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The role of comorbidity in the assessment of intermittent claudication in older adults

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Abstract

The prevalence of intermittent claudication (IC) in older adults by questionnaire is less than 5% while the prevalence of peripheral arterial disease (PAD) by non-invasive testing is 2–4-fold higher. Comorbid conditions may result in under-reporting intermittent claudication (IC) as assessed by the Rose Questionnaire. We examined characteristics of those who report leg pain in relationship to other comorbid conditions and disability in 5888 participants of the Cardiovascular Health Study (CHS). Older adults with exertional leg pain, not meeting criteria for IC, had a higher prevalence of PAD on non-invasive testing with the ankle–arm index than those without pain, as well as a higher prevalence of arthritis. The pattern of responses suggested that pain for both conditions was reported together. The Rose Questionnaire for IC is specific for PAD, but a negative questionnaire does not indicate a lack of symptoms, rather the presence of PAD along with other conditions that can cause pain.

Keywords: Atherosclerosis; Intermittent claudication; Peripheral arterial disease

1. Introduction

Intermittent claudication (IC), as determined using the Rose Questionnaire, is considered to be the classic manifestation of chronic arterial obstruction in the legs [1]. Several epidemiologic studies have reported that the proportion of older adults reporting IC is less than 5% [2–4]. Prevalence estimates are about three-fold higher using non-invasive testing for peripheral arterial disease (PAD) [5]. The Rose Questionnaire is specific for classic exertional pain in the lower leg but can be insensitive to those with pain that is atypical in location, precipitants or character [6]. Even with modifications of the questionnaire [7] to improve its sensitivity by defining a broader range of symptoms and locations [8], prevalence of IC is low. For example, in a primary care patient group over age 55, the prevalence of a positive modified questionnaire was only 3.8% while prevalence of PAD, defined as an ankle–arm index (AAI) $\leqslant$0.9, was 13% [6]. This is consistent with other population studies of PAD [2–4]. The Cardiovascular Health Study (CHS) found a prevalence of IC in 2% of community dwelling older adults and an AAI $\leqslant$0.90 in 12.4% [2]. The Rose Questionnaire was quite specific for a low AAI, yet the majority (91.4%) of those with a low AAI did not have IC.

To determine if those with PAD as evidenced by a low AAI were truly asymptomatic, we compared item responses on the Rose Questionnaire between those with a low AAI and those with a normal AAI. We also evaluated demographic characteristics, comorbidity and disability that might influence the presence of symptoms. We hypothesized that a high proportion of those with a low AAI may have atypical responses to the Rose Questionnaire.

2. Methods and materials

The Cardiovascular Health Study (CHS) included 5888 adults, aged 65 and older, recruited from a random sample of Medicare enrollees. This included 5201 examined between June 1989 and June 1990 and an additional 687 African-American participants recruited in 1992–93 who underwent the same baseline examination. Details of the study design and recruitment have been published [9,10]. Participants were recruited from a random sample of the Health

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Care Finance Administration Medicare eligibility lists in four communities in the United States: Forsyth County, NC; Sacramento County, CA, Washington County, MD; and Allegheny County, PA. Subjects were excluded if they were living in an institution, wheelchair-bound in the home or currently under treatment for cancer. Of the 5888 participants, Rose Questionnaire data were available on 5883 (99.9%) and AAI data were available in 5743 (97.5%). AAI data were valid for 5717 (97.1%) due to exclusion of those with non-compressible vessels [2] or bilateral leg lesions (ulcerations) which precluded the use of blood pressure cuffs. Those with history of leg bypass and/or angioplasty ($n = 109$) were excluded leaving 5572 with complete data for this analysis.

Of these 5572 participants, 57.5% were women and 16% were African American or ethnicity other than Caucasian. Most (71%) had at least a high school education. To identify characteristics associated with a negative Rose Questionnaire in those with PAD, we also performed analysis on a subset of participants ($n = 723$) with an AAI <0.90 in either leg who had complete Rose Questionnaire data.

2.1. Exertional leg pain

We first categorized participants by presence or absence of any leg pain on walking, then by presence or absence of IC. Those who reported pain in either leg on walking, but who did not meet criteria for IC, were categorized as having exertional leg pain.

2.2. Intermittent claudication

Intermittent claudication was assessed using the original Rose Questionnaire [1]. An algorithm summarized the answers to individual items and resulted in a positive questionnaire for IC when pain occurred in either leg on walking, the pain did not begin when standing still or sitting, the pain occurred in the calf (or calves), pain occurred either when the patient walked uphill or hurried or when walking at an ordinary pace on the level ground, the pain did not disappear while walking, the pain caused the participant to stop or slow down when the pain occurred and the pain subsided within 10 minutes after the participant stopped walking.

2.3. Ankle–arm index

The AAI is the ratio of the ankle-to-arm systolic blood pressure and is reduced when there is atherosclerotic obstruction from the heart to the leg. A participant was classified as having a low AAI if either leg had an ankle-to-arm systolic blood pressure ratio of less than .90. Systolic pressures were measured with a Doppler stethoscope (8 MHz, Parks Electronics, Aloha, OR). Details of the methods have been published [2].

2.4. Comorbidity

Cardiovascular disease, diabetes, hypertension, pulmonary disease, arthritis and depression were evaluated and hypothesized to modify responses to the questionnaire. Myocardial infarction (MI), angina, stroke, hypertension and diabetes were defined at the CHS baseline exam using self-report with validation by medication records, electrocardiogram, and medical records [11]. Diabetes is defined according to the American Diabetic Association guidelines of 1997; that is, diabetes is present if the participant uses insulin or oral hypoglycemics or if glucose level exceeded 126 mg/dL (7.0 mmol/L) [12]. Cerebrovascular disease is defined as history of stroke, transient ischemic attack or carotid endarterectomy. Chronic obstructive pulmonary disease (COPD) (defined as asthma, bronchitis or emphysema at study entry) and arthritis were assessed by self-report. Depression was assessed using the modified Center for Epidemiologic Studies Depression scale of 0–30 [13]. In this analysis, a participant with a score of 10 or higher (greater than the 90th percentile) was considered to have "depression."

Smoking history was assessed by self-report of current or past use and reported number of pack-years. Relative body weight was assessed using body mass index, calculated as kg/m^2. Alcohol use was assessed by self-report and classified in tertiles of drinks per week.

2.5. Disability

Disability was defined as self-reported difficulty with one or more activities of daily living (ADLs) or instrumental activities of daily living (IADLs) [9].

2.6. Statistical analysis

Chi-square was used to test associations between categorical variables and the outcome variable of interest. Continuous variables were assessed using the Student's *t*-test if normally distributed or nonparametric (Wilcoxon Rank Sum or Kruskal–Wallis) if non-normally distributed. Logistic regression was performed to examine independent associations among those variables which were significantly related in bivariate analysis to the outcome variable. Analyses were performed using SAS (Statistical Analysis System, version 6.12 for Windows).

3. Results

Among the 5572 CHS participants, 4358 (78.2%) reported no leg pain upon walking, 1124 (20.2%) reported exertional leg pain not meeting criteria for IC and 90 (1.6%) had a positive Rose Questionnaire for IC. A low AAI (AAI <0.90) was present in 9.8% of those without leg pain, 20.8% of those with exertional leg pain but not IC and in 68.9% of those with IC (Table 1).

With the addition of the minority cohort to this report, we recalculated the sensitivity and specificity of a positive questionnaire for IC predicting a low AAI. The sensitivity was 8.6% and the specificity was 99.4%, similar to that previously published [2]. The prevalence of specific items assessed by the Rose Questionnaire in those with a low AAI

Table 1
Prevalence of a low AAI by presence or absence of exertional lower-extremity leg pain in the Cardiovascular Health Study (n = 5572)

Ankle–arm index	No leg pain (n = 4358, 78.2%) n (%)	Exertional leg pain (n = 1124, 20.2%) n (%)	Intermittent claudication (n = 90, 1.6%) n (%)
<0.90	427 (9.8)	234 (20.8)	62 (68.9)

(<0.9) were compared to those with a normal AAI (Table 2). Those with a low AAI were more likely to answer "yes" to questions that would be consistent with classic claudication. However, most of those who reported any leg pain on walking were also likely to report that the pain was relieved in "10 minutes or less" regardless of the presence or absence of a low AAI. Thus the relief of exertional leg pain with rest was not specific for PAD.

Demographics, comorbidity and physical function were compared in those with no leg pain, exertional leg pain and IC in pairwise fashion (Table 3). Those with exertional leg pain were less likely to have a low AAI than those with IC (20.8% vs. 68.9%, P < .001), but more likely to have a low AAI than those with no leg pain (9.8%, P < .001). Those with exertional leg pain were more likely to be women than either of the other two groups, while those with IC were older than the other groups.

Those with exertional leg pain had a higher prevelance of several co-morbid conditions than those with no pain, including diabetes, angina, cerebrovascular disease, any clinical cardiovascular disease other than PVD, COPD and depression. In most cases, the prevalence of these comorbidities in the group with exertional leg pain was similar to or higher than the prevalence in those with IC. Arthritis prevalence was higher in those with exertional leg pain (73.2%) than in either of the other two groups (46.1% in those with no pain and 57.3% in those with IC).

Those with exertional leg pain reported similar prevalence of difficulties in the activities of daily living (ADL) (18% vs 12%, P = .17) and in the instrumental activities of daily living (42% vs 43%, P = .74) compared to those with IC. Multivariate analyses showed that the only variable predictive of exertional pain vs IC was arthritis (P = .004, odds ratio 1.964, 95% confidence interval 1.2, 3.1).

To better assess why most individuals with a low AAI do not report classic IC, we examined comorbidity in the subgroup with a low AAI by the responses to the questionnaire (Table 4). Of 723 participants with a low AAI and complete IC questionnaires, 427 (58.7%) reported no leg pain, 234 (32.2%) had exertional leg pain and 62 (8.5%) had IC. In this subgroup with a low AAI, those with exertional leg pain had more arthritis than either of the other two groups yet had a similar mean AAI to those with IC. The prevalences of other comorbidity and disability were similar in those with exertional leg pain or IC (except for arthritis and depression which are significantly higher in those with exertional leg pain), and those with exertional leg pain had more comorbidities and disabilities than those reporting no leg pain.

We then compared the responses of Rose Questionnaire items between those with a low AAI and exertional leg pain by presence or absence of arthritis (Table 5). The pattern of responses suggested that those with both conditions answered the questions with respect to pain from both conditions simultaneously. This resulted in a large proportion with both arthritis and lower-extremity disease (as evidenced by a low AAI) who did not meet criteria for IC, in part because the item regarding pain at rest excluded IC. Inspection of the item responses in those without PAD also suggests that arthritis pain can come on with exertion and be relieved by rest just as is found with claudication.

We also examined the proportion of those with no pain, exertional pain and IC in those with an ankle–arm index below 0.90 by decrements of 0.10 (Fig. 1). Both the propor-

Table 2
Rose Questionnaire item responses by presence or absence of a low AAI (AAI < 0.9) for CHS participants with complete questionnaire information who did not have a history of lower-extremity procedures or a positive coding for IC (n = 5482) and questionnaire responses for those with a positive coding of IC as comparison

Question	Rose IC n = 90 n (%)	Normal AAI n = 4821 n (%)	Low AAI n = 661 n (%)	Normal AAI vs low AAI P-value
Do you get a pain in either leg on walking?	90 (100.0)	890 (18.5)	234 (35.4)	.001
Does pain begin when standing still or sitting?		N = 868	N = 233	
Answer = No	90 (100.0)	300 (34.4)	116 (49.8)	.001
Do you get this pain in your calf/calves?		N = 870	N = 231	
Answer = Yes	90 (100.0)	517 (59.4)	175 (75.8)	.001
Do you get it if you walk uphill or hurry?		N = 739	N = 188	
Answer = Yes	77 (85.6)	477 (64.5)	142 (75.5)	.005
Do you get it when you walk at an ordinary pace on the level?		N = 867	N = 225	
Answer = Yes	62 (68.9)	539 (62.2)	145 (64.4)	.55
Does it ever disappear while walking?		N = 851	N = 227	
Answer = No	90 (100.0)	384 (45.1)	128 (56.4)	.70
What do you do if you get it while walking?		N = 835	N = 225	
Answer = Stop or Slow Down	90 (100.0)	553 (66.2)	179 (79.6)	.001
What happens to the pain if you stand still?		N = 416	N = 143	
Answer = Relieved in 10 min or less	82 (91.0)	383 (92.1)	127 (88.8)	.23

Table 3
Characteristics for CHS participants by presence or absence of lower-extremity pain with exertion and intermittent claudication [n = 5572/5888 (94.6%)]

	No leg pain (n = 4358, 78.2%) n (%)	Exertional leg pain (n = 1124, 20.2%) n (%)	Intermittent claudication (n = 90, 1.6%) n (%)
Ankle–arm index <0.90	427 (9.8)	234 (20.8)**††	62 (68.9)‡‡
Demographics			
Age, mean (SD)	72.7 (5.5)	73.0 (5.6)†	74.9 (5.8)‡‡
Gender			
Women	2463 (56.5)	701 (62.4)**	44 (48.9)
Men	1895 (43.5)	423 (37.6)	46 (51.1)
Comorbidity			
Arthritis	1985 (46.1)	810 (73.2)**††	51 (57.3)‡
Diabetes (ADA)	637 (14.8)	213 (19.3)**	22 (24.4)‡
Angina	710 (16.3)	283 (25.2)*†	33 (36.7)‡‡
Cerebrovascular disease	261 (6.0)	113 (10.1)**	11 (12.2)‡
Clinical CVD other than PAD	1823 (41.8)	582 (51.8)**	52 (57.8)
COPD	983 (22.6)	370 (32.9)**	25 (27.8)
Depression	784 (18.0)	361 (32.2)**†	19 (21.1)
Physical Function			
ADL			
Any difficulty	204 (4.7)	202 (18.0)**	11 (12.2)‡‡
IADL			
Any difficulty	893 (20.5)	466 (41.6)**	39 (43.3)‡‡

AAI = Ankle–arm index; ADA = American Diabetes Association; Clinical CVD other than PAD = heart disease (MI, angina, history of heart procedure, congestive heart failure, atrial fibrillation or major abnormality on electrocardiogram, use of digitalis or antiarrhythmic medication) or cerebrovascular disease (stroke, transient ischemic attack or carotid artery surgery); COPD = Chronic obstructive pulmonary disease; ADL = Activities of daily living (walking around the home, getting out of bed, eating, dressing, bathing, using the toilet); IADL = instrumental activities of daily living (heavy housework, light housework, shopping, preparing meals, paying bills, using the phone).

* = $P < 0.05$, ** = $P < 0.01$, for comparison of those with no pain versus those with exertional pain.

† = $P < 0.05$, †† = $P < 0.01$, for comparison of those with exertional pain versus those with IC.

‡ = $P < 0.05$, ‡‡ = $P < 0.01$, for comparison of those with no pain versus those with IC.

tions of those with exertional leg pain and IC increased as the AAI decreased. In those with an AAI <0.7, 43.5% reported no pain, 43.5% reported exertional leg pain and 13% reported IC, while for those with AAI ≥0.7, 67.9% had no pain, 26.0% had exertional leg pain and 6.1% had IC. Conversely, an AAI <0.7 was found in 26.7% of those without leg pain, 48.7% of those with exertional leg pain and 54.8% of those with IC ($P = 0.001$).

To examine whether modifications to the questionnaire might improve the sensitivity, we calculated sensitivity and specificity based on selected items that differed significantly between those with a low AAI and a normal AAI from Table 2. Based on positive responses to items 1, 4 and 8, the sensitivity increased from 8.6% to 27% and the specificity decreased from 99% to 92%. Using only the first question, "Do you get a pain in either leg on walking," the sensitivity improved again to 41% but the specificity decreased to only 81%. Thus, to maximize sensitivity, the first question can be used and, in order to maintain a high degree of specificity, the full questionnaire should be used.

4. Discussion

In this study, we found that older adults with exertional leg pain that does not meet criteria for IC have a higher prevalence of a low AAI than those without leg pain and have a higher prevalence of comorbidity and disability. The other comorbid conditions appeared to result in responses that were not specific for claudication, but characteristic of pain in general. Review of the pattern of responses in those with and without a low ankle–arm index showed that leg pain with exertion was common in older adults and such pain was often relieved by stopping, regardless of the AAI. Those with exertional leg pain had similar comorbidity to those with classic IC with the exception of arthritis, which was present in a larger proportion of those with exertional leg pain compared to the other groups. Further examination of those with a low AAI demonstrated that those with both a low AAI and arthritis appeared to respond to the questionnaire in a pattern that may reflect the reporting for both conditions simultaneously. These findings are consistent with other studies that have shown an increased prevalence of PAD in those with atypical claudication symptoms [6,14]. It has been suggested that the lack of IC in older adults with coronary artery disease may be due to lowered physical activity [15]. Our findings suggest that many of those with PAD are not asymptomatic but have leg pain that does not meet the criteria for IC.

The Rose Questionnaire has been shown to be quite specific for PAD [8]. Modifications [7] have improved its sensitivity yet are unlikely to address the problem of distinguishing between multiple causes of leg pain. This was noted in a study that compared PAD patients to those

Table 4
Characteristics for CHS participants by presence or absence of lower-extremity pain, among those with a low ankle–arm index (AAI <0.9), *n* = 723

	Subgroup with AAI <0.9		
	No leg pain (*n* = 427) *n* (%)	Exertional leg pain (*n* = 234) *n* (%)	Intermittent claudication (*n* = 62) *n* (%)
Ankle–arm index, mean (SD)	0.76 (0.12)	0.69 (0.14)**	0.69 (0.13)‡‡
Comorbidity			
Arthritis	195 (46.5)	156 (67.2)**††	25 (41.0)
Diabetes (ADA)	109 (26.0)	57 (25.0)	16 (25.8)
Angina	107 (25.1)	92 (39.3)**	25 (40.3)‡
Cerebrovascular disease	54 (12.7)	49 (20.9)*	7 (11.3)
Clinical CVD other than PAD	256 (60)	169 (72.2)**	40 (64.5)
COPD	87 (20.4)	64 (27.4)**	14 (22.6)
Depression	88 (20.7)	74 (31.6)**†	11 (17.7)
Physical function			
ADL			
Any difficulty	40 (9.4)	37 (15.8)*	4 (6.5)
IADL			
Any difficulty	118 (27.8)	101 (43.2)**	25 (40.3)‡

AAI = Ankle–arm index; ADA = American Diabetes Association; Clinical CVD other than PAD = heart disease (MI, angina, history of heart procedure, congestive heart failure, atrial fibrillation or major abnormality on electrocardiogram, use of digitalis or antiarrhythmic medication) or cerebrovascular disease (stroke, transient ischemic attack or carotid artery surgery); COPD = Chronic obstructive pulmonary disease; ADL = Activities of daily living (walking around the home, getting out of bed, eating, dressing, bathing, using the toilet); IADL = instrumental activities of daily living (heavy housework, light housework, shopping, preparing meals, paying bills, using the phone).

* = $P < 0.05$, ** = $P < 0.01$, no pain versus exertional pain.

† = $P < 0.05$, †† = $P < 0.01$, exertional pain vs IC.

‡ = $P < 0.05$, ‡‡ = $P < 0.01$, no pain versus IC.

screened for PAD in a general medical clinic [16]. As in our study, these general medical patients were noted to more often have a positive response to the first question regarding the presence of leg symptoms with exertion and also more likely to respond to having pain at rest. It is difficult to structure a questionnaire for patients that would ask them to attribute the pain to a specific cause. Additionally, those with PAD may well have symptoms other than leg pain that should be assessed in addition to classic exertional symptoms [16,17].

This study is based on the original Rose Questionnaire which has since been modified to address some of the concerns about low sensitivity. These modifications do not appear to have addressed the issue of multifactorial leg pain, but we were unable to directly assess that here. Also, we do not mean to imply that a low AAI measured in an epidemiologic study is the gold standard for the diagnosis of PAD. We used a cut-point of 0.9 to define PAD non-invasively because of its association with total and CVD morbidity and mortality [18], and because the Rose Questionnaire has been shown to have high specificity for this cut-point. The test characteristics would vary with a lower cut-point.

Table 5
Rose Questionnaire answers by presence or absence of arthritis for those with a low AAI and with exertional leg pain but without positive Rose Questionnaire for IC, *n* = 234

	Those without arthritis *n* = 73		Those with arthritis *n* = 156		P-value
Do you get a pain in either leg on walking?	73	100%	156	100%	
Does pain begin when standing still or sitting?					
Answer = No	57	78.1	60	38.5	.001
Do you get this pain in your calf/calves?					
Answer = Yes	55	75.3	118	76.1	.897
Do you get it if you walk uphill or hurry?					
Answer = Yes	55	82.1	86	72.3	.133
Do you get it when you walk at an ordinary pace on the level?					
Answer = Yes	46	62.2	97	65.5	.620
Does it ever disappear while walking?					
Answer = No	22	29.7	76	50.7	.003
What do you do if you get it while walking?					
Answer = Stop or Slow Down	54	72.0	123	83.7	.041
What happens to the pain if you stand still?					
Answer = Relieved in 10 min. or less	59	95.2	82	72.6	.001

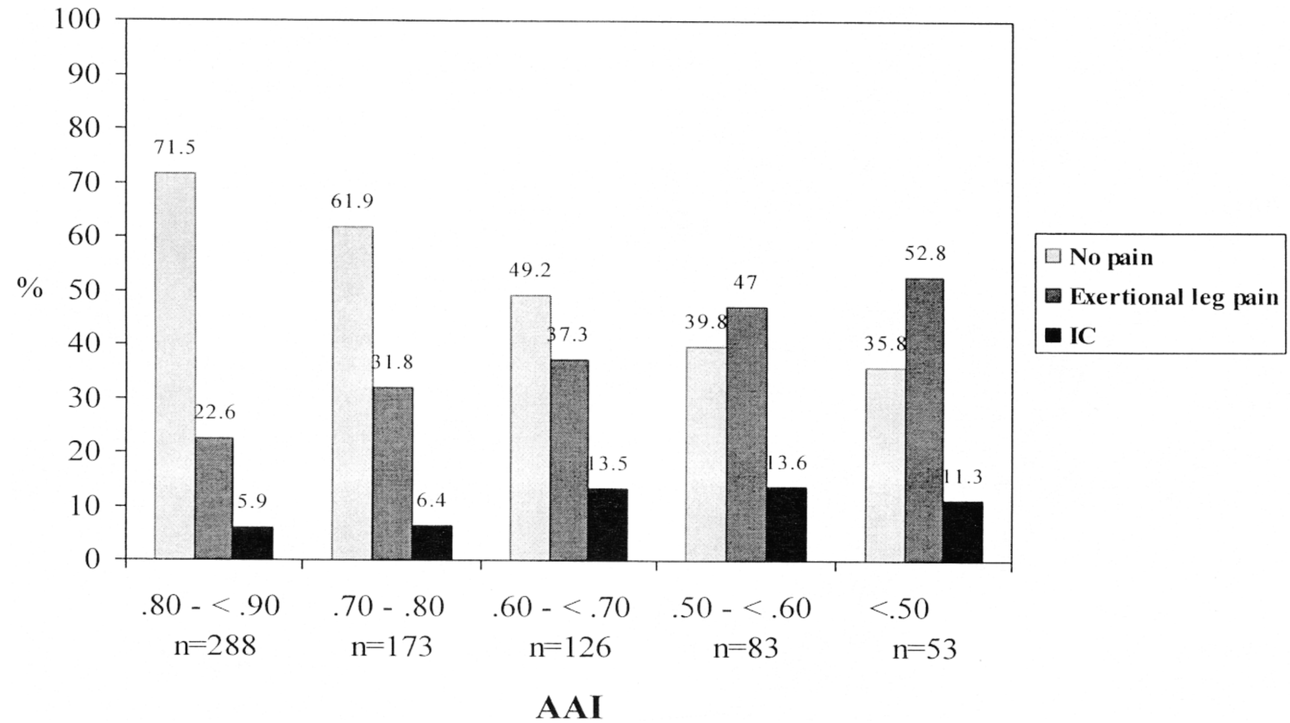

Fig. 1. No leg pain, exertional leg pain and IC: Proportions in groups classified by decreasing level of AAI. The Cardiovascular Health Study, $n = 723$.

Although none of these analyses provide direct answers as to how the questionnaires could be improved, we suggest that the current questionnaire be scored as "possible claudication," based on the first item with specificity retained by using the full questionnaire. Further study of symptoms other than claudication is needed and may also suggest improvements. It is quite possible, however, that other symptoms associated with PAD are nonspecific and will not distinguish between coexisting conditions, which are so common in older adults. For example, those with mild PAD may have symptoms of sensory or motor neuropathy resulting in gait abnormalities and weakness. Until the true spectrum of symptoms is well described, it is difficult to suggest improvements. Finally, these analyses do not reflect the ability of a skilled clinician to sort out the types of pain present in a given patient. A clinician would have more detailed information that would be used to diagnose multiple types of pain or pain that is atypical for claudication.

These findings have important implications for research and clinical care. Older adults with symptoms that do not meet criteria for the Rose Questionnaire for claudication should not be classified as asymptomatic in population studies or in clinical practice. One-third of those with a low AAI in our study had exertional pain, not meeting the specific criteria for IC, but were not "asymptomatic." Older adults reporting leg pain with exertion should be thought of as having an increased risk of PAD. In research studies using this questionnaire, those with pain on exertion should be classified as having atypical symptoms for claudication. This study also illustrates an important limitation of using disease-specific instruments in older adults. Comorbidity, especially arthritis, may result in a low prevalence of IC because those multiple conditions may not be able to distinguish between sources of pain. In older adults, multiple causes of a condition is often the rule, not the exception. In the case of PAD, a non-invasive test may be needed to determine its role in contributing to pain.

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