



## Inadequate Treatment of Hypertension in Peripheral Arterial Disease Affecting Patient Outcomes

Mahmud Saedon<sup>1</sup>, Mimi M Li<sup>2\*</sup>, Athanasios Saratzis<sup>3</sup> and Donald RJ Singer<sup>1,4</sup>

<sup>1</sup>Nottingham University Hospital NHS Trust, UK

<sup>2</sup>Department of Vascular Surgery, South Tees Hospitals NHS Foundation Trust, UK

<sup>3</sup>University of Warwick, UK

<sup>4</sup>Fellowship of Postgraduate Medicine, London, UK

### Abstract

**Background:** Hypertension is major risk-factor for Peripheral Arterial Disease (PAD). We prospectively assessed the prevalence of undertreated hypertension in patients presenting with PAD across a region in the UK and estimated its impact on presentation and outcome.

**Methods:** We prospectively assessed the adequacy of BP-control and hyperlipidaemia in 284 patients [age  $71 \pm 7$  years (SD), 34 (12%) females] attending a PAD-clinic after being referred by their GP in two regional centers (West-Midlands, UK). NICE Guidance was used as standard to define hypertension [Blood Pressure (BP)  $>140$  mmHg systolic and  $>90$  mmHg diastolic]. BP was measured according to British Hypertension Society (BHS) guidelines. 105 (37%) patients had critical ischaemia at baseline and 94 (33%) were diabetic.

**Results:** Mean BP was  $147/83 \pm 21/18$  mmHg, 131 patients (80%) were already on some treatment for hypertension when referred. 210 (74%) were receiving antiplatelet-agents and 204 (72%) a statin or other lipid-lowering medication; 202 (71%) were on “best medical therapy”. All individuals with critical limb ischaemia had a BP above the NICE standard. Blood-pressure treatment was not guideline-compliant in 55% of patients.

**Conclusion:** Hypertension is undertreated in PAD despite well-established guidelines. Undertreated patients were most likely to present with critical ischaemia and undergo amputation. Urgent review of hypertension treatment in PAD, both in the community and in hospital-based services, is necessary.

### OPEN ACCESS

#### \*Correspondence:

Mimi M Li, Department of Vascular Surgery, South Tees Hospitals NHS Foundation Trust, The James Cook University Hospital, Marton Road, Middlesbrough, Cleveland TS4 3BW, UK,

E-mail: [mimi.mz.li@gmail.com](mailto:mimi.mz.li@gmail.com)

Received Date: 18 Jan 2019

Accepted Date: 11 Feb 2019

Published Date: 15 Feb 2019

#### Citation:

Saedon M, Li MM, Saratzis A, Singer DRJ. Inadequate Treatment of Hypertension in Peripheral Arterial Disease Affecting Patient Outcomes. *World J Vasc Surg.* 2019; 2(1): 1017.

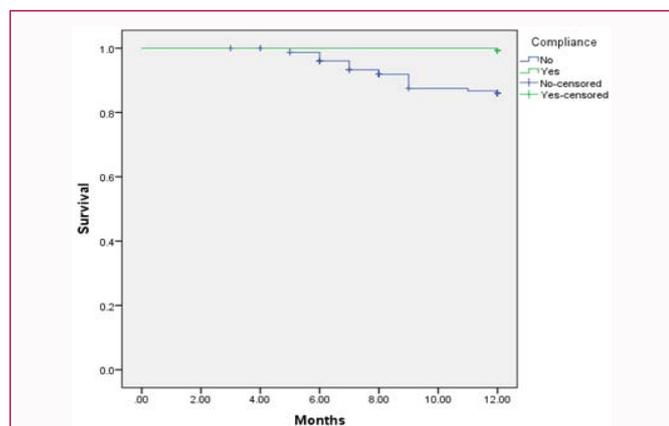
**Copyright** © 2019 Mimi M Li. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### Introduction

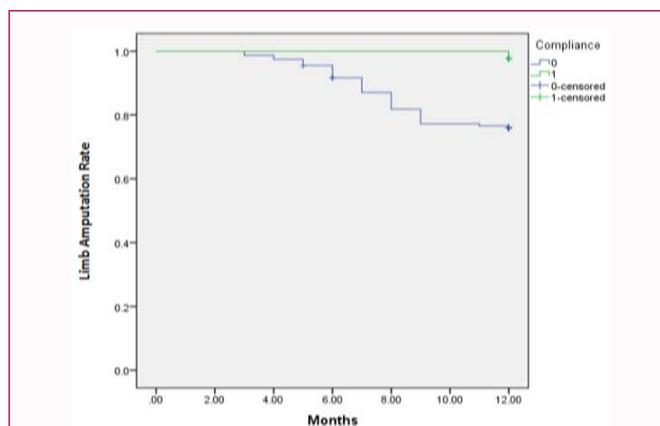
Peripheral Arterial Disease (PAD) is a common manifestation of atherosclerosis, affecting up to 20% of the over-70 population. It has seen a global increase in prevalence of 23.5% in the preceding decade [1]. Symptomatic PAD most commonly presents as intermittent claudication, but can also manifest as critical limb ischaemia. With a plethora of risk factors such as hypertension, hyperlipidaemia, diabetes and smoking, PAD patients have a high risk of mortality from cardiovascular events [2]. Hypertension is an important modifiable risk factor known to increase the risk of cardiovascular complications in established PAD [3]. An estimated 50% to 92% of PAD patients have concomitant hypertension [4]. The HOPE study established the impact of the antihypertensive ramipril on prevention of major cardiovascular events in both clinical and subclinical PAD [5]. Use of lipid-lowering therapy has also been shown to be effective in significantly reducing the risk of cardiovascular events in PAD [6].

In the United Kingdom (UK), there are clear guidelines produced by the National Institute of Health and Care Excellence (NICE) regarding Blood Pressure (BP) in secondary prevention. NICE guidelines recommend a target BP of 140/90 mmHg in those under 80 with treated hypertension. Treatment is a stepwise approach with initial commencement of an Angiotensin-Converting Enzyme (ACE) inhibitor, Angiotensin II Receptor Blocker (ARB) or Calcium Channel Blocker (CCB) depending on patient factors [7]. General risk factor management with lipid-lowering and antiplatelet therapy, as well as lifestyle advice and diabetic control, is also recommended for PAD patients [8].

The aim of this study was to assess the adequacy of BP control in patients presenting to secondary care with symptomatic PAD, and assess the possible impact of this on patient outcomes. Secondary



**Figure 1:** Comparison of all-cause mortality in patients compliant and non-compliant with recommended therapy.



**Figure 2:** Comparison of amputation rate in patients compliant and non-compliant with recommended therapy.

aims were to also assess the use of lipid-lowering and antiplatelet therapy in this patient group.

**Methods**

This was a prospective audit of patients presenting to vascular clinics following GP referral with a diagnosis of PAD confirmed by a vascular specialist. Compliance was tested against the NICE guideline for hypertension (CG127), with a target of systolic BP <140 mmHg and diastolic BP <90 mmHg. Data was collected for patients presenting over a 1-year period (August 2013 to August 2014) at three UK vascular centres: Good Hope Hospital (Birmingham), University Hospital Coventry, and Leicester General Hospital. At initial presentation to vascular clinic, BP was measured according to British Hypertension Society guidelines using a validated Omron BP monitor (Omron Corporation, Kyoto, Japan) by a trained nurse [9]. BP was measured in each arm, with recordings 1 to 2 minutes apart, and the higher arm value being used to assess BP control. If a large difference (>10 mmHg) between the two arm readings was found, a third measurement was made and the average of the three readings taken. Hypertension was defined as a BP of ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic. From the patient history it was established whether any antihypertensive medication had been commenced. Patients were followed-up for one year, with outcomes for limb amputation and all-cause mortality recorded. Data was also recorded on severity of PAD (presence/absence of critical limb ischaemia), patient age, gender, cardiovascular risk factors, regular medications, and co-morbidities.

Regional Research Ethics Committee (REC) review was not required under the harmonised Governance Arrangement for REC (GafREC) for research because this study was considered part of service evaluation (audit). Therefore, patient consent was not required. Statistical analysis was performed using IBM SPSS Statistics (IBM Corp, New York, USA).

**Results**

**Baseline characteristics**

A total of 284 patients were included in this study. Mean age was 71 (± 7SD), with 80% (227) of patients over the age of 55. 12% (34) of patients were female. 33% (94) of patients were diabetic, 18% (51) were current smokers, 50% (142) ex-smokers, and 37% (105) had critical limb ischaemia at baseline (Table 1). Patients had been prescribed the following medications: statin 72% (204), ezetimibe

**Table 1:** Patient demographics.

Characteristic	Number (%)
Age: mean ± SD	71 ± 7 years
Age >55 years	227 (80%)
Critical Limb Ischaemia	105 (37%)
Diabetes Mellitus	94 (33%)
Smoker	51 (18%)
Ex-Smoker	142 (50%)

**Table 2:** Patient medications.

Medication	Number (%)
Statin	204 (72%)
Ezetimibe	2 (0.7%)
ACE Inhibitor	80 (28%)
Beta Blocker	34 (12%)
Calcium Channel Blocker	22 (7.8%)
Diuretic	205 (72%)
Antiplatelet	210 (74%)

0.7% (2), ACE inhibitor 28% (80), beta blocker 12% (34), calcium channel blocker 7.8% (22), diuretic 72% (205), antiplatelet agent 74% (210) (Table 2).

**Risk factor control**

Average blood pressure (mean ± SD) was 146 ± 18 mmHg systolic and 81 ± 12 mmHg diastolic. 46% (184) of patients had a systolic BP>140 mmHg, 40% (113) had a diastolic BP>90. For patients without critical limb ischaemia, average BP was 141 ± 17 systolic and 79 ± 15 diastolic. For critical limb ischaemia patients, this was significantly higher at 148 ± 21 systolic and 82 ± 21 diastolic (p=0.02). Only 45% (128) of patients were on antihypertensive therapy with adequately treated BP. 20% (57) of patients were not on any antihypertensive therapy despite being hypertensive.

**Patient outcomes**

Patients not being compliant with best medical therapy (taking antihypertensive, lipid-lowering and antiplatelet therapy) was associated with an increased presence of critical limb ischaemia (odds ratio: 1.9, 95% CI 0.8-2.6, p<0.001). Patients not compliant with best medical therapy also had a significantly increased all-cause mortality

of 13% at 1 year, compared with 1% for those that were compliant ( $p < 0.0001$ , log-rank test) (Figure 1). Patients not compliant with best medical therapy had a 20% rate of limb amputation at 1 year compared with 2% in those compliant ( $p < 0.0001$ , log-rank test) (Figure 2).

## Discussion

A large proportion of patients in this study were identified as hypertensive. Despite the availability of clear guidelines for management in the community, less than half of patients were receiving adequate treatment. With hypertension control a known modifiable risk factor affecting patient outcomes, this is a significant finding and area for improvement [3,5]. Worryingly, a fifth of patients found to be hypertensive had not been started on any antihypertensive medication, suggesting that this could be more than a simple patient compliance problem. Lipid control with statin therapy and commencement of an antiplatelet agent are also recommended in all PAD patients for secondary prevention of cardiovascular events [8], with well-documented benefits on cardiovascular event risk reduction [6,10]. Use of lipid-lowering therapy fell short of the guidelines, with over a quarter of patients not taking a statin; antiplatelet therapy was also similarly underused.

Looking at patient outcomes, the all-cause mortality rate at one year is significantly lower for those on best medical therapy than for those that aren't. This difference between the two groups begins to manifest around 6 months after presentation to vascular clinic. All-cause mortality is a relatively crude measure for progression of vascular disease, however, as no adjustments have been made for other co-morbidities. Amputation rate is a measure which is more closely linked to vascular disease progression. Again, there is a significant difference between the two groups, with the guideline non-compliant group ten times more likely to have a limb amputation at one year. Undertreated patients were more likely to present with critical limb ischaemia. The impact of undertreated modifiable risk factors is evident in our studied patient population: non-compliance with treatment led to significantly worse outcomes at one year, with greater likelihood of mortality and amputation.

It is known that blood pressure can be artificially raised in a clinical setting due to anxiety, leading normotensive patients to be classified as hypertensive [9]. Taking multiple measurements with an interval rather than one isolated measurement aimed to counteract this. Even with the assumption that some patients may have artificially raised BP, a significant difference in BP between patients with and without critical limb ischaemia was still found.

Although a large proportion of patients with undertreated risk factors were identified, potential barriers to uptake of treatment still

need to be explored. Poor patient compliance or patient preference may be a cause, with improved patient education and regular monitoring in the primary care setting may be potential solutions for poor patient compliance or patient preference. Other factors such as consultation time restraints or lack of physician awareness could also be contributory.

## Conclusion

Modifiable risk factors, particularly hypertension, are undertreated in PAD despite well-established guidelines. Undertreated patients were more likely to present with critical limb ischaemia and had a significantly increased risk of undergoing amputation. An urgent review of modifiable risk-factor treatment in PAD, both in the community and hospital-based services, is necessary.

## References

1. Fowkes FGR, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet*. 2013;382(9901):1329-40.
2. Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med*. 1992;326(6):381-6.
3. Singer DR, Kite A. Management of hypertension in peripheral arterial disease: does the choice of drugs matter?. *Eur J Vasc Endovasc Surg*. 2008;35(6):701-8.
4. Olin JW. Hypertension and peripheral arterial disease. *Vasc Med*. 2005;10(3):241-6.
5. Ostergren J, Sleight P, Dagenais G, Danisa K, Bosch J, Qilong Y, et al. Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. *Eur Heart J*. 2004;25(1):17-24.
6. Aung PP, Maxwell H, Jepson RG, Price J, Leng GC. Lipid-lowering for peripheral arterial disease of the lower limb. *Cochrane Database Syst Rev*. 2007;17(4):CD000123.
7. National Institute of Health and Care Excellence. Hypertension in adults: diagnosis and management. NICE CG127. 2011.
8. National Institute for Health and Care Excellence. Peripheral arterial disease: diagnosis and management. NICE CG147. 2012.
9. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion J-M, Mancia G, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens*. 2003;21(5):821-48.
10. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ*. 2002;324(7329):71-86.