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Nutritional status and body composition in patients with peripheral arterial disease: A cross-sectional examination of disease severity and quality of life

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Abstract

Nutritional and body weight recommendations for cardiovascular diseases are well established, yet there are no equivalent guidelines for peripheral arterial disease (PAD). This cross-sectional study measured the prevalence of cardiovascular-related nutritional and body composition risk factors in sixty PAD patients and their association with PAD severity. A diet that exceeds daily recommended intake of fat and that falls short of recommended intakes of fiber, folate, and vitamin D was associated with increased leg pain and walking difficulty. Increased body fat and waist circumference were associated with diminished walking ability and poorer psychosocial quality of life. Future prospective investigations are merited to inform both PAD clinical care and disease management guidelines.

Keywords

Body composition; nutrition; obesity; peripheral arterial disease; quality of life

Introduction

Background

Peripheral arterial disease (PAD) is a pressing public health concern. Despite its known high prevalence (Mahoney et al. 2008; Norgren et al. 2010) and very high health economic costs (Smolderen et al. 2010), PAD garners substantially less investigational attention than other cardiovascular diseases (CVDs). PAD is biologically distinct in its effect on ambulation and physical function, and unlike other CVDs, is often associated with major exertional lower extremity ischemic symptoms (claudication) that are experienced as muscle fatigue, discomfort, pain, and diminished walking capacity. It is also associated with progressive

functional impairment that profoundly affects physical and psychosocial quality of life and is the single most frequent cause of limb amputation (Hirsch et al. 2006). Currently, the key intervention offered to PAD patients is revascularization; however, the benefits are not always durable (Stoner et al. 2008). Intersocietal ACC-AHA Guidelines for the Management of Patients with PAD (2005 and 2011) provide no focus on prevention of incident PAD or on the potential efficacy of nutritional or body composition–related interventions (Rooke et al. 2013).

Table 1 presents the current CVD evidence and guidelines for nutrition, body composition, and related factors in comparison to existing PAD research. There is evidence suggesting an association between certain nutrition and body composition–related variables and PAD; however, the data are limited and several aspects remain unexamined. There remains a need to establish whether existing CVD guidelines for nutrition and body composition can be applied to individuals with PAD, or whether PAD is sufficiently biologically distinct so as to warrant its own clinical guidelines. This study's purpose is two-fold: first, to evaluate the prevalence of CVD-related nutritional and body composition markers in a PAD population and second, to assess whether and to what extent these markers may be associated with the severity of patients' PAD disease burden. We hypothesize that (1) the prevalence of risk factors in the sample population is equal to or greater than that of the general CVD population and that (2) increased severity of patients' disease, whether defined as physical symptoms or as psychosocial burden, is significantly associated with having more or more severe nutritional and body composition risk factors. If there is evidence to suggest such associations, then future interventions may aim to benefit PAD symptoms and clinical progression by targeting these nutritional and body composition factors.

Methods and materials

Study design

We conducted a cross-sectional study of the nutritional status, body composition, and disease burden of sixty PAD patients. Comparable data for CVD-specific cohorts and the general U.S. population are well documented (Wright and Ervin 1994), and both served as comparisons for this pilot's findings. Therefore, no separate control group was used.

Recruitment and study population

Participants were identified through a search of a university-affiliated hospital clinical database and through direct referral from three Twin Cities metropolitan vascular specialty clinics. To be eligible, a patient had to have an established clinical PAD diagnosis, regardless of revascularization history or symptom status. Other inclusion criteria were consistent access to a telephone, the ability to read and understand spoken English, and the ability to attend research clinic visits. Patients were excluded from participation if they were bilateral amputees, thus rendering ankle-brachial index (ABI) measurement impossible. Patients were also excluded if they had undergone a revascularization procedure within the previous 6 months, thereby making the distinction between postoperative and PAD-related symptoms difficult. Potential participants were initially contacted by telephone and then met at an initial screening visit to provide written informed consent. The study protocol and study-

related documents were approved by the University of Minnesota Institutional Review Board.

Anthropomorphic, dietary, and clinical measures

Participants were asked to come to a university-affiliated research clinic for data collection. Surveyed information included general demographics and tobacco, alcohol, and prescription medication use. Survey questions regarding medical history included previous diagnoses of PAD, myocardial infarction, stroke, cancer, overweight/obesity, and diabetes. Questions regarding physical activity assessed the strenuousness (e.g., mild activity such as leisurely walking or strenuous activity such as jogging), duration, and weekly frequency of exercise. Each participant underwent a total-body dual X-ray absorptiometry (DXA) scan (Kendler et al. 2013) to assess adiposity, and a staff clinician measured height, weight, and hip circumference. Participants were asked to complete three nonconsecutive 24-hour dietary recall interviews within a 2-month period; the first was conducted in person, with two additional recalls over the telephone. For participants who completed all three recalls, one recall assessed food intake on a weekend day, and two recorded weekday intakes. This multipass approach to recording nutritional intakes on varying days of the week is considered the optimal method for collecting a reliable assessment of dietary habits (Wright 1994). A certified interviewer assessed eating habits using the Nutrition Data System for Research (NDSR), a software application developed at the University of Minnesota Nutrition Coordinating Center (NCC) that facilitates standardized recall collection (Feskanih et al. 1989). Participants used scale models of foods and serving sizes to report their food intake and were given the NCC Food Amounts Booklets for use during telephone surveys. Participants' daily dietary intakes were calculated using the NCC Food and Nutrient Database (Sievert, Schakel, and Buzzard 1989) and evaluated for portion size, ingredients, nutrient composition, and preparation method. Average daily intake values were computed for analysis.

Measures of PAD severity included ABI, the Walking Impairment Questionnaire (WIQ) (Gardner et al. 1991), and the King's College Hospital's Vascular Quality of Life Questionnaire (VascuQOL) (Morgan et al. 2001). The ABI was measured using a 5 mHz Doppler device (Elite-100 R, Nicolet Vascular Inc., Golden, CO). Systolic blood pressures were recorded at the brachial arteries of both upper extremities and at the dorsalis pedis and posterior tibial arteries using a standard technique (Aboyans et al. 2012). The same technique was employed on each patient, regardless of the revascularization status of either leg. Each participant underwent two ABI measurements while in a supine position, and the average of each pair of readings was recorded. For this study, we utilized the lower ABI value for each participant. Scores were recorded as continuous measures, as well as categorized by standard clinical guideline-based diagnostic cut points (Fowkes et al. 2008): abnormal (< 0.90), borderline ($0.91-0.99$), normal ($1.00-1.40$), or noncompressible (> 1.40).

The WIQ is a validated (Sagar et al. 2012) twenty-item survey designed to measure the severity of PAD limitation of physical function. It is the predominant instrument used for capturing self-reported walking ability in PAD patients with symptomatic claudication and evaluates four components: distance, speed, stair climbing, and pain (Hirsch et al. 2006;

Mays et al. 2011), with ranges of difficulty within each component, (e.g., the distance component assesses difficulty ranging from walking indoors around one's home to walking the equivalent of five city blocks, or 1,500 feet; the stairs component assesses a range from the ability to climb one flight of stairs to the ability to climb three flights of stairs). Participants answered items on a Likert scale from 0 for "unable to do" to 4 for "no difficulty," and responses were weighted according to the relative difficulty of tasks within the range of each component. When respondents avoided certain activities altogether due to PAD symptoms, they were asked to choose "Didn't do for other reasons."

The VasculQOL is a validated twenty-five-item survey (Morgan et al. 2001) that assesses patients' perceived quality of life in five domains, two physical and three psychosocial—pain, activity, symptoms, emotional, and social. All questions are equally weighted and scored from 1 to 7; for example, in response to "In the last 2 weeks I have had pain in the foot or leg when I am at rest," choosing "All of the time" is coded as a 1, and choosing "None of the time" is coded as a 7. Domain subscores were calculated as averages of the questions assigned to each domain.

Biomarkers

A fasting blood sample was collected from each participant, aliquoted and separated, and frozen at -20°C until analysis. Folic acid concentrations were assessed from whole erythrocytes using chemiluminescent immunoassay (Quest Diagnostics, Wood Dale, IL). Serum vitamin D (25-hydroxy calcidiol[ng/mL]) was measured using the Diasorin LIAISON[®] chemiluminescence method (Heartland Assays, Ames, IA). All but nine participants reported taking prescription medications for lowering cholesterol and/or altering blood lipid profiles, and therefore these factors were not measured. Commercially available Quantikine human ELISA kits (R&D Systems, Minneapolis, MN) were used to measure serum adiponectin concentrations (Kurzer Lab, Saint Paul, MN). For genotyping, whole blood was extracted using a QIAamp Mini Blood Kit (Qiagen) and manufacturer's protocol. The methylenetetrahydrofolate reductase (*MTHFR*) gene encodes and determines the efficiency of MTHFR, an enzyme that is crucial for folate metabolism and homocysteine (Hcy) homeostasis. Amplified 15 ng DNA was assessed for *MTHFR* C667T SNPs using a TaqMan SNP Genotyping Assay (Life Technologies Co, Grand Island, NY). The Lightcycler 480 Probes Master (Roche) master mix was run under cycling conditions established by the manufacturer and collected on a real-time PCR machine (Institute of Human Genetics, University of Minnesota Masonic Cancer Center, Minneapolis, MN).

Data analysis

Data analyses tested first the prevalence and frequency of CVD-related risk factors in the population and second, the extent to which these risk factors were associated with PAD severity in terms of ABI, WIQ scores, and VasculQOL scores. All analyses were conducted with the sample as a whole and stratified by revascularization status. Since PAD is a progressive disease and participants had varying durations since diagnosis, stratification accounted for possible improvements in pain and symptoms that revascularized patients may have experienced relative to patients who had never undergone such treatment(s).

Continuous exposure variables, such as ABI and serum biomarkers, were first analyzed against severity measures using linear regression modeling. Severity measures were modeled individually as ABI, WIQ scores and sub-scores, VascuQOL scores and subscores, and as aggregates of physical severity and psychosocial severity. The initial model used the full data set, and a second refined model omitted outliers and heavily influential data points. Only associations that were significant in both models were considered statistically significant. No significant confounding by key demographic variables (age, gender, level of educational attainment) was detected, and Spearman's correlation coefficients were generated to evaluate monotonic relationships. Ordinal exposure variables, such as binary yes/no nutrient deficiency and obesity status, were analyzed using Cochran-Mantel-Haenszel tests and proportional-odds cumulative logit modeling. Categories with small frequencies (< 5) were analyzed both separately and as collapsed categories. As this was a limited patient sample, we purposefully did not set any Bonferroni corrections to limit the significance of these multiple comparisons. Statistical analyses were conducted using SAS software, version 9.3 (SAS Institute Inc., Cary, NC).

Results

Sixty-four PAD patients consented to participation; however, sixty completed data collection. Demographic, nutritional, body composition, and PAD severity characteristics of the study cohort are presented in Table 2.

All revascularized patients had undergone their procedures a minimum of 6 months prior to data collection. Half ($n = 30$) of the cohort reported having a previous clinical diagnosis of coronary heart disease; nine participants reported a history of stroke; and four had a history of both conditions. Over a third were diagnosed with type 2 DM, and approximately 75% were classified as overweight or obese. Sixty percent of participants fell into the low-cardiovascular risk category of waist circumference (< 88 cm for females, < 102 cm for males [“Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults—The Evidence Report. National Institutes of Health” 1998]), but 95% fell into the high-risk waist-to-hip-ratio (WHR) category (mean = 0.99) (Nishida, Ko, and Kumanyika 2010)). DXA scan results similarly yielded a mean android:gynoid ratio of 1.07, and means of both percent total body fat and percent truncal fat were approximately 35%.

Twenty-five participants completed all three dietary recalls; two completed two recalls; and thirty-three completed only the initial in-person recall. Mean daily energy intake was $1,976 \pm 789$ kcal, and revascularized patients were significantly more likely than patients with native vasculature (NV) to consume the AHA-recommended daily diet of 2,000 calories or less ($p = .03$) (Lichtenstein et al. 2006). NV patients, however were significantly more likely than revascularized patients to consume the minimum recommended daily calcium intake (1,000 mg) (Institute of Medicine Committee to Review Dietary Reference Intakes for Vitamin D and Calcium 2011), ($p = .04$). Over 58% of the participants had insufficient or clinically deficient serum 25(OH)D concentrations. Participants generally reported consuming diets that exceed the daily recommended amount of protein, refined carbohydrates (e.g., white bread and pasta, no more than 65 g/day), saturated fat, cholesterol, and added sodium. Participants consumed ≥ 2 servings/day of fruits, vegetables, and whole

grains (versus recommended intakes [U.S. Department of Agriculture and U.S. Department of Health and Human Services 2010]), and despite multivitamin supplement use in over half of participants, the majority did not meet daily recommended intakes (DRI) (“Dietary Guidelines for Americans 2010)) for zinc or vitamins A, C, E, or K. For *MTHFR*, five participants were homozygous for the CC wild type, and the remaining fifty-five were split between CT and TT genotypes.

Participants did not differ by revascularization status for any other dietary variable, body composition factor, ABI, WIQ component, or VasculQOL domain. WIQ scores for speed and distance components were worse (lower) than for pain and stairs. On average, patients scored no higher than 4.9 on VasculQOL domains (7 being the most adversely affected and 0 the least), with social and emotional scores worse (higher) than those for the physical domains of pain, activity, or symptoms.

Table 3 presents results of linear regression tests for various nutritional and body composition factors in relation to WIQ scores. Nine comparisons are significantly associated with WIQ scores in both the total and refined models. Of particular note, increasing percentages of total body fat are significantly associated with decreasing WIQ scores for the overall, distance, speed, and stairs scores. Increasing BMI and waist circumference are significantly associated with lower WIQ stairs scores (-1.7 ± 0.6 ; $p = .008$ and -0.6 ± 0.3 ; $p = 0.038$, respectively). Selected regression estimates are visually presented as scatter plots in Figure 1. Spearman correlation analysis for ABI and WIQ scores (not pictured) yield comparable findings. Among dietary variables, dietary cholesterol is inversely correlated with WIQ pain scores ($r = -0.26$; $p = .05$), and dietary fiber is positively related to WIQ stairs ($r = +0.26$; $p = .04$). The percent of energy intake as fat is inversely associated with ABI ($r = -0.31$; $p = .02$), whereas red blood cell folate is inversely associated with WIQ speed ($r = -0.29$; $p = .03$). Mirroring regression estimates, both BMI and waist circumference are inversely correlated with WIQ stairs ($r = -0.32$; $p = .01$ and $r = -0.27$; $p = .04$, respectively).

Figure 2 presents nine selected Cochran-Mantel-Haenszel tests comparing nutrition and body composition variables to ABI measurements and VasculQOL scores. Participants with larger waist circumferences are significantly more likely to report increasingly severe VasculQOL symptoms ($p = .02$). Similarly, participants who fall in higher BMI categories are significantly more likely to report a greater VasculQOL social, emotional, and total burden (p -values .01, .001, and .02, respectively). Among dietary variables, lower serum vitamin D status is associated with higher VasculQOL pain scores ($p = .007$), and as with the Spearman correlation analysis, increasing total percent of energy intake as fat is associated with lower ABI scores ($p = .04$). Participants who exercise more frequently are more likely to report less severe total VasculQOL and VasculQOL social scores ($p = .02$ and $p = .005$, respectively). Finally, proportional-odds cumulative logit modeling (not pictured) yields one significant association for dietary fat and ABI: At the 21%–35% level of caloric intake as fat, the estimated odds of an ABI score below any diagnostic threshold (abnormal, borderline, normal, noncompressible) are 0.23 times the estimate of odds at the >35% level of fat intake ($p = .04$, CI 0.06–0.91).

Discussion

Few prior studies have reported the dietary patterns, nutritional status, and body composition of patients with PAD, and fewer still have assessed how these factors may be associated with parameters of disease severity (Brostow et al. 2012; McDermott et al. 1997). In this study, we find that the prevalence of nutritional and body composition–related risk factors in PAD patients equals or exceeds that found in CVD cohorts and the general U.S. population. We also find that several, but not all, established CVD risk factors are significantly associated with having a greater physical or psychosocial PAD disease burden.

Of sixty participants, sixteen were normal weight (BMI 18.5–24.99), twenty were clinically overweight (BMI 25–29.99), and twenty-four were clinically obese (BMI ≥ 30). Participants did not vary by BMI (neither continuous nor categorical BMI) for any demographic factor. Nevertheless, higher BMI is significantly associated with a decreased capacity to climb stairs (WIQ stairs) and with a significant negative effect on VasculQOL emotional and social well-being. Similarly, increased total body fat is significantly associated with a decreased ability to climb stairs, shorter maximal walking distances, and impaired walking speed. Obesity research has not reached a clear consensus on what measure of adiposity is most accurate or predictive of disease risk (Heo et al. 2012); however, according to World Health Organization recommendations (WHO 1995), this cohort exceeded recommended cutoffs for both sexes: on average, 31% total body fat among men (versus < 25%) and, on average, 42% total body fat among women (versus < 35%). The association between increased adiposity and diminished physical function and poorer psychosocial quality of life is well established, even independent of other health conditions (Arranz, Rafecas, and Alegre 2014; Preiss, Brennan, and Clarke 2013). Given that PAD is also independently associated with a poorer quality of life and greater risk of depressive-type symptoms (Grenon et al. 2012; O’Neil et al. 2012; Remes et al. 2010), our observations in this study suggest that both dynamics may have an effect on total well-being.

Although over half of participants fell into the low-risk category for waist circumference. Increased waist circumference is associated with a hampered stair-climbing ability and with more severe overall leg pain and discomfort (WIQ overall). Nevertheless, while all but three participants fell into the high-risk category for waist-to-hip ratio, and over two-thirds of the participants had android-gynoid ratios over 1.0, neither factor is associated with any parameter of PAD severity. There is an overall paucity of data examining specific measures of abdominal adiposity in relation to physical function or ambulation; however, a recent longitudinal study observed a significant correlation between increased waist circumference and slower walking speeds, further supporting this study’s findings (Batsis et al. 2014).

Previous research has also established that adiponectin, which is secreted by abdominal adipocytes, is inversely correlated with abdominal adiposity and vascular risk (Berg and Scherer 2005). We observe that a 1 ng/mL increase in adiponectin concentration is associated with a 19-point decrease in WIQ distance scores. The biological mechanisms involved are unclear, and to date there have been no other studies of adiponectin and quality of life. However, our results are supported by Golledge et al.’s finding of a positive

association between serum adiponectin concentrations and mean walking distance in PAD patients (Golledge et al. 2007).

This study also observed a significant association between physical activity and total (VasculQOL total) and social quality of life. Cochran-Mantel-Haenszel graphs in Figure 2 suggest that participants who engage in any type of physical activity, whether mild, moderate, or strenuous, on any regular basis, are less likely to feel that PAD adversely affects their social lives, independent of weight status. Although further proportional-odds analysis did not reveal significant associations, these trends indicate that sedentary patients may experience more social isolation and depressed moods than their more active counterparts. Depressive mood disorders are highly prevalent among patients with various CVD conditions, and a depressed state can significantly contribute to worse vascular outcomes (Arseven et al. 2001; Grenon et al. 2012). Depressed patients may also be less likely to participate in research studies, which underscores the need to develop more comprehensive assessment tools and recruitment methodologies.

Given the sample size and cross-sectional nature of this study, causal associations cannot be formulated. Nevertheless, it can be concluded that excess adiposity is associated with diminished walking ability and a poorer quality of life among PAD patients. Established CVD guidelines promote the benefits of weight modification and dietary changes in reducing disease risk and progression (Jensen et al. 2013). Prospective studies of PAD patients are needed to determine whether specific factors such as percent body fat and waist circumference are indeed significant, modifiable predictors of disease burden, or whether they are proxies for a more physically active lifestyle.

Nutritional factors show variable associations. Nearly all participants were taking lipid-modifying medications, and we elected not to analyze serum lipid profiles. Nevertheless, increased dietary cholesterol is correlated with a more severe pain burden among participants (WIQ pain). Compared to endogenous synthesis, dietary cholesterol constitutes the minor fraction of total cholesterol in the body, and this result is likely indicative of broader dietary patterns within the cohort. The percent of energy intake as fat is negatively correlated with ABI values, and participants consuming fat calories in excess of the recommended 35% (USDHHS 2010) experienced significantly greater odds of having lower (more severe) ABI values. Greater total energy intake is unexpectedly associated with higher WIQ distance scores. However, given that over half the participants reported consuming fewer than 2,000 calories per day, it is possible that participants with greater energy intake were more likely to consume a more nutritionally complete diet.

Increased dietary fiber consumption is associated with a greater ability to climb stairs. PAD patients consumed a daily average of 22 grams of dietary fiber, which, although higher than the U.S. average of 15 grams, still falls short of recommendations (McGuire 2011; Trumbo et al. 2002). As with other CVD, it is thought that dietary fiber influences PAD symptoms by improving blood glucose control and by mediating cholesterol synthesis (Satija and Hu 2012). This study also observed a 26-point increase in WIQ stairs scores for every 1 gram increase in fiber intake. Although a finding of such magnitude is likely a spurious anomaly,

there is evidence of a link between increased fiber intake and decreased CVD events and related mortality (Bazzano et al. 2003; Pereira et al. 2004).

Subjects with increased serum vitamin 25(OH)D reported less-severe limb pain on the VasculQOL pain domain. Thirty-five (58%) participants had serum 25(OH)D concentrations at suboptimal levels (< 30 ng/mL). Recent NHANES data observed that approximately 43% of the assessed U.S. population had insufficient or deficient serum vitamin D concentrations (Deng et al. 2013), whereas other estimates concluded that between half and two-thirds of adults may be vitamin D deficient (Norman et al. 2007). Hypovitaminosis D is a significant risk factor for both PAD (Fahrleitner-Pammer et al. 2005; Melamed et al. 2008) and CHD and stroke (Holick 2005, 2009), although the mechanisms for vitamin D's action in vascular disease etiology remain unclear. One hypothesized pathway includes promotion of calcium deposition in endothelial tissue. As well, increased calcium loss may lead to bone pain (Garcia-Canton et al. 2011; Zagura et al. 2011). Calcium metabolism is dependent on vitamin D intake and synthesis, and while the majority of participants met daily calcium intake requirements (revascularized participants were significantly more likely both to meet intake requirements and to use calcium supplements), our findings suggest inadequate vitamin D might contribute to unabsorbed dietary calcium and more-severe PAD-related pain. McDermott et al.'s recent prospective analysis observes a greater prevalence of vitamin D insufficiency in PAD patients compared to healthy controls (20% versus 14%), and also observes that participants with lower vitamin D levels experience a significantly faster decline in maximal walking distance and velocity (McDermott et al. 2014), although there is no association with mortality. Stricker et al. (2012) do not observe significant changes in endothelial function or coagulation markers in a small vitamin D supplementation trial, and larger supplementation trials are needed to determine whether this functional decline can be slowed or mitigated.

Greater RBC folate concentrations are significantly associated with lower WIQ speed scores, but since the score decrease is minimal (~one-tenth of a point per 1 ng/mL), this association may be spurious. Over 30% of participants were clinically deficient in folate, likely resulting from the participants' generally low intake of folate-rich foods (e.g., fruits, vegetables, and whole grains). Inadequate folate intake is associated with increased CHD and PAD risk, as well as with increased serum Hcy concentrations, which is an independent risk factor for PAD (Hirsch et al. 2006; Santos et al. 2010). *MTHFR* genotype might mediate these associations, and in this study, heterozygous type frequency was nearly identical to the general population (45% compared to 43%) (Guerzoni et al. 2007; Wald, Law, and Morris 2002). Unexpectedly, and after reconfirming genotyping data, we observe that only 8.3% of the participants had the CC wild type, compared to 47% in the general population (Guerzoni et al. 2007; Wald, Law, and Morris 2002), and 46.7% was homozygous for the TT variant, compared to 5%–10% of the general population (Guerzoni et al. 2007; Jacques et al. 1996; Wald, Law, and Morris 2002). The TT variant encodes a less efficient MTHFR protein (~50% reduced activity [Verhoeff et al. 1998]), which in turn results in decreased folate metabolism and may drive increases in Hcy concentrations. It remains unclear, however, whether the TT genotype is an important mediator of folate and Hcy-related PAD risk (Zintzaras and Zdoukopoulos 2009), and we are unable to substantiate why the majority of our participants were homozygous for the variant. Previous CHD and PAD genotyping

studies have yielded discordant results, with some reporting moderately higher frequency of the TT type and others observing equal or lower frequencies (Guerzoni et al. 2007; Jacques et al. 1996; Verhoeff et al. 1998).

To our knowledge, this is the first attempt to comprehensively assess markers of PAD severity in relation to nutrition and body composition. This is also the first study to use precise quantitative and qualitative tools to measure PAD patients' dietary habits without relying on generalized surveys. As participants tended to have consistent daily eating habits with minimal intrapersonal variation, this strengthens the reliability of our findings. We find that overarching dietary patterns mirror dietary trends observed in both CVD-specific populations and the total U.S. population (Britten et al. 2012; Grooms et al. 2013; Troesch et al. 2012). Like CVD patients and adult Americans in general, participants consumed a diet that is relatively low in essential micronutrients and high in refined carbohydrates, added sodium, and added sugars. Given the similarities in diet between this cohort and other CVD populations, it is reasonable to conclude that modeling future PAD intervention trials on existing CVD dietary guidelines merits exploration.

There were a number of limitations inherent in this study. First, we note the relatively small sample size. However, our modest sample size is typical for PAD clinical treatment or outcome studies. The WIQ and VasuQOL surveys are validated for PAD patients in studies of this size and are correlated (Mehta et al. 2003), and we were able to detect significant associations. As our sample was recruited from a vascular specialty clinic (convenience) population, our findings may not be generalizable to the larger PAD disease burden than might be derived from a primary care population. Patients with severely limited physical mobility or age-related cognitive difficulties might differ in eating habits or body composition from a broader population-based sample. This study also excluded participation of individuals with PAD who were asymptomatic and excluded individuals "at risk" for incident PAD. As a cross-sectional study, the associations we have reported between nutritional variables and PAD severity cannot establish directions of causality. Finally, self-reported dietary and lifestyle habits may have been affected by recall bias such as underreporting of energy intake and other sources of error. Difficulties with recall also limited our ability to gauge the effect of duration of PAD illness on participants' disease severity, as the majority of patients reported having PAD for multiple years and were not able to recall a reliable time of diagnosis.

Conclusions

These data demonstrate, for the first time, potential associations between clinical and psychosocial PAD symptoms and self-reported nutritional status and body composition. We observe that individuals with PAD report eating habits that are similar to those of the broader U.S. population and to other cohorts with other CVDs. However, since PAD biologically differs from other common CVDs, it is possible that the nutritional contributions to each PAD risk factor may differ as well. Therefore, these data can provide the basis for a much broader evaluation of the effect of nutrition on incident PAD, PAD progression, recovery from revascularization interventions, and psychosocial well-being. The current data suggest that individuals with PAD might benefit from increased consumption of dietary fiber,

vitamin D-rich foods, folate-rich foods, as well as from efforts to modify body composition for overweight and obese PAD patients. These actionable nutritional measures should be incorporated into future intervention trials to assess potential efficacy. Future research can be designed that would confirm the likely effect of nutrition on PAD outcomes and that could inform PAD care guidelines, with a potential benefit on both patient outcomes and health-care costs.

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Figure 1.

Selected scatter plots of regression estimates for nutritional and body composition variables in relation to Walking Impairment Questionnaire (WIQ) scores.

Figure 2. Selected Cochran-Mantel-Haenszel associations comparing nutritional and body composition variables to ankle-brachial index and Vascular Quality of Life (VascuQOL) scores.

Table 1.

Dietary, body composition, and related guidelines for CVD compared to existing PAD data.

Factor	Current consensus	Guideline/ recommendation	Supporting evidence in PAD research ¹
Total energy intake	↑ intakes associated with ↑ risk of CVD and CVD-related events	2,000 kcal/day ± kcal depending on activity level	-
Cholesterol		300 mg/day	✓
Total fat		20%–35% of total energy intake	✓
Saturated fat		5%–6% of total energy intake (~13 gm/day)	✓
Added sugars		Maximum 100–150 kcal/day (6–9 teaspoons)	-
Sodium		Aim for < 1,500 mg/day, maximum 2,400 mg/day	-
Body mass index	↑ values associated with ↑ CVD risk	Maintain weight within normal range (18.5–24.99)	✓
Waist circumference		88 cm women, 102 cm men	✓
Waist-to-hip ratio		< 0.85 women, < 0.90 men	✓
Vitamin D	Deficiency associated with ↑ CVD risk	15 µg/day	✓
Folate		400 µg/day	✓
n-3 fatty acids	↑ intakes associated with ↓ CVD risk	2 servings fish/wk (1.1–1.6 gm/day)	✓
n-6 fatty acids		Use n-6-rich cooking oils (13–17 gm n-6/day)	✓
Whole grains		Constitute at minimum 50% of grains eaten	✓
Fiber		25 gm/day women, 38 gm/day men	✓
<i>MTHFR</i> genotype	Cys667Thr variant reduces efficiency of homocysteine regulation, may ↑ CVD risk	N/A	✓
Serum adiponectin	↑ concentrations associated with ↑ obesity and ↓ blood glucose control	N/A	✓

Source: Derived from the National Institutes of Health, World Health Organization, and the American Heart Association guidelines.

¹Cholesterol: (59); Total fat: (60); Saturated fat: (59); Body Mass Index: (61–66); Waist circumference: (30,63); Waist-to-hip ratio: (67); Vitamin D: (41,42,68,69); Folate: (70–73); n-3 fatty acids: (70,74); n-6 fatty acids: (59,75); Whole grains: (76,77); fiber: (59,60); *MTHFR* genotype: (78–80); Serum adiponectin: (30,81)

Table 2.

Demographic, nutritional, body composition, and PAD severity characteristics of the study cohort, by revascularization status¹.

	Total n = 60	(%)	NV n = 25	(%)	RV n = 35	(%)	<i>p</i> value
Sex							
Male	40	(66.7)	18	(72.0)	22	(62.9)	0.581
Female	20	(33.3)	7	(28.0)	13	(37.1)	
Age (mean ± SD)	68.7	±10.7	67.8	±10.4	69.3	±11.1	0.587
Race/ethnicity							
White, non-Hispanic	53	(88.3)	22	(88.0)	31	(88.6)	0.642
Non-white	7	(11.7)	3	(12.0)	4	(11.4)	
Annual household income							
< \$20,000	10	(17.0)	4	(16.0)	6	(17.1)	0.919
\$20,000–\$39,999	14	(23.7)	5	(20.0)	9	(25.7)	
\$40,000–\$59,999	12	(20.3)	5	(20.0)	7	(20.0)	
> \$60,000	23	(39.0)	11	(44.0)	12	(34.3)	
Education							
High school	9	(15.0)	1	(4.0)	8	(22.9)	0.382
Some college/vocational school	24	(40.0)	13	(52.0)	11	(31.4)	
College graduate	27	(45.0)	11	(44.0)	16	(45.7)	
Alcohol (drinks/wk)							
0–3	47	(78.3)	18	(72.0)	29	(82.9)	0.324
4–6	4	(6.7)	2	(8.0)	2	(5.70)	
7 +	9	(15.0)	5	(20.0)	4	(11.4)	
Medical history							
History of cardiovascular disease	30	(50.0)	11	(44.0)	19	(54.3)	0.601
History of stroke	10	(16.7)	5	(20.0)	5	(14.3)	0.728
Emphysema and/or COPD	12	(20.0)	5	(20.0)	7	(20.0)	1.000
Cancer	14	(23.3)	4	(16.0)	10	(28.6)	0.357
Atherosclerosis risk factors							
Current smoker	12	(20.0)	6	(24.0)	6	(17.1)	0.337
Former smoker	38	(63.3)	17	(68.0)	21	(60.0)	0.787
Never smoker	10	(16.7)	2	(8.0)	8	(22.9)	
Type 2 diabetes	21	(35.0)	8	(32.0)	13	(37.1)	
Hypertension	45	(75.0)	22	(88.0)	23	(65.7)	0.071
Obesity diagnosis	10	(16.7)	4	(16.0)	6	(17.1)	1.000
Physical activity ² (times/wk)							
None	4	(6.6)	2	(8.0)	2	(5.7)	0.611
1x	10	(16.7)	6	(24.0)	4	(11.4)	
2–3x	12	(20.0)	4	(16.0)	8	(22.9)	
> 3	34	(56.7)	13	(52.0)	21	(60.0)	

	Total n = 60	(%)	NV n = 25	(%)	RV n = 35	(%)	p value
Total energy intake							
Daily mean kcal $\pm$ SD	1976	± 788.6	1899	± 720.0	2031	± 840.1	0.529 ³
< 1,500	16	(26.7)	10	(40.0)	6	(17.1)	
1,500–1,999	19	(31.7)	3	(12.0)	16	(45.7)	
2,000–2,499	15	(25.0)	7	(28.0)	8	(22.9)	
≥ 2,500	10	(16.6)	5	(20.0)	5	(14.3)	0.030
Total fat (% of total kcal)⁴							
Daily mean grams $\pm$ SD	76.8	± 44.5	69.9	± 34.2	81.8	± 50.4	0.283
20%	3	(5.0)	2	(8.0)	1	(2.9)	
21–35%	34	(56.7)	14	(56.0)	20	(57.1)	
> 35%	23	(38.3)	9	(36.0)	14	(40.0)	0.749
Dietary n-3 fatty acids							
Daily mean grams $\pm$ SD	1.7	± 1.2	1.5	± 0.8	1.8	± 1.4	0.246
Dietary cholesterol							
Daily mean mg $\pm$ SD	276.9	± 165.2	270.6	± 141.9	281.4	± 181.9	0.806
DRI ⁴ < 300 mg	37	(61.7)	15	(60.0)	22	(62.9)	
Exceeds DRI	23	(38.3)	10	(40.0)	13	(37.1)	1.000
Protein							
Daily mean grams $\pm$ SD	79.3	± 31.7	77.4	± 24.3	80.6	± 36.3	0.692
DRI (46 g Fern, 56 g Male)	9	(15.0)	4	(16.0)	5	(14.3)	
Exceeds DRI	51	(85.0)	21	(84.0)	30	(85.7)	1.000
Carbohydrates							
Daily mean grams $\pm$ SD	238.3	± 112.5	233.6	± 108.6	241.6	± 201.5	0.788
DRI (130 g)	8	(13.3)	4	(16.0)	4	(11.4)	
Exceeds DRI	52	(86.7)	21	(84.0)	31	(88.6)	0.708
Dietary fiber							
Daily mean grams $\pm$ SD	22.0	± 16.6	22.3	± 17.5	21.7	± 16.2	0.897
DRI (25 g Fern, 38 g Male)	5	(8.3)	1	(4.0)	4	(11.4)	
Below DRI	55	(91.7)	24	(96.0)	31	(88.6)	0.634
Added dietary sugars							
Daily mean kcal $\pm$ SD	264.1	± 236.0	286.1	± 268.0	248.3	± 212.9	0.546
DRI (25% total kcal)	56	(93.3)	23	(92.0)	33	(94.3)	
Exceeds DRI	4	(6.7)	2	(8.0)	2	(5.7)	1.000
Caffeine⁵ (no. 8-oz servings)							
1.5	14	(23.3)	6	(24.0)	8	(22.9)	
1.6–2.5	15	(25.0)	5	(20.0)	10	(28.6)	
2.6–4	11	(18.3)	4	(16.0)	7	(20.0)	
> 4	20	(33.3)	10	(40.0)	10	(28.6)	0.712
Dietary sodium							
Daily mean mg $\pm$ SD	2282	± 1370	2129	± 1392	2391	± 1364	0.471

	Total n = 60	(%)	NV n = 25	(%)	RV n = 35	(%)	p value
DRI (< 1500 mg)	22	(36.7)	11	(44.0)	11	(31.4)	
Exceeds DRI	38	(63.3)	14	(56.0)	24	(68.6)	0.417
Dietary calcium							
Daily mean mg ± SD	1439	±821	1685	±1064	1264	±544	0.078
DRI (1000 mg)	44	(73.3)	22	(88.0)	22	(62.9)	
Below DRI	16	(26.7)	3	(12.0)	13	(37.1)	0.040 ³
Dietary niacin							
Daily mean mg ± SD	31.1	±16.3	33.2	±19.4	29.6	±13.5	0.440
DRI (16 mg)	50	(83.3)	22	(88.0)	28	(80.0)	
Below DRI	10	(16.7)	3	(12.0)	7	(20.0)	0.499
Serum 25(OH)D⁶							
Mean ng/mL ± SD	30.0	±15.8	32.1	±19.0	28.4	±13.2	0.384
Optimal (30 ng/mL)	25	(41.7)	13	(52.0)	12	(34.3)	
Insufficient (20–30 ng/mL)	20	(33.3)	5	(20.0)	15	(42.9)	
Deficient (< 20 ng/mL)	15	(25.0)	7	(28.0)	8	(22.9)	0.190
Red blood cell folate⁶							
Mean ng/mL ± SD	665.1	±182.1	689.3	±186.6	648.4	±179.7	0.401
Sufficient (280 ng/mL)	37	(61.7)	17	(68.0)	19	(54.3)	
Deficient (< 280 ng/mL)	22	(36.7)	7	(28.0)	15	(42.9)	0.336
MTHFR C667 T Genotype							
CC genotype (wild type)	5	(8.3)	2	(8.0)	3	(8.6)	
CT genotype	27	(45.0)	13	(52.0)	14	(40.0)	
TT genotype (variant)	28	(46.7)	10	(40.0)	18	(51.4)	0.686
Body Mass Index							
Mean ± SD	28.8	+5.6	28.7	±5.2	28.9	±6.0	0.924
Underweight (< 18.5)	0	(0.0)	0	(0.0)	0	(0.0)	
Normal (18.5–24.99)	16	(26.7)	6	(24.0)	10	(28.6)	
Overweight (25.0–29.99)	20	(33.3)	8	(40.0)	12	(34.3)	
Obese class I (30.0–34.99)	19	(31.7)	10	(32.0)	9	(25.7)	
Obese class II (35.0–39.99)	2	(3.3)	0	(0.0)	2	(5.7)	
Waist circumference⁷ (cm)							
Mean ± SD	106	±13.9	107	±13.8	105	±14.1	0.526
Low risk (Fern 88, Male 102)	36	(60.0)	17	(68.0)	19	(54.3)	
High risk (Fern > 88, Male > 102)	24	(40.0)	8	(32.0)	16	(45.7)	0.423
Waist-to-hip ratio⁷							
Mean ± SD	0.99	±0.09	1.01	±0.09	0.98	±0.08	0.102
Low risk (Fern 0.85, Male 0.90)	3	(5.0)	1	(4.0)	2	(5.7)	
High risk (Fem > 0.85, Male > 0.90)	57	(95.0)	24	(96.0)	33	(94.3)	1.000

	Total n = 60	(%)	NV n = 25	(%)	RV n = 35	(%)	<i>p</i> value
Android-gynoid ratio (mean ± SD)	1.07	±0.19	1.11	±0.22	1.05	±0.16	0.196
% Total body fat (mean ± SD)	34.7	±7.3	34.5	±5.8	34.8	±8.2	0.884
% Truncal fat (mean ± SD)	35.3	±7.2	35.4	±5.9	35.2	±8.0	0.929
Adiponectin (mean ng/mL ± SD)	103	±76.4	102	±85.4	103	±70.6	0.828
Ankle-brachial index (index leg)							
Mean ± SD	0.69	±0.32	0.72	±0.29	0.67	±0.35	0.583
> 1.40 (noncompressible)	1	(1.7)	0	(0.0)	1	(2.9)	
1.00–1.40 (normal)	5	(8.3)	3	(12.0)	2	(5.7)	
0.91–0.99 (borderline)	12	(20.0)	4	(16.0)	8	(22.9)	
0.90 (abnormal)	41	(68.3)	18	(72.0)	23	(65.7)	0.782
WIQ Scores⁸ (mean % ± SD)							
Overall	52.4	±23.2	48.1	±22.1	55.5	±23.7	0.224
Pain	68.8	±20.6	65.3	±19.4	71.3	±21.3	0.264
Distance	45.6	±35.8	40.0	±35.8	49.7	±35.8	0.303
Speed	42.9	±26.9	37.3	±25.8	46.9	±27.4	0.177
Stairs	52.4	±28.4	49.8	±27.8	54.2	±29.1	0.565
VasculQOL Scores⁹ (mean ± SD)							
Total	5.3	±1.1	5.4	±1.0	5.3	±1.2	0.949
Pain	4.9	±1.5	5.0	±1.6	4.9	±1.5	0.834
Activity	5.0	±1.2	4.9	±1.1	5.1	±1.3	0.693
Symptoms	5.4	±1.2	5.5	±1.1	5.3	±1.3	0.730
Emotional	5.8	±1.2	5.9	±1.0	5.7	±1.3	0.535
Social	6.0	±1.2	5.8	±1.4	6.2	±1.1	0.178

¹Participants who have a history of 1+ endovascular or operative procedure(s) to treat PAD are categorized as revascularized (RV) versus participants with native vasculature (NV).

²Physical activity is defined as an aggregate of frequency of 15+ minute intervals of mild (minimal effort) exercise, moderate (not exhausting) exercise, and strenuous (rapid heartbeat) exercise.

³Participants' total caloric intake differed significantly by revascularization status, $p = .03$; dietary calcium intake differed significantly by revascularization status, $p = .04$.

⁴% kcal as dietary fat guidelines from the Department of Health and Human Services 2010 (22); Dietary Reference Intakes (DRI) from the Institutes of Medicine (38,82).

⁵Caffeinated beverages include regular and half-caffeine coffees, teas (black, green, and white), and caffeinated soft drinks.

⁶Serum vitamin 25(OH)D cutoffs derived from current clinical guidelines (44); Red blood cell folate (5-methyltetrahydrofolate) cutoffs based on diagnostic lab reference ranges (83).

⁷Waist circumference cutoff thresholds from the National Institutes of Health (18); waist-to-hip ratio cutoff thresholds from 2008 World Health Organization Expert Consultation (19).

⁸WIQ scores (15,16) are defined as percentages of maximum possible points for a given component (overall, pain, distance, speed, stairs); each component is the product of predefined values multiplied by degree of difficulty.

⁹The King's College Hospital's Vascular Quality of Life Questionnaire (VascuQOL) (12) assesses responses to twenty-five questions in five domains, with each scored between 1 (lowest quality of life) and 7 (highest quality of life).

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Table 3.

Linear regression estimates¹ for nutritional and body composition variables in relation to Walking Impairment Questionnaire scores.

	WIQ overall				WIQ pain				WIQ distance				WIQ speed				WIQ stairs			
	n	Estimate	(SE)	p value	n	Estimate	(SE)	p value	n	Estimate	(SE)	p value	n	Estimate	(SE)	p value	n	Estimate	(SE)	p value
Total Kcal (per 250 kcal)	58	0.8	(1.1)	0.464	52	-0.9	(0.9)	0.329	60	3.5	(1.4)	0.018 ²	58	0.3	(1.3)	0.837	52	5.5	(1.70)	0.002 ⁴
Dietary Cholesterol	57	-0.03	(0.02)	0.159	54	-0.04	(0.01)	0.009 ⁴	56	-0.05	(0.04)	0.190	56	-0.03	(0.02)	0.255	57	-0.01	(0.02)	0.697
Total dietary fat (log)	50	-2.0	(7.7)	0.799	53	-3.7	(4.2)	0.391	51	-7.9	(12.4)	0.526	49	4.8	(7.8)	0.546	54	10.5	(8.2)	0.204
Serum vitamin D (log)	56	10.7	(6.9)	0.079	55	1.3	(3.9)	0.739	58	18.3	(9.2)	0.051	55	9.4	(6.7)	0.168	53	20.5	(7.2)	0.006 ⁴
Vitamin D supplementation	52	-7.8	(5.2)	0.141	46	-8.5	(3.1)	0.009 ⁴	60	-0.5	(9.3)	0.954	51	5.4	(5.9)	0.366	55	-19.5	(6.7)	0.005 ⁴
Calcium supplementation	57	-7.0	(7.4)	0.347	55	-8.8	(4.6)	0.064	53	-35.2	(12.7)	0.008 ⁴	58	0.02	(8.4)	0.999	58	-5.5	(8.7)	0.527
Serum Folate	51	-0.08	(0.02)	<0.0001 ⁴	49	-0.01	(0.01)	0.307	51	-0.1	(0.02)	<0.0001 ⁴	52	-0.1	(0.02)	<0.0001 ³	51	-0.1	(0.02)	0.001 ⁴
MTHFR genotype	55	-10.1	(4.9)	0.042 ⁴	54	0.6	(3.4)	0.861	58	7.1	(8.0)	0.377	55	3.3	(5.9)	0.577	57	-15.7	(5.6)	0.007 ⁴
% Total body fat	59	-1.5	(0.4)	0.0002 ³	56	-0.5	(0.3)	0.087	50	-2.9	(0.6)	<0.0001 ³	53	-1.6	(0.4)	0.001 ³	55	-2.9	(0.4)	<0.0001 ³
Body Mass Index	50	0.7	(0.9)	0.385	47	-0.1	(0.5)	0.849	48	2.7	(1.3)	0.044 ⁴	51	2.0	(0.9)	0.027 ⁴	60	-1.7	(0.6)	0.008 ²
Waist circumference	49	-0.5	(0.3)	0.036 ⁴	53	0.2	(0.2)	0.271	56	-0.3	(0.4)	0.428	52	0.04	(0.3)	0.901	56	-0.6	(0.3)	0.038 ²
Android:gynoid ratio	56	3.3	(17.0)	0.846	51	17.3	(13.3)	0.200	57	17.2	(26.3)	0.516	51	6.1	(19.9)	0.759	55	2.9	(21.4)	0.894
Serum adiponectin (log)	55	-7.7	(3.7)	0.042 ⁴	44	-13.5	(3.9)	0.001 ⁴	57	-19.0	(5.9)	0.002 ²	55	-0.5	(4.4)	0.919	56	-1.6	(4.9)	0.741

¹ The initial regression model analyzed the full data set; a second refined model omitted outliers and heavily influential data points. Only associations that were significant in both models were considered statistically significant in this table.

² Statistically significant at $\alpha = 0.05$.

³ Statistically significant at $\alpha = 0.001$.

⁴ Only statistically significant in the refined model, omitting outliers and heavily influential data points.