Heart and Vessels (2019) 34:590–596
https://doi.org/10.1007/s00380-018-1274-6

ORIGINAL ARTICLE

Comparison of leg loader and treadmill exercise for evaluating patients with peripheral artery disease

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Received: 1 May 2018 / Accepted: 28 September 2018 / Published online: 4 October 2018

Abstract

The exercise ankle-brachial index (ABI) helps diagnose lower extremity peripheral artery disease (PAD). Patients with comorbidities may be unable to perform treadmill exercise, the most common stress loading test. While the active pedal plantar flexion (APP) test using the leg loader, simple and easy stress loading device, could be an alternative, there are no data comparing the leg loader and treadmill exercise. Therefore, we aimed to compare APP using the leg loader and treadmill exercise to evaluate PAD. A total of 27 patients (54 limbs) diagnosed with PAD with intermittent claudication and considered for angiography and/or endovascular treatment were recruited prospectively, and both the leg loader and treadmill were performed. There was a strong correlation ($r = 0.925$, $p < 0.001$) between the leg loader ABI and treadmill ABI; however, the decrease rate of the leg loader ABI was significantly less than that of treadmill ABI (14.0% [5.6, 30.1] vs. 25.8% [6.1, 53.1], $p < 0.001$). The number of patients who terminated the exercise prematurely due to dyspnea was four during the treadmill and zero during the leg loader. There was a good correlation between the leg loader ABI and treadmill ABI. Although leg loader, a simple, safe, and easy method, could be an alternative to diagnose PAD, further studies are needed to evaluate the diagnostic value of the leg loader in patients with borderline ABI or those unable to perform the treadmill.

Keywords Ankle-brachial index · Diagnosis · Exercise test · Peripheral artery disease

Introduction

Peripheral arterial disease (PAD) of the lower extremities is associated with a high risk of cardiovascular mortality and morbidity and is considered as an indicator of generalized atherosclerosis [1–3]. Patients with PAD tend to be elderly, with a low exercise capacity and a host of comorbidities such as cardiac, cerebrovascular, orthopedic, and neurologic diseases. Intermittent claudication, which is one of the representative symptoms of PAD, is also seen in patients with musculoskeletal and neurologic diseases; hence, it can be misleading at times.

Ankle-brachial index (ABI) is defined as an ankle to arm systolic blood pressure ratio and ABI ≤ 0.9 is considered the cutoff point for a PAD diagnosis. Resting ABI is the most common, noninvasive diagnostic method for PAD; however, it can at times misdiagnose the presence of PAD and its severity. Lower extremity exercise enhances the diagnostic accuracy of ABI by reducing the ABI in the presence of PAD. Exercise ABI is recommended for the accurate diagnosis of PAD in symptomatic patients, when resting ABI is normal or borderline, and distinguishes PAD from spinal canal stenosis [4,5]. Although treadmill exercise is the standard method to diagnose PAD in patients with borderline or normal ABI, some patients are unable to perform treadmill exercise due to walking intolerance caused by several comorbidities, including cardiac, cerebral, musculoskeletal, and neurologic diseases. Active pedal plantar flexion (APP) with a stress-loading device is a simpler, safer, and easier alternative diagnostic method to add load only to the lower extremities [6]. However, there are no data comparing APP using the leg loader and treadmill exercise. Therefore, the purpose of this study was to compare the leg loader and treadmill exercise to evaluate patients with PAD.

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Materials and methods

Study population

From April 2016 to November 2016, consecutive patients with intermittent claudication of either one or both limbs who were diagnosed PAD and considered for angiography and/or endovascular treatment were recruited prospectively. Exclusion criteria included critical limb ischemia, non-compressible vessels (ABI > 1.4), and inability to walk on a treadmill or perform APP with leg loader. Written informed consent was obtained from the patients before enrollment. This study was approved by the ethics committee at Shinshu University Hospital and performed in accordance with the Declaration of Helsinki. Target lesion was defined as stenosis ≥50% of the diameter, observed on angiography.

ABI measurement

Ankle-brachial index (ABI) was measured using the form PWV/ABI (BP-203RPE; Omron Healthcare, Kyoto, Japan), which is an automated oscillometric device designed to measure ABI using blood pressure in all four limbs. Four oscillometric cuffs, which incorporated pressure sensors, were wrapped around both arms and ankles. Ankle pressures were measured over the dorsalis and posterior tibial arteries and were used to calculate the ABI [7]. ABI was measured before and immediately after APP and treadmill. Exercise ABI was performed in the order (1) APP using the leg loader and (2) treadmill. Each protocol was symptom limited; therefore, premature termination of exercise due to lower extremity discomfort, dyspnea, angina, or arrhythmia was allowed.

APP was performed using a stress-loading device, leg loader (VSL-100A; FUKUDA DENSHI, Tokyo, Japan). Exercise load could be adjusted to 2 loads: weak strength level (3.3 J) and high strength level (5.3 J). The previously reported protocol was modified and applied in this study [6]. A standard load was set at the high strength (5.3 J) in the previous study; however, we included 2 phasic loads, a weak and high strength because it was expected that most patients with PAD would not perform the high strength level adequately. After a rest of at least 30 min, calf muscle fatigue was induced by isotonic APP exercise, in which the patients were asked to step on the foot pedal until the pedals stopped against a stopper, with the left and right feet alternatively, in a supine position [6]. The patients had to press the pedal in time to an audible signal set at 60 beats per minute: one signal to push, and the next signal to release the pedal, and push with the other foot. After repeating 100 cycles of the weak strength level (3.3 J), thesubjects were asked to perform cycles at the high strength level (5.3 J) up to 100 consecutive repetitions. The knees were to stay fully extended. Post-leg loader ABI was measured without changing the posture.

The treadmill test was performed 1 h or more after APP with the leg loader. The treadmill protocol consisted of a 5-min walk on a 12% grade at 2.4 km/h [8].

Duplex ultrasound

Duplex ultrasound (DUS) was performed by trained sonographers. Target lesions were considered significant if a peak systolic velocity ratio (PSVR) of ≥ 2.5 was measured or an occlusion was observed [9,10].

Statistical analysis

Continuous variables were reported as means ± standard deviations or medians (interquartile ranges [IQRs]), and binary and categorical variables were reported as frequencies (percentages). Leg loader ABI and treadmill ABI were compared using the paired *t* test and the decrease rate of ABI was compared using the Wilcoxon signed rank test. Pearson correlation coefficients were calculated to assess the relationship between mean post-leg loader ABI and post-treadmill ABI and the decrease rate of leg loader ABI and treadmill ABI. The receiver operator characteristic (ROC) curve was used to evaluate the diagnostic ability of the leg loader and treadmill for significant lesions. The areas under the ROC curve of leg loader and treadmill were compared using DeLong's test. *p* values were 2-tailed and considered statistically significant at values < 0.05 in all analyses. Data were analyzed using SPSS 24.0 (IBM, New York, USA).

Results

Baseline clinical and angiographic characteristics

A total of 27 patients (54 limbs) were enrolled. Patient and limb characteristics are summarized in Tables 1 and 2, respectively. Patients' mean age was 74.2 ± 7.0 years, and about 70% were male. There were 24 patients with either one or both limbs with abnormal ABI (≤ 0.9) and 3 with either one or both limbs with borderline ABI (0.91 to 0.99). There were 37 limbs with abnormal ABI (≤ 0.9), 11 with borderline ABI (0.91 to 0.99), and 6 with normal ABI (1.00–1.40) [5]. Among limbs with abnormal ABI (≤ 0.9), 11 lesions (40.9%) were present in the iliac artery, and 26 (59.1%) in the superficial femoral artery. Twenty-one lesions (56.7%) were classified as Trans-Atlantic Inter-Society Consensus (TASC) II type A/B, and 16 (43.3%) were classified as TASC II type C/D. Among limbs with borderline ABI (0.91

Table 1 Patient clinical characteristics

Variables ($n=27$)	
Age (years)	74.2 ± 7.0
Male sex	19 (70.4)
Body mass index (kg/m^2)	22.0 ± 3.6
Hypertension	21 (77.8)
Dyslipidemia	21 (77.8)
Diabetes mellitus	14 (51.9)
Smoking	22 (81.5)
Coronary artery disease	12 (44.4)
Previous myocardial infarction	3 (11.1)
Cerebrovascular disease	4 (14.8)
Previous endovascular treatment	10 (37.0)
Hemodialysis	3 (11.1)
Rutherford classification	
I	7 (25.9)
II	8 (29.6)
III	12 (44.4)
Ejection fraction (%)	69.5 ± 10.3
eGFR (mL/min/1.73m^2)	48.2 ± 21.7
Low-density lipoprotein (mg/dL)	87.0 ± 24.3
High-density lipoprotein (mg/dL)	50.9 ± 14.3
Medication	
Aspirin	15 (55.6)
Clopidgrel	14 (51.9)
Cilostazol	16 (59.3)
Statins	19 (70.4)
Calcium channel blocker	14 (51.9)
ACE-I/ARB	16 (59.3)
β-blocker	10 (37.0)

Values are presented as numbers (percentages) or mean ± standard deviation

eGFR estimated glomerular filtration rate, *ACE-I* angiotensin converting enzyme inhibitor, *ARB* angiotensin receptor blocker

to 0.99), there were 2 iliac artery lesions (TASC II type A) and 8 superficial femoral artery lesions (TASC II type A). Among the limbs with normal (ABI 1.00 to 1.40), there was 1 iliac artery lesion (TASC II type A).

Exercise ABI

Patients completed 102.4 ± 48.1 APP repetitions; of these, 3 patients completed the full 200 repetitions, while 24 terminated prematurely due to lower extremity discomfort. Patients walked 106.3 ± 61.7 m on the treadmill; 7 completed the full 5-min protocol, and others terminated prematurely due to lower extremity discomfort ($n=15$), dyspnea ($n=4$), and lower back pain ($n=1$). There were no adverse events related to exercises. The results of the leg loader ABI and treadmill ABI are summarized in Table 3. Overall, there was no significant difference between pre-leg loader ABI and pre-treadmill ABI (0.78 ± 0.21 vs. 0.78 ± 0.20, $p=0.391$), while post-leg loader ABI was significantly higher than post-treadmill ABI (0.63 ± 0.33 vs. 0.57 ± 0.37, $p=0.002$). The difference between post-leg loader ABI and post-treadmill ABI was greater in limbs with abnormal ABI (≤ 0.9) (0.48 ± 0.28 vs. 0.39 ± 0.28, $p<0.001$). There was no significant difference between post-leg loader ABI and post-treadmill ABI in limbs with borderline ABI (0.91 to 0.99) (0.90 ± 0.15 vs. 0.87 ± 0.14, $p=0.402$). There was a strong correlation between post-leg loader ABI and post-treadmill ABI (overall: $r=0.925$, $p<0.001$, ABI ≤ 0.9: $r=0.881$, $p<0.001$, 0.9 < ABI < 1.0: $r=0.769$, $p=0.006$) (Fig. 1). Moreover, the decrease rate of the treadmill ABI was significantly lower than that of leg loader ABI in overall (14.0% [5.6, 30.1] vs. 25.8% [6.1, 53.1], $p<0.001$) and in limbs with abnormal ABI (≤ 0.9) (23.3% [9.3, 42.3] vs. 32.6% [16.8, 97.5], $p<0.001$) (Fig. 2). There was also a strong correlation between the decrease rate of leg loader ABI and treadmill ABI (overall: $r=0.807$, $p<0.001$, ABI ≤ 0.9: $r=0.780$, $p<0.001$, 0.9 < ABI<1.0: $r=0.784$, $p=0.004$) (Fig. 2).

Leg loader versus treadmill

The ROC curve for significant lesions (stenosis with PSVR ≥ 2.5 or chronic total occlusion) is shown in Fig. 3. When the cutoff value of leg loader ABI was set to 7.1% decrease, the sensitivity was 87.5%, and the specificity was 71.4% (C statistics = 0.85, $p<0.001$). Similarly, when the cutoff value of treadmill was set to 11.2% decrease, the sensitivity was 82.5%, and the specificity was 78.6% (C statistics = 0.86, $p<0.001$). C-statistics of leg loader and treadmill were not significantly different ($p=0.836$).

Discussion

To the best of our knowledge, the present study is the first to compare APP using the leg loader and treadmill exercise in patients with PAD. The major finding of the study was that there was a strong correlation between the leg loader ABI and treadmill ABI, although the decrease rate of the leg loader ABI was less than that of treadmill ABI.

Several exercise ABI methods such as treadmill [11–14], ergometer [15], pedalator [16], and APP [17] have been used for the evaluation and diagnosis of PAD. Among them, treadmill exercise has been the most common method. It can objectively evaluate not only the degree of decrease in ABI after exercise but also the walking distance based on leg symptoms, which cannot be evaluated by the leg loader. However, there are several concerns regarding treadmill

Table 2 Limb characteristics

	ABI ≤ 0.9 (n = 37)	ABI 0.91–0.99 (n = 11)
ABI	0.67 ± 0.14	0.94 ± 0.03
Target lesion	37	10
Significant lesion	34 (91.9)	5 (45.5)
Chronic total occlusion	17 (50.0)	0 (0)
Peak systolic velocity ratio ≥ 2.5	17 (50.0)	5 (100.0)
Iliac artery	11 (29.7)	2 (20.0)
TASC II		
Type A	8 (72.7)	2 (100.0)
Type B	1 (9.1)	0 (0)
Type C	0 (0)	0 (0)
Type D	2 (18.2)	0 (0)
Superficial femoral artery	26 (70.3)	8 (80.0)
TASC II		
Type A	9 (34.6)	8 (100.0)
Type B	3 (1.5)	0 (0)
Type C	7 (26.9)	0 (0)
Type D	7 (26.9)	0 (0)
In-stent restenosis	4 (10.8)	1 (10.0)

Values are presented as numbers (percentages) or mean ± standard deviations

ABI ankle-brachial index, *TASC* Trans-Atlantic Inter-Society Consensus

ABI: (1) removing and installing cuffs is troublesome; (2) therefore, it can delay the measurement immediately after treadmill exercise and may reduce the effect of stress loading, and (3) treadmill exercise can be a risk in patients with severe comorbidities and cannot be performed in some cases.

Against these concerns of treadmill, potential strengths of leg loader ABI are: (1) convenient to perform, and (2) safe method with high applicability. The leg loader, which places a load only on the calf muscles, is an easier method to evaluate exercise ABI than the treadmill exercise. Previous studies reported that oxygen consumption of the calf muscles increases more than tenfold while walking, accompanied by a 20–30 times increase in blood flow in normal subjects; hence, calf muscles are considered as an adequate target for measuring exercise ABI [5,18]. In fact, leg loader ABI showed a median 14.0% decrease, a good correlation of the decrease rate with treadmill ($r = 0.807$, $p < 0.001$), and comparable diagnostic ability for significant lesions with the treadmill (c-statistics: leg loader 0.85 vs. treadmill 0.86) in the present study. Moreover, the leg loader may be an adequate exercise for patients who cannot perform the treadmill due to walking impairment caused by cerebrovascular diseases and/or orthopedic diseases. In terms of safety, there were 4 premature terminations of the treadmill due to dyspnea, while there was no termination of the leg loader in the present study. This finding may imply the superior safety of the leg loader compared with that of the treadmill, although objective evidences to support the safety of leg loader were not available (i.e., ECG during stress test).

Therefore, APP using leg loader might be useful for patients with severe comorbidities including coronary artery disease, heart failure, and aortic stenosis. With regard to clinical benefit of leg loader, the convenience and safety of leg loader might contribute to early detection and correct diagnosis of PAD among patients with borderline ABI, normal ABI but with claudication, and exercise intolerance, although further studies are warranted to test the utility of leg loader among such population.

An earlier randomized control trial comparing APP and treadmill exercise reported that APP in the standing position was comparable with treadmill exercise for the assessment

Table 3 Comparison of leg loader and treadmill ABI

	Leg loader ABI	Treadmill ABI	Mean difference	p value
Overall (n = 54)				
Pre	0.78 ± 0.21	0.78 ± 0.20	0.004 ± 0.038	0.391
Post	0.63 ± 0.33	0.57 ± 0.37	0.063 ± 0.140	0.002
ABI ≤ 0.9 (n = 37)				
Pre	0.67 ± 0.14	0.67 ± 0.13	0.005 ± 0.042	0.513
Post	0.48 ± 0.28	0.39 ± 0.28	0.092 ± 0.137	<0.001
0.9 < ABI < 1.0 (n = 11)				
Pre	0.94 ± 0.03	0.95 ± 0.04	0.009 ± 0.024	0.242
Post	0.90 ± 0.15	0.87 ± 0.14	0.025 ± 0.096	0.402

Valuesare presented as mean ± standard deviation

ABI ankle-brachial index

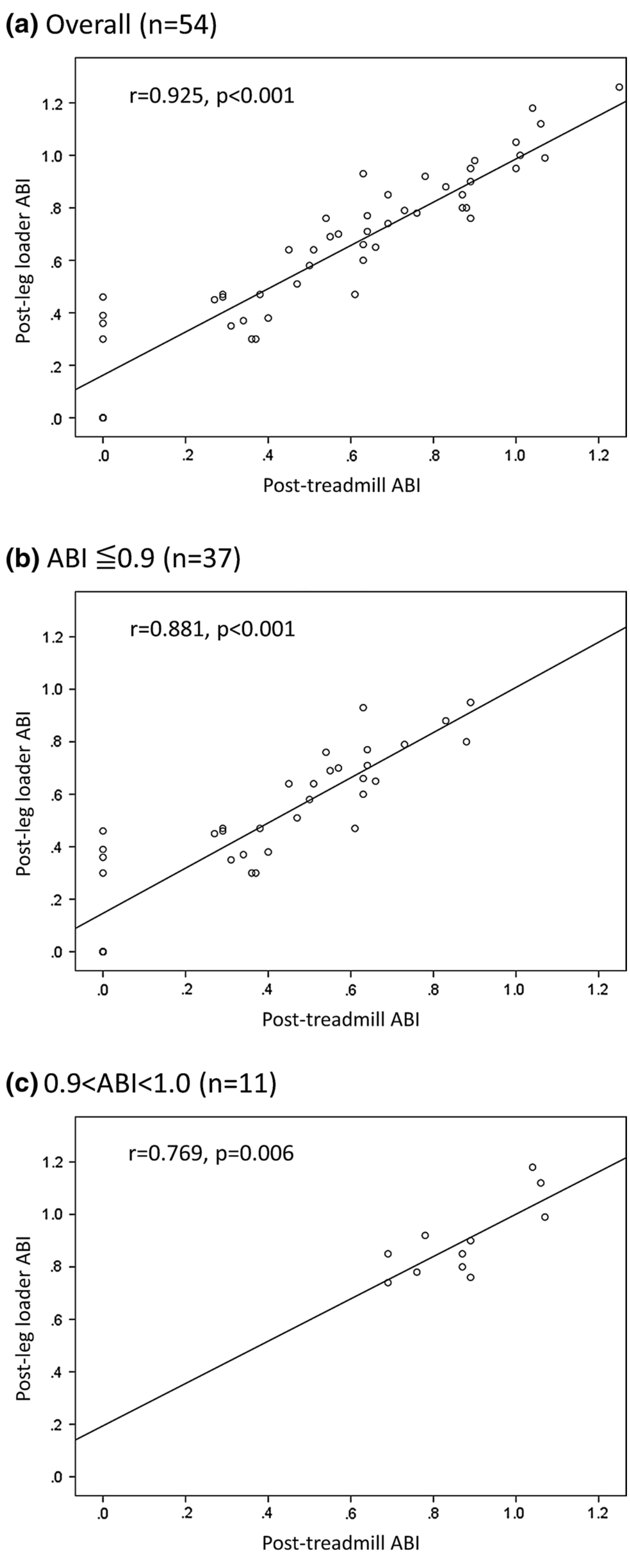
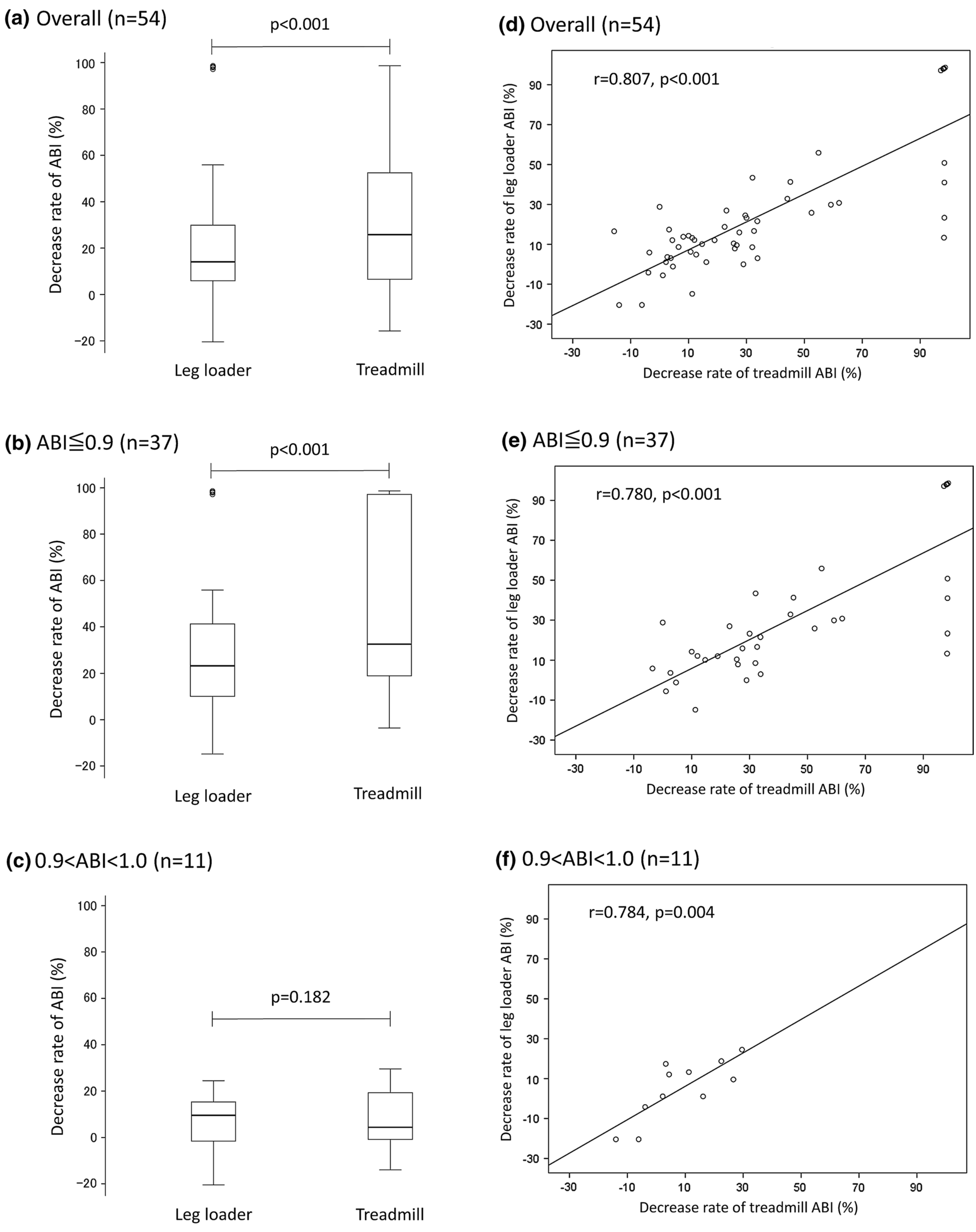


Fig. 1 Correlation between post-leg loader ABI and post-treadmill ABI in overall (**a**), limbs with ABI ≤ 0.9 (**b**), and limbs with 0.9 < ABI < 1.0 (**c**). *ABI* ankle-brachial index

of PAD [17]. The decrease in ABI was similar in both methods, whereas, in the present study, a difference of absolute and percent decrease of treadmill ABI was significantly higher than that of leg loader ABI. There are several possible reasons for the lower decrease of leg loader ABI in this study: (1) the order of stress testing was not randomized. Although there was enough rest time between the leg loader and treadmill and we confirmed the recovery of ABI before the treadmill, there might have been an influence on the treadmill; (2) the termination of stress testing was according to the physicians' discretion. Although physicians terminated examinations based on patients' symptoms, there may have been an observer bias, which led to inadequate stress loading of the leg loader; (3) almost all patients performing the leg loader terminated prematurely due to leg fatigue. The calf muscle pain might occur mainly because of muscle fatigue irrespective of intermittent claudication caused by insufficient blood supply; (4) stress load of the leg loader might have been simply less than that of the treadmill. The load of the leg loader applied only on calf muscles unlike that of the treadmill, which utilized the entire lower body.

There were several limitations in the present study. First, the small number of patients from a single center, which was not based on statistical power or sample size calculations, may affect the results of the present study. Second, in the limb analysis, the contralateral leg had inadequate load because of premature termination of exercise and this led to underestimation of the effect of each exercise method. Third, appropriateness of leg loader protocol should be considered in the further study in light of lots of premature terminations of leg loader, although strong correlation and comparable diagnostic ability between leg loader and treadmill were shown in this study. Finally, the present study was not designed to compare the diagnostic ability for PAD of the leg loader and the treadmill in patients with normal/borderline ABI. Further studies are needed to evaluate the diagnostic ability of the leg loader in those patients.

In conclusion, there was a good correlation between leg loader ABI and treadmill ABI despite smaller decrease rate of leg loader ABI than that of treadmill ABI. Although we surmise that leg loader, a simple, safe, and easy method to add load only to the lower extremities could be an alternative to diagnose PAD, further studies are necessary to evaluate the diagnostic value of the leg loader in patients with borderline ABI or those unable to perform the treadmill.


(a) Overall (n=54)
p<0.001
Decrease rate of ABI (%)
Leg loader
Treadmill
(b) ABI≦0.9 (n=37)
p<0.001
Decrease rate of ABI (%)
Leg loader
Treadmill
(c) 0.9<ABI<1.0 (n=11)
p=0.182
Decrease rate of ABI (%)
Leg loader
Treadmill
(d) Overall (n=54)
r=0.807, p<0.001
Decrease rate of leg loader ABI (%)
Decrease rate of treadmill ABI (%)
(e) ABI≦0.9 (n=37)
r=0.780, p<0.001
Decrease rate of leg loader ABI (%)
Decrease rate of treadmill ABI (%)
(f) 0.9<ABI<1.0 (n=11)
r=0.784, p=0.004
Decrease rate of leg loader ABI (%)
Decrease rate of treadmill ABI (%)

◂**Fig. 2** The decrease rate of leg loader ABI and treadmill ABI in overall (**a**), limbs with ABI ≤ 0.9 (**b**), and limbs with 0.9 < ABI < 1.0 (**c**). Correlation between decrease rate of leg loader ABI and treadmill ABI in overall (**d**), limbs with ABI ≤ 0.9 (**e**), and limbs with 0.9 < ABI < 1.0 (**f**). The top, middle, and bottom lines of the box indicate the 75th percentile, median, and 25th percentile values, respectively. Outliers indicate a value that is more than 1.5 times the interquartile range away from the top or bottom of the box. The top and bottom whiskers indicate the greatest and least values excluding outliers, respectively. *ABI* ankle-brachial index

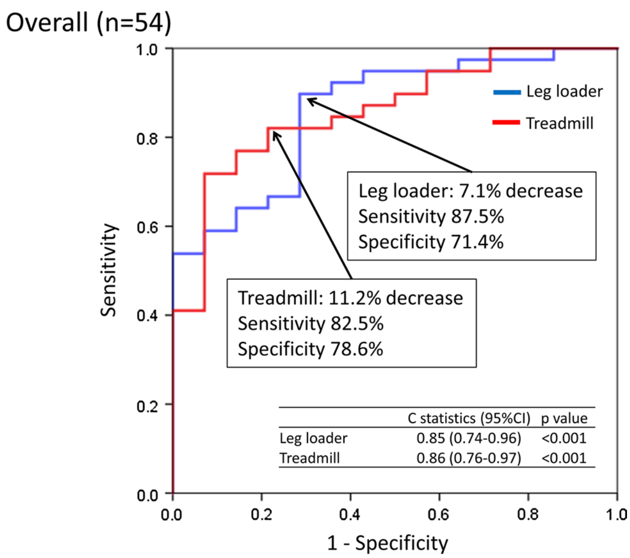


Fig. 3 The receiver operating characteristic curve of significant lesions for the leg loader and treadmill in overall. *ABI* ankle-brachial index, *CI* confidence interval

Acknowledgements The authors thank the staff of physiological laboratory for their kind help.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclosure.

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