0	40.0	76.0	78.5	Y
233	132.0	10.3	154.0	53.0	75.0	87.0	Y
234	105.0	9.0	145.0	33.0	73.0	139.1	Y
235	98.0	3.5	174.0	54.0	109.0	56.0	Y
236	192.0	12.9	122.0	44.0	58.0	78.7	Y
237	108.0	60.0	169.0	60.0	98.0	62.0	Y
238	165.0	16.4	138.0	29.0	78.0	119.9	Y
239	101.0	6.4	134.0	35.0	80.0	96.0	Y
240	97.0	10.6	131.0	32.0	78.0	73.9	Y
241	87.0	2.7	204.0	96.0	103.0	26.0	Y
242	94.0	22.5	192.0	37.0	125.0	190.0	Y
243	-	-	-	-	-	-	-
244	-	-	-	-	-	-	-
245	-	-	-	-	-	-	-
246	-	-	-	-	-	-	-
247	-	-	-	-	-	-	-
248	-	-	-	-	-	-	-
249	-	-	-	-	-	-	-
250	-	-	-	-	-	-	-
251	-	-	-	-	-	-	-
252	-	-	-	-	-	-	-
253	-	-	-	-	-	-	-
254	-	-	-	-	-	-	-
255	-	-	-	-	-	-	-
256	-	-	-	-	-	-	-
257	-	-	-	-	-	-	-
258	-	-	-	-	-	-	-
259	-	-	-	-	-	-	-
260	106.0	8.5	143.0	37.0	86.0	-	N
261	125.0	-	117.0	39.0	51.0	-	N

262	227.0	-	227.0	33.0	80.0	-	N
263	152.0	-	137.0	35.0	79.0	-	N
264	-	-	-	-	-	-	-
265	-	-	217.0	51.0	152.0	71.0	Y
266	-	-	177.0	60.0	92.0	125.0	Y
267	124.0	10.7	225.0	55.0	141.0	127.3	Y
268	98.0	38.6	154.0	45.0	82.0	120.1	N
269	89.0	8.8	145.0	44.0	84.0	85.0	N
270	87.0	5.6	130.0	38.0	76.0	81.0	N
271	105.0	5.6	212.0	37.0	147.0	122.8	Y
272	127.0	19.9	210.0	46.0	118.0	203.0	N
273	134.0	25.4	142.0	50.0	69.0	104.1	Y
274	115.0	11.5	414.0	93.0	288.0	148.6	Y
275	101.0	4.5	206.0	57.0	137.0	59.0	Y
276	94.0	2.0	214.0	78.0	115.0	92.6	Y
277	130.0	62.5	130.0	25.0	68.0	162.9	N
278	149.0	18.9	186.0	36.0	75.0	333.0	Y
279	92.0	6.5	155.0	62.0	80.0	67.0	Y
280	82.0	6.4	179.0	52.0	106.0	91.7	Y
281	86.0	14.5	144.0	62.0	62.0	89.9	N
282	98.0	24.3	161.0	38.0	99.0	105.0	Y
283	92.0	5.9	252.0	40.0	179.0	147.7	Y
284	97.0	8.1	136.0	39.0	69.0	123.7	Y
285	93.0	5.4	176.0	44.0	101.0	138.0	Y
286	97.0	12.2	155.0	54.0	85.0	82.0	Y
287	123.0	10.7	171.0	55.0	86.0	133.5	Y
288	95.0	4.9	169.0	59.0	86.0	105.0	Y
289	98.0	14.6	186.0	64.0	104.0	91.0	Y
290	95.0	7.0	147.0	54.0	64.0	130.8	Y
291	110.0	4.9	286.0	53.0	209.0	106.8	N
292	98.0	6.6	132.0	53.0	67.0	62.0	N
293	122.0	20.7	152.0	51.0	80.0	92.6	Y
294	94.0	4.6	156.0	65.0	74.0	84.0	Y

295	99.0	3.4	230.0	54.0	131.0	200.3	Y
296	214.0	44.5	156.0	35.0	99.0	97.0	Y
297	178.0	29.7	123.0	47.0	57.0	95.0	N
298	98.0	8.3	147.0	53.0	74.0	98.0	Y
299	117.0	6.0	110.0	50.0	54.0	31.0	Y
300	109.0	9.8	152.0	48.0	90.0	69.0	N
301	181.0	41.3	136.0	42.0	73.0	93.5	N
302	132.0	-	138.0	49.0	70.0	95.0	N
303	-	-	270.0	45.0	197.0	64.0	Y
304	93.0	8.2	166.0	41.0	82.0	190.5	N
305	88.0	4.2	214.0	97.0	109.0	38.0	Y
306	94.0	3.7	110.0	40.0	57.0	63.0	Y
307	89.0	2.5	230.0	86.0	126.0	88.0	Y
308	113.0		140.0	28.0	67.0	198.5	Y
309	89.0	11.3	147.0	39.0	89.0	96.0	Y
310	99.0	9.8	116.0	75.0	30.0	53.0	Y
311	88.0	11.5	150.0	39.0	87.0	107.7	Y
312	95.0	7.8	176.0	85.0	79.0	59.0	Y
313	105.0	5.5	171.0	66.0	90.0	75.0	Y
314	107.0	8.6	181.0	68.0	100.0	64.0	Y
315	-	-	-	-	-	-	-
316	-	-	-	-	-	-	-
317	-	-	-	-	-	-	-
318	-	-	-	-	-	-	-
319	99.0	11.9	116.0	31.0	68.0	87.0	Y
320	106.0	9.8	195.0	55.0	114.0	128.0	Y
321	105.0	5.5	171.0	66.0	90.0	75.0	Y
322	132.0	10.3	154.0	53.0	75.0	87.0	Y
323	192.0	12.9	122.0	44.0	58.0	101.0	-
324	101.0	6.4	134.0	35.0	80.0	96.0	-
325	97.0	10.6	131.0	32.0	78.0	105.0	Y
326	94.0	22.5	192.0	37.0	125.0	253.0	Y

Abbreviations: TC-total cholesterol; HDL-C-high density lipoprotein-cholesterol; LDL-C-low density lipoprotein-cholesterol; TG-triglycerides; MetSyn-metabolic syndrome.

Chapter 4 Raw Data

Table 4. Subject Characteristics

Subject	OSA-risk	BRS	Age (yr)	AAA (cm)	BMI (kg/m2)	WC (cm)	HC (cm)	W/H ratio	SBP (mmHg)	DBP (mmHg)	Anti-HTN med	Anti-lipemic Med	Diabetic Med
1	Y	2	53.00	2.3	51.9	182.9	148.6	1.23	156	98	Y	Y	Y
2	Y	2	62.00	2.2	33.8	109.2	102.9	1.06	118	68	Y	N	Y
3	Y	1	51.00	2.8	34.3	104.1	94.0	1.11	134	88	Y	N	Y
4	Y	2	74.00	2.4	28.8	102.9	109.2	0.94	150	66	Y	Y	N
5	N	1	59.00	2.3	29.1	92.7	101.6	0.91	126	80	N	Y	N
6	Y	3	58.00	2.3	39.8	121.9	124.5	0.98	138	84	Y	N	N
7	N	2	59.00	2.2	30.7	100.3	105.4	0.95	122	84	N	N	N
8	N	1	76.00	2.6	26.7	96.5	101.6	0.95	132	72	Y	Y	N
9	Y	1	62.00	1.9	24.7	88.9	104.1	0.85	144	90	Y	Y	N
10	N	3	83.00	1.9	27.6	97.8	101.6	0.96	158	84	Y	Y	Y
11	N	1	68.00	2.0	33.6	109.2	113.0	0.97	122	76	Y	Y	Y
12	Y	3	61.00	2.1	35.0	124.5	115.6	1.08	130	90	Y	Y	Y
13	N	2	61.00	1.9	30.0	94.0	96.5	0.97	128	78	Y	Y	Y
14	Y	2	60.00	2.0	37.5	116.8	116.8	1.00	134	80	Y	Y	Y
15	Y	1	71.00	2.2	27.0	100.3	108.0	0.93	144	86	Y	Y	Y
16	Y	3	60.00	6.1	31.2	109.2	101.6	1.08	160	98	Y	N	N
17	N	3	62.00	1.9	29.4	96.5	96.5	1.00	132	78	Y	Y	N
18	N	1	79.00	2.4	27.0	86.4	95.3	0.91	138	80	Y	Y	N
19	N	1	52.00	2.6	31.6	95.3	106.7	0.89	140	82	Y	N	Y
20	Y	2	64.00	1.9	26.1	94.0	101.6	0.92	130	78	Y	Y	N
21	N	0	65.00	1.9	20.1	81.3	86.4	0.94	138	84	Y	N	N
22	N	0	64.00	2.3	29.4	91.4	104.1	0.88	130	78	N	Y	N
23	N	0	64.00	2.2	21.1	73.7	88.9	0.83	140	80	N	Y	N
24	N	2	70.00	4.4	24.7	102.9	96.5	1.07	140	68	-	-	-
25	Y	1	63.00	3.0	28.6	101.6	105.4	0.96	139	73	Y	Y	N
26	Y	1	76.00	4.3	30.6	113.0	110.5	1.02	134	78	Y	Y	Y
27	N	2	86.00	3.7	32.6	114.3	120.7	0.96	118	74	-	-	-
28	Y	2	71.00	3.1	27.6	94.0	97.8	0.96	124	65	Y	Y	N

29	N	2	79.00	3.6	26.1	88.9	100.3	0.89	162	85	Y	Y	N
30	Y	1	80.00	3.5	31.5	114.3	118.1	0.97	168	89	-	-	-
31	N	2	73.00	4.7	25.5	100.3	101.6	0.99	150	93	Y	Y	N
32	Y	2	75.00	3.7	30.9	109.2	111.8	0.98	116	62	Y	N	Y
33	N	2	73.00	3.0	23.8	83.8	95.3	0.88	130	79	-	-	-
34	Y	1	76.00	3.7	26.7	91.4	94.0	0.97	145	78	-	-	-
35	N	1	67.00	3.7	23.2	82.6	91.4	0.90	109	68	Y	Y	N
36	Y	1	64.00	4.6	28.3	102.9	102.9	1.00	118	72	-	-	-
37	Y	2	82.00	4.1	36.5	111.1	114.3	1.00	152	78	N	N	N
38	N	1	86.00	4.8	23.0	94.0	101.6	0.90	124	78	N	Y	N
39	N	1	83.00	4.8	19.6	76.8	88.9	0.90	144	65	N	Y	N
40	N	1	77.00	4.8	21.6	87.6	96.5	0.90	160	80	Y	Y	N
41	Y	1	55.00	3.8	26.8	94.0	101.6	0.90	122	98	N	Y	N
42	Y	1	77.00	4.5	29.9	109.2	109.2	1.00	150	74	N	N	N
43	N	2	57.00	3.4	34.5	102.9	120.7	0.90	110	76	Y	Y	N
44	Y	1	75.00	3.6	24.5	91.4	96.5	1.00	134	80	N	N	N
45	N	1	74.00	3.3	26.9	83.8	106.7	0.80	153	70	Y	N	N
46	N	2	70.00	4.2	29.3	102.9	105.4	1.00	137	88	N	N	N
47	Y	2	60.00	3.3	27.6	94.0	99.1	1.00	161	94	N	Y	N
48	Y	2	73.00	3.6	28.4	100.3	102.9	1.00	130	70	Y	N	N
49	Y	1	71.00	4.6	25.9	101.1	108.0	0.90	154	78	Y	N	N
50	Y	2	72.00	3.9	27.3	99.1	101.6	1.00	148	84	Y	N	N
51	N	0	80.00	4.3	21.4	83.8	96.5	0.90	145	75	N	N	N
52	Y	1	72.00	3.5	30.9	110.5	113.0	1.00	163	74	N	N	N
53	Y	2	72.00	3.4	24.7	92.7	99.1	0.94	130	80	Y	Y	N
54	Y	1	62.00	4.4	49.9	125.7	153.7	0.80	114	68	Y	N	N
55	Y	1	73.00	4.2	32.5	109.2	108.0	1.00	128	68	Y	Y	N
56	Y	3	61.00	4.2	32.2	102.9	106.7	1.00	130	82	Y	Y	N
57	Y	2	67.00	4.5	29.3	105.4	102.9	1.00	150	88	Y	Y	N
58	N	2	70.00	4.4	24.7	102.9	96.5	1.07	140	68	N	Y	N
59	Y	2	64.00	3.5	31.0	102.9	104.1	1.00	120	70	Y	Y	N
60	N	0	74.00	4.2	25.1	82.6	94.0	0.90	120	80	Y	Y	N
61	Y	0	78.00	3.9	27.3	92.7	100.3	0.90	126	76	Y	Y	N

62	Y	2	68.00	3.4	32.0	110.5	114.3	1.00	155	90	Y	Y	N
63	Y	1	78.00	3.8	26.7	90.2	102.9	0.90	134	84	Y	Y	N
64	Y	1	82.00	3.0	28.1	94.0	101.6	0.90	132	80	Y	Y	Y
65	Y	2	72.00	4.1	30.7	108.0	106.7	1.00	150	84	Y	Y	N
66	N	1	80.00	3.1	30.0	106.7	114.3	0.90	120	73	Y	Y	N
67	N	1	79.00	3.9	34.8	116.8	115.6	1.00	120	62	N	Y	N
68	N	3	74.00	3.3	32.4	104.1	104.1	1.00	110	78	N	N	N
69	Y	1	81.00	3.8	30.1	100.3	108.0	0.90	118	61	Y	Y	N
70	N	1	72.00	4.4	23.3	94.0	91.4	1.00	153	87	N	Y	N
71	Y	2	54.00	3.4	31.3	109.2	111.8	1.00	108	72	Y	Y	N
72	N	1	84.00	3.2	25.1	92.7	99.1	0.90	124	70	Y	Y	N
73	Y	2	75.00	3.6	29.2	102.9	105.4	1.00	138	76	N	Y	N
74	Y	3	71.00	3.6	27.8	111.8	110.5	1.00	140	62	Y	Y	Y
75	N	1	71.00	4.1	28.2	96.5	94.0	1.00	138	78	Y	Y	N
76	Y	1	74.00	4.1	30.4	106.7	111.8	1.00	145	88	Y	Y	N
77	Y	3	79.00	4.0	24.2	91.4	96.5	1.00	145	74	Y	Y	Y
78	Y	1	86.00	3.4	23.1	78.7	96.5	0.80	136	67	Y	N	N
79	Y	2	69.00	4.0	24.4	96.5	101.6	1.00	126	69	Y	Y	N
80	N	1	77.00	3.3	27.3	108.0	113.0	1.00	116	66	N	Y	N
81	Y	1	62.00	4.0	30.0	106.7	104.1	1.00	143	84	Y	Y	N
82	N	1	81.00	3.3	16.1	68.6	87.6	0.80	150	70	Y	Y	N
83	Y	2	86.00	3.7	32.6	114.3	120.7	1.00	118	74	Y	Y	N
84	Y	3	78.00	3.4	21.6	92.7	99.1	0.94	142	84	Y	Y	Y
85	N	1	80.00	3.5	31.5	114.3	118.1	1.00	168	89	Y	Y	N
86	N	2	73.00	3.0	23.8	83.8	95.3	0.90	130	79	Y	Y	N
87	Y	1	76.00	3.7	26.7	91.4	94.0	1.00	145	78	Y	Y	N
88	N	2	68.00	3.2	22.9	95.9	95.3	1.00	140	78	N	Y	N
89	Y	0	72.00	4.0	28.8	111.8	111.8	1.00	118	76	Y	N	N
90	Y	1	64.00	3.5	26.6	100.3	99.1	1.00	149	81	Y	N	N
91	Y	2	63.00	4.0	22.6	106.7	96.5	1.10	152	90	Y	Y	N
92	Y	2	80.00	3.6	25.6	99.1	121.9	1.00	132	60	N	N	Y
93	Y	0	81.00	2.5	23.4	88.9	91.4	1.00	136	64	Y	Y	N
94	Y	2	75.00	3.7	30.9	108.0	105.4	1.00	138	64	Y	N	N

95	N	1	77.00	3.2	20.7	81.3	92.7	0.90	108	70	N	N	N
96	Y	3	78.00	3.9	33.5	121.9	119.4	1.00	144	88	Y	Y	N
97	Y	1	73.00	3.8	34.9	118.1	118.1	1.00	149	81	N	N	N
98	Y	1	82.00	3.3	28.7	99.1	106.7	0.90	142	78	Y	Y	N
99	N	1	76.00	3.7	26.2	97.8	99.1	1.00	112	66	N	N	N
100	Y	1	64.00	4.6	28.3	102.9	102.9	1.00	118	72	Y	Y	N
101	N	2	64.00	3.3	24.4	85.1	94.0	0.90	104	74	Y	N	N
102	Y	3	68.00	3.0	33.8	110.5	105.4	1.10	150	87	Y	Y	Y
103	Y	2	82.00	3.8	29.3	91.4	99.1	0.90	138	74	N	N	N
104	Y	1	82.00	3.8	24.4	83.8	96.5	0.90	120	64	Y	N	N
105	N	1	75.00	4.0	23.1	85.1	96.5	0.90	116	78	N	N	N
106	N	1	77.00	4.3	24.6	88.9	101.6	0.90	128	78	Y	Y	N
107	Y	2	87.00	4.2	23.8	97.8	104.1	0.90	158	86	N	N	N
108	Y	2	62.00	4.7	32.2	106.7	104.1	1.00	160	101	Y	N	N
109	N	1	77.00	3.5		106.7	100.3	1.10	132	70	Y	N	N
110	N	2	63.00	3.3	24.5	88.9	99.1	0.90	138	90	N	N	N
111	N	0	74.00	3.0	23.0	86.4	96.5	0.90	116	66	Y	N	N
112	N	1	78.00	3.3	33.3	108.0	111.8	1.00	116	66	N	Y	N
113	Y	3	72.00	4.0	27.8	102.9	100.3	1.00	130	72	Y	N	N
114	N	2	71.00	3.8	63.0	114.3	99.1	1.20	128	76	-	-	-

Abbreviations: OSA-obstructive sleep apnea; BQ-Berlin Questionnaire; BRS-Berlin Risk Score; AAA-abdominal aortic aneurysm; BMI-body mass index; WC-waist circumference; HC-hip circumference; W/H-waist/hip; SBP-systolic blood pressure; DBP-diastolic blood pressure; HTN-hypertension; Med-medication.

Table 5. Cardiopulmonary Exercise Test Variables at Rest, Ventilatory Threshold, Peak Exercise, and Recovery

Subject	Rest			Ventilatory Threshold (VT)			Peak Exercise					Recovery	
	HR-supine (bt/min)	SBP supine (mmHg)	DBP supine (mmHg)	HR (bt/min)	VO^2 (ml/kg/min)	RER	HR (bt/min)	SBP (mmHg)	DBP (mmHg)	VO^2 (ml/kg/min)	RER	HR min1 (bt/min)	SBP min1 (bt/min)
1	72	142	84	112	13.6	0.84	124	246	106	12.3	1.05	87	210
2	52	118	68	86	12.2	0.93	104	120	158	14.7	1.18	64	130
3	61	144	92	99	17.0	0.90	115	170	88	29.8	1.12	86	148
4	65	124	68	92	16.9	0.97	119	210	76	28.7	1.36	93	204
5	63	126	80	140	24.5	0.94	172	180	90	37.8	1.18	137	180
6	62	138	84	127	16.6	0.83	163	180	84	24.5	1.15	102	182
7	70	122	84	-	-	-	137	170	76	18.2	0.90	103	148
8	54	138	72	109	15.0	0.81	136	214	88	17.5	1.13	110	194
9	67	144	90	-	-	-	165	228	100	42.0	1.15	-	-
10	87	170	90	108	11.9	0.71	130	190	86	14.0	1.08	125	190
11	68	122	76	110	13.2	0.99	146	200	90	21.4	1.32	124	176
12	67	130	90	149	18.0	0.86	156	190	98	16.5	1.01	91	170
13	76	128	78	107	17.8	0.81	127	190	76	26.6	1.07	102	182
14	69	158	98	117	15.1	0.98	142	208	70	24.2	1.11	120	168
15	75	144	86	140	21.7	0.95	155	186	76	27.3	1.11	130	188
16	77	160	98	113	11.4	0.72	118	220	104	13.3	0.97	105	190
17	59	132	78	111	20.5	0.94	152	200	70	36.8	1.28	119	196
18	55	138	80	111	17.3	0.91	125	190	70	23.1	1.12	102	186
19	65	140	82	-	-	-	-	-	-	-	-	-	-
20	58	130	78	-	-	-	115	166	82	26.3	1.13	85	162
21	96	138	84	-	-	-	175	122	78	24.9	1.14	-	-
22	60	130	78	118	20.2	0.96	152	218	74	34.3	1.25	110	200
23	63	130	80	-	-	-	149	172	84	33.3	1.14	-	-
24	86	138	72	134	16.6	1.02	147	214	80	18.8	1.11	128	212
25	68	100	60	98	13.1	0.94	-	160	50	16.6	1.15	113	132
26	63	154	86	-	10.3	0.77	112	184	92	15.1	1.03	93	184
27	-	-	-	-	11.4	0.81	-	-	-	-	-	-	-

28	75	118	70	116	11.9	0.70	166	180	76	22.4	1.09	155	158
29	54	136	76	80	18.4	0.83	112	190	80	29.0	1.12	61	180
30	68	150	88	113	13.4	0.79	127	208	70	15.7	1.25	96	208
31	65	158	80	99	15.7	0.86	95	170	80	17.6	1.29	90	180
32	61	144	72	111	12.8	0.89	128	196	76	14.6	1.07	118	190
33	52	116	78	80	7.8	0.70	133	160	84	20.4	1.32	108	164
34	60	126	70	82	11.4	0.94	98	180	70	11.8	1.16	83	120
35	64	142	88	128	19.9	0.75	166	208	86	27.9	1.23	152	206
36	60	118	72	92	14.5	0.71	130	158	80	22.3	1.16	102	158
37	55	152	80	-	15.6	1.00	129	200	80	17.4	1.13	90	194
38	47	124	86	75	15.7	0.90	106	174	80	21.0	1.19	95	190
39	60	138	52	73	9.7	0.77	83	160	82	16.0	1.18	75	150
40	70	164	72	83	10.1	0.72	110	164	70	14.6	1.10	105	145
41	44	132	78	83	13.6	0.97	109	170	84	15.5	1.17	75	198
42	62	141	78	-	14.1	0.76	125	182	80	15.2	1.21	129	172
43	73	136	84	-	9.6	0.90	123	180	86	10.6	0.93	101	182
44	70	114	80	129	16.0	0.82	174	180	86	35.9	1.16	138	160
45	54	120	74	-	12.7	0.77	83	128	60	15.1	0.96	113	144
46	50	110	76	-	15.7	0.88	102	164	76	21.7	0.93	82	160
47	66	134	80	-	11.3	0.67	140	178	86	22.2	1.10	121	196
48	68	136	76	101	11.3	0.67	120	206	74	18.9	1.14	103	198
49	60	150	74	103	13.8	0.84	119	195	90	15.1	1.25	62	194
50	53	122	70	83	12.1	0.72	110	142	68	22.7	1.01	77	162
51	51	102	68	102	18.5	0.95	116	174	105	22.2	1.05	97	-
52	51	132	72	101	16.5	0.99	110	142	70	17.5	1.13	84	130
53	87	151	89	-	27.5	0.73	169	230	100	33.6	0.95	142	280
54	55	140	74	-	15.8	0.85	106	200	84	20.7	1.15	70	164
55	62	120	78	103	14.2	0.99	133	214	90	19.6	1.09	117	176
56	48	118	64	-	19.4	1.03	120	174	80	23.6	1.09	94	170
57	65	158	80	-	21.0	1.00	139	168	80	23.5	1.23	115	128
58	86	138	72	134	16.6	1.02	147	214	80	18.8	1.11	128	212
59	56	130	72	69	9.7	0.83	82	144	74	12.1	1.11	68	180
60	60	114	76		19.1	0.99	156	178	88	21.1	1.14	115	158

61	75	122	88	147	12.6	0.98	170	170	70	15.7	1.18	140	180
62	64	118	76	103	12.6	0.93	138	226	94	17.6	1.17	118	218
63	62	120	68	89	10.1	0.86	98	156	74	12.3	0.96	91	156
64	83	132	74	114	14.7	0.90	124	160	52	17.3	1.00	106	150
65	60	124	66	122	15.5	1.00	130	200	80	15.8	1.05	106	218
66	51	128	66	117	29.7	1.04	126	180	40	34.3	1.14	105	158
67	61	120	78	-	-	-	110	146	76	18.4	0.90	78	136
68	54	142	80	90	15.3	0.89	132	210	86	23.0	1.19	92	215
69	65	108	64	96	20.3	1.07	109	160	84	21.3	1.20	86	172
70	93	130	68	-	-	-	135	170	76	-	0.00	122	184
71	49	152	86	83	12.8	0.75	109	152	76	18.1	1.03	94	164
72	63	160	78	96	10.9	0.78	138	170	78	20.6	1.14	115	146
73	60	136	72	107	14.5	0.80	158	208	84	20.7	1.22	111	202
74	47	146	84	71	11.2	0.82	89	166	80	15.3	1.09	65	170
75	73	164	90	103	12.5	0.99	127	208	70	15.7	1.25	96	208
76	58	142	74	85	10.0	0.77	106	172	66	13.0	1.10	100	176
77	62	140	80	96	16.3	0.81	119	240	76	19.3	1.12	91	224
78	55	134	68	96	16.0	1.01	116	184	76	19.4	1.15	88	194
79	67	140	92	97	17.8	0.78	132	200	74	27.0	1.22	116	184
80	60	122	78	92	9.9	0.68	155	214	86	20.3	1.23	131	206
81	86	126	68	124	10.0	0.76	149	170	76	13.7	1.04	132	176
82	53	120	68	83	12.4	0.81	105	174	84	16.6	1.09	84	178
83	-	-	-	-	11.4	0.81	-	-	-	-	-	-	-
84	68	100	90	88	14.1	0.76	111	172	76	20.4	1.10	89	154
85	68	150	88	113	13.4	0.79	127	208	70	15.7	1.25	96	208
86	52	116	78	80	7.8	0.70	133	160	84	20.4	1.32	108	164
87	60	126	70	82	11.4	0.94	98	180	70	11.8	1.16	83	120
88	54	104	74	-	16.6	0.78	124	148	64	25.0	1.03	96	144
89	55	138	78	106	15.7	0.99	112	184	90	16.7	1.08	95	214
90	65	136	80	-	15.4	0.91	140	240	108	19.6	1.02	105	218
91	75	138	70	104	14.8	0.84	133	190	78	22.3	1.11	122	170
92	53	128	78	94	12.7	0.69	149	210	96	26.4	1.17	120	186
93	57	142	82	-	16.6	0.84	167	224	70	-	1.05	112	226

94	64	130	76	-	23.5	0.93	135	220	78	36.6	1.12	101	210
95	69	120	62	99	6.7	0.72	132	206	60	14.1	1.16	119	204
96	63	132	78	-	19.1	0.99	129	206	86	24.5	1.25	109	188
97	56	108	72	86	12.6	0.71	124	168	80	19.5	1.04	87	178
98	70	118	60	-	13.9	0.80	156	148	64	17.3	1.00	129	170
99	57	158	80	93	15.0	0.77	136	148	60	21.1	1.12	118	148
100	60	118	72	92	14.5	0.71	130	158	80	22.3	1.16	102	158
101	63	150	88	123	14.2	0.84	122	170	78	18.4	1.16	126	200
102	61	-	-	97	9.8	0.81	152	230	90	20.9	1.30	134	210
103	57	144	88	-	12.6	0.85	98	140	74	15.8	1.13	95	136
104	66	132	90	128	19.1	0.95	146	182	80	22.2	1.05	134	176
105	85	128	78	-	14.1	0.82	142	194	80	21.6	1.11	124	190
106	59	138	74	-	9.4	0.85	132	160	84	10.3	1.09	97	164
107	64	118	72	95	10.9	0.96	114	234	66	-	1.13	102	184
108	62	146	72	73	10.2	0.75	86	204	86	11.6	0.98	67	210
109	68	120	71	-	20.7	0.98	169	180	72	39.4	1.24	144	174
110	64	138	90	88	14.1	0.80	127	220	78	26.4	1.23	85	176
111	61	112	70	117	17.6	0.81	152	240	80	26.3	1.10	131	220
112	102	118	78	140	16.6	0.83	156	160	90	18.6	1.11	155	-
113	47	122	56	72	12.5	0.98	74	132	60	12.5	1.02	56	124
114	75	128	76	103	11.8	0.83	106	168	82	13.9	-	90	170

Abbreviations: HR-heart rate; SBP-systolic blood pressure; DBP-diastolic blood pressure; VO^2-oxygen consumption; RER-respiratory exchange ratio; PA-physical activity.

APPENDIX F

STATISTICAL OUTPUT TABLES

Chapters 2 and 3 Statistical Output Tables

Table 1. Independent Samples Test for Subject Characteristics and VAPAQ by Clinical Berlin OSA Risk

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Age	Equal variances assumed	.471	.493	2.299	324	.022	2.17205	.94476	.31341	4.03068
	Equal variances not assumed			2.287	291.531	.023	2.17205	.94974	.30283	4.04126
AAA_size	Equal variances assumed	.000	.992	-.687	296	.492	-.06145	.08940	-.23740	.11450
	Equal variances not assumed			-.695	279.951	.487	-.06145	.08838	-.23543	.11253
BMI	Equal variances assumed	3.009	.084	-4.352	320	.000	-2.92162	.67129	-4.24233	-1.60092
	Equal variances not assumed			-4.514	318.212	.000	-2.92162	.64721	-4.19497	-1.64828
Waist_cm	Equal variances assumed	.025	.875	-3.686	304	.000	-6.33267	1.71808	-9.71351	-2.95183
	Equal variances not assumed			-3.728	284.371	.000	-6.33267	1.69853	-9.67597	-2.98938
Hip_cm	Equal variances assumed	2.463	.118	-3.132	304	.002	-4.34237	1.38634	-7.07041	-1.61433
	Equal variances not assumed			-3.259	301.896	.001	-4.34237	1.33233	-6.96421	-1.72053
Waist_Hip_ratio	Equal variances assumed	.013	.908	-2.681	304	.008	-.02405	.00897	-.04171	-.00639
	I::qual vanances not assumed			-2.713	284.977	.007	-.02405	.00886	-.04150	-.00660
SBP_rest	Equal variances assumed	.000	.999	.825	303	.410	1.68106	2.03732	-2.32802	5.69013
	Equal variances not assumed			.826	274.343	.410	1.68106	2.03616	-2.32743	5.68954
DBP_rest	Equal variances assumed	1.420	.234	-.393	304	.694	-.47402	1.20531	-2.84582	1.89778
	Equal variances not assumed			-.400	288.161	.690	-.47402	1.18616	-2.80865	1.86061
Blocks_walked_day	Equal variances assumed	15.630	.000	2.459	324	.014	2.61609	1.06382	.52322	4.70895
	Equal variances not assumed			2.337	233.380	.020	2.61609	1.11943	.41062	4.82156
Stairs_climbed_day	Equal variances assumed	12.655	.000	2.433	274	.016	1.37674	.56591	.26266	2.49083
	Equal variances not assumed			2.142	141.249	.034	1.37674	.64280	.10599	2.64750
Blocks_flights_day	Equal variances assumed	16.821	.000	3.143	271	.002	32.48890	10.33784	12.13622	52.84159
	Equal variances not assumed			2.926	176.442	.004	32.48890	11.10196	10.57918	54.39863

Table 2. Analysis of Variance for Subject Characteristics and VAPAQ by Berlin Risk Score

ANOVA

		Sum or Squares	df	Mean Square	F	SIg.
Age	Between Groups	450.252	3	150.084	2.103	.100
	Within Groups	22984.104	322	71.379		
	Total	23434.356	325			
AM_size	Between Groups	2.286	3	.762	1.318	.269
	Within Groups	170.051	294	.578		
	Total	172.338	297			
BMI	Between Groups	1170.110	3	390.037	11.454	.000
	Within Groups	10828.832	318	34.053		
	Total	11998.942	321			
Waist_cm	Between Groups	5169.579	3	1723.193	8.052	.000
	Within Groups	64630.719	302	214.009		
	Total	69800.298	305			
Hlp_cm	Between Groups	2164.102	3	721.367	5.097	.002
	Within Groups	42743.064	302	141.533		
	Total	44907.166	305			
Waist_Hip_ratio	Between Groups	.088	3	.029	4.991	.002
	Within Groups	1.777	302	.006		
	Total	1.865	305			
SBP_rest	Between Groups	758.887	3	252.962	.820	.484
	Within Groups	92871.624	301	308.544		
	Total	93630.511	304			
DBP_rest	Between Groups	74.979	3	24.993	.230	.876
	Within Groups	32825.138	302	108.693		
	Total	32900.118	305			
Blocks_walked_day	Between Groups	885.343	3	295.114	3.289	.021
	Within Groups	28896.460	322	89.741		
	Total	29781.804	325			
Stairs_climbed_day	Between Groups	198.747	3	66.249	3.125	.026
	Within Groups	5767.195	272	21.203		
	Total	5965.942	275			
Blocks_flights_day	Between Groups	83514.656	3	27838.219	3.966	.009
	Within Groups	1887967.395	269	7018.466		
	Total	1971482.051	272			

Table 3. Bonferroni Post Hoc Test for Subject Characteristics and VAPAQ by Berlin Risk Score

Muniple Compar sons

Bonferroni

Deoendent Variable	I Berlin Risk Score	(J) Berlin Risk Score	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Age	.00	1 Category positive	-2.17401	2.13434	1.000	-7.8400	3.4919
		2 Categoricpoitivc	.28780	2.12184	1.000	5.3450	5.0206
		3 Categories positive	.25926	2.29942	1.000	-5.8449	6.3634
	1 Category positive	00	2.17401	2.13434	1.000	-3.4919	7.8400
		2 Categories positive	2.46182	1.06141	.126	-.3559	5.2795
		3 Categories positive	2.43327	1.38266	.476	-1.2372	6.1038
	2 Categories positive	00	-.28780	2.12184	1.000	-5 9206	5.3450
		1 Category positive	-2.46182	1.06141	.126	-5.2795	3559
		3 Categories positive	-.02854	1.36328	1.000	-3.6476	3.5905
	3 Categories postive	.00	-.25926	2.29942	1.000	-6.3634	5.8449
		1 Category postive	-2.43327	1.38266	.476	-6.1038	1.2372
		2 Categories positive	.02854	1.36328	1.000	-3.5905	3.6476
AAA_size	.00	1 Category postive	-.29199	.19832	.852	-.8188	.2348
		2 Categories positive	-.35534	.19669	.431	-.8778	.1671
		3 Categories positive	-.20735	.21465	1.000	-.7775	.3628
	1 Category positive	00	29199	.19832	.852	-.2348	8188
		2 Categories positive	-.06335	.09986	1.000	-.3286	2019
		3 Categories positive	08463	13174	1.000	-.2653	4346
	2 Categories positive	00	35534	.19669	.431	-.1671	8778
		1 Category positive	06335	.09986	1.000	-.2019	3286
		3 Categories positive	14798	.12929	1.000	-.1954	.4914
	3 Categories positive	.00	.20735	.21465	1.000	-.3628	.7775
		1 Category postive	-.08463	.13174	1.000	-.4346	.2653
		2 Categories positive	-.14798	.12929	1.000	-.4914	.1954
BMI	.00	1 Category postive	-3.73662	1.47662	.071	-7.6569	.1836
		2 Categories positive	-5.37687"	1.46622	.002	-9.2695	-1.4842
		3 Categories positive	-8.08704	1.58822	.000	-12.3035	-3.8705
	1 Category positive	00	3.73662	1.47662	.071	-.1836	7.6569
		2 Categories positive	-1.64025	.73930	.163	-3.6030	3225
		3 Categories positive	-4.35042_..	95875	000	-6.8958	-1.8051
	2 Categories positive	00	5.37687	1.46622	.002	1.4842	92695
		1 Category positive	1.64025	.73930	.163	-.3225	3.6030
		3 Categories positive	-2.71017"	.94265	.026	-5.2128	-.2076
	3 Categories positive	.00	8.08704	1.58822	.000	3.8705	12.3035
		1 Category postive	4.35042"	.95875	.000	1.8051	6.8958
		2 Categories positive	2.71017"	.94265	.026	.2076	5.2128
Waist_cm	.00	1 Category postive	-8.62899	3.71953	.126	-18.5071	1.2492
		2 Categories positive	-12.22248	3.68436	.006	-22.0072	-2.4377
		3 Categories positive	-17.54758	4.01069	.000	-28.1990	-6.8962
	1 Category positive	00	8.62899	3.71953	.126	-1.2492	18.5071
		2 Categories positive	-3.59349	1.90543	.362	-8_6538	1.4668
		3 Categories positive	-8.91959"	2.47826	002	-15.5002	-2.3369
	2 Categories positive	00	12.22248	3.68436	.006	2.4377	22 0072
		1 Category positive	3.59349	1.90543	.362	-1.4668	8.6538
		3 Categories positive	-5.32511	2.42515	.173	-11.7657	1.1155
	3 Categories positive	.00	17.54758	4.01069	.000	6.8962	28.1990
		1 Category postive	8.91859"	2.47826	.002	2.3369	15.5002
		2 Categories positive	5.32511	2.42515	.173	-1.1155	11.7657
Hip_Cn"l	0 0	1 Category poitive	-a.aa1 2a	3.02484	.317		2.1!J20
		2 Categories positive	-8.68400..	2.99623	.024	-16.6412	-.7268
		3 Categories positive	-11.17102..	3.26161	.004	-19.8331	-2.5090
	1 Category positive	.00	5.88125	3.02484	.317	-2.1520	13.9145
		2 Categories positive	-2.80275	1.54955	.429	-6.9180	1.3125
		3 Categories positive	-5.28977	2.01540	.055	-10.6422	.0626
	2 Categories postive	.00	8.68400	2.99623	.024	.7268	16.6412
		1 Category postive	2.80275	1.54955	.429	-1.3125	6.9180
		3 Categories positive	-2.48702	1.97221	1.000	-7.7247	2.7507
	3 Categories postive	00	11.17102	3.26161	.004	2.5090	19.8331
		1 Category postive	5.28977	2.01540	.055	-.0626	10.6422
		2 Categories positive	2.48702	1.97221	1.000	-2.7507	7.7247
Waist_Hip_ratio	00	1 Category postive	- 03065	01950	703	-.0824	0212
		2 Categories positive	-.04209	.01932	.181	-.0934	0092
		3 Categories positive	-.071as·	.02103	.005	-.1269	- 0152
	1 Category positive	.00	.03065	.01950	.703	-.0212	.0824
		2 Categories positive	-.01144	.00999	1.000	-.0380	.0151
		3 Categories positive	-.04040"	.01300	.012	-.0749	-.0059
	2 Categories positive	.00	.04209	.01932	.181	-.0092	.0934
		1 Category postive	.01144	.00999	1.000	-.0151	.0380
		3 Categories positive	- 02895	.01272	.141	-.0627	.0048
	3 Categories positive	00	07105	.02103	.005	.0152	1269
		1 Category positive	04040..	.01300	.012	.0059	0749
		2 Categories positive	02895	01272	.141	-.0048	0627

•. The mean difference 1s s1gmficant at the 0.05 level.

Table 3. Bonferroni Post Hoc Test for Subject Characteristics and VAPAQ by Berlin Risk Score con't

Multiple Comparisons

Bonferroni

Deoendent Variable	(I) Berlin Risk Score	(J) Berlin Risk Score	Mean Difference (J)	Std.Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
SBP_ rest	.00	1 Category positive	1.65859	4.46612	1.000	-10.2026	13.5t98
		2 Categories positive	4.18254	4.42607	1.000	-7.5722	15.9373
		3 Categories positive	.44771	4.81572	1.000	-12.3419	13.2374
	1 Category postive	_00	-1.65859	4.46612	1.000	-13.5t 98	10.2026
		2 Categories positive	2.52395	2.29210	1.000	-3.5634	8.6t13
		3 Categories positive	-1.21087	2.97570	1.000	-9.1t38	6.6920
	2 Categories positive	_00	-4.18254	4.42607	1.000	-15.9373	7.5722
		1 Category positive	-2.52395	2.29210	1.000	-8.6t13	3.5634
		3 Categories positive	-3.73483	2.91524	1.000	-1t.4772	4.0075
	3 Categori es postive	_00	-_44771	4.81572	1.000	-13.2374	12.3419
		1 Category positive	1.21087	2.97570	1.000	-6.6920	9.1t38
		2 Categories positive	3.73483	2.91524	1.000	-4.0075	11.4772
DBP_rest	.00	1 Category positive	1.76970	2.65077	1.000	-5.2701	8.8095
		2 Categories positive	1.19554	2.62570	1.000	-5.7777	8.1688
		3 Categories positive	.67647	2.85827	1.000	-6_9t 44	8.2673
	1 Category positive	.00	-1.76970	2.65077	1.000	-8.8095	5.2701
		2 Categories positive	-.57416	1.35792	1.000	-4.1805	3.0322
		3 Categories positive	-1.09323	1.76617	1.000	-5.7837	3.5973
	2 Categories positive	.00	-1.19554	2.62570	1.000	-8.1688	5.7777
		1 Category positive	.57416	1.35792	1.000	-3.0322	4.1805
		3 Categories positive	-.51907	1.7283t	1.000	-5.1090	4.0709
	3 Categories positive	.00	-.67647	2.85827	1.000	-8.2673	6.9t 44
		1 Category positive	t.09323	t .76617	1.000	-3.5973	5.7837
		2 Categories positive	.51907	t.7283t	1.000	-4.0709	5.1090
Blocks_walked_day	.00	1 Category positive	4.37466	2.39317	.411	-t.9784	10.7277
		2 Categories positive	6.13033	2.37914	.063	-.1855	12.446t
		3 Categories positive	7.14815	2.57826	.035	.3037	13.9926
	1 Category positive	_00	-4.37466	2.39317	.411	-10.7277	t.9784
		2 Categories positive	1.75567	t.19013	.847	-t.4037	4.9t50
		3 Categories positive	2.77349	1.55033	.44 7	-t.3421	6.8891
	2 Categories positive	_00	-6.13033	2.37914	.063	-12.4461	.1855
		1 Category positive	-1.75567	1.19013	.847	-4.9t 50	t.4037
		3 Categories positive	1.01782	1.52860	1.000	-3.0401	5.0757
	3 Categori es postive	_00	-7.14815	2.57826	.035	-13.9926	-_3037
		1 Category positive	-2.77349	1.55033	.44 7	-6.8891	1.3421
		2 Categories positive	-1.01782	1.52860	1.000	-5.0757	3.0401
Stairs_climbed_day	.00	1 Category positive	-1.91827	1.2126t	.689	-5.1410	1.3045
		2 Categories positive	-_47570	1.19650	1.000	-3.6556	2.7042
		3 Categories positive	.27851	1.29613	1.000	-3.1662	3.7232
	1 Category positive	_00	1.91827	1.21261	.689	-t.3045	5.1410
		2 Categories positive	1.44256	.63841	.148	-_2541	3.1392
		3 Categories positive	2.19678	.80988	.043	.0444	4.3492
	2 Categories positive	_00	.47570	1.19650	1.000	-2.7042	3.6556
		1 Category positive	-1.44256	.63841	.148	-3.1392	.2541
		3 Categories positive	.75421	.78555	1.000	-1.3335	2.8420
	3 Categori es positive	_00	-_27851	1.29613	1.000	-3.7232	3.1662
		1 Category positive	-2.19678	.80988	.043	-4.3492	-_0444
		2 Categories positive	-.75421	.78555	1.000	-2.8 420	1.3335
Blocks_fiights_day	.00	1 Category positive	24.48197	22 09793	1.000	-34.2524	83.2163
		2 Categories positive	49.35294	21.78110	.146	-8.5393	107.2452
		3 Categories positive	62.10804	23.58145	.054	-_5694	124.7855
	1 Category positive	.00	-24.48197	22.09793	1.000	-83.2163	34.2524
		2 Categories positive	24.87097	11.70610	.207	-6.2428	55.9848
		3 Categories positive	37.62607	14.78856	.069	-t.6806	76.9327
	2 Categories positive	.00	-49.35294	2t .78110	.146	-107.2452	8.5393
		1 Category positive	-24.87097	1t .70610	.207	-55.9848	6.2428
		3 Categories positive	12.75510	14.31082	1.000	-25.2818	50.7920
	3 Categories positive	.00	-62.10804	23.58145	.054	-124.7855	.5694
		1 Category positive	-37.62607	14.78856	.069	-76.9327	t.6806
		2 Categories positive	-12.75510	14.31082	1.000	-50.7920	25.2818

***. The mean difference 1s s1gmficant at the 0.051evel.**

Table 4. Independent Samples Test for Cardiovascular and Metabolic Biomarkers by Clinical Berlin OSA Risk

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Glucose_fasting_serum	Equal variances assumed	3.307	.070	-.564	282	.573	-1.831	3.245	-8.218	4.556
	Equal variances not assumed			-.537	205.052	.592	-1.831	3.409	-8.551	4.889
Insulin_fasting_serum	Equal variances assumed	6.870	.009	-2.474	274	.014	-4.306	1.741	-7.733	-.879
	Equal variances not assumed			-2.636	269.421	.009	-4.306	1.633	-7.522	-1.090
TC	Equal variances assumed	.154	.695	-.291	300	.771	-1.45609	5.00246	-11.30044	8.38826
	Equal variances not assumed			-.288	263.904	.773	-1.45609	5.04994	-11.39938	8.48720
HDL	Equal variances assumed	.263	.608	1.491	300	.137	2.46363	1.65278	-.78889	5.71615
	Equal variances not assumed			1.503	281.926	.134	2.46363	1.63863	-.76187	5.68913
LDL	Equal variances assumed	.540	.463	-.588	298	.557	-2.31091	3.93109	-10.04712	5.42530
	Equal variances not assumed			-.592	278.136	.554	-2.31091	3.90432	-9.99669	5.37487
TG	Equal variances assumed	.213	.645	-2.094	292	.037	-11.72803	5.60030	-22.75009	-.70596
	Equal variances not assumed			-2.121	276.643	.035	-11.72803	5.52841	-22.61112	-.84494

Table 5. Analysis of Variance for Cardiovascular and Metabolic Biomarkers by Berlin Risk Score

ANOVA

		Sum of Squares	d'	Mean Square	F	Sig.
Glucose_fasting_serum	Between Groups	6805.932	3	2268.644	3.189	.024
	Within Groups	199184.265	280	711.372		
	Total	205990.197	283			
Insulin_fasting_serum	Between Groups	1996.539	3	665.513	3.279	.021
	Within Groups	55213.727	272	202.992		
	Total	57210.266	275			
TC	Between Groups	5190.500	3	1730.167	.940	.422
	Within Groups	548621.888	298	1841.013		
	Total	553812.387	301			
HDL	Between Groups	687.297	3	229.099	1.134	.335
	Within Groups	60197.687	298	202.006		
	Total	00884.983	301			
LDL	Between Groups	6699.250	3	2233.083	1.997	.114
	Within Groups	330955.747	296	1118.094		
	Total	337654.997	299			
TG	Between Groups	15736.537	3	5245.512	2.338	.074
	Within Groups	650767.245	290	2244.025		
	Total	666503.782	293			

Table 6. Bonferroni Post Hoc Test for Cardiovascular and Metabolic Biomarkers by Berlin Risk Score

Muhiple Compar sons

Bonferroni

DeoendentVariable	I Berlin Risk Score	J Berlin Risk Score	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Glucose_fasting_serum	.00	1 Category positive	-18.337	7.162	.066	-37.37	.70
		2 Categories positive	-15.591	7.106	.174	-34.47	3.29
		3 Categories positive	-23.190-	7.741	.018	-43.76	-2.62
	1 Category positive	.00	18.337	7.162	.066	-.70	37.37
		2 Categories positive	2.745	3.587	1.000	-6.79	12.28
		3 Categories positive	-4.854	4.723	1.000	-17.40	7.70
	2 Categories positive	.00	15.591	7.106	.174	-3.29	34.47
		1 Category positive	-2.745	3.587	1.000	-12.28	6.79
		3 Categories positive	-7.599	4.636	.614	-19.92	4.72
	3 Categories positive	.00	23.190	7.741	.018	2.62	43.76
		1 Category positive	4.854	4.723	1.000	-7.70	17.40
		2 Categories positive	7.599	4.636	614	-4.72	19.92
Insulin_fasting_serum	.00	1 Category positive	-3.271	3.834	1.000	-13.46	6.92
		2 Categories positive	-5.929	3.802	.720	-16.03	4.17
		3 Categories positive	-10.268	4.159	.085	-21.32	.79
	1 Category positive	.00	3.271	3.834	1.000	-6.92	13.46
		2 Categories positive	-2.658	1.943	1.000	-7.82	2.51
		3 Categories positive	-6.997"	2.574	.042	-13.84	-.16
	2 Categories positive	.00	5.929	3.802	.720	-4.17	16.03
		1 Category positive	2.658	1.943	1.000	-2.51	7.82
		3 Categories positive	-4.339	2.526	.522	-11.05	2.37
	3 Categories positive	.00	10.268	4.159	.085	-.79	21.32
		1 Category positive	6.997"	2.574	.042	.16	13.84
		2 Categories positive	4.339	2.526	.522	-2.37	11.05
TC	.00	1 Category positive	-2.77071	10.90940	1.000	-31.7459	26.2045
		2 Categories positive	-7.16489	10.81696	1.000	-35.8946	21.5648
		3 Categories positive	4.65193	11.82583	1.000	-26.7573	36.0612
	1 Category positive	00	2.77071	10.90940	1.000	-26.2045	31.7459
		2 Categories positive	-4.39418	5.60933	1.000	-19.2925	10.5041
		3 Categories positive	7.42263	7.36941	1.000	-12.1504	26.9957
	2 Categories positive	.00	7.16489	10.81696	1.000	-21.5648	35.8946
		1 Category positive	4.39418	5.60933	1.000	-10.5041	19.2925
		3 Categories positive	11.81682	7.23186	.620	-7.3909	31.0245
	3 Categories positive	.00	-4.65193	11.82583	1.000	-36.0612	26.7573
		1 Category positive	-7.42263	7.36941	1.000	-26.9957	12.1504
		2 Categories positive	-11.81682	7.23186	.620	-31.0245	7.3909
HDL	.00	1 Category positive	3.43737	3.61372	1.000	-6.1606	13.0354
		2 Categories positive	5.05956	3.58310	.954	-4.4571	14.5762
		3 Categories positive	6.33107	3.91728	643	-4.0732	16.7353
	1 Category positive	00	-3.43737	3.61372	1.000	-13.0354	6.1606
		2 Categories positive	1.62218	1.85808	1.000	-3.3129	6.5572
		3 Categories positive	2.89369	2.44110	1.000	-3.5898	9.3772
	2 Categories positive	.00	-5.05956	3.58310	.954	-14.5762	4.4571
		1 Category positive	-1.62218	1.85808	1.000	-6.5572	3.3129
		3 Categories positive	1.27151	2.39554	1.000	-5.0910	7.6340
	3 Categories positive	.00	-6.33107	3.91 728	.643	-16.7353	4.0732
		1 Category positive	-2.89369	2.44110	1.000	-9.3772	3.5898
		2 Categories positive	-1.27151	2.39554	1.000	-7.6340	5.0910
LDL	.00	1 Category positive	-2.26249	8.50729	1.000	-24.8588	20.3338
		2 Categories positive	-7.97111	8.42977	1.000	-30.3615	14.4193
		3 Categories positive	5.43056	9.24175	1.000	-19.1165	29.9776
	1 Category positive	.00	2.26249	8.50729	1.000	-20.3338	24.8588
		2 Categories positive	-5.70862	4.38206	1.000	-17.3479	5.9306
		3 Categories positive	7.69304	5.79235	1.000	-7.6921	23.0782
	2 Categories positive	00	7.97111	8.42977	1.000	-14.4193	30.3615
		1 Category positive	5.70862	4.38206	1.000	-5 9306	17.3479
		3 Categories positive	13.40167	5.67788	.113	-1.6794	28.4827
	3 Categories positive	.00	-5.43056	9.24175	1.000	-29.9776	19.1165
		1 Category positive	-7.69304	5.79235	1.000	-23 0782	7.6921
		2 Categories positive	-13.40167	5.67788	.113	-28.4827	1.6794
TG	.00	1 Category positive	-11.99203	12.07634	1.000	-44.0726	20.0885
		2 Categories positive	-19.02594	11.96719	.678	-50.8165	12.7647
		3 Categories positive	-29.27222	13.05620	.154	-63.9558	5.4113
	1 Category positive	.00	11.99203	12.07634	1.000	-20 0885	44.0726
		2 Categories positive	-7.03391	6.30204	1.000	-23.7751	9.7073
		3 Categories positive	-17.28019	8.18330	.213	-39.0190	4.4586
	2 Categories positive	00	19.02594	11.96719	678	-12.7647	50.8165
		1 Category positive	7.03391	6.30204	1.000	-9.7073	23.7751
		3 Categories positive	-10.24628	8.02135	1.000	-31.5548	11.0623
	3 Categories positive	.00	29.27222	13.05620	.154	-5.4113	63.9558
		1 Category positive	17.28019	8.18330	.213	-4.4586	39.0190
		2 Categories positive	10.24628	8.02135	1.000	-11.0623	31.5548

..... The mean difference 1s s1gmficant at the 0.05 level.

Chapter 4 Statistical Output Tables

Table 7. Independent Samples Test for Subject Characteristics by Clinical Berlin OSA Risk

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Age	Equal variances assumed	.158	.692	2.217	112	.029	3.44630	1.55419	.36687	6.52572
	Equal variances not assumed			2.214	110.007	.029	3.44630	1.55653	.36163	6.53096
AAA_size	Equal variances assumed	.033	.856	.591	112	.556	.09096	.15384	-.21385	.39578
	Equal variances not assumed			.588	107.689	.558	.09096	.15461	-.21552	.39744
BMI	Equal variances assumed	1.010	.317	-2.363	111	.020	-2.65796	1.12461	-4.88644	-.42948
	Equal variances not assumed			-2.332	96.428	.022	-2.65796	1.13996	-4.92063	-.39529
Waist_cm	Equal variances assumed	.308	.580	-2.989	112	.003	-7.43209	2.48669	-12.35915	-2.50503
	Equal variances not assumed			-2.961	103.749	.004	-7.43209	2.51025	-12.41015	-2.45403
Hip_cm	Equal variances assumed	.048	.828	-1.421	112	.158	-2.74167	1.92998	-6.56567	1.08234
	Equal variances not assumed			-1.425	111.707	.157	-2.74167	1.92434	-6.55462	1.07128
Waist_Hip_ratio	Equal variances assumed	2.500	.117	-4.183	112	.000	-.05369	.01283	-.07911	-.02826
	Equal variances not assumed			-4.182	110.609	.000	-.05369	.01284	-.07913	-.02824
SBP_rest	Equal variances assumed	.004	.952	-.943	112	.348	-2.62963	2.78800	-8.15370	2.89444
	Equal variances not assumed			-.943	110.682	.348	-2.62963	2.78841	-8.15523	2.89597
DBP_rest	Equal variances assumed	2.388	.125	-1.822	112	.071	-3.02778	1.66155	-6.31993	.26437
	Equal variances not assumed			-1.802	102.161	.074	-3.02778	1.67987	-6.35973	.30418

Table 8. Analysis of Variance for Subject Characteristics by Berlin Risk Score

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Age	Between Groups	342.960	3	114.320	1.637	.185
	Within Groups	7683.505	110	69.850		
	Total	8026.465	113			
AAA_size	Between Groups	1.928	3	.643	.960	.414
	Within Groups	73.642	110	.669		
	Total	75.570	113			
BMI	Between Groups	297.999	3	99.333	2.805	.043
	Within Groups	3859.322	109	35.407		
	Total	4157.321	112			
Waist_em	Between Groups	2467.514	3	822.505	4.816	.003
	Within Groups	18785.830	110	170.780		
	Total	21253.344	113			
Hip_cm	Between Groups	640.258	3	213.419	2.054	.111
	Within Groups	11430.061	110	103.910		
	Total	12070.319	113			
Waist_Hip_ratio	Between Groups	.093	3	.031	6.618	.000
	Within Groups	.514	110	.005		
	Total	.606	113			
SBP_rest	Between Groups	484.580	3	161.527	.727	.538
	Within Groups	24454.543	110	222.314		
	Total	24939.123	113			
DBP_rest	Between Groups	372.249	3	124.083	1.573	.200
	Within Groups	8676.216	110	78.875		
	Total	9048.465	113			

Table 9. Bonferroni Post Hoc Tests for Subject Characteristics by Berlin Risk Score

Multiple Comparisons

Bonferroni

Deoendent Variable	II Berlin Risk Score	(J) Berlin Risk Score	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Age	.00	1.00	-.83007	3.02171	1.000	-8.9488	7.2887
		2.00	2.71274	3.07649	1.000	-5.5532	10.9787
		3.00	2.82906	3.62411	1.000	-6.9082	12.5664
	1.00	.00	.83007	3.02171	1.000	-7.2887	8.9488
		2.00	3.54280	1.75307	.274	-1.1674	8.2530
		3.00	3.65913	2.59667	.970	-3.3176	10.6359
	2.00	.00	-2.71274	3.07649	1.000	-10.9787	5.5532
		1.00	-3.54280	1.75307	.274	-8.2530	1.1674
		3.00	.11632	2.66021	1.000	-7.0312	7.2638
	3.00	.00	-2.82906	3.62411	1.000	-12.5664	6.9082
		1.00	-3.65913	2.59667	.970	-10.6359	3.3176
		2.00	-.11632	2.66021	1.000	-7.2638	7.0312
AAA_size	.00	1.00	-.45516	.29583	.761	-1.2500	.3397
		2.00	-.32108	.30119	1.000	-1.1303	.4882
		3.00	-.21658	.35480	1.000	-1.1699	.7367
	1.00	.00	.45516	.29583	.761	-.3397	1.2500
		2.00	.13408	.17163	1.000	-.3270	.5952
		3.00	.23858	.25421	1.000	-.4444	.9216
	2.00	.00	.32108	.30119	1.000	-.4882	1.1303
		1.00	-.13408	.17163	1.000	-.5952	.3270
		3.00	.10450	.26044	1.000	-.5952	.8042
	3.00	.00	.21658	.35480	1.000	-.7367	1.1699
		1.00	-.23858	.25421	1.000	-.9216	.4444
		2.00	-.10450	.26044	1.000	-.8042	.5952
BMI	.00	1.00	-3.53782	2.15458	.621	-9.3277	2.2521
		2.00	-5.51588	2.19035	.079	-11.4019	.3702
		3.00	-6.09838	2.58024	.119	-13.0322	.8354
	1.00	.00	3.53782	2.15458	.621	-2.2521	9.3277
		2.00	-1.97806	1.25368	.705	-5.3470	1.3909
		3.00	-2.56055	1.85249	1.000	-7.5387	2.4176
	2.00	.00	5.51588	2.19035	.079	-.3702	11.4019
		1.00	1.97806	1.25368	.705	-1.3909	5.3470
		3.00	-.58250	1.89398	1.000	-5.6721	4.5071
	3.00	.00	6.09838	2.58024	.119	-.8354	13.0322
		1.00	2.56055	1.85249	1.000	-2.4176	7.5387
		2.00	.58250	1.89398	1.000	-4.5071	5.6721
Waist_cm	.00	1.00	-9.98818	4.72485	.221	-22.6829	2.7066
		2.00	-15.03350	4.81050	.014	-27.9584	-2.1086
		3.00	-18.72436	5.66679	.008	-33.9499	-3.4988
	1.00	.00	998818	4.72485	.221	-2.7066	22.6829
		2.00	-5.04532	2.74117	.410	-12.4103	2.3197
		3.00	-8.73618	4.06024	.202	-19.6453	2.1729
	2.00	.00	15.03350	4.81050	.014	2.1086	27.9584
		1.00	5.04532	2.74117	.410	-2.3197	12.4103
		3.00	-3.69086	4.15961	1.000	-14.8669	7.4852
	3.00	.00	18.72436	5.66679	.008	3.4988	33.9499
		1.00	8.73618	4.06024	.202	-2.1729	19.6453
		2.00	3.69086	4.15961	1.000	-7.4852	14.8669

*. The mean difference is significant at the 0.05 level.

Table 9. Bonferroni Post Hoc Tests for Subject Characteristics by Berlin Risk Score con't

Multiple Comparisons

Bonferroni

Dependent Variable	(I) Berlin Risk Score	(J) Berlin Risk Score	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Hip_cm	.00	1.00	-7.41503	3.68551	.280	-17.3173	2.4872
		2.00	-8.85664	3.75232	.120	-18.9384	1.2251
		3.00	-9.63675	4.42025	.188	-21.5131	2.2396
	1.00	.00	7.41503	3.68551	.280	-2.4872	17.3173
		2.00	-1.44161	2.13818	1.000	-7.1865	4.3033
		3.00	-2.22172	3.16710	1.000	-10.7311	6.2877
	2.00	.00	8.85664	3.75232	.120	-1.2251	18.9384
		1.00	1.44161	2.13818	1.000	-4.3033	7.1865
		3.00	-.78011	3.24460	1.000	-9.4977	7.9375
	3.00	.00	9.63675	4.42025	.188	-2.2396	21.5131
		1.00	2.22172	3.16710	1.000	-6.2877	10.7311
		2.00	.78011	3.24460	1.000	-7.9375	9.4977
Waist_Hip_ratio	.00	1.00	-.02725	.02470	1.000	-.0936	.0391
		2.00	-.07138	.02515	.032	-.1390	-.0038
		3.00	-.09410	.02963	.012	-.1737	-.0145
	1.00	.00	.02725	.02470	1.000	-.0391	.0936
		2.00	-.04413*	.01433	.016	-.0826	-.0056
		3.00	-.06685*	.02123	.013	-.1239	-.0098
	2.00	.00	.07138	.02515	.032	.0038	.1390
		1.00	.04413*	.01433	.016	.0056	.0826
		3.00	-.02272	.02175	1.000	-.0812	.0357
	3.00	.00	.09410	.02963	.012	.0145	.1737
		1.00	.06685	.02123	.013	.0098	.1239
		2.00	.02272	.02175	1.000	-.0357	.0812
SBP_rest	.00	1.00	-4.83660	5.39079	1.000	-19.3206	9.6474
		2.00	-5.94038	5.48852	1.000	-20.6870	8.8062
		3.00	-9.26496	6.46550	.928	-26.6365	8.1066
	1.00	.00	4.83660	5.39079	1.000	-9.6474	19.3206
		2.00	-1.10378	3.12752	1.000	-9.5068	7.2993
		3.00	-4.42836	4.63251	1.000	-16.8750	8.0183
	2.00	.00	5.94038	5.48852	1.000	-8.8062	20.6870
		1.00	1.10378	3.12752	1.000	-7.2993	9.5068
		3.00	-3.32458	4.74588	1.000	-16.0758	9.4267
	3.00	.00	9.26496	6.46550	.928	-8.1066	26.6365
		1.00	4.42836	4.63251	1.000	-8.0183	16.8750
		2.00	3.32458	4.74588	1.000	-9.4267	16.0758
DBP_rest	.00	1.00	-.75163	3.21098	1.000	-9.3789	7.8757
		2.00	-2.87263	3.26919	1.000	-11.6563	5.9111
		3.00	-6.17094	3.85112	.672	-16.5182	4.1763
	1.00	.00	.75163	3.21098	1.000	-7.8757	9.3789
		2.00	-2.12099	1.86288	1.000	-7.1262	2.8842
		3.00	-5.41931	2.75932	.312	-12.8331	1.9945
	2.00	.00	2.87263	3.26919	1.000	-5.9111	11.6563
		1.00	2.12099	1.86288	1.000	-2.8842	7.1262
		3.00	-3.29831	2.82685	1.000	-10.8935	4.2969
	3.00	.00	6.17094	3.85112	.672	-4.1763	16.5182
		1.00	5.41931	2.75932	.312	-1.9945	12.8331
		2.00	3.29831	2.82685	1.000	-4.2969	10.8935

*. The mean difference is significant at the 0.05 level.

Table 10. Independent Samples Test for CPET Variables at Rest and the Ventilatory Threshold by Clinical Berlin OSA Risk

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
HR_sup	Equal variances assumed	.004	.948	.369	110	.713	.75769	2.05117	-3.30726	4.82264
	Equal variances not assumed			.371	109.479	.711	.75769	2.04006	-3.28545	4.80083
SBP_sup	Equal variances assumed	.000	.998	-1.076	109	.284	-3.01471	2.80291	-8.56998	2.54057
	Equal variances not assumed			-1.074	105.475	.285	-3.01471	2.80720	-8.58057	2.55116
DBP_sup	Equal variances assumed	.001	.974	-1.632	109	.106	-2.63039	1.61162	-5.82458	.56379
	Equal variances not assumed			-1.630	105.523	.106	-2.63039	1.61392	-5.83031	.56953
HR_vt	Equal variances assumed	.000	.993	.971	80	.335	4.03399	4.15530	-4.23532	12.30330
	Equal variances not assumed			.970	79034	.335	4 03399	4.15770	-4.24164	12.30962
V02mlkg_vt	Equal variances assumed	.012	.913	.571	104	.569	.44311	.77633	-1.09639	1.98261
	Equal variances not assumed			.572	103.914	.569	.44311	.77535	-1.09444	1.98067
RER_vt	Equal variances assumed	.243	.623	1.027	104	.307	.02055	.02001	-.01913	.06023
	Equal variances not assumed			1.027	103.695	.307	.02055	.02002	-.01915	.06024

Table 11. Independent Samples Test for CPET Variables at Peak Exercise and Recovery by Clinical Berlin OSA Risk

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
HR_max	Equal variances assumed	1.503	.223	1.342	108	.183	5.78183	4.30975	-2.76084	14.32450
	Equal variances not assumed			1.349	107.999	.180	5.78183	4.28446	-2.71071	14.27437
SBP_max	Equal variances assumed	2.455	.120	-1.542	109	.126	-8.01760	5.20042	-18.32467	2.28947
	Equal variances not assumed			-1.528	101.595	.130	-8.01760	5.24830	-18.42808	2.39288
DPB_max	Equal variances assumed	.244	.622	-1.659	109	.100	-4.17080	2.51339	-9.15225	.81066
	Equal variances not			-1.646	102.225	.103	-4.17080	2.53447	-9.19777	.85618
V02mlkg_max	Equal variances assumed	.590	.444	.074	106	.941	.09636	1.30401	-2.48897	2.68168
	Equal variances not assumed			.075	105.417	.941	.09636	1.29055	-2.46244	2.65516
RER_max	Equal variances assumed	.026	.872	-.364	108	.717	-.00994	.02732	-.06409	.04422
	Equal variances not assumed			-.375	99.369	.708	-.00994	.02647	-.06246	.04259
HRR1	Equal variances assumed	.310	.579	1.487	106	.140	6.11813	4.11327	-2.03682	14.27309
	Equal variances not assumed			1.489	105.707	.140	6.11813	4.10986	-2.03032	14.26658
SBP_reef	Equal variances assumed	.010	.919	-1.459	104	.148	-7.69160	5.27343	-18.14900	2.76581
	Equal variances not assumed			-1.456	102.661	.148	-7.69160	5.28109	-18.16580	2.78261
LastYearRecPA	Equal variances assumed	2.762	.099	1.257	107	.211	285.69699	227.28189	-164.86286	736.25684
	Equal variances not assumed			1.294	96.648	.199	285.69699	220.81928	-152.58833	723.98231

Table 12. Analysis of Variance for CPET Variables at Rest and the Ventilatory Threshold by Berlin Risk Score

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
HR_sup	Between Groups	69.081	3	23.027	.194	.900
	Within Groups	12839.338	108	118.883		
	Total	12908.420	111			
SBP_sup	Between Groups	647.873	3	215.958	.996	.398
	Within Groups	23209.766	107	216.914		
	Total	23857.640	110			
DBP_sup	Between Groups	329.123	3	109.708	1.531	.211
	Within Groups	7666.246	107	71.647		
	Total	7995.369	110			
HR_vt	Between Groups	1416.408	3	472.136	1.356	.263
	Within Groups	27166.092	78	348.283		
	Total	28582.500	81			
VO2mlkg_vt	Between Groups	55.538	3	18.513	1.173	.324
	Within Groups	1610.096	102	15.785		
	Total	1665.634	105			
RER_vt	Between Groups	.049	3	.016	1.550	.206
	Within Groups	1.066	102	.010		
	Total	1.114	105			

Table 13. Bonferroni Post Hoc Tests for CPET Variables at Rest and the Ventilatory Threshold by Berlin Risk Score

Muniple Cornpar-i ons

Bonferroni

Deoendent Variable	rn Berlin Risk Score	J Be r in Risk Score	Mean Difference (1- J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
HR_sup	.00	1.00	.02614	3.94211	1.000	-10.5692	10.6214
		2.00	.19658	4.03206	1.000	-10.6405	11.0336
		3.00	2.52991	4.72800	1.000	-10.1777	15.2375
	1.00	00	-.02614	3.94211	1.000	-10.6214	10.5692
		2.00	.17044	2.31933	1.000	-6.0633	6.4042
		3.00	2.50377	3.38760	1.000	-6.6012	11.6087
	2 00	00	-.19658	4.03206	1.000	-11.0336	10.6405
		1.00	-.17044	2.31933	1.000	-6.4042	6.0633
		3.00	2.33333	3.49186	1.000	-7.0518	11.7185
	3.00	00	-2.52991	4.72800	1.000	-15.2375	10.1777
		1.00	-2.50377	3.38760	1.000	-11.6087	6.6012
		2.00	-2.33333	3.49186	1.000	-11.7185	7.0518
SBP_sup	00	1.00	-6.76471	5.32492	1.000	-21.0791	7.5497
		2.00	-8.23077	5.44641	.802	-22.8718	6.4102
		3.00	-10.50000	6.49443	.653	-27.9583	6.9583
	1.00	.00	6.76471	5.32492	1.000	-7.5497	21.0791
		2.00	-1.46606	3.13291	1.000	-9.8879	6.9558
		3.00	-3.73529	4.72539	1.000	-16.4381	8.9675
	2.00	.00	8.23077	5.44641	.802	-6.4102	22.871a
		1.00	1.46606	3.13291	1.000	-6.9558	9.8879
		3.00	-2.26923	4.86190	1.000	-15.3389	10.8005
	3.00	00	10.50000	6.49443	.653	-6.9583	27.9583
		1.00	3.73529	4.72539	1.000	-8.9675	16.4381
		2.00	2.26923	4.86190	1.000	-10.8005	15.3389
DBP_sup	00	1.00	2.59477	3 06033	1.000	-5 6320	10.8215
		2.00	29915	3.13016	1.000	-8.1153	8.7136
		3.00	-2.77778	3.73248	1.000	-12.8114	7.2558
	1.00	00	-2.59477	3 06033	1.000	-10.8215	5.6320
		2.00	-2.29563	1.80054	1.000	-7.1358	2.5446
		3.00	-5.37255	2.71578	.303	-12.6731	1.9280
	2.00	00	-.29915	3.13016	1.000	-8.7136	8.1153
		1.00	2.29563	1.80054	1.000	-2.5446	7.1358
		3.00	-3.07692	2.79423	1.000	-10.5883	4.4345
	3.00	.00	2.77778	3.73248	1.000	-7.2558	12.8114
		1.00	5.37255	2.71578	.303	-1.9280	12.6731
		2.00	3.07692	2.79423	1.000	-4.4345	10.5883
HR_vt	.00	1.00	15.36842	8.8781a	.524	-8.6667	39.4035
		2.00	18.25000	9.06065	.285	-6.2791	42.7791
		3.00	16 00000	10 06572	696	-11.2500	43.2500
	1.00	00	-15.36842	8.87818	.524	-39.4035	8.6667
		2.00	2.88158	4.64801	1.000	-9.7016	15.4647
		3.00	63158	6.38964	1.000	-16.6665	17.9297
	2 00	00	-18.25000	9.06065	285	-42.7791	6.2791
		1.00	-2.88158	4.64801	1.000	-15.4647	9.7016
		3.00	-2.25000	6.64084	1.000	-20.2282	15.7282
	3.00	00	-16.00000	10.06572	.696	-43.2500	11.2500
		1.00	.63158	6.38064	1.000	17.0207	16.6665
		2.00	2.25000	6.64084	1.000	-15.7282	20.2282
V02mlkg_vt	00	1.00	2.66249	1.60963	607	-1.6685	6.9935
		2.00	2.97451	1.63089	.427	-1.4137	7.3627
		3.00	2.11835	1.86260	1.000	-2.8933	7.1300
	1.00	.00	-2.66249	1.60963	.607	-6.9935	1.6685
		2.00	31201	86059	1.000	-2 0036	26276
		3.00	-.54414	1.24503	1.000	-3.8941	2.8059
	2.00	.00	-2.97451	1.63089	.427	-7.3627	1.4137
		1.00	-.31201	.86059	1.000	-2.6276	2.0036
		3.00	-.85615	1.27240	1.000	-4.2798	25675
	3.00	00	-2.11835	1.86260	1.000	-7.1300	2.8933
		1.00	.54414	1.24503	1.000	-2.8059	3.8941
		2.00	85615	1.27240	1.000	-2.5675	4.2798
RER_vt	00	1.00	07547	04141	428	-.0360	1869
		2.00	09040	.04196	.201	-.0225	.2033
		3.00	.07374	.04792	.762	-.0552	.2027
	1.00	00	-.07547	.04141	.428	-.1869	.0360
		2.00	01493	02214	1.000	-.0446	.0745
		3.00	-.00173	.03203	1.000	-.0879	.0845
	2 00	00	- 09040	04196	201	- 2033	0225
		1.00	-.01493	.02214	1.000	-.0745	.0446
		3.00	-.01667	.03274	1.000	-.1048	.0714
	3.00	00	-.07374	.04792	.762	-.2027	.0552
		1.00	00173	03203	1.000	-.0845	0879
		2.00	01667	.03274	1.000	-.0714	.1048

Table 14. Analysis of Variance for CPET Variables at Peak Exercise and Recovery by Berlin Risk Score

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
HR_max	Between Groups	4437.803	3	1479.268	3.046	.032
	Within Groups	51479.188	106	485.653		
	Total	55916.991	109			
SBP_max	Between Groups	2553.203	3	851.068	1.128	.341
	Within Groups	80700.761	107	754.213		
	Total	83253.964	110			
DPB_max	Between Groups	668.345	3	222.782	1.265	.290
	Within Groups	18844.214	107	176.114		
	Total	19512.559	110			
V02mlkg_max	Between Groups	116.615	3	38.872	.854	.468
	Within Groups	4735.279	104	45.532		
	Total	4851.894	107			
RER_max	Between Groups	.006	3	.002	.091	.965
	Within Groups	2.202	106	.021		
	Total	2.208	109			
HRR1	Between Groups	1593.854	3	531.285	1.157	.330
	Within Groups	47771.109	104	459.338		
	Total	49364.963	107			
SBP_reef	Between Groups	5687.349	3	1895.783	2.667	.052
	Within Groups	72494.274	102	710.728		
	Total	78181.623	105			
LastYearRecPA	Between Groups	11130872.42	3	3710290.807	2.761	.046
	Within Groups	141082058.3	105	1343638.651		
	Total	152212930.8	108			

Table 15. Bonferroni Post Hoc Test for CPET Variables at Peak Exercise and Recovery by Berlin Risk Score

Multiple Comparisons

Bonferroni

Deoendent Variable	m Berlin Risk Score	(J) Berlin Risk Score	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
HR_max	.00	1.00	21.50113	7.99204	.050	.0132	42.9891
		2.00	24.14530*	8.14948	.023	2.2340	46.0566
		3.00	23.35043	9.55611	.097	-2.3428	49.0437
	1.00	.00	-21.50113	7.99204	.050	-42.9891	-.0132
		2.00	2.64417	4.72905	1.000	-10.0707	15.3590
		3.00	1.84929	6.87526	1.000	-16.6360	20.3346
	2.00	.00	-24.14530	8.14948	.023	-46.0566	-2.2340
		1.00	-2.64417	4.72905	1.000	-15.3590	10.0707
		3.00	-.79487	7.05766	1.000	-19.7706	18.1809
	3.00	.00	-23.35043	9.55611	.097	-49 0437	2.3428
		1.00	-1.84929	6.87526	1.000	-20.3346	16.6360
		2.00	.79487	7.05766	1.000	-18.1809	19.7706
SBP_max	.00	1.00	7.46889	9.94413	1.000	-19.2629	34.2006
		2.00	-.18803	10.15580	1.000	-27.4888	27.1127
		3.00	-6.18803	11.90873	1.000	-38.2010	25.8249
	1.00	.00	-7.46889	9.94413	1.000	-34.2006	19.2629
		2.00	-7.65692	5.86712	1.000	-23.4289	8.1150
		3.00	-13.65692	8.54989	.679	-36.6407	9.3268
	2.00	.00	.18803	10.15580	1.000	-27.1127	27.4888
		1.00	7.65692	5.86712	1.000	-8.1150	23.4289
		3.00	-6.00000	8.79518	1.000	-29.6431	17.6431
	3.00	.00	6.18803	11.90873	1.000	-25.8249	38.2010
		1.00	13.65692	8.54989	.679	-9.3268	36.6407
		2.00	6.00000	8.79518	1.000	-17.6431	29.6431
DPB_max	.00	1.00	4.87111	4.80526	1.000	-8.0464	17.7886
		2.00	.16239	4.90754	1.000	-13.0300	13.3548
		3.00	-.65812	5.75461	1.000	-16.1276	14.8114
	1.00	.00	-4.87111	4.80526	1.000	-17.7886	8.0464
		2.00	-4.70872	2.83514	.598	-12.3301	2.9127
		3.00	-5.52923	4.13153	1.000	-16.6356	5.5771
	2.00	.00	-.16239	4.90754	1.000	-13.3548	13.0300
		1.00	4.70872	2.83514	.598	-2.9127	12.3301
		3.00	-.82051	4.25006	1.000	-12.2455	10.6045
	3.00	.00	.65812	5.75461	1.000	-14.8114	16.1276
		1.00	5.52923	4.13153	1.000	-5.5771	16.6356
		2.00	.82051	4.25006	1.000	-10.6045	12.2455
V02mlkg_max	.00	1.00	4.07564	2.57306	.697	-2.8450	10.9963
		2.00	3.48046	2.62481	1.000	-3.5794	10.5403
		3.00	3.94933	3.03214	1.000	-4.2061	12.1048
	1.00	.00	-4.07564	2.57306	.697	-10.9963	2.8450
		2.00	-.59518	1.45857	1.000	-4.5182	3.3279
		3.00	-.12631	2.10515	1.000	-5.7884	5.5358
	2.00	.00	-3.48046	2.62481	1.000	-10.5403	3.5794
		1.00	.59518	1.45857	1.000	-3.3279	4.5182
		3.00	.46887	2.16809	1.000	-5.3626	6.3003
	3.00	.00	-3.94933	3.03214	1.000	-12.1048	4.2061
		1.00	.12631	2.10515	1.000	-5.5358	5.7884
		2.00	-.46887	2.16809	1.000	-6.3003	5.3626

*.The mean difference is significant at the 0.051evel.

Table 15. Bonferroni Post Hoc Test for CPET Variables at Peak Exercise, Recovery and Recreational PA by Berlin Risk Score con't

Multiple Comparisons

Bonferroni

OtWI:!!Idt:Hil Va'ioiJit!'	I Bt:!'llin Rik Scull:!!	!Jl Bollin Ri:sk Stul!:!	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence InteiVal	
						Lower Bound	Upper Bound
RER_max	.00	1.00	.01736	.05219	1.000	-.1230	.1577
		2.00	.00687	.05343	1.000	-.1368	.1505
		3.00	-.00137	.06250	1.000	-.1694	.1667
	1.00	.00	-.01736	.05219	1.000	-.1577	.1230
		2.00	-.01048	.03102	1.000	-.0939	.0729
		3.00	-.01872	.04487	1.000	-.1394	.1019
	2.00	.00	-.00687	.05343	1.000	-.1505	.1368
		1.00	.01048	.03102	1.000	-.0729	.0939
		3.00	-.00824	.04631	1.000	-.1328	.1163
	3.00	.00	.00137	.06250	1.000	-.1667	.1694
		1.00	.01872	.04487	1.000	-.1019	.1394
		2.00	.00824	.04631	1.000	-.1163	.1328
HRR1	.00	1.00	7.79592	8.65990	1.000	-15.4963	31.0881
		2.00	11.77289	8.79759	1.000	-11.8896	35.4354
		3.00	16.43956	10.04755	.629	-10.5849	43.4641
	1.00	.00	-7.79592	8.65990	1.000	-31.0881	15.4963
		2.00	3.97698	4.59914	1.000	-8.3932	16.3471
		3.00	8.64364	6.68640	1.000	-9.3405	26.6278
	2.00	.00	-11.77289	8.79759	1.000	-35.4354	11.8896
		1.00	-3.97698	4.59914	1.000	-16.3471	8.3932
		3.00	4.66667	6.86379	1.000	-13.7946	23.1279
	3.00	.00	-16.43956	10.04755	.629	-43.4641	10.5849
		1.00	-8.64364	6.68640	1.000	-26.6278	9.3405
		2.00	-4.66667	6.86379	1.000	-23.1279	13.7946
SBP_reel	.00	1.00	27.77083	11.54390	.108	-3.2902	58.8318
		2.00	17.20513	11.69096	.865	-14.2516	48.6618
		3.00	16.35897	13.15774	1.000	-19.0444	51.7623
	1.00	.00	-27.77083	11.54390	.108	-58.8318	3.2902
		2.00	-10.56571	5.74723	.413	-26.0297	4.8983
		3.00	-11.41186	8.33536	1.000	-33.8397	11.0160
	2.00	.00	-17.20513	11.69096	.865	-48.6618	14.2516
		1.00	10.56571	5.74723	.413	-4.8983	26.0297
		3.00	-.84615	8.53787	1.000	-23.8189	22.1266
	3.00	.00	-16.35897	13.15774	1.000	-51.7623	19.0444
		1.00	11.41186	8.33536	1.000	-11.0160	33.8397
		2.00	.84615	8.53787	1.000	-22.1266	23.8189
LasiYearRecPA	.00	1.00	1027.95355	420.37410	.097	-102.5006	2158.4077
		2.00	1077.25071	429.71164	.082	-78.3136	2232.8150
		3.00	1378.89529*	502.64302	.043	27.2067	2730.5839
	1.00	.00	-1027.95355	420.37410	.097	-2158.4077	102.5006
		2.00	49.29716	250.55959	1.000	-624.4982	723.0925
		3.00	350.94174	361.63243	1.000	-621.5465	1323.4300
	2.00	.00	-1077.25071	429.71164	.082	-2232.8150	78.3136
		1.00	-49.29716	250.55959	1.000	-723.0925	624.4982
		3.00	301.64458	372.44561	1.000	-699.9220	1303.2112
	3.00	.00	-1378.89529	502.64302	.043	-2730.5839	-27.2067
		1.00	-350.94174	361.63243	1.000	-1323.4300	621.5465
		2.00	-301.64458	372.44561	1.000	-1303.2112	699.9220

*. The mean difference is significant at lhe 0.05 level.

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