Younger women with symptomatic peripheral arterial disease are at increased risk of depressive symptoms

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Objectives: **Gender disparities, particularly among young women with cardiovascular disease, are a growing cause for concern. Depression is a prevalent and prognostically important comorbidity in peripheral arterial disease (PAD), but its prevalence has not been described as a function of gender and age. Therefore, we compared depressive symptoms at the time of PAD diagnosis and 6 months later by gender and age in PAD patients.**

Methods: **The study enrolled 444 newly diagnosed patients with PAD (32% women) from two Dutch vascular outpatient clinics. Patients' depressive symptoms were assessed with the 10-item Center for Epidemiological Studies Depression Scale (CES-D) at baseline and 6 months later (CES-D scores ≥4 indicate significant depressive symptoms). Logistic regression models were constructed to evaluate the relationship among four gender-age groups (women <65 and ≥65 years; men <65 and ≥65 years [reference category]) and baseline and 6-month follow-up depressive symptoms.**

Results: **Initially, 33% of women <65 years had significant depressive symptoms, and 6 months later, significant depressive symptoms had developed in 19% of the other younger women. These rates were much higher than other gender-age groups (range at baseline, 11%-16%; 6-month incidence, 6%-10%; $P \leq .03$). Adjusting for demographics and clinical factors, women <65 years experienced a fourfold greater odds of baseline (odds ratio [OR], 4.3; 95% confidence interval [CI], 2.2-8.7) and follow-up depressive symptoms (OR, 4.1; 95% CI, 2.0-8.4) compared with men ≥65 years, whereas other gender-age groups were not at risk. Additional adjustment for change in the ankle-brachial index did not explain the increased depression risk in younger women (OR, 3.5; 95% CI, 1.2-10.2).**

Conclusions: **Significant depressive symptoms are more common in younger women with PAD than in other gender-age groups, both at the time of diagnosis and 6 months later. To eradicate gender-based disparities in PAD, depression screening and monitoring in younger women may be an important direction for future research and intervention. (J Vasc Surg 2010;52:637-44.)**

Morbidity and mortality rates in patients with peripheral arterial disease (PAD) range from 30% to 70% during the 5 to 15 years after their diagnosis.[1] PAD greatly affects physical functioning, and PAD patients have greater functional impairment and more rapid functional decline than patients without PAD.[2] Preliminary findings suggest that women with PAD are at particularly high risk to experience leg pain on exertion and rest, have poorer functioning, and greater walking impairment than men with PAD.[3]

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Apart from the physical burden, depression is a common comorbidity in PAD patients, affecting approximately one of five PAD patients.[4-7] Depressive symptoms among PAD patients are associated with substantially compromised functional status[6] and poor prognosis.[8] Research in patients with coronary artery disease, and in the general population, suggest that younger women may be at particularly increased risk of experiencing significant depressive symptoms than other gender-age groups.[9] The degree to which depressive symptoms differ as a function of gender and age has not been examined in PAD, but is important to establish because it may mediate the worse health status and poorer outcomes of young women and may emerge as an important potential target for intervention.

Given prior findings of depression in patients with coronary artery disease, we hypothesized that relatively younger women with PAD are especially at risk of experiencing an increased risk of depressive symptoms compared with other gender-age groups. The current study examined baseline and 6-month follow-up rates of significant depressive symptoms according to gender and age groups in a prospective registry of PAD patients to identify potentially actionable targets to improve the outcomes of young women, a particularly vulnerable group of PAD patients.

METHODS

This study was approved by the Institutional Review Board at each participating hospital. All participants provided written informed consent.

Participants and study design. PAD patients presenting with symptomatic disease were consecutively enrolled from two vascular outpatient clinics of the St. Elisabeth Hospital (between September 2001 and June 2008) and the TweeSteden Hospital (March 2006 to May 2008) in Tilburg, The Netherlands. Patients were included if they had an abnormal resting ankle-brachial index (ABI) (≤0.90) or an abnormal postexercise ABI (ABI decrease of 15% after exercise).[10] The study excluded patients who had ischemic rest pain, tissue loss, ulcers, gangrene, significant cognitive impairment, severe psychiatric comorbidities (eg, psychosis), insufficient knowledge of the Dutch language, or life-threatening conditions.

All participating patients received a diagnostic workup, including vascular laboratory assessment, and completed self-report questionnaires at baseline and at 6 months of follow-up. Information about clinical factors was obtained through medical record abstraction at baseline. A subset of patients (those enrolled after March 2006) underwent repeated vascular laboratory assessment at 6 months of follow-up.

Assessment of depressive symptoms. Depressive symptoms were evaluated with an abbreviated 10-item version of the Center for Epidemiological Studies Depression Scale (CES-D).[11,12] This measure has good reliability, with a Cronbach α of .88. Using an optimal cutoff score of ≥4, the 10-item CES-D has a sensitivity of 97% and a specificity of 84% for a diagnosis of major depression using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) criteria[13] in younger individuals, and a sensitivity of 100% and specificity of 93% in adults aged >60.[11]

Vascular laboratory assessment. A handheld Doppler ultrasonic instrument (Imexlab 9000; Imex Medical Systems Inc, Golden, Colo) was used by trained technicians to obtain systolic blood pressure readings in the right and left brachial arteries, right and left dorsalis pedis arteries, and right and left posterior tibial arteries. The ABI at rest and after walking on a treadmill was registered according to the current TransAtlantic Inter-Society Consensus guidelines.[10] Walking distance until pain occurred (pain-free walking distance) and maximum walking distance was registered in all patients.

Statistical analysis. Baseline characteristics were compared among four gender-age groups—women <65 years and ≥65 years and men <65 and ≥65 years—with the latter serving as the referent group. Mean depressive symptom scores and depressive symptom rates (CES-D ≥4) were compared among these four gender-age groups using analysis of variance for continuous variables and χ^2 tests for categoric variables. Bonferroni correction was used in post hoc analyses to control for type I errors. Three pairwise comparisons between men ≥65 years and the other gender-age categories were performed. Assuming $\alpha = .05$ and three pairwise comparisons, a value of $P = .02$ was considered statistically significant in post hoc analyses.

To compare the relative strength of the association between patient characteristics and baseline depressive symptoms, we compared standardized measures of effect using Cohen's d ($mean_1 - mean_2$/pooled standard deviation). This was calculated for those patient characteristics that were considered to be clinically important, including gender-age groups, partner status, education, working status, hypercholesterolemia, hypertension, diabetes mellitus, prior cardiac disease, prior cerebrovascular disease, chronic renal failure, chronic lung disease, chronic back pain, hip or knee osteoarthritis, smoking, body mass index, ABI, and pain-free walking distance.

Multiple logistic regression models were then constructed to evaluate the unadjusted and adjusted relationship among the four gender-age groups (men ≥65 years were used as reference category) and baseline and 6-month follow-up depressive symptoms. Baseline and 6-month follow-up depressive symptoms were defined as CES-D scores ≥4. Follow-up depressive symptoms consisted of patients with persistent depressive symptoms (CES-D score ≥4 at baseline and follow-up) and incident depressive symptoms (CES-D score <4 at baseline, but ≥4 at follow-up).

Multivariable analyses were performed with adjustment for disease severity (ABI), clinical factors (diabetes mellitus, prior cardiac disease, prior cerebrovascular disease, chronic lung disease, chronic back pain), and sociodemographic variables (marital status, education, working status). Follow-up analyses were additionally adjusted for baseline depressive symptoms and whether patients received peripheral revascularization within the 6-month follow-up period.

Secondary analyses were performed in patients with repeated vascular laboratory assessment. The changes in ABI scores were calculated and added as a covariate in the model to evaluate whether changes in disease severity contributed to the association with depressive symptoms at the 6-month follow-up. All analyses were performed with SPSS 17.0 software (SPSS Inc, Chicago, Ill). Values of $P < .05$ were considered statistically significant.

RESULTS

At baseline, 634 eligible patients were screened for depressive symptoms. At 6 months, 32 patients were not able to provide follow-up data on depressive symptoms (17 died, 7 had a life-threatening condition, 4 were hospitalized, and 4 could not be contacted), and 132 did not return the questionnaire, resulting in 470 patients (78.1%). Of these, the CES-D questionnaires were incomplete for 26, which precluded derivation of a score, leaving 444 patients for our final analyses. Nonresponders did not systematically differ from responders on baseline characteristics, including age and gender, except that nonresponders were less likely to have a partner (35% vs 26%, $P = .01$) and had a shorter maximum walking distance (329 vs 378 meters, $P = .04$). Importantly, mean baseline depressive symptoms were not

Table I. Baseline characteristics of the total sample and stratified by gender and age

Variables	*Women <65 years (n = 63)*	*≥65 years (n = 81)*	*Men <65 years (n = 150)*	*≥65 years[a] (n = 150)*	P *value*
Demographics					
Age, mean (SD, range), y	56.4 (6.1, 37-64)[b]	72.2 (6.0, 65-92)	57.5 (5.0, 39-64)[b]	72.6 (5.0, 65-85)	<.0001
Socioeconomic, No. (%)					
No partner	17 (27)	39 (48)[b]	21 (14)[b]	36 (24)	<.0001
<High school education	17 (27)	28 (35)	23 (15)[b]	52 (35)	.001
Working full- or part-time	31 (49)[b]	9 (11)[b]	71 (47)[b]	5 (3)	<.0001
Medical history, No. (%)					
Hypercholesterolemia	43 (68)	52 (64)	95 (63)	95 (63)	.91
Hypertension	28 (44)[b]	48 (59)	77 (51)	90 (60)	.10
Diabetes mellitus	11 (18)	17 (21)	30 (20)	39 (26)	.47
Prior cardiac disease	11 (18)[b]	31 (38)	36 (24)[b]	75 (50)	<.0001
Prior cerebrovascular disease	6 (10)	4 (5)[b]	22 (15)	32 (21)	<.01
Chronic renal failure	2 (3)	8 (10)	9 (6)	14 (9)	.31
Chronic lung disease	9 (14)	11 (14)	12 (8)	22 (15)	.29
Chronic back pain	8 (13)	15 (19)	16 (11)	22 (15)	.40
Knee or hip osteoarthritis	6 (10)	15 (19)	18 (12)	29 (19)	.14
Life-style factors					
Smoked ≤30 days, No. (%)	45 (71)[b]	34 (42)	93 (62)[b]	53 (35)	<.0001
Body mass index, mean (SD)	26.9 (5.9)	26.3 (5.5)	26.7 (5.0)	26.3 (4.9)	.80
Vascular laboratory assessment					
Ankle-brachial index, mean (SD)	0.66 (0.15)	0.59 (0.15)	0.67 (0.17)	0.63 (0.19)	.01
Walking distance					
Pain-free, mean (SD), m	97.3 (121.1)	92.5 (106.6)	124.5 (131.8)	122.7 (151.9)	.08
Maximum (SD), m	372.7 (307.2)	266.6 (241.8)	444.6 (321.4)	370.0 (314.0)	.001
Revascularization, No. (%)					
PTA	26 (41)	23 (28)	48 (32)	40 (27)	.19
Bypass surgery	3 (5)	4 (5)	7 (5)	4 (3)	.77
Endarterectomy	2 (3)	0 (0)	3 (2)	6 (4)	.29
Medication use, No. (%)					
Statins	45 (71)	54 (66.7)	88 (59)	105 (70)	.14
Aspirin	30 (48)[b]	52 (64)	87 (58)	103 (69)	.03
ACE inhibitors	12 (19)	26 (32)	49 (33)	57 (38)	.06
Anticoagulants	7 (11)	15 (19)	17 (11)	28 (19)	.20
Calcium antagonists	5 (8)[b]	15 (19)	35 (23)	37 (25)	.04
β-Blockers	13 (21)[b]	36 (44)	40 (27)[b]	72 (48)	<.0001
Diuretics	9 (14)	18 (22)	26 (17)	30 (20)	.61
Nitrates	0 (0)[b]	5 (6)	3 (2)[b]	12 (8)	.02
Digoxin	0 (0)	2 (3)	1 (1)	3 (2)	.45
Antiarrhythmics	0 (0)	4 (5)	2 (1)	8 (5)	.08
Depression treatment, No. (%)					
Antidepressants	6 (10)	3 (4)	6 (4)	6 (4)	.30
Currently receiving counseling[c]	2 (4)	1 (2)	4 (3)	1 (1)	.35

ACE, Angiotensin-converting enzyme; *PTA,* percutaneous transluminal angioplasty; *SD,* standard deviation.

[a]Reference group for the other three gender-age categories.

[b]Values are statistically significantly different between men ≥ 65 years and gender-age category. Three pairwise comparisons between men ≥ 65 years and other gender-age categories were made using analysis of variance (Bonferroni correction). A value of $P = .02$ was used as the level of statistical significance for the pairwise comparisons.

[c]Available in 253 patients.

significantly different between responders and non-responders (1.9 vs 2.0, $P = .60$).

Gender-age groups. The cohort consisted of 14% women <65 years, 18% women ≥65 years, 34% men <65 years, and 34% men ≥65 years. There were significant baseline differences among these gender-age groups in marital status, education, working status, prior cardiac and cerebrovascular disease, smoking status, ABI, use of aspirin, calcium antagonists, β-blockers, and nitrates (Table I).

Younger women with PAD were less likely to have prior cardiac disease and to be treated with cardioprotective medication than men ≥65 years. Importantly, younger women were more likely to be active smokers (71%). Women ≥65 years were more likely to live without a partner than men ≥65 years. Finally, younger men were more likely to be more educated, to be actively working, and to be smokers, but were less likely to have a history of cardiac disease than men ≥65 years.

Significant depressive symptoms. Of the 444 patients screened for depressive symptoms, 75 (17%) had significant baseline depressive symptoms (CES-D ≥4). Mean CES-D scores and depressive symptom rates (CES-D

Table II. Mean depressive symptom scores and depressive symptoms rates at baseline and at 6 months of follow-up by gender-age groups

Score variables	*Women <65 years (n = 63)*	*≥65 years (n = 81)*	*Men[a] <65 years (n = 150)*	*≥65 years (n = 150)*	P *value*
Baseline					
CES-D score, mean (SD)	2.7 (1.9)[b]	2.0 (1.8)	1.8 (1.8)	1.8 (1.5)	.01
CES-D ≥4, No. (%)	21 (33.3)[b]	13 (16.0)	24 (16.0)	17 (11.3)	.001
6-month follow-up					
CES-D score, mean (SD)	2.7 (1.8)	2.4 (2.0)	1.9 (1.9)	2.0 (1.9)	.02
CES-D ≥4, No. (%)	25 (39.7)[b]	17 (21.0)	26 (17.3)	26 (17.3)	.001
Incident CES-D ≥4, No. (%)	12 (19.0)[b]	8 (9.9)	9 (6.0)	14 (9.3)	.03

CES-D, Center for Epidemiological Studies Depression.

[a]Reference group for the other 3 gender-age categories.

[b]Values are statistically significantly different between men ≥ 65 years and gender-age category. Three pairwise comparisons between men ≥ 65 years and other gender-age categories were made using analysis of variance (Bonferroni correction). A value of $P = .02$ was used as the level of statistical significance for the pairwise comparisons.

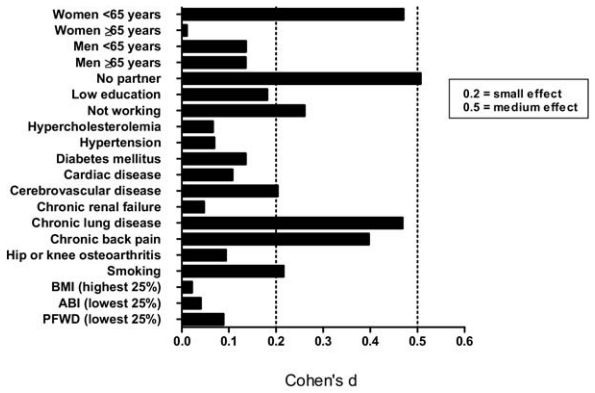

Fig 1. Effect sizes of patient characteristics associated with baseline depressive symptoms. *ABI,* Ankle-brachial index; *PFWD,* pain-free walking distance.

≥4) are presented in Table II. The depressive symptom rates at baseline were highest in women <65 years (33%), followed by women ≥65 years and male PAD patients (range, 11%-16%; $P = .001$). Importantly, at the 6-month follow-up, significant depressive symptoms affected up to 40% of women <65 years, compared with 17% to 21% in other gender-age groups ($P = .001$). The incidence of new, significant depressive symptoms at 6 months among patients who had not screened positive at baseline was 19% in women <65 years, which was significantly higher compared with the incidence of 6% to 10% in the other gender-age groups ($P = .03$).

To facilitate the interpretation of these gender-age associations, Cohen's d effect sizes were calculated for the association between gender-age groups and baseline depressive symptoms, for relevant sociodemographic and clinical factors, and disease severity indices (Fig 1). A much larger effect size was observed for the association between younger women and depressive symptoms compared with the effect sizes for PAD severity indices. Other factors with moderate effect sizes with baseline depressive symptoms were having no partner and chronic lung disease.

Risk estimates for gender-age groups and baseline depressive symptoms. Risk estimates for the gender-age groups and baseline depressive symptoms (CES-D ≥4) are shown in Fig 2. Women <65 years had more than threefold greater odds for experiencing baseline depressive symptoms (unadjusted odds ratio [OR], 3.2, 95% confidence interval [CI] 1.5-6.8) compared with men ≥65 years (reference group; Fig 2, *A,* left). Other gender-age groups were not significantly associated with baseline depressive symptoms.

After adjusting for disease severity and clinical factors in multivariable models, women <65 years remained at increased risk of having significant depressive symptoms (adjusted OR, 4.3; 95% CI, 2.2-8.7; $P < .0001$; Fig 2, *A,* right). Further adjustment for sociodemographic variables did not change these results (adjusted OR for women <65 years, 5.4; 95% CI, 2.6-11.4; $P < .0001$).

Risk estimates for gender-age groups and 6-month depressive symptoms. At the 6-month follow-up, women <65 years had a threefold increased odds of depressive symptoms (unadjusted OR, 3.1; 95% CI, 1.6-6.1; Fig 2, *B,* left), but other gender-age groups were not significantly associated with 6-month depressive symptoms. Adjusting for PAD severity, clinical factors, revascularization, and baseline depressive symptoms, women <65 years remained at increased risk of having significant depressive symptoms (adjusted OR, 4.1; 95% CI, 2.0-8.4, $P = .03$; Fig 2, *B,* right). Further adjustment for sociodemographic variables (ie, marital status, education, working status) did not change these results (adjusted OR for women <65 years, 2.9; 95% CI, 1.2-7.2; $P < .0001$).

Changes in PAD severity and depressive symptoms. To evaluate whether changes in PAD severity explained the association between gender-age and depressive symptoms at 6 months of follow-up, change ABI scores were calculated. Repeated vascular laboratory assessment was available in 269 patients. Mean increase in ABI was 0.12 in women <65 years, 0.09 in women ≥65 years, 0.10 in men <65 years, and 0.05 in men ≥65 years ($P = .18$). Risk estimates of gender-age groups and depressive symptoms at 6 months of follow-up were evaluated, while adding

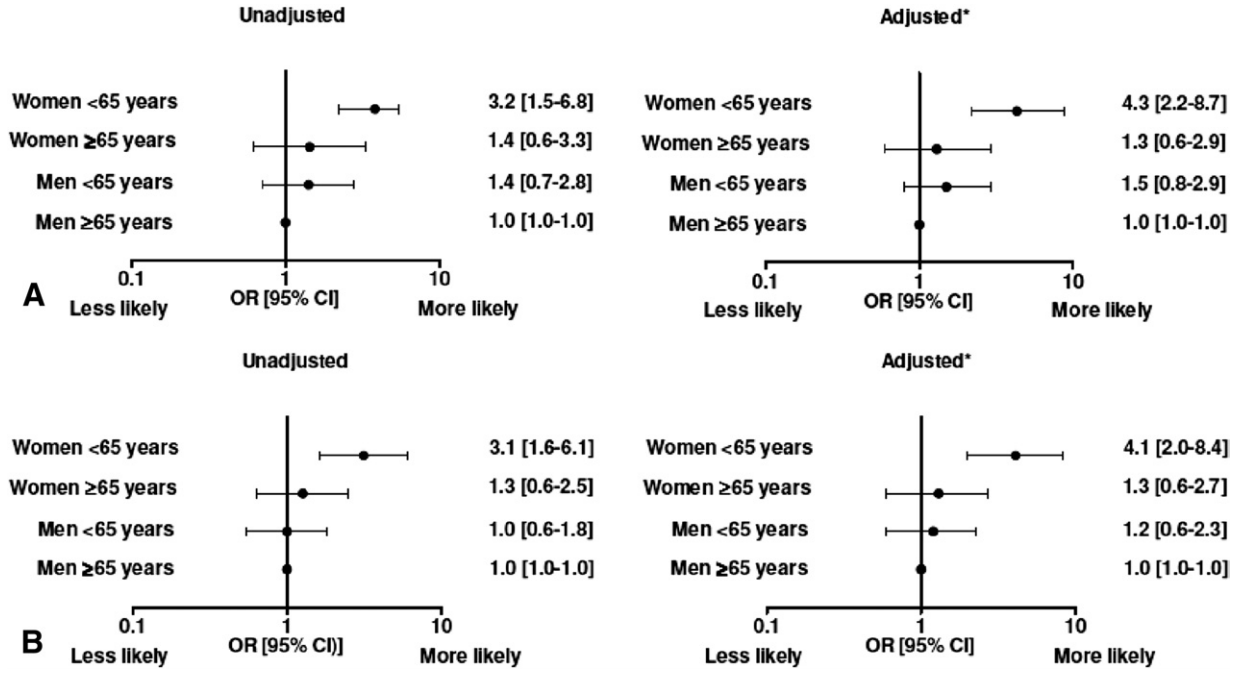

Fig 2. Model estimates presented with odds ratios *(OR)* and 95% confidence intervals (*CI*) of risk for **(A)** baseline depressive symptoms defined as Center for Epidemiological Studies Depression (*CES-D*) score ≥4, and **(B)** 6 months' follow-up depressive symptoms (CES-D ≥4) for gender-age groups. *Multivariable analyses adjusted for ankle-brachial index, diabetes mellitus, prior cardiac disease, prior cerebrovascular disease, chronic lung disease, and chronic back pain. Follow-up analysis was additionally adjusted for baseline depressive symptoms and peripheral revascularization during follow-up.

change ABI in the logistic regression model. A trend was observed for the association between increased ABI and a lower risk of follow-up depressive symptoms (OR, 0.9; 95% CI, 0.9-1.1; $P = .13$), but women <65 years remained at increased risk of experiencing depressive symptoms at the 6-month follow-up (OR, 3.5; 95% CI, 1.2-10.2; $P = .02$), after adjusting for their greater improvements in ABIs.

DISCUSSION

In this prospective multicenter PAD registry, we found that depressive symptoms were present in up to 33% of women aged <65 years at the time of PAD diagnosis, which was significantly more common than the 11% to 16% rate in the other gender-age groups. Moreover, prevalence rates significantly increased over time, affecting 40% of younger women at 6 months of follow-up. Even after adjustment for PAD severity, clinical factors, and sociodemographic variables, younger women experienced a more than fourfold increased odds of significant depressive symptoms, both at baseline and at follow-up, than men ≥65 years. The other gender-age groups had no increased risk of having significant depressive symptoms at baseline or at follow-up. Importantly, the increased risk of depressive symptoms in younger women may represent a large difference: point estimates for younger women were not overlapping with the estimates for the other gender-age groups, with the CIs showing little overlap.

To our knowledge, this is the first study that highlights the vulnerability of younger women with PAD in terms of their mental health. Although depressive symptoms have been demonstrated to be prevalent in approximately one of five patients with PAD,[6,7,14] they have never been specifically evaluated and found to be significantly high (40%) among the subgroup of younger women with PAD. To put these proportions in perspective, the average prevalence of depression in age groups comparable to the PAD population has been estimated to be 2% for a major depressive disorder and 10% for minor depression in community-dwelling people,[15] with female/male depression ratios being similar to those that were found in our study. Significant depressive symptoms have been reported to occur in about 16% to 31% of patients that have recently experienced an acute myocardial infarction[16] and in approximately 30% in patients with diabetes.[17]

Recently, there has been an increased awareness for the disproportionate high rates of depressive symptoms in female—especially younger—cardiac patients, in whom, similar to our study, prevalence rates up to 40% have been reported[9] and gender disparities in terms of adverse outcomes[18,19] and impaired health status.[20,21] In contrast, there is a paucity of research describing gender-specific differences in PAD.

Although epidemiologic studies have demonstrated that PAD is at least as common in women and men,[22-24] a

discrepancy still exists between these findings and the proportion of women enrolled in clinical studies among patients with PAD and the awareness for gender-based differences in patients with PAD in daily clinical practice.[25] Women with PAD are more likely to be undertreated,[26] experience more physical disability,[3] and have more adverse outcomes after revascularization.[27] Our current findings support these prior reports of undertreatment, although atherosclerotic risk factor control could have been more optimal across all gender-age groups. Younger women, especially, were less likely to receive cardioprotective medication (eg, aspirin) than the other gender-age groups.

It is not clear why younger women are more susceptible than the other gender age-groups to depressive symptoms. Their cardiovascular profile or PAD severity did not explain the higher rates of depressive symptoms in the current study. In fact, PAD severity indices only accounted for a small amount of the variation in baseline depressive symptoms, whereas the contribution of being a woman aged <65 years was associated with a much larger effect size. Moreover, although the change in ABI severity over 6 months was larger in young women, they had more persistent and new-onset depressive symptoms than other gender-age groups. Other factors that were substantially associated with depressive symptoms were having no partner and chronic lung disease. However, adjusting for clinical factors and sociodemographic factors such as education, working, or marital status did not alter our findings.

Alternative explanations for higher rates of depressive symptoms in younger women include the differential social roles and demands they face, care responsibilities for their families, combining work and home responsibilities, lower income and job inequality, and being a single parent. All of these may partially explain the increased susceptibility of younger women to depressive symptoms and warrant further investigation.[28] Evidence for biologic mechanisms (hormonal factors, gender differences in neurotransmitter systems or genetic factors) that might explain these gender differences is inconclusive and deserves further study.[28] Finally, the tendency of women to report more depressive symptoms than men[29] could not explain our findings, because prevalence rates of depressive symptoms in elderly women were similar to men.

Although disease severity—as expressed by younger women's baseline ABI and 6-month changes in ABI—could not explain their higher prevalence rates of depression, it is important to pay attention to the clinical profile of younger women with PAD in the current study. The observation that smoking rates were high in this group is especially worrisome, because smoking is one of the most powerful risk factors for PAD progression, and the number of pack-years is associated with disease severity, increased risk of amputation, peripheral graft occlusion, and death.[10,30] Therefore, smoking cessation is considered a cornerstone of PAD risk management.

From a clinical perspective, smoking cessation will be an enormous challenge in those presenting with depressive symptoms because the two are often intertwined, and smoking may be considered as a way of self-medicating patients' levels of distress.[31] Taking away this "medication" in depressed patients will require intense follow-up, additional supportive strategies, and referral for counseling should be considered to prevent further exacerbation of depressive symptoms.[31] Our results suggest that younger women may particularly benefit from such additional supportive measures.

Finally, despite the disproportionate distribution of depressive symptoms across gender-age groups, it is notable that receiving antidepressants or counseling for depressive symptoms did not significantly differ as a function of gender-age in the current study, suggesting undertreatment of depressive symptoms in younger women. The low proportion of depression treatment in patients with significant depressive symptoms highlights a potential opportunity to improve their treatment, particularly given that previous reports have demonstrated that depressive symptoms are associated with greater physical disability in men and women with PAD[6,7] and with poor prognosis in men with PAD.[8]

Apart from the implications for prognosis, depressive symptoms deserve to be treated in their own right to reduce the burden of depression itself. Increasing awareness by clinicians for the increased depressive symptom burden and the potential challenges associated with untreated depressive symptoms among patients with PAD in general, and particularly in younger women with PAD, will be an important first step. The preparedness to incorporate quality-of-care improvements in routine clinical care for PAD patients that target these symptoms may be crucial action steps in this regard.

Collaborative care models—led by a depression care manager—that focus on improving case finding, referral, patient education, and activation have been previously successfully implemented in other patient groups[32,33] and have been able to improve depression recognition and quality of life.[34,35] These quality-of-care improvements aimed at improving depression detection and outcomes among patients with a chronic disease may also be necessary to optimize risk management in patients with PAD.

Our study results should be interpreted in the context of the following potential limitations: no systematic depression screening protocol using a psychiatric interview was implemented; therefore, no diagnosis of major depression according to DSM-IV criteria could be established. On the other hand, the brief self-report instrument that was used can be easily implemented in clinical practice and has been shown to have high concordance with the diagnosis of major depression.[11]

Furthermore, our findings may not be generalizable to community-dwelling individuals with PAD or to PAD patients seen in primary care, because our patients represented only those that consulted a vascular surgeon for symptomatic PAD. As such, we may have underestimated the magnitude of the problem, because PAD is often under-recognized in women, possibly due to the atypical presentation of PAD symptoms.[25]

Given the relatively high invasive intervention rates (33% to 49%), the present study results may also not be generalizable to clinics that have lower invasive treatment rates among this population.

Finally, although we were able to adjust for clinically important confounders in our analyses, the possibility of residual confounding remains. More specifically, a larger sample size for each of the gender-age groups, and especially among female subgroups, would have enabled us to more reliably adjust for all potential confounders of depression. Future mediation studies in larger samples will thus be needed to give more insight in mechanisms that explain these increased prevalence rates. Clinicians, however, do not have the capacity to adjust for multiple risk factors in daily clinical practice, and as such, crude prevalence rates seem to provide important insights as well. Therefore, the current findings should not stop clinicians involved in care for patients with PAD from being aware of the increased prevalence of depressive symptoms among relatively younger women with PAD, and especially the challenging copresentation of depressive symptoms with increased smoking rates.

CONCLUSIONS

The present study suggests that younger women with PAD are more prone to significant depressive symptoms than are other gender-age groups: up to 33% experienced depressive symptoms at baseline, and this increased to 40% at follow-up. Future research will need to further develop this body of research, examining explanations for these gender-age related differences. Meanwhile, opportunities to improve detection and treatment facilities for depressed PAD patients need to be explored, because these strategies will be necessary to further optimize PAD management in all patients, but especially in younger women with PAD.

AUTHOR CONTRIBUTIONS

Conception and design: KS, JS, PV, JD
Analysis and interpretation: KS, JS, PV
Data collection: KS, PV, SK, MN
Writing the article: KS
Critical revision of the article: KS, SK, MN, JD, JS, MN, PV
Final approval of the article: KS, SK, MN, JD, JS, MN, PV
Statistical analysis: KS
Obtained funding: JD
Overall responsibility: KS

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