Factors Affecting the Success Rate of Percutaneous Transluminal Angioplasty in Patients with Peripheral Arterial Disease Rutherford Degrees 2-6 At Prof. Dr. I G. N. G. Ngoerah Hospital Denpasar

Alex Toman Fernando[1*], IGAB Krisna Wibawa[2], Tjokorda Gde Bagus Mahadewa[3]

[1]Department of General Surgery, Faculty of Medicine, Udayana University,
Prof. Dr. IGNG Ngoerah General Hospital, Denpasar, Indonesia (80113)

[2]Division of Vascular Surgery, Department of Surgery, Faculty of Medicine, Udayana University,
Prof. Dr. IGNG Ngoerah General Hospital, Denpasar, Indonesia (80113)

[3]Department of Neurosurgery, Faculty of Medicine, Udayana University,
Prof. Dr. IGNG Ngoerah General Hospital, Denpasar, Indonesia (80113)

*Corresponding author details: Alex Toman Fernando; alextf.saragih@gmail.com

ABSTRACT

Background: Peripheral arterial disease (PAD) is a growing arterial disease that becomes a problem at the age of >50 years. About 12% of the adult population worldwide is reported to be affected by PAD with equal prevalence between men and women and 50% of them are asymptomatic. Percutaneous Transluminal Angioplasty (PTA) has developed rapidly and from several sources, it is found that the success rate is quite high in handling complaints that can be monitored through the Ankle Brachial Index. Several factors that can affect the incidence of restenosis in PTA according to some literature include the levels of albumin, uric acid, potassium, ferritin, phosphorus, LDL, total bilirubin, and the length of atherosclerotic lesions. *Method:* This study used a retrospective cohort using secondary data in the form of medical records from January 2020 to June 2022. This study involved 46 samples of PAD patients who performed PTA. Data analysis in this study consisted of bivariate analysis and multivariate analysis using SPSS Windows version 24. *Results:* 32 (69.2%) PAD patients with Rutherford 2-6 had successful PTA outcomes based on improvement in ankle-brachial index (ABI) values before and after treatment. Multivariate analysis performed with a logistic regression test showed that lipid levels <160 independently increased the risk of successful PTA outcomes by 6.318 times higher than patients with a history of hyperlipidemia (adjusted p=0.047; CI95%=1.026-38.992). The number of single lesions also independently increased the risk of successful PTA outcomes by 8.941 times higher than patients with multiple lesions (adjusted p=0.033; CI95%=1.195-66.026). *Conclusion:* Patients with LDL levels <160 mg/dl and a single atherosclerotic lesion type are contributing factors to the success of PTA based on ABI in patients with Rutherford grade 2-6 PAD.

Keywords: percutaneous transluminal angioplasty; peripheral arterial disease; ankle-brachial index; Rutherford

INTRODUCTION

Peripheral Arterial Disease (PAD) is an occlusive disease of the peripheral arteries that is a form of manifestation of atherosclerosis in the lower extremities that is often associated with an increased risk of cardiovascular diseases such as myocardial infarction and stroke (Behroozian and Beckman, 2021). PAD is most commonly caused by atherosclerosis, where atherosclerotic plaques cause stenosis or occlusion of arteries and result in decreased blood flow to the affected limb (Morley *et al.*, 2018; Conte *et al.*, 2019).

About 12% of the adult population worldwide is reported to be affected by PAD with equal prevalence between men and women and 50% of them are asymptomatic (Conte dan Vale, 2018). In Indonesia, according to Basic Health Research data in 2018, the prevalence of the population suffering from

cardiovascular disease, hypertension, and diabetes mellitus as risk factors for PAD were 1.5%, 34.11%, and 1.5%, respectively, an increase from the data found in 2013 (RI Kemenkes, 2018).

One alternative that can be used to screen, diagnose, and prognose PAD is the ankle-to-brachial pressure index (ABI) with good sensitivity (80%) and excellent specificity (95%). The diagnosis of PAD is made when the ABI score is <0.9, but in general, patients with PAD present with an ankle ABI index <0.4 and systolic pressure at the toes <30 mmHg (Campia *et al.*, 2019).

The Fontaine and Rutherford classification standards are the most adopted systems by vascular surgeons and are divided into 4 stages for Fontaine and 3 grading and 6 classes for Rutherford (Jaff *et al.*, 2015; Conte *et al.*, 2019).

The therapeutic approach to PAD can be done especially by controlling the risk factors, including by modifying lifestyle, antiplatelet therapy, etc (Morley *et al.*, 2018). However, in some patients, arterial revascularization therapy is the primary option to prevent the risk of amputation or limb loss, especially in Critical Limb Ischaemia conditions (Yuksel *et al.*, 2018). Revascularization therapies commonly used in medical practice include open revascularization therapy involving surgery and endovascular therapy. Currently, endovascular therapy is preferred due to its relatively less invasive nature compared to surgery and the high risk of morbidity and mortality (Dominguez *et al.*, 2015; Kinlay, 2017).

One of the endovascular therapies that is currently the choice of PAD therapy is percutaneous transluminal angioplasty (PTA). PTA is a type of invasive endovascular therapy commonly applied to Critical Limb Ischaemia patients, in which this therapy will dilate the stenosed artery using a small catheter. The success rate and 5-year survival rate of PAD patients treated with PTA are quite high, at 97.3% and 88.5% (Notash, Elyasinia dan Molavi, 2019; Choi *et al.*, 2021). Several factors that can affect the incidence of restenosis in PTA according to some literature include the levels of albumin, uric acid, potassium, ferritin, phosphorus, LDL, total bilirubin, and the length of atherosclerotic lesions (Notash, Elyasinia dan Molavi, 2019; Wu *et al.*, 2022).

Until now, studies related to factors affecting the success of PTA as one of the therapies of choice in PAD using ABI scoring are still very rare, especially in Indonesia, especially in the Bali area. If known early, modifiable factors such as clinical factors that affect the success of PTA are very important to control so that it can help success in patients who will be performed PTA, especially in patients with Rutherford stages 2-6 with moderate claudication symptoms to ischemic rest pain or who have gangrene.

METHODS
Design, time, and place of the study
This study was an analytic observational study to examine the influence of various factors on the success of PTA treatment. The purpose of this study was to see if there is a relationship between the independent variable and the dependent variable. Researchers observed and followed patients with peripheral arterial disease (PAD) Rutherford class 2-6 who treated percutaneous transluminal angioplasty (PTA) therapy through the medical records of patients admitted to Prof. Dr. I.G.N.G. Ngoerah Hospital during the period January 2022 to June 2022. Then the researchers evaluated age, gender, diabetes mellitus, hypertension, hyperlipidemia, smoking, type, and number of atherosclerotic lesions.

Sample characteristics
The target population in this study were all patients with PAD who were treated with PTA at Prof. Dr. I G. N. G. Ngoerah Hospital.

The affordable population in this study were all patients aged more than or equal to 18 years with PAD Rutherford 2-6 post-PTA who underwent treatment at Prof. DR. I G. N. G. Ngoerah Denpasar Hospital in the period January 2020 to June 2022 when this study was conducted, declared successful if there was a difference in ABI values after PTA with ABI values before PTA of at least 0.1.

Data analysis
Before analyzing the data, a data completeness check was first carried out. The research analysis was carried out with several stages of data analysis consisting of:
1. *Descriptive analysis*
This analysis aims to describe the characteristics of subjects and research variables, based on exposed and unexposed groups. Descriptive statistical analysis displays the frequency distribution. Data were then displayed in a cross-distribution table.

2. *Bivariate analysis*
Bivariate analysis was performed to determine differences in age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking, type, and the number of atherosclerotic lesions between successful and unsuccessful PTA treatment for numerical data using the independent t-test if the data were normally distributed and the Mann Whitney U test if the data were not normally distributed with a 95% confidence interval and an accepted significance limit with a p-value <0.05.

To obtain the Odd Ratio value, the data were analyzed by presenting data on age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking, type, and a number of atherosclerotic lesions in categorical form so that cross-tabulation analysis can be carried out using a 2x2 table.

3. *Multivariate analysis*
Multivariate analysis aims to analyze the independent variables of age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking, type of lesion, and number of atherosclerotic lesions so as to obtain an adjusted OR value with a 95% confidence interval and significance p value <0.05.

RESULTS
Characteristic of the study
This study used 46 medical records of patients with PAD Rutherford 2-6 post PTA who underwent treatment at Prof. DR. I G. N. G. Ngoerah Denpasar Hospital in the period January 2020 to June 2022. Respondent characteristics were described based on age, gender, diabetes mellitus, hypertension, hyperlipidemia, smoking, type and number of atherosclerotic lesions on the success of PTA based on ABI. The normality test on the age variable with the Shapiro-Wilk test showed that the data was not normally distributed (p=0.002). The data is presented in Table 1.

TABLE 1: Respondent Characteristics.

Characteristics	Number (N=46)	Percentage (%)
Age (years)		
18-66	23	50
≥66	23	50
Gender		
Male	22	47,8
Female	24	52,2
Diabetes Mellitus		
No	3	6,5
Yes	43	93,5
Hypertension		
No	24	52,2
Yes	22	47,8
Hyperlipidemia		
No (LDL<160)	24	52,2
Yes (LDL≥160)	22	47,8
Smoking		
Occasional	28	60,9
Heavy	18	39,1
Number of Lesions		
Single	24	52,2
Multiple	22	47,8
Lesion Type		
TASC A	27	58,7
TASC B	19	41,3
PTA Outputs		
Success	32	69,6
Failed	14	30,4

The median age of the sample was 66 years, with the youngest age being 17 years and the oldest being 89 years. The median value was used to classify the age variable. A total of 32 (69.6%) samples had successful PTA outcomes, while the remaining 14 (30.4%) had failed PTA. Most of the PAD patients in this study had a history of diabetes mellitus (93.5%).

The Effect of Demographic Factors on the Success of Percutaneous Transluminal Angioplasty (PTA) in Patients with Peripheral Arterial Disease (PAD)
The demographic factors evaluated in this study were age and gender. Most patients with successful PTA outcomes were in the age group of 18-66 years (78.3%). Chi-square test showed that age and gender were not factors significantly associated with successful PTA (p=0.200 and p=0.655, respectively).

TABLE 2: Effect of Demographic Factors on the Success of PTA.

Demographic Factors	PTA Outcomes		Odds Ratio (OR)	Confidence Interval (CI) 95%	P value
	Success (N=32)	Fail (N=14)			
Age (years)					
18-66	18 (78,3)	5 (21,7)	2,314	0,632-8,469	0,200
≥66	14 (60,9)	9 (39,1)			
Gender					
Male	16 (72,7)	6 (27,3)	1,333	0,376-4,725	0,655
Female	16 (66,7)	8 (33,3)			

The Effect of Clinical Factors on the Success of Percutaneous Transluminal Angioplasty (PTA) in Patients with Peripheral Arterial Disease (PAD)
Clinical factors assessed in this study included a history of comorbidities such as diabetes mellitus, hypertension, and hyperlipidemia, and a history of

smoking. The absence of hyperlipidemia was a significant factor for successful PTA outcomes (odds ratio [OR]=4.167; 95% confidence interval [CI]=1.067-16.277; p=0.034). Patients without a history of diabetes mellitus or hypertension had a lower risk of a successful PTA outcome (72.1% vs

33.3% and 77.3% vs 62.5%, respectively) compared to patients with a history of diabetes mellitus or hypertension. The absence of a history of diabetes mellitus or hypertension acted as a protective factor of successful PTA outcomes (OR<1) but was not statistically significant (p=0.216 and p=0.277, respectively). A history of occasional smoking increased PTA success by 1.909 times compared to a history of heavy smoking, but the result was not statistically significant (p=0.318).

TABLE 3: Effect of Clinical Factors on the Success of PTA.

Clinical Factors	PTA Outcomes		Odds Ratio (OR)	Confidence Interval (CI) 95%	P value
	Success (N=32)	Fail (N=14)			
Diabetes Mellitus					
No	1 (33,3)	2 (66,7)	0,194	0,016-2,337	0,216
Yes	31 (72,1)	12 (27,9)			
Hypertension					
No	15 (62,5)	9 (37,5)	0,490	0,134-1,790	0,277
Yes	17 (77,3)	5 (22,7)			
Hyperlipidemia					
No(<160)	20 (83,3)	4 (16,7)	4,167	1,067-16,277	0,034
Yes (≥160)	12 (54,5)	10 (45,5)			
Smoking					
Occasional	21 (65,6)	7 (50,0)	1,909	0,533-6,843	0,318
Heavy	11 (61,1)	7 (50,0)			

The Effect of Lesion Factors on the Success of Percutaneous Transluminal Angioplasty (PTA) in Patients with Peripheral Arterial Disease (PAD)

The lesion factors evaluated in this study were the number and type of lesions. The number of single lesions was a factor that significantly increased the risk of successful PTA outcomes by 4.167 times higher than multiple lesions (p=0.034). TASC A lesion type also increased the risk of successful PTA outcome by 6.389 times higher than TASC B (p=0.006).

TABLE 4: Effect of lesion factors on the success of PTA.

Lesion Factor	PTA Outcomes		Odds Ratio (OR)	Confidence Interval (CI) 95%	P value
	Success (N=32)	Fail (N=14)			
Number of Lesions					
Single	20 (83,3)	4 (16,7)	4,167	1,067-16,277	0,034
Multiple	12 (54,5)	10 (45,5)			
Lesion Type					
TASC A	23 (85,3)	4 (14,8)	6,389	1,588-25,708	0,006
TASC B	9 (47,4)	10 (52,6)			

Multivariate Analysis Results

Multivariate analysis was performed with a logistic regression test to assess the influence of age, gender, diabetes mellitus, hypertension, hyperlipidemia, smoking, number of lesions, and type of lesions on the success of PTA in PAD patients. The results showed that lipid levels <160 and the number of single lesions were significant independent risk factors of successful PTA outcomes.

Lipid levels <160 independently increased the risk of successful PTA outcomes by 6.318 times higher than patients with a history of hyperlipidemia (adjusted p=0.047; CI95%=1.026-38.992). The number of single lesions also independently increased the risk of successful PTA outcomes by 8.941 times higher than patients with multiple lesions (adjusted p=0.033; CI95%=1.195-66.026).

TABLE 5: Multivariate Analysis of Factors Affecting the Success of PTA.

Risk Factor	B	*Adjusted* OR (aOR)	CI 95%	*Adjusted* p
Age (18-65years)	1,772	5,883	0,649-54,119	0,118
Gender (male)	-1,273	0,280	0,036-2,169	0,223
Diabetes Mellitus (No)	-0,543	0,581	0,028-11,976	0,725
Hypertension (No)	-0,326	0,722	0,101-5,179	0,746
No Hyperlipidemia (<160)	**1,843**	**6,318**	**1,026-38,992**	**0,047**
Smoking (Occasional)	1,514	4,544	0,573-36,060	0,152
Number of Lesions (Single)	**2,191**	**8,941**	**1,195-66,026**	**0,033**
Lesion Type (TASC a)	1,605	4,979	0,747-33,200	0,097

DISCUSSION

In this study, 32 (69.2%) PAD patients with Rutherford 2-6 had successful PTA outcomes based on improvement in ankle-brachial index (ABI) values before and after the procedure. This is supported by a previous consecutive study in 70 patients with critical limb ischemia (CLI) who received PTA therapy below the knee showing that 11 patients required amputation within the first year after the procedure. The amputation-free survival (AFS) rate was high at 68% and 58% at 1- and 2 years post-PTA respectively (Strom et al., 2016).

The Effect of Age on the Success of PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)

The prevalence of PAD is reported to increase with age. One study of 2,174 samples reported that the prevalence of PAD increased with age, with a prevalence of 1% in the population aged 40-49 years to 15% of the population aged over 70 years (Vitalis et al., 2017). Most patients with successful PTA outcomes were in the age group of 18-66 years (78.3%), but multivariate and bivariate analysis showed that age was not a significant factor in PTA success (p<0.05). The results of this study are supported by previous research by Zheng et al. (2021) which showed that patients with arterial stenosis after PTA were significantly older than patients with patent arteries within 12 months. A systematic review study by Schreuder et al. (2017) on 10 articles also reported that age is a predictive factor of amputation-free survival (AFS) or limb salvage and survival after PTA.

The Effect of Gender on the Success of PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)

The prevalence of PAD by gender still varies. Data collected and categorized by the Center for Global Health Research Edinburgh UK in 2015, found that women dominated the number of PAD patients compared to men. PAD cases were found to be 11.88 million in women and 10.75 million in men in 2015 (Peige et al., 2015). This study showed that the proportion of male patients with successful PTA outcomes was higher than that of females (72.7% vs 66.7%). However, statistical test results showed that gender was not an independent factor that significantly influenced the success of PTA. A study by Graziani et al. (2007) showed similar results, where male patients with PAD after PTA who underwent amputation were higher than those who did not need amputation, but not statistically significant (76% vs 69%). These results confirm that gender is a demographic factor that does not independently influence PTA outcomes, but rather through other factors with a stronger influence.

The Effect of Hypertension on Successful PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)

Hypertensive patients' risk of PAD is not as high as those with a history of diabetes mellitus and smoking, but hypertension is reported to increase the risk of PAD by 1.5 - 2 times higher than without hypertension (Hernando and Conejero, 2007; Norgren et al., 2007). This study showed that the proportion of patients without hypertension was higher than those with hypertension (52.2% vs 47.8%). Patients with hypertension had more successful PTA outcomes than those without hypertension (77.3% vs 62.5%) although this result was not significant based on statistical analysis. A study by Graziani et al. (2007) reported that the proportion of hypertensive patients who underwent amputation after PTA was higher than those who did not (82% vs 78%), but it was not statistically significant. A study by Morley et al. (2018) reported that the use of ramipril as first-line therapy in the management of hypertension and cardiovascular risk in PAD was not shown to improve symptoms of intermittent claudication, which was also found in PAD patients.

Relationship of Diabetes Mellitus in Successful PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)

Diabetes mellitus is a qualitative and quantitative risk factor for PAD. Every 1% increase in glycosylated hemoglobin (HbA1c) is associated with a 15% increased risk of PAD (Hernando and Conejero, 2007). A more severe and prolonged course of diabetes mellitus is also associated with a higher risk of PAD development (Criqui and Aboyans, 2015). The majority of PAD patients in this study were also diagnosed with diabetes mellitus (DM), with only 3 samples (6.5%) not diagnosed with DM. The proportion of DM patients with successful PTA outcomes was also reported to be higher than patients without DM (72.1% vs. 33.3%) and an OR<1 was obtained so that the absence of DM was concluded to be a protective factor against successful PTA outcomes.

However, this result was not significant based on bivariate and multivariate analysis. A previous study by Vossen et al. (2018) showed that diabetes mellitus was an independent risk factor for loss of primary clinical patency post-PTA in PAD patients. Patients with diabetes had a 1.47 times higher risk of losing patency post-PTA (Vossen et al., 2018).

The Effect of LDL <160mg/dl in Successful PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)
A retrospective study of 467 men and 1,444 women with an average age of 81 years and symptomatic PAD showed that every 1 mg/dl increase in LDL cholesterol was associated with a 1.9% increased risk of PAD prevalence. However, another study showed no significant association between LDL cholesterol and incident PAD in the female study after adjusting for age in the regression model (Aday and Everett, 2020). This study defined hyperlipidemia as cholesterol levels ≥160 mg/dl. Most patients in this study did not have hyperlipidemia (cholesterol <160 mg/dl). Bivariate and multivariate analysis in this study proved that hyperlipidemia was a factor that significantly and independently influenced successful PTA outcomes. The absence of hyperlipidemia independently increased the risk of successful PTA outcomes by 6.318 times higher than patients with hyperlipidemia (CI95%=1.195-66.026; p=0.033). Hyperlipidemia was reported to be higher in patients who did not undergo amputation than those who did, although not statistically significant (28% vs 12%) (Graziani et al., 2007).

In a study by SHARP, Baigent et al. (2011) reported that lowering LDL cholesterol reduced the incidence of major atherosclerotic events (such as non-fatal myocardial infarction, death from coronary disorders, non-hemorrhagic stroke, and complications after arterial revascularization procedures) in patients with chronic kidney disease. Hypercholesterolemia was reported as a risk factor (HR 1.05) and the use of stati was a protective factor (HR 0.81) for clinical patency outcomes (recurrence of symptoms and need for revascularization) after PTA, but the results were not statistically significant (Vossen et al., 2018). Different results were reported by Aiello et al (2012) in a retrospective study that examined 646 critical limb ischemia (CLI) patients who received endovascular therapy. The results showed that at 24 months post-intervention, the group taking statins at the time of intervention had significantly higher rates of primary patency, secondary patency, limb salvage, and overall survival than patients who did not get statins. The group of patients taking statins had a significantly higher incidence of diabetes mellitus, coronary artery disease, congestive heart failure, previous myocardial infarction, and coronary artery bypass grafting than patients not taking statins (Ailleo et al., 2012).

The Effect of Smoking on Successful PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)
Half of all PAD diagnoses can be attributed to smoking history. It is concluded that heavier smokers have a higher potential to suffer from PAD than light smokers. In addition, the risk of PAD will also increase in former smokers compared to non-smokers. Quitting smoking can also prevent the worsening of symptoms in patients already diagnosed with PAD (Armstrong et al., 2014). This study showed that the majority of patients with PAD were light smokers based on WHO categories. The proportion of successful PTA outcomes in patients with light smokers was higher compared to patients with heavy smokers (65.6% vs 61.1%), although not statistically significant. Research by Strom et al (2012) also showed that smoking history was not associated with the risk of post-PTA amputation. Patients with a history of smoking were reported to have a higher risk of amputation compared to non-smokers (35% vs 18%) but it was not statistically significant (Graziani et al., 2007).

The Effect of Atherosclerotic Lesion Type on the Success of PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)
The majority of PAD patients in this study had TASC A lesion type in this study. Based on lesion type, a higher proportion of patients with successful PTA outcomes had TASC A lesion type compared to TASC B (85.3% vs 47.4%), but this result was not statistically significant. Previous studies reported that the most common PAD classification was TASC B (53%) followed by TASC A (41%). The results of this study are supported by previous studies. This TASC classification was also reported to be unrelated to symptom recurrence and the need for revascularization after PTA (Vossen et al., 2018). The same results were also reported by Dosluoglu et al., (2012) where the need for infrapopliteal intervention was a factor that increased the risk of limb loss by 2 times higher than other intervention sites.

The Effect of Lesion Count on Successful PTA in Patients with Rutherford Grade 2-6 Peripheral Arterial Disease (PAD)
The atherosclerotic process that occurs in the lower extremities starts from the infrarenal aorta to the final branches of the tibial artery. When clinical symptoms appear, obstruction usually occurs at several levels of blood vessels (Okataviono, 2014). More than half of the PAD patients in this study had a single lesion (52.2%). Based on the number of lesions, a higher proportion of patients with successful PTA outcomes had single lesions compared to multiple (83.3% vs 54.4%) and this difference was statistically significant (p=0.033). The number of single lesions was an independent factor that had a significant effect on successful PTA outcomes. Patients with a single lesion had 8.941 times higher odds of achieving a successful PTA outcome than those with multiple lesions (CI95%=1.195-66.926).

The location of PAD has also been reported to be associated with successful outcomes and resilience after PTA. Research by Strom et al. (2016) showed that there was no relationship between the amount of recanalization of the cruris blood vessels. Sites of stenosis or occlusion in the peroneal artery had more

success after PTA, compared to other sites such as the anterior and posterior tibia (Faglia et al., 2012). Percutaneous transluminal angioplasty (PTA) is also used as first-line therapy for stenosis and occlusion of vascular accesses, such as arteriovenous fistulas (AVF) and arteriovenous grafts (AVG). A study in 284 hemodialysis patients who received PTA showed that multiple stenosis was a factor associated with post-intervention patency. Multiple stenosis was reported to increase the risk of recurrent stenosis by 6.332 times higher than single stenosis (Zheng et al., 2021).

CONCLUSIONS

Patients with LDL levels <160 mg/dl and a single atherosclerotic lesion type are contributing factors to the success of PTA based on ABI in patients with Rutherford grade 2-6 PAD.

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