Published in final edited form as:

Angiology. 2011 November ; 62(8): 657–661. doi:10.1177/0003319711404025.

Gender Differences in the Prevalence and Management of Metabolic Syndrome and its Components in Patients with Peripheral Arterial Disease

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Abstract

We compared the prevalence and management of metabolic syndrome (MetS) and its components in men and women with peripheral arterial disease (PAD). Seventy men and 70 women with PAD were evaluated for presence of MetS. There was no significant gender difference in presence of MetS ($P=0.399$) and the number of MetS components ($P=0.411$). Among PAD patients with each MetS component, there was no significant gender difference in the use ($P=0.617$) and number ($P=0.716$) of blood pressure medications, the use ($P=0.593$) and number ($P=0.591$) of lipid lowering medications, and the number ($P=0.155$) of diabetic medications. Significantly more women were treated with diabetic medications compared with men (85 vs 57%, $P=0.026$).

The prevalence and management of MetS and its components was similar between men and women with PAD, except that more women were treated for diabetes. PAD patients with MetS did not receive optimal medical management.

Keywords

Claudication; Gender; Metabolic Syndrome; Peripheral Artery Disease

Introduction

Peripheral arterial disease (PAD) affects up to 30% of the population > 70 years of age^{1–2}. In addition to producing life-style limiting symptoms of claudication and the potential for progression to critical limb ischemia and amputation, PAD is associated with 2 to 6- fold

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Presented at the Society for Vascular Medicine meeting, June, 2008, Minneapolis, Minnesota.

increased risk of cardiovascular and cerebrovascular events, with an annual mortality rate of 4–6%^{1,3–5,6–9}.

Gender difference in patients with PAD has not been well-studied. Studies suggest that women remain asymptomatic and present later in life with more advanced disease^{10–11}. Symptomatic women with PAD are more limited functionally by their disease than their male counterparts^{12–14}. Few studies have investigated differences in risk factors between men and women with PAD^{15–16}.

Metabolic syndrome (MetS) represents a significant risk factor for PAD, and is associated with more advanced PAD^{16–19}. The aims of this study were: 1) to evaluate gender differences in the prevalence of MetS and its components in patients with PAD, and, 2) to identify gender differences in the management of MetS components.

Patients and Methods

Patients

One hundred forty patients (70 men and 70 women) with stable intermittent claudication (IC) and established PAD (ankle-brachial index [ABI] <0.9) were evaluated in this cross-sectional study at the General Clinical Research Center (GCRC) at the University of Oklahoma Health Sciences Center (OUHSC). Patients were recruited from the non-invasive vascular laboratory and the vascular outpatient clinic on the OUHSC campus and from advertisement in the local newspaper.

Inclusion criteria included: (a) history of IC, (b) limited ambulation during a graded treadmill test due to IC, and, (c) ABI 0.90 at rest, or an ABI 0.73 after exercise. Exclusion criteria included: (a) absence of PAD, (b) inability to obtain ABI due to non-compressible vessels, (c) asymptomatic PAD, (d) rest pain PAD, (e) limited exercise tolerance due to factors other than IC (severe coronary artery disease, dyspnea, uncontrolled blood pressure [BP]), and, (f) active cancer, renal, or liver disease. The procedures used in this study were approved by the Institutional Review Board.

MetS classification

We adapted our definition for MetS from the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III, by defining MetS as the presence of greater than 3 of the following criteria: (1) obesity, (2) dyslipidemia, (3) hypertension, and (4) diabetes²⁰. We defined obesity as body mass index (BMI) > 30 since we did not collect waist circumference data on all our patients. Dyslipidemia was used to define patients with elevated triglycerides or low high density lipoprotein (HDL). In addition, treatment with medications was used to define presence of MetS components.

Medical History and Physical Exam and Anthropometry

Medical History—Demographic information, height, weight, cardiovascular risk factors, co-morbid conditions, claudication history, and a list of current medications were collected during a medical history and physical examination interview conducted by an internal medicine physician.

Blood Pressure Measurements—The systolic and diastolic BP's were obtained with the patient sitting upright for 5 min using the Dynamap automatic BP cuff.

Ankle/Brachial Index—After 10 min of rest in supine position, the ankle and brachial systolic BP's were obtained. The ABI was calculated as the highest ankle systolic pressure on each side/highest brachial systolic pressure.

Body Mass Index—The BMI was calculated as the weight (kg)/height (m²).

Waist/Hip Ratio—The minimum circumference of the waist and the maximum circumference of the hips were obtained with a plastic measuring tape. The waist/hip ratio was calculated as the waist circumference (cm)/hip circumference (cm).

Fasting Laboratory Data—All patients underwent a fasting blood draw for complete metabolic profile, lipid profile and insulin.

Ambulatory Activity Monitoring—Ambulatory activity was measured during seven consecutive days using an accelerometer (Step Watch 3, Cyma Inc, Mountlake Terrace, Wash) placed over the right ankle. The monitor continuously recorded the number of steps taken on a minute- to- minute basis during waking hours. The monitor was removed before retiring to bed.

Statistical analysis

Unpaired t-tests and Mann-Whitney tests were used to assess differences between men and women in prevalence and management of MetS and its components. All analyses were performed using the SPSS-PC statistical package. All analyses were performed with a two-tailed significance level of $p < 0.05$. Measurements are presented as means $\pm$ standard deviations.

Results

Demographics and Prevalence of MetS

As shown in Table 1, women were similar to men in age ($P=0.076$), current smoking status ($P=0.336$), and resting ABI ($P=0.395$). There was a significantly higher number of Caucasian women compared with men ($P<0.001$). Women had a lower body weight ($P=0.017$), but significantly higher BMI ($P=0.044$), while men had a significantly higher waist to hip ratio ($P=0.002$). Women also had a significantly higher total cholesterol ($P=0.012$) and HDL ($P=0.001$). Prevalence of MetS was similar between women and men with PAD ($P=0.400$), and there was no significant difference between women and men in the number of MetS components ($P=0.445$) (Table 2).

Management of MetS components

Among PAD patients with hypertension, there was no significant difference between men and women in the use of BP medications ($P=0.617$), and the number of BP medications ($P=0.716$) (Table 3). Men and women with hypertension had similar SBP ($P=0.315$) and DBP ($P=0.488$).

The use of lipid-lowering medications ($P=0.593$) and number of medications ($P=0.591$) did not differ between men and women with dyslipidemia (Table 3). Men and women had similar triglycerides ($P=0.844$) and low density lipoprotein (LDL) ($P=0.159$). However, women had higher total cholesterol ($P=0.031$) and HDL ($P=0.002$).

More women with diabetes were treated with diabetic medications ($P=0.026$) than men (Table 3). In the treated patients, men and women received similar number of diabetic

medications ($P=0.155$). The fasting glucose ($P=0.179$) and insulin ($P=0.392$) did not differ between men and women with diabetes.

Among obese patients with PAD, men and women had similar BMI ($P=0.259$). Among those whose waist and hip circumference data was collected, men had a significantly higher waist/hip ratio compared to women ($P=0.002$). There was no significant difference between men and women in the total ambulatory strides per day ($P=0.112$) and the total activity per day ($P=0.091$).

Discussion

The major findings of this study were: 1) there was no significant gender difference in the prevalence of MetS and its components among patients with PAD, 2) there was no significant difference in the management of MetS components among men and women with PAD, with the exception that more women received diabetic medications, and, 3) patients with PAD had suboptimal control of their MetS components.

The overall prevalence of MetS among PAD patients with IC was 53% in this study. This finding supports a number of other studies, which have demonstrated that MetS is present in more than 50% of patients with PAD^{15–16}. In the Second Manifestation of Arterial Disease (SMART) study, Gorter *et al* reported an overall prevalence of 58% among patients with PAD¹⁵. They also found that the prevalence of MetS was significantly greater among PAD patients (58%) than those with coronary heart disease (41%), cerebrovascular disease (43%), and abdominal aortic aneurysms (47%)¹⁵. Similar to our findings, Gorter *et al* demonstrated that hypertension is the most prevalent MetS component followed by hyperlipidemia, diabetes, and obesity in patients with PAD¹⁵. Brevetti, *et al* reported an overall prevalence of 52% among patients with symptomatic PAD¹⁶. This study also found that hypertension is the most prevalent MetS component among patients with PAD¹⁶. However, they reported a higher prevalence of diabetes than hyperlipidemia among patients with PAD¹⁶.

Our study did not demonstrate a significant gender difference in the prevalence of MetS and its components in PAD patients with IC (57% in women vs 50% in men). Previous studies have reported a higher prevalence of MetS among women compared with men with PAD^{15–16}. Gorter *et al* reported a prevalence of 65% in women versus 55% in men with PAD¹⁵. Brevetti *et al* reported a prevalence of 74% in women vs 43% in men with symptomatic PAD¹⁶. This may be explained by differences in the study population. Gorter's study included all patients with PAD, including those with asymptomatic PAD, IC and critical limb ischemia¹⁵. Brevetti's study included patients with symptomatic PAD, including those with IC and critical limb ischemia¹⁶. Previous studies have shown that women with PAD more commonly present with asymptomatic disease or present later with more advanced disease^{10–11}. Our study population of patients with IC may underestimate the prevalence of MetS in women with PAD by excluding those with asymptomatic disease and critical limb ischemia.

To our knowledge, this is the first study evaluating gender differences in the management of MetS among patients with PAD. Although no significant gender differences were detected in the management of MetS among PAD patients, with the exception that more women were treated for diabetes, this study demonstrates that MetS components are not optimally controlled in this high risk patient population. For example, among PAD patients with hypertension, only 70–80% were on antihypertensive medications and the mean systolic BP was higher than the recommended goal of 140 mmHg for non-diabetics and 130 mmHg for diabetics and those with renal insufficiency^{1, 21}. Among PAD patients with dyslipidemia, only 70–80% were on lipid lowering medications, with the mean LDL level above the

recommended goal of 100 mg/dL for this patient population^{1, 21}. Among PAD patients with diabetes, only 57% of men and 85% of women were on diabetic medications, with the mean fasting glucose level above 119 mg/dL, which correlates with a glycosylated hemoglobin value between 6.0–7.0%²². Current guidelines recommend a glycosylated hemoglobin level of < 7.0% or as close to 6.0% as possible^{1, 21}. The mean BMI placed women in the obese category and men in the overweight category²¹. Of those who were defined as obese, many approached a morbidly obese value of 40, particularly the women patients. The majority of these patients had limited physical activity as measured by the number of ambulatory strides and minutes of activity accumulated each day.

Limitations of this study include the following: (1) definition for MetS was modified since waist circumference data was not collected on all patients and the use of medications to treat dyslipidemia was added as a criteria, (2) our study population was limited to PAD patients with IC, excluding those with asymptomatic disease and critical limb ischemia, (3) we did not assess the influence of having both MetS and diabetes on the outcome measures, which has been shown to worsen ABI compared with having MetS without diabetes²³, (4) the racial composition of men and women was different, but was not used as a covariant because several statistical assumptions were not met, (5) patients were referred and volunteered to participate in this cross-sectional study, and therefore this study does not represent a random sample. That fact that an equal number of men and women were studied indicates that PAD is as prevalent in women as in men, but the group sample size was not designed to be equal prior to the investigation.

In summary, this study demonstrates that: 1) there is no significant gender differences in the prevalence of MetS among patients with PAD, 2) there is no significant gender difference in the management of MetS components among patients with PAD, with the exception that more women were treated for diabetes, and, 3) that MetS components are not managed optimally among this high risk patient population. Measures aimed at improving symptomatic PAD and decreasing the risk of associated morbidity and mortality should include diet, exercise, and optimal medical management of MetS components.

Acknowledgments

This research was supported by grants from the National Institute on Aging (NIA) (R01-AG-24296; AWG), by a Oklahoma Center for the Advancement of Science and Technology grant (HR04-113S; AWG), and by the University of Oklahoma Health Sciences Center General Clinical Research Center grant (M01-RR-14467), sponsored by the National Center for Research Resources from the National Institutes of Health.

References

1. Hirsch AT, Haskal ZJ, Hertzner NR, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease); endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; Trans Atlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation*. 2006; 113 (11):e463–654. [PubMed: 16549646]
2. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA*. 2001; 286(11):1317–1324. [PubMed: 11560536]
3. Criqui MH, Denenberg JO, Langer RD, Fronek A. The epidemiology of peripheral arterial disease: importance of identifying the population at risk. *Vasc Med*. 1997; 2:221–226. [PubMed: 9546971]

4. Ness J, Aronow WS. Prevalence of coexistence of coronary artery disease, ischemic stroke, and peripheral arterial disease in older persons, mean age 80 years, in an academic hospital-based geriatrics practice. *J Am Geriatr Soc.* 1999; 47:1255–1256. [PubMed: 10522961]
5. Stoffers HE, Rinkens PE, Kester AD, Kaiser V, Knottnerus JA. The prevalence of asymptomatic and unrecognized peripheral arterial occlusive disease. *Int J Epidemiol.* 1996; 25:282–290. [PubMed: 9119553]
6. Criqui MH, Langer RD, Fronek A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med.* 1992; 326:381–386. [PubMed: 1729621]
7. McKenna M, Wolfson S, Kuller L. The ratio of ankle and arm arterial pressure as an independent predictor of mortality. *Atherosclerosis.* 1991; 87:119–128. [PubMed: 1854359]
8. McDermott MM, Feinglass J, Slavensky R, Pearce WH. The ankle brachial index as a predictor of survival in patients with peripheral vascular disease. *J Gen Intern Med.* 1994; 9:445–449. [PubMed: 7965239]
9. Howell MA, Colgan MP, Seeger RW, Ramsey DE, Sumner DS. Relationship of severity of lower limb peripheral vascular disease to mortality and morbidity: a six-year follow-up study. *J Vasc Surg.* 1989; 9:691–696. discussion 696–697. [PubMed: 2724457]
10. Cheanvechai V, Harthun N, Graham L, Freischlag J, Gahtan V. Incidence of peripheral vascular disease in women: Is it different from that in men? *J Thorac Cardiovasc Surg.* 2004; 127 (2):314–317. [PubMed: 14762335]
11. Sigvant B, Wiberg-Hedman K, Bergqvist D, et al. A population-based study of peripheral arterial disease prevalence with special focus on critical limb ischemia and sex differences. *J Vasc Surg.* 2007; 45 (6):1185–1191. [PubMed: 17543683]
12. Gardner AW. Sex differences in claudication pain in subjects with peripheral arterial disease. *Med Sci Sports Exerc.* 2002; 34(11):1695–1698. [PubMed: 12439070]
13. McDermott MM, Greenland P, Liu K, et al. Sex differences in peripheral arterial disease: leg symptoms and physical functioning. *J Am Geriatr Soc.* 2003; 51(2):222–228. [PubMed: 12558719]
14. Collins TC, Suarez-Almazor M, Bush RL, Peterson NJ. Gender and peripheral arterial disease. *J Am Board Fam Med.* 2006; 19(2):132–140. [PubMed: 16513901]
15. Gorter PM, Olijhoek JK, van der Graaf Y, Algra A, Rabelink TJ, Visseren FL. the SMART Study Group. Prevalence of the metabolic syndrome in patients with coronary heart disease, cerebrovascular disease, peripheral arterial disease or abdominal aortic aneurysm. *Atherosclerosis.* 2004; 173(2):363–369. [PubMed: 15064114]
16. Brevetti G, Schiano V, Sirico G, Giugliano G, Laurenzano E, Chiariello M. Metabolic syndrome in peripheral arterial disease: Relationship with severity of peripheral circulatory insufficiency, inflammatory status, and cardiovascular morbidity. *J Vasc Surg.* 2006; 44(1):101–136. [PubMed: 16753279]
17. Olijhoek JK, van der Graaf Y, Banga JD, Algra A, Rabelink TJ, Visseren FL. the SMART Study Group. *Eur Heart J.* 2004; 25(4):342–348. [PubMed: 14984924]
18. Gardner AW, Montgomery PS, Parker DE. Metabolic syndrome impairs physical function, health-related quality of life, and peripheral circulation in patients with intermittent claudication. *J Vasc Surg.* 2006; 43(6):1191–1196. [PubMed: 16765237]
19. Gardner AW, Montgomery PS. The Effect of Metabolic Syndrome Components on Exercise Performance in Patients with Intermittent Claudication. *J Vasc Surg.* 2008; 47(6):1251–1258. [PubMed: 18407453]
20. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA.* 2001; 285:2486–2497. [PubMed: 11368702]
21. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg.* 2007; 45(Suppl S):S5–67. [PubMed: 17223489]
22. Nathan DM, Singer DE, Hurxthal K, Goodson JD. The clinical information value of the glycosylated hemoglobin assay. *N Engl J Med.* 1984; 310 (6):341–346. [PubMed: 6690962]

23. Lee IT, Lee WJ, Sheu WH. Metabolic syndrome exacerbating ankle-brachial index in asian type 2 diabetic patients. *Angiology*. 2010; 61(5):482–6. [PubMed: 20395227]

Table 1

Patient Demographics.

Variables	Men (n = 70)	Women (n = 70)	P-Value
Race n (%) white	40 (57%)	58 (83%)	< 0.001
Current smoking n (%)	47 (67%)	50 (73%)	0.336
Age (years)	69 ± 10	66 ± 10	0.076
Rest ABI	0.69 ± 0.21	0.72 ± 0.24	0.395
Weight (kg)	86 ± 19	78 ± 17	0.017
BMI	28±6	31±15	0.044
Waist Girth (cm)	104±12	97±18	0.056
Hip Girth (cm)	107±8	112±12	0.087
Waist/Hip	0.97±0.07	0.87±0.13	0.002
SBP (mmHg)	140±21	139±21	0.662
DBP (mmHg)	72±19	69±21	0.451
Cholesterol (mg/dL)	171±40	187±37	0.012
Triglycerides (mg/dL)	158±132	161±350	0.963
LDL (mg/dL)	100±34	111±35	0.071
HDL (mg/dL)	42±13	50±14	0.001
Glucose (mg/dL)	94±33	103±43	0.165
Insulin (mg/dL)	10±8	13±12	0.345

Values are means ± SD, or number (n) and percentage (%) of subjects with each characteristic. ABI = Ankle Brachial Index, BMI = Body Mass Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein

Table 2

Prevalence of Metabolic Syndrome and its Components in Men and Women with Peripheral Arterial Disease.

Variables	Men (n = 70)	Women (n = 70)	P-Value
MetS Prevalence n(%)	35 (50%)	40 (57%)	0.400
MetS Components (n)	2.60±1.07	2.74±1.14	0.445
Hypertension n(%)	59 (84%)	65 (93%)	0.113
Dyslipidemia n(%)	59 (84%)	58 (81%)	0.657
Diabetes n(%)	23(33%)	27 (39%)	0.484
Obesity n(%)	22(31%)	33 (47%)	0.058

Values are mean ± SD, or number (n) and percentage (%) of subjects with each characteristic.

MetS = Metabolic Syndrome

Table 3

Management of Men and Women who are Positive on Components of Metabolic Syndrome.

Variables	Men	Women	P-Value
Patients with Hypertension	n = 59	n = 65	
BP med. N(%)	45 (76%)	52 (80%)	0.617
No. BP med. n(%)	1.7±1.2	1.7±1.2	0.716
SBP (mmHg)	144±20	141±21	0.315
DBP (mmHg)	76±12	75±8	0.488
Patients with Dyslipidemia *	n = 59	n = 58	
Lipid lowering med. n(%)	43(73%)	44(77%)	0.593
No. lipid lowering med. n(%)	1.0±0.8	0.9±0.6	0.591
Cholesterol (mg/dL)	169±41	185±39	0.031
Triglycerides (mg/dL)	171±139	182±387	0.844
LDL (mg/dL)	100±35	109±35	0.159
HDL (mg/dL)	39±12	47±15	0.002
Patients with Diabetes	n = 23	N = 27	
Diabetic med. n(%)	13(57%)	23(85%)	0.026
No. Diabetic med. n(%)	1.2±1.4	1.7±1.0	0.155
Glucose (mg/dL)	119±40	136±50	0.179
Insulin (mg/dL)	10±7	14±9	0.392
Patients with Obesity	n = 22	N = 33	
Total strides/day	2927±1179	2976±1409	0.112
Total activity time/day	222±76	266±106	0.091
BMI	34±6	39±20	0.259
Waist girth (cm)	114±13	102±22	0.095
Hip girth (cm)	111±10	119±12	0.067
Waist/Hip	1.03±0.05	0.86±0.17	0.002

Values are means ± SD, or number (n) and percentage (%) of subjects with each characteristic.

* Dyslipidemia was defined as either having elevated triglyceride or low high density lipoprotein cholesterol

BP = Blood Pressure, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein, BMI = Body Mass Index