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Original Article

Low Adherence to Guideline for the Control of Major Cardiovascular Risk Factors in Diabetic Patients with Peripheral Arterial Disease: A Study in Northern Part of Thailand

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Abstract

Objective: **The control of major cardiovascular risk factors is an important issue in the treatment of patients with peripheral arterial diseases (PAD), and several large trials and many guidelines have stressed the importance of detection and treatment of these risk factors. This is even critical in diabetic patients with PAD because such patients carry higher risk of cardiovascular problem than non diabetic patients. However, it is not known to what extent this has been applied to such patients. The objective of this study was to investigate the adequacy of risk factor management in diabetic patients with PAD.**

Methods: **A cross-sectional study was conducted in 286 consecutive diabetic patients with PAD. A medical history, medication history, and fasting venous blood sample were taken for each patient. The plasma concentrations of cholesterol were determined. PAD was diagnosed when patients had low ankle brachial index (≤ 0.9). Then we classified whether patients had good or poor control in each criteria according to the recommended guidelines between PAD and non PAD.**

Results: **There were 2,247 diabetic patients, 874 (38.9) males and 1373 (61.1) females. Among them were 286 PAD patients. Diabetic patients with PAD had histories of cardiovascular events (angina pectoris, myocardial infarction, unstable angina, stroke and transient ischemic attack) more than those without PAD. Apart from smoking, the percentage of appropriate control of risk factors was around only 15-30% in PAD patients. When authors focused on further details between non PAD, mild PAD and severe PAD, severe PAD had lower BMI and lower waist circumference than those in other groups. Eighteen out of 286 PAD patients were still smoking.**

Conclusion: **Although the risk factors in vascular disease management are well understood and many guidelines have been published, they do not seem to be well managed in diabetic patients with PAD.**

Keywords: **blood pressure, diabetes, dyslipidemia, peripheral arterial disease, smoking**

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Introduction

Hyperlipidaemia, hypertension, smoking, obesity and hyperglycemia are the most important risk factors in atherosclerosis, which is the major cause of arterial diseases[1]. Aggressive risk reduction to prevent cardiovascular events in patients with arterial disease is well known[2]. Many recommendations have been made specifically for PAD patients[2-5]. Some even more focus on PAD in diabetic patients, because these patients are remarkably at high risk for cardiovascular morbidity and mortality. The guidelines of the American Heart Association (AHA) and The Royal College of Physicians of Thailand indicated risk factor control in diabetic patients with PAD as in Table 1[3-5].

Despite much evidence about the danger of inappropriate risk factor control in diabetic patients with PAD, it is not known to what extent this has been applied to Thai patients. The objective of this study was to study the extent to which participants' risk factors this study had been managed with regard to such guidelines.

Materials and Methods

This study recruited outpatients aged 45 years with diabetic mellitus between May 2014 and August 2014. This study was conducted in three hospitals in Northern part of Thailand namely Maharaj Nakorn Chiang Mai Hospital, Chiangrai Prachanukroh Hospital and Lamphun Hospital. Medical records were reviewed. Patients' records and the drug charts in the patient's notes were checked for record of laboratory within three months during enrolment including low density lipoprotein (LDL) and HbA1C. The test consisted of the participants sitting quietly in a room at the clinic for at least 20 minutes. Twice, at intervals of 5-10 minutes, their blood pressure was measured on left arm at heart level. The mean of these two measurements was used for the analysis. Anthropometric measurements were performed. While wearing indoor clothes, the participant's height, weight, and waist circumference measurement were taken. Each participant filled out questionnaires on various cardiovascular risk factors, such as family history of smoking experience, cardiovascular disease, current drug habits, and past medical history. Ankle brachial index (ABI) was determined in all patients using autonomic machine. The criteria for diagnosis of PAD is the ABI ≤ 0.9 or a history of leg ischemia with a previous intervention (angioplasty, bypass graft or other vascular intervention including amputation)[2]. Then authors further classified PAD group into mild PAD (ABI 0.9-0.5) and severe PAD (ABI < 0.5 or history of a previous intervention).

Statistical methodology

The data was showed in descriptive study in percentage. We categorized each risk factor as "controlled" if it was at the target level of the American Heart Association recommendation and The Royal College of Physician of Thailand as Table 1. Chi-squared test was used to analyse the difference between PAD and non PAD group. The protocol was approved by our local ethic committee in each hospital and signed, informed consent was obtained for all patients. Analysis was performed by STATA for Windows version 13.0.

Results

There were 2,247 diabetic patients 874 (38.9) males and 1373 (61.1) females (Table1). There were 286 PAD patients. The number of severe and mild PAD was 35 and 251 cases respectively. Diabetic patients with PAD had histories of cardiovascular events (angina pectoralis, myocardial infarction, unstable angina, stroke and transient ischemic attack) more than those without PAD (Table 2). Apart from smoking, the percentage of appropriate control of risk factors was around only 15-30% in PAD patients (Table 3). Non PAD patients had more BMI and waist circumference than those in PAD patients. When authors focused on

Table 1 Criteria of good control of risk factors according to AHA guideline and the guideline of The Royal College of Physicians of Thailand

Item	"Good control" definition
Blood pressure (BP)	systolic BP < 130 mmHg and diastolic BP < 80 mmHg
LDL	< 70 mg/dL
HbA1C	< 7%
Body mass index	≤ 23
Waist circumference	< 90 cm (male) or < 80 cm (female)
Smoking	Stop

LDL low density lipoprotein

Table 2 Baseline clinical data

Characteristics	Total (2247 patients) N (%)	PAD (286 patients) N (%)	Non-PAD (1961patients) N (%)
Age (years)			
45 - 49	151 (6.7)	11 (3.9)	140 (7.1)
50 - 59	759(33.8)	63 (22.0)	696 (35.5)
60 - 69	813(36.2)	97 (33.9)	716 (36.5)
70 - 79	400(17.8)	81 (28.3)	319 (16.3)
≥ 80	124 (5.5)	34 (11.9)	90 (4.6)
Gender			
Male	874(38.9)	112 (39.2)	762 (38.9)
Female	1373(61.1)	174 (60.8)	1199 (61.1)
Previous history of cardiovascular events			
1. Chronic stable angina	8 (0.4)	3 (1.1)	5 (0.3)
2. Myocardial infarction	73 (3.3)	19 (6.6)	54 (2.8)
3. Unstable angina	35 (1.6)	9 (3.2)	26 (1.3)
4. Stroke (ischemic)	55 (2.5)	15 (5.2)	40 (2.0)
5. Transient ischemic attack	3 (0.13)	1 (0.35)	2 (0.10)

PAD = peripheral arterial disease

Table 3 Distribution of patients according to recommended criteria between PAD and non PAD

Item	Non PAD	PAD	*P* value
Blood pressure (BP)			
Systolic BP < 130 mmHg and Diastolic BP < 80 mmHg)	29.8	28.7	0.70
Systolic BP _ 130 mmHg or BP Diastolic _ 80 mmHg)	70.2	71.3	
LDL			
< 70 mg/dL	18.7	18.8	0.95
_ 70 mg/dL	81.4	81.3	
HbA1C (%)			
< 7	25.8	30.1	0.18
≥ 7	74.2	69.9	
BMI (kg/m^2)			
≤ 23	31.1	37.1	0.04
>23	68.9	62.9	
Waist circumference (cm.)			
< 90 (Male) or < 80 (Female)	29.9	35.6	0.05
≥ 90 (Male) or ≥ 80 (Female)	70.1	64.4	
Smoking			
Never or Former	96.8	93.7	0.008
Current	3.2	6.3	

PAD = peripheral arterial disease, BP = blood pressure, LDL = low density lipoprotein, BMI=body mass index

further details between non PAD, mild PAD and severe PAD, severe PAD had lower BMI and waist circumference than those in other groups (Table 4).

Discussion

Although a huge amount of evidence supports the proper treatment of risk factor control in patients with PAD, it does not seem to be well managed in clinical practice[6]. Indeed mismanagement is evident in patients in this study, only 15-30% of diabetic patients with PAD had proper control in each risk factor. It seems that some patients are not aware of this problem, which may imply that clinicians fail to stress the

Table 4 Distribution of patients according to recommended criteria between non PAD, Mild PAD (ABI 0.5-0.9), severe PAD (ABI < 0.5)

Item	Non PAD	Mild PAD	Severe PAD	*P* Value
Blood pressure (BP)				
Systolic BP < 130 mmHg and Diastolic BP < 80 mmHg)	29.8	27.9	34.3	0.69
Systolic BP ≥ 130 mmHg or BP Diastolic ≥ 80 mmHg)	70.2	72.1	65.7	
LDL				
< 70 mg/dL	18.7	16.6	35.0	0.14
≥ 70 mg/dL	81.4	83.5	65.0	
HbA1C (%)				
< 7	25.8	30.9	22.7	0.29
≥ 7	74.2	69.1	77.3	
BMI (kg/m^2)				
≤ 23	31.1	32.7	68.6	<0.001
>23	68.9	67.3	31.4	
Waist circumference (cm.)				
< 90 (Male) or < 80 (Female)	29.9	33.3	51.4	0.01
≥ 90 (Male) or ≥ 80 (Female)	70.1	66.7	48.6	
Smoking				
Never or Former	96.8	93.6	94.3	0.03
Current	3.2	6.4	5.7	

PAD = peripheral arterial disease, BP = blood pressure, LDL = low density lipoprotein, BMI=body mass index

importance of the risk factor control to the patients with PAD. Only 20-35 % of severe PAD group had good control in blood pressure, LDL and HbA1C.

Since severe PAD patients mainly came to see physicians due to rest pain, gangrene or ulcer, they are waiting for surgery. We hypothesised that some physicians believe that once a patient has PAD, risk factor control is no longer beneficial. In other words, it is already too late to treat a severely stenotic lesion. While it is true that a severely stenotic lesion is highly unlikely to regress in a short period, it can reduce the cardiovascular event. For example, in many trials statins have reduced the incidence of myocardial infarction, which is the main cause of death peri-operatively and long-term after surgery[7]. To achieve a good outcome for these patients, adequate risk factor management would be beneficial.

This study found that hyperlipidemia was not well controlled in clinical practice in Thailand. The main reason is probably no one takes responsibility for the management of hyperlipidaemia. Some general practitioners treat hyperlipidemia intensively in patients with PAD and some do not. Some vascular surgeons do not treat it because of the expense and ask general practitioners to handle it instead, which makes this matter even more complicated if general practitioners do not understand the importance of risk factor management in these patients. There had been a lack of direct evidence about the benefits of risk factor modifications such as lipid-lowering therapy for diabetic patients with PAD. Some clinicians might be concerned about the cost-effectiveness of lipid-lowering treatment, more specifically about its lack of cost-effectiveness for patients with PAD. This might come from confusion about the correct values for good control of plasma cholesterol. There are several recommendations in clinical practice. For example, in the USA, the National Cholesterol Education Program used 100 mg/dl as the desirable blood cholesterol level[8]. However, for PAD patients who have a high risk of developing associated ischaemic heart disease the recommendation is 70 mg/dl rather than 100 mg/dl (AHA guideline)[3,4]. Therefore, it is important to educate all clinicians who take care of vascular patients about proper management of risk factor control.

In addition, serum cholesterol is an independent predictor of atherosclerosis[9,10] and the level of hyperlipidaemia is a prognostic factor for recurrence of peripheral artery stenosis following carotid endarterectomy (CEA)[11,12]. If hyperlipidaemia can be adequately treated, the patency of the artery may last longer. Ultrasonic evidence has shown that lipid-

lowering treatments result in regression of carotid plaques and Furberg et al. found that the average intimal medial thickness was significantly lower in patients taking lovastatin than in those of control group[13]. This might be particularly beneficial for patients with bilateral PAD who have a unilateral leg surgery and conservative treatment for the other lesion. Thus proper management of hyperlipidaemia after surgery for PAD on one side may prevent progression of the disease on the non-operative side.

It is interesting to note that patients in severe PAD group had significantly lower BMI and waist circumference than those in other groups. This can partially be explained by BMI in PAD patients which was lower than those in non PAD patients. Although originally we believe obesity is an important risk factor of PAD, this seems contrast to our original concept. We hypothesized an explanation that these patients were in starvation stage due to excruciating foot pain in severe PAD. Further nutritional analysis is needed to confirm this hypothesis.

Another risk factor that can be managed is smoking. Eighteen patients (6.3%) in our study were still smoking (Table 3). It is well known that smoking is strongly associated with atherogenesis, and it has been reported in many papers that smoking is associated with recurrent PAD after surgery[14]. Cessation of smoking rapidly decreases the risk of ischaemic stroke and myocardial infarction[15,16]. This is another way in which long-term results for these patients may be improved.

Limitations

There are some limitations of this study. Firstly, all patients in this study came from one region in Northern part of Thailand, which might not represent all PAD patients in this country, including those in other settings. Secondly, only the LDL was used as a measurement of lipid abnormality, but low serum HDL and high triglyceride levels may be better measures of lipid abnormality in some subgroup.

Conclusion

In this study it was found that one-third of PAD patients had proper control for each risk factor according to the recommended value. Awareness of the significance of risk factor control is inadequate in clinical practice. This problem persists in spite of much evidence of the benefits of risk factor control. Management of risk factor should be strictly performed. The findings in current study support the need for greater education of clinicians who involved in the management of risk factor of PAD patients. To control the majority of these risk factors effectively, much expertise is needed and many services are involved, including those that lead to a cessation of smoking. A risk factor clinic with a multidisciplinary approach might therefore be beneficial.

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REFERENCES

1. Castelli WP. Epidemiology of coronary heart disease: the Framingham study. Am J Med 1984;76:4-12.
2. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vas Surg 2007;45 Suppl S:S5-67.
3. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines. J Am Coll Cardiol 2006;47:1239-312.
4. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, et al. 2011 ACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011;58:2020-45.

5. Thai Medical Council TRCoPoT. Guideline for tertiary care in arterial disease prevention Bangkok: 2011.
6. Aspry KE, Holcroft JW, Amsterdam EA. Physician recognition of hypercholesterolemia in patients undergoing peripheral and carotid artery revascularization. Am J Prev Med 1995;11:336-41.
7. Musser DJ, Nicholas GG, Reed JF 3rd. Death and adverse cardiac events after carotid endarterectomy. J Vas Surg 1994;19:615-22.
8. Talbert RL. New therapeutic options in the National Cholesterol Education Program Adult Treatment Panel III. Am J Managed Care 2002;8:S301-7.
9. Joensuu T, Salonen R, Winblad I, Korpela H, Salonen JT. Determinants of femoral and carotid artery atherosclerosis. J Int Med 1994;236:79-84.
10. Rittoo D, Cramb R, Odogwu S, Khaira H, Duddy M, Smith S, et al. Worsening lipid profile is associated with progression of carotid artery stenosis. Int Angiol 2001;20:47-50.
11. Das MB, Hertzer NR, Ratliff NB, O'Hara PJ, Beven EG. Recurrent carotid stenosis. A five-year series of 65 reoperations. Ann Surg 1985;202:28-35.
12. Rapp JH, Qvarfordt P, Krupski WC, Ehrenfeld WK, Stoney RJ. Hypercholesterolemia and early restenosis after carotid endarterectomy. Surgery 1987;101:277-82.
13. Furberg CD, Adams HP Jr, Applegate WB, Byington RP, Espeland MA, Hartwell T, et al. Effect of lovastatin on early carotid atherosclerosis and cardiovascular events. Asymptomatic Carotid Artery Progression Study (ACAPS) Research Group. Circulation 1994;90:1679-87.
14. Cuming R, Worrell P, Woolcock NE, Franks PJ, Greenhalgh RM, Powell JT. The influence of smoking and lipids on restenosis after carotid endarterectomy. Eur J Vas Surg 1993;7:572-6.
15. Ockene IS, Miller NH. Cigarette smoking, cardiovascular disease, and stroke: a statement for healthcare professionals from the American Heart Association. American Heart Association Task Force on Risk Reduction. Circulation 1997; 96:3243-7.
16. Wolf PA, D'Agostino RB, Kannel WB, Bonita R, Belanger AJ. Cigarette smoking as a risk factor for stroke. The Framingham Study. JAMA 1988;259:1025-9.