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## **The sensitivity, specificity, and predictive value of traditional clinical evaluation of peripheral arterial disease: results from noninvasive testing in a defined population**

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**ABSTRACT** In a companion article we have reported the prevalence, in an older, defined population, of traditional assessments (intermittant claudication and abnormal pulse examination) of peripheral arterial disease (PAD) as compared with the results of highly accurate noninvasive testing. In this article we report the sensitivity, specificity, and positive and negative predictive values for claudication and abnormal pulses for the diagnosis of large-vessel and small-vessel PAD as determined by noninvasive testing. Claudication and abnormal pulses were completely unrelated to isolated small-vessel PAD. In contrast, both claudication and abnormal pulses were significantly correlated with large-vessel PAD. Claudication and an abnormal femoral pulse showed a high specificity and positive predictive value but a low sensitivity for large-vessel PAD. Conversely, an abnormal dorsalis pedis pulse showed a good sensitivity but low specificity and positive predictive value. The best single discriminator was an abnormal posterior tibial pulse, which had high sensitivity, specificity, and positive predictive value. Various combinations of claudication and pulse abnormalities revealed a good sensitivity for broader criteria but at the expense of specificity, whereas stricter criteria had a good specificity and positive predictive value but a poor sensitivity. No combination was superior to an abnormal posterior tibial pulse alone. Additional analyses revealed that atypical leg pain was more common in patients with large-vessel PAD than in those without, that subjects with isolated large-vessel PAD in the posterior tibial artery did not have claudication, that claudication was rare until large-vessel PAD could be detected bilaterally by noninvasive testing, and finally that in the presence of large-vessel PAD concomitant small-vessel PAD was a marker for more severe large-vessel PAD. These results provide a useful guide to the utility and to the limitations of traditional clinical evaluation of PAD.  
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IN A COMPANION ARTICLE,<sup>1</sup> we have outlined the prevalence of peripheral arterial disease (PAD) in a defined population as assessed first by traditional clinical evaluation (intermittent claudication and pulse palpation) and second by highly accurate, recently developed noninvasive testing procedures. This article evaluates the degree of overlap between traditional clinical evaluation and noninvasive testing results to determine the sensitivity, specificity, and predictive value of positive and negative findings of claudication

and pulse palpation, both individually and in combination, for noninvasively diagnosed PAD. These results also shed light on the nature and degree of PAD sufficient to cause symptoms.

### **Methods**

All 624 subjects were members of a geographically defined population initially studied under a Lipid Research Clinics (LRC) protocol.<sup>2,3</sup> Subjects were recruited for the study with an introductory letter, followed by a telephone call to schedule an appointment. About half of the subjects (51.7%) were from a random sample of the LRC cohort and the others were selected from the same earlier study for hyperlipidemia, defined as being at or above age- and sex-specific 90th percentiles for cholesterol concentration or 95th percentiles for triglyceride concentration or use of lipid-lowering medications. Subjects were from a predominantly white, upper-middle-class community in southern California, and informed consent was obtained after the procedures had been fully explained.

Eleven subjects (1.8%) were excluded because of missing

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data or unreliable results of noninvasive testing. Two hundred seventy-five men and 338 women ranging in age from 38 to 82 years (mean 66) remained. One hundred fifty-eight subjects were 38 to 59 years old, 161 were 60 to 69 years old, and 294 were 70 to 82 years old.

**Criteria for PAD measurements**

*Intermittent claudication.* Claudication was assessed by the standardized Rose questionnaire developed at the London School of Hygiene and Tropical Medicine.<sup>4</sup> Claudication was defined by the Rose criteria: exercise calf pain not present at rest relieved within 10 min by rest. We also defined as “possible” claudication, exercise calf pain not present at rest but otherwise not fully concordant with the Rose criteria. The remaining subjects, including subjects with leg pain at rest and subjects with exercise pain not including the calf, were categorized as not having claudication.

*Pulse palpation.* On 508 (82.9%) of the subjects, a single examiner performed a standardized bilateral palpation of the femoral, posterior tibial, and dorsalis pedis arteries, with pulses subjectively graded from 0 to 4, and auscultation of the groin for femoral bruits. Pulses lower than grade 3 or audible bruits were considered abnormal. This examination was done before noninvasive testing, and the examiner was unaware of the subject’s responses to the claudication questionnaire.

*Noninvasive testing.* Four different noninvasive measurements of limb perfusion in the lower extremities were made: segmental blood pressure, flow velocity, postocclusive reactive hyperemia, and pulse reappearance half-time.

**SEGMENTAL BLOOD PRESSURE.** The ratio of arm systolic blood pressure to pressure at five different levels of the lower extremity (upper thigh, above knee, below knee, above ankle, and toe) was recorded by the sphygmomanometric technique and a mercury-in-Silastic gauge attached to the toe.<sup>5-7</sup>

**FLOW VELOCITY.** The Doppler effect produced by back-scattered ultrasound from red blood cells in motion was used to measure flow velocity in the femoral and posterior tibial arteries.<sup>8</sup>

**POSTOCCLUSIVE REACTIVE HYPEREMIA.** This phenomenon was used to mimic exercise blood flow requirements. Arterial flow was halted by inflating a cuff below the knee to a suprasystolic value for 4 min. Upon release of the cuff, the Doppler flow velocity response (reactive hyperemia) was recorded from the femoral artery. The percentage increase above baseline as well as the time for the response to fall to 50% of peak were recorded.<sup>9</sup>

**PULSE REAPPEARANCE HALF-TIME.** Simultaneously with the postocclusive reactive hyperemia test, the pulse reappearance half-time, or the time it took after releasing the cuff for the pulse amplitude to reach one-half the baseline value, was recorded.<sup>10</sup>

*Large-vessel PAD.* Large-vessel PAD was defined as either an abnormal segment-to-arm blood pressure ratio (LV<sub>BP</sub>+) or an abnormal large-vessel flow velocity (LV<sub>FV</sub>+).

LV<sub>BP</sub> + was defined as  
(both an above ankle and below knee ratio ≤ 0.8)

or

( an above ankle or below knee ratio ≤ 0.8, and  
[ a toe ratio ≤ 0.7 or  
[ an above knee ratio ≤ 0.8 or  
[ an upper thigh ratio ≤ 0.8 ] ] )

LV<sub>FV</sub> + was defined as either a  
(femoral peak forward flow of ≤ 20 cm/sec)

and

(a femoral pulse decay of ≥ 260 msec or  
(a femoral deceleration of ≤ 100 cm/sec<sup>2</sup>)

or

(a posterior tibial peak forward flow of ≤ 10 cm/sec)  
and

(a posterior tibial pulse decay of ≥ 220 msec or  
(a posterior tibial deceleration of ≤ 70 cm/sec<sup>2</sup>)

Although these tests measure dynamic aspects of perfusion rather than the degree of anatomic obstruction, they have been demonstrated to have a good correlation with moderate or greater large-vessel PAD determined angiographically.<sup>5-8</sup>

*Small-vessel PAD.* Small-vessel PAD was defined by an isolated toe pressure abnormality or a pulse reappearance half-time abnormality or a combination of abnormalities in pulse reappearance half-time, postocclusive reactive hyperemia, and time for hyperemic response to fall to 50% of peak.

Specifically, the presence of small-vessel PAD was defined as

(a T ratio ≤ 0.7 with the above ankle ratio and the below knee ratio normal)

or

(a pulse reappearance half-time ≥ 20 sec)

or

(a pulse reappearance half-time ≥ 15 sec and a post-occlusive reactive hyperemia ≤ 75% and time for hyperemic response to fall to 50% of peak ≥ 40 sec)

The cutpoints chosen represent extreme values from previous studies of normal control subjects.<sup>9, 10</sup> Since small-vessel PAD cannot be reliably assessed angiographically, anatomic correlation of these tests is impractical.

*Surgery for PAD.* Subjects were asked whether they had ever had surgery for poor circulation to the extremities, other than for varicose veins, and the nature and location of the surgery. Subjects with documented surgery for PAD underwent the noninvasive testing along with other subjects. For this analysis, the 1.2% of subjects with a history of surgery for PAD were grouped with the other subjects.

*Statistical analysis.* Tests for association in 2 × 2 tables were performed with Pearson’s chi square with Yates’ correction. The Mantel-Haenszel chi-square procedure corrected for continuity was used to test for association in ordered contingency tables.<sup>11</sup>

**Results**

Table 1 shows the association of Rose, possible, and absent claudication with large-vessel PAD and isolated small-vessel PAD. Numbers of subjects vary slightly in this and subsequent tables because of missing data. The overall prevalence of large-vessel PAD was 11.3% and that of isolated small-vessel PAD was 15.6%. There was a highly statistically significant association between Rose or possible claudication and large-vessel PAD (p < .001). In contrast, claudication was completely unrelated to isolated small-vessel PAD (p = NS).

Table 2 shows the prevalence, sensitivity (the proportion of positive findings in subjects with large-vessel PAD), specificity (the proportion of negative findings in subjects without large-vessel PAD), positive predictive value (the proportion with large-vessel PAD in subjects with positive findings), and negative predictive value (the proportion without large-vessel PAD in subjects with negative findings) for each of the traditional clinical findings. There was essentially no corre-

**TABLE 1**  
**Association of claudication with large-vessel PAD and isolated small-vessel PAD**

Claudication — all subjects	LV-PAD <sup>A</sup>			Isolated SV-PAD <sup>B</sup>		
	+	–	Total	+	–	Total
Rose	6	5	11 (1.9)	1	10	11 (1.9)
Possible	7	16	23 (4.0)	4	20	24 (4.1)
Absent	52	489	541 (94.1)	87	468	555 (94.1)
Total	65 (11.3)	510 (88.7)	575 (100.0)	92 (15.6)	498 (84.4)	590 (100.0)

Values in parentheses are percentages.

LV-PAD = large-vessel peripheral arterial disease; SV-PAD = small-vessel peripheral arterial disease.

<sup>A</sup>Large-vessel PAD and claudication association significant at  $p < .001$ .

<sup>B</sup>Small-vessel PAD and claudication association,  $p = \text{NS}$ .

lation between traditional clinical findings and isolated small-vessel PAD, and thus these values are not shown. The data are limited to clinical findings of routine interest, i.e., Rose or possible claudication, femoral bruit, abnormal femoral or posterior tibial pulse, and various combinations of these findings. This analysis allows examination, for example, of the difference in sensitivity for large-vessel PAD between Rose claudication alone and Rose claudication combined with a pulse abnormality.

Rose claudication was present in only 1.9% of subjects, with an additional 4% of subjects having possible claudication. Of the individual pulse abnormalities, dorsalis pedis abnormalities had the highest prevalence (29.3%), reflecting relatively common congenital absence.<sup>12, 13</sup> Of the various combinations in the lower half of the table, the strictest criteria, Rose claudication *and* a pulse abnormality, had the lowest prevalence (0.9%), whereas the broadest category,

Rose *or* possible claudication or any pulse abnormality, had the highest (24.1%).

Rose claudication had a very high specificity (99%) and a positive predictive value of 54.5% but a low sensitivity (9.2%). Thus, although there was a highly significant association between claudication and large-vessel PAD, only 9.2% of the subjects with large-vessel PAD had Rose claudication. Conversely, only 54.5% of the subjects with Rose claudication had large-vessel PAD.

Expanding the Rose definition of claudication to include possible claudication-induced pain predictably increased the sensitivity but reduced the specificity and positive predictive value. A femoral pulse abnormality or bruit also had a high specificity but low sensitivity. Among the individual abnormalities, a posterior tibial pulse abnormality appeared to be the single best discriminator of large-vessel PAD, with the highest sensitivity (71.2%), highest negative predictive value

**TABLE 2**  
**Prevalence, sensitivity, specificity, and predictive value of traditional PAD symptoms and findings (%)**

Symptoms/findings	Prevalence	Sensitivity	Specificity	Predictive value	
				+	–
Rose claud.	1.9	9.2	99.0	54.5	89.5
Rose or poss. claud.	5.9	20.0	95.9	38.2	90.4
Femoral bruit	6.0	20.0	95.7	36.7	90.7
Abn. femoral pulse	3.0	12.7	98.2	46.7	90.1
Abn. post. tibial pulse	15.1	71.2	91.3	48.7	96.5
Abn. dorsalis pedis pulse	29.3	50.0	73.1	17.7	92.7
Any abn. pulse <sup>A</sup>	20.1	76.9	86.4	39.6	97.0
Rose or any abn. pulse	21.3	78.2	85.6	39.8	97.0
Rose or poss. or any abn. pulse	24.1	82.1	83.1	37.4	97.4
Rose and any abn. pulse	0.9	4.8	99.6	60.0	89.8
Rose or poss. and any abn. pulse	2.2	11.5	98.8	53.8	90.5

<sup>A</sup>Dorsalis pedis abnormalities excluded.

(96.5%), second highest positive predictive value (48.7%), and a reasonably high specificity (91.3%). An abnormal dorsalis pedis pulse had a fairly high sensitivity (50.0%) but by far the lowest specificity (73.1%) and positive predictive value (17.7%).

Because of this low specificity and positive predictive value for the dorsalis pedis, this pulse was excluded from the “any pulse abnormality” category. The “any pulse” category was not much of an improvement over the posterior tibial alone, with a slightly higher sensitivity but a somewhat lower specificity and positive predictive value. The categories of “any pulse” or Rose, or “any” or Rose or possible, predictably increased sensitivity slightly with a slight loss of specificity. The strictest category, Rose claudication and any pulse abnormality, had a very high specificity (99.6%) and the highest positive predictive value (60.6%) but a very low sensitivity (4.8%).

About one-sixth of the subjects with large-vessel PAD had their disease manifested by both blood pressure (LV<sub>BP</sub>+) and flow (LV<sub>FV</sub>+) abnormalities. In this small, severely affected subset the sensitivity of the traditional clinical findings, particularly claudication, was greater (not shown).

Because of the modest correlation between claudication and large-vessel PAD, we undertook additional analyses. Among subjects not reporting claudication, the prevalence of large-vessel PAD in subjects with leg pain at rest was more than twice that in subjects without pain (19.0% vs 8.5%;  $p = .02$ ), suggesting that some nonambulatory pain was likely ischemic in origin. However, 81.0% of the subjects with leg pain at rest did not have large-vessel PAD.

Table 3 shows the association in the subjects with large-vessel PAD between claudication and isolated posterior tibial artery disease, defined as LV<sub>BP</sub> normal, femoral LV<sub>FV</sub> normal, but LV<sub>FV</sub> + in a posterior tibial artery. Strikingly, none of the subjects with isolated

**TABLE 3**  
Claudication in subjects with isolated posterior tibial artery LV<sub>FV</sub> + compared with other large-vessel PAD<sup>A</sup>

Claudication	Iso. post. tib. LV <sub>FV</sub> +	Other LV-PAD	Total
Rose or possible	0	13	13
Absent	31	18	49
Total	31	31	62

LV-PAD = large-vessel peripheral arterial disease.

<sup>A</sup>Isolated posterior tibial artery LV<sub>FV</sub> + defined as LV<sub>BP</sub> normal, LV<sub>FV</sub> in femoral artery normal, and LV<sub>FV</sub> + in a posterior tibial artery. Comparison significant at  $p < .001$ .

**TABLE 4**  
Number and percentage of subjects with Rose or possible claudication by large-vessel PAD category<sup>A</sup>

Claudication	LV-PAD			Total
	Bilateral	Unilateral	None	
Rose or possible	10 (35.7)	2 (6.5)	20 (4.0)	32
Absent	18 (64.3)	29 (93.5)	486 (96.0)	533
Total	28	31	506	565

LV-PAD = large-vessel peripheral arterial disease.

Values in parentheses are percentages.

<sup>A</sup>Bilateral large-vessel PAD and claudication association significant at  $p < .001$ .

posterior tibial disease had Rose or possible claudication, a highly significant difference from those with other large-vessel PAD ( $p < .001$ ). Subjects with isolated posterior tibial disease constituted half the large-vessel PAD group, resulting in a large “diluting” effect on the sensitivity calculations in table 2.

Because of this “diluting” effect, we reanalyzed all table 2 categories necessarily involving claudication, excluding subjects with isolated posterior tibial disease. There was a more than doubling of sensitivity in each category, and the negative predictive value increased somewhat. Specificity and the positive predictive value were unchanged, since no normal subjects were excluded and no excluded subject had Rose or possible claudication.

We were also interested in whether subjects with bilateral large-vessel PAD might be more likely to be symptomatic. Table 4 shows the association of claudication with bilateral vs unilateral large-vessel PAD. The results are striking, showing that 35.7% (10/28) of subjects with bilateral large-vessel PAD had Rose or possible claudication vs only 6.5% (2/31) of subjects with unilateral PAD, ( $p < .001$ ), which was barely more than the 4.0% (32/565) claudication rate in subjects without large-vessel PAD. However, in the small number of subjects with presumably more severe disease, i.e., LV<sub>BP</sub> + and LV<sub>FV</sub> +, subjects with both bilateral and unilateral disease had high claudication rates, 66.7% and 62.5%, respectively (not shown).

Finally, we were curious as to whether the pulse reappearance half-time, a highly reliable test of small-vessel PAD, would predict more severe large-vessel PAD when it was abnormal with coexisting large-vessel PAD. Table 5 shows the association between the pulse reappearance half-time and claudication separately in subjects with and without large-vessel PAD. The top half of the table indicates that in subjects

TABLE 5

Percentage of subjects with Rose or possible claudication by pulse reappearance half-time (PRT<sup>1/2</sup>) category and without and with large-vessel PAD

% Rose or possible claudication	PRT <sup>1/2</sup> (sec)					Total
	<10	10–19	20–29	30–39	40+	
LV-PAD absent <sup>A</sup>	4.3 (12/281)	3.8 (6/156)	1.9 (1/52)	7.7 (1/13)	16.7 (1/6)	4.1 (21/508)
LV-PAD present <sup>B</sup>	5.0 (1/20)	6.3 (1/16)	25.0 (4/16)	33.3 (1/3)	55.6 (5/9)	18.8 (12/64)

Actual numbers are in parentheses.

LV-PAD = large-vessel peripheral arterial disease.

<sup>A</sup>Claudication and PRT<sup>1/2</sup> association, *p* = NS.

<sup>B</sup>Claudication and PRT<sup>1/2</sup> association, significant at *p* < .001.

without large-vessel PAD, claudication was essentially unrelated to the pulse reappearance half-time (*p* = NS). However, in subjects with large-vessel PAD, the proportion of subjects with claudication increased with each 10 sec increment in the pulse reappearance half-time, so that more than half the subjects with a half-time of 40 sec or greater had probable or questionable claudication, a highly significant trend (*p* < .001). Thus, in the presence of large-vessel PAD, a prolonged pulse reappearance half-time appears to be a marker for more severe disease.

## Discussion

The association between classic (Rose) claudication and noninvasively assessed large-vessel PAD was highly statistically significant but nonetheless modest. The proportion of subjects with Rose claudication having large-vessel PAD was only 54.5%, suggesting neuromuscular, venous, or other origins for nearly half the subjects reporting typical ischemic pain. A lesser predictive value for claudication (30%) was reported from a study in Sweden, which used abnormal venous plethysmographic results as the end point.<sup>14</sup> A recent study from Finland reported similar results, confirming significant PAD in only one-third of men and one-fifth of women with typical claudication. However, the diagnosis of PAD was based on “clinical examination.”<sup>15</sup> A study from Denmark, however, reported a higher predictive value; 72.0% of subjects with Rose claudication had a reduced systolic ankle blood pressure as measured by Doppler techniques.<sup>16</sup>

Only 9.2% of the subjects with large-vessel PAD had Rose claudication with an additional 10.8% having possible claudication. When subjects with isolated posterior tibial disease (none of whom reported claudication [table 3] were removed, these numbers improved to 19.4% and 22.5%. It thus seems clear that even when subjects with isolated posterior tibial dis-

ease are excluded, only 20% to 40% of subjects with hemodynamically significant large-vessel PAD have Rose or possible claudication. Even if leg pain at rest is included, over half the subjects with large-vessel PAD in our study did not complain of calf pain. Similarly, in the Danish study only 18.9% of subjects with decreased ankle systolic blood pressure had Rose claudication,<sup>16</sup> and a French study found only an 11.6% claudication rate among subjects with decreased ankle pressure.<sup>17</sup> It is unclear why so much disease is asymptomatic. Perhaps some subjects do not routinely exercise sufficiently to cause ischemic pain. Collateral circulation may prevent symptoms in others.

In a study of 458 diabetics, Marinelli *et al.*<sup>18</sup> evaluated the association of Rose claudication and abnormal pulses with noninvasive testing of resting and exercise ankle blood pressures and abnormal wave forms on Doppler velocimetry. They found a higher sensitivity than in our study for Rose claudication, but a lower specificity. Both the sensitivity and specificity for abnormal pulses or a category of Rose claudication *or* abnormal pulses were lower than in our study. A major design difference was that their population was exclusively diabetic and predictably had a much higher prevalence of PAD (36.0%), Rose claudication (10.9%), and abnormal pulses (43.4%) compared with 11.3%, 1.9%, and 20.1%, respectively, in our study. The positive predictive value increases and negative predictive value decreases with increased disease prevalence<sup>19</sup> and a comparison of the results from their study (high disease prevalence) and ours (lower disease prevalence) demonstrate this phenomenon.

The findings for possible claudication (table 1) and for leg pain at rest indicate that these complaints are more frequent with large-vessel PAD than in its absence and suggest patients with occlusive disease can present with atypical symptoms. One frequent finding in our study in subjects with possible claudication and

large-vessel PAD was exercise calf pain that disappeared with continued walking or exercise; that is, subjects could “walk through” their pain.

Our study protocol involved the standardized Rose questionnaire, administered to all subjects in the same manner, a necessary prerequisite for epidemiologic studies. We have little doubt that an experienced clinician with longer and more extensive questioning, perhaps on more than one visit, could better discriminate true claudication than by a standardized questionnaire. Nonetheless, we would caution the clinician that nearly half of our subjects with Rose “claudication” did not have large-vessel PAD and well over half of subjects with large-vessel PAD did not have Rose claudication or even calf pain.

The results in table 2 indicate that clinical findings in the femoral artery were little better than the subjective symptoms of claudication for diagnosing large-vessel PAD. Only 17.7% of subjects with an abnormal dorsalis pedis pulse had large-vessel PAD, a finding reflecting the 4% to 12% congenital absence of this artery.<sup>12, 13</sup> The posterior tibial pulse was the best single measure, as might be expected since it can be abnormal in either proximal or distal disease and is almost never congenitally absent, but still fewer than half the subjects with an abnormal posterior tibial pulse had large-vessel PAD, and about 30% of subjects with large-vessel PAD had a normal posterior tibial pulse. Combinations of findings followed a predictable pattern. The strictest criteria, which required Rose claudication *and* a pulse abnormality, had a high specificity and positive predictive value but a low sensitivity.

It seems probable that the data for specificity and positive predictive value in table 2 involving pulse palpation would have been improved had we required an absent rather than diminished pulse. However, the numbers would have become small and unstable, and any improvement in specificity would almost certainly have been at the expense of sensitivity.

Interestingly, the data in table 4 suggest that until large-vessel PAD becomes extensive enough to be detected bilaterally, it is largely asymptomatic. Once it is demonstrable by noninvasive testing bilaterally, over a third of subjects have Rose or possible claudication.

Isolated small-vessel PAD (table 1) was completely unrelated to Rose or possible claudication or to abnormal pulses. These findings were expected, since isolated disease of distal small vessels should not affect perfusion of proximal larger vessels, but to our knowledge this concept has not been previously documented. However, the data in table 5 suggest that in the pres-

ence of large-vessel PAD, the extent of prolongation of pulse reappearance half-time was predictive of the probability of claudication and thus presumably the severity of disease, a conclusion supported by the results from a previous study.<sup>20</sup> Thus the presence of small-vessel PAD with large-vessel PAD appears to be a marker for more severe large-vessel PAD, or alternatively, inadequate compensatory collateral circulation.

In conclusion, earlier studies addressing the association of clinical findings and large-vessel PAD have involved a much more limited assessment of this issue than the current report. Our data suggest that hemodynamically significant large-vessel PAD is frequently asymptomatic, although the probability of symptoms increases with the severity of disease. Conversely, symptoms and abnormal pulses do not invariably indicate large-vessel PAD, although the probability increases with the severity of the symptoms. Thus symptoms and clinical evaluation are important, but both clinicians and investigators should be aware of their limitations, and this population-based study should be a useful guide to the value of traditional clinical evaluation of PAD.

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