Original Article

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Factor Associated with Abnormal Ankle-Brachial Index Among Diabetic Patients in Songklanagarind Hospital: A Retrospective Cohort Study

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Abstract:

Objective: To find the correlation between type 2 diabetic patients who had abnormal ankle-brachial index (ABI) among factors affected diabetes and cardiovascular outcomes including acute coronary syndrome (ACS), myocardial infarction (MI), coronary revascularization stroke, renal replacement therapy, leg revascularization and limb amputation

Material and Methods: Retrospective cohort study collecting the data of 548 diabetic patients examined ABI at Out-patient Departments from 1st January 2009 to 31st December 2015.

Results: From 548 medical records including only normal-ABI group and low-ABI group, we found that hypertension, chronic kidney disease (CKD), smoking, history of previous MI, history of previous stroke and age were the significant associated factor of low-ABI. The survival analyses revealed the significantly higher rate of ACS, MI, and coronary revascularization in low-ABI group (p-value=0.04, <0.01, <0.01 respectively) after exposed to low-ABI around 4 years. However, the study found no significant difference of other outcomes between the 2 groups.

Conclusion: Songklanagarind's diabetic patients with low-ABI were associated with the significantly higher rate of multiple cardiovascular risk factors including hypertension, CKD, smoking, history of previous MI, history of previous stroke and age and they tend to significantly experience more ACS, MI and coronary revascularization after 4 years exposed to low-ABI.

Keywords: ankle-brachial index, diabetic patients

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Introduction

Currently, diabetes plays a crucial role in national health problem. The number was rising annually and reached 670,664 in 2014.[1] It is predicted that its number will rise continuously.[1] Failure to achieve the appropriate blood sugar level may cause long-term complications. Remaining in high blood sugar level leads to multiple complication composed of diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic foot and cardiovascular diseases.[2] Only 30.0% of patient's glycemic levels are well-controlled.[2] Ankle-brachial index (ABI) is the ratio of systolic blood pressure between ankle artery and brachial artery invented by Winsor in 1951.[3] The ratio mainly acts as an alternative tool in peripheral artery disease (PAD) diagnosis (ABI 0.90-1.40 indicated as normal, ABI <0.90 indicated as PAD and ABI>1.40 indicated as vascular calcification).[3] Moreover it is also the atherosclerotic index and cardiovascular prognostic factor.[3] In Songklanagarind's Primary Care Unit (PCU), examining of ABI were inconsistent and mostly occur after the presence of impaired pulse strength. As a result, less than half of diabetic patients received the examination. Knowing the importance of ABI may encourage health care providers to examine their patients. This research was conducted to find the future events of acute coronary syndrome (ACS), myocardial infarction (MI), coronary revascularization, stroke, renal replacement therapy, leg revascularization and limb amputation in those who had abnormal ABI.

Material and Methods

Setting

Songklanagarind Hospital is a university hospital belonging to the Faculty of Medicine, Prince of Songkla University. The hospital is a medical school, residency training, and referral center for the southern part of Thailand. The average of outpatients was 2,200-2,400 patients per day.

Study population and samples

A retrospective longitudinal medical records review was conducted in 548 diabetic adult attending PCU and internal medicine clinic of Songklanagarind Hospital, Thailand, from January 2009 until end of study in December 2015. All diabetic patients those who attended PCU and internal medicine clinic followed up from 1st January 2009 to 31st December 2015 were included in this study. The exclusion criteria were missing baseline and follow-up data for patients with fewer than 2 visits. The data of this study were recorded in the data extraction form which was reviewed from the patients with diabetes who have record of ABI measurement from 1st January 2009 to 31st December 2015. The data was entered into a computer database management system (Microsoft Excel 2010®). The hospital number were encoded in terms of patient confidentiality.

Data analysis

The data was recorded, categorized, and analyzed by Epidata®, Microsoft Excel 2010®, and R version 3.4.3 respectively. There are descriptive statistical analysis, and survival analyses. For the descriptive data, we used demographic data then continue data as median and categorical data as percentile (%). Survival analysis was conducted by univariate analyses using Nelson-Aalen cumulative hazard estimate model and statistical significant of difference by log-rank test. Covariates were also analyzed using a cox proportional hazard model and considered significant. Survival analyses were performed using record of cardiovascular events as end-point.

Results

Figure 1 exhibits 548 eligible participants including only normal-ABI and low-ABI individuals (absence of high-ABI patients). In addition, ratio of follow-up time (3 years or less and over 3 years) seems to be similar between normal and low-ABI patients (p-value=0.23). The study population tends to be followed more than 3 years. The minimum of follow-up time, median day at risk, interquartile range and maximum follow-up time were 732, 2,021, 1,436 and 3,263 days respectively.

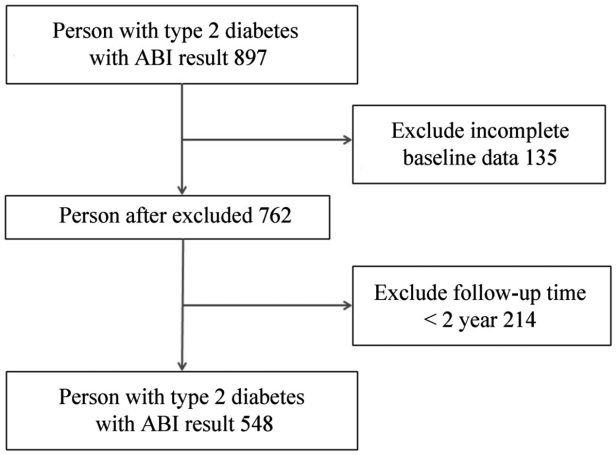

Figure 1 Eligible participants included in this study

According to the Table 1, the individuals with low-ABI tend to have significantly higher age, history of amputation, history of smoking, duration of diabetes and medical conditions including hypertension, chronic kidney disease (CKD), PAD, history of MI and history of stroke. In the other hands, patients who had normal-ABI tend to be higher body mass index (BMI) and dyslipidemia (p-value= 0.01 and 0.02 respectively).

The data illustrated in Table 2 reveals that calcium channel blocker and nitrates were more significantly used in low-ABI group (p-value<0.01 and 0.01 respectively) while there are no statistically significant difference in other antihypertensive drug. Individuals who use insulin were higher in low-ABI group (p-value=0.04) whereas metformin uses were significantly higher in the rest group (p-value<0.01). Additionally, using of aspirin were found significantly common in the low-ABI group (p-value< 0.01). In the other hands, there were no significant different of lipid lowering agent usage.

Cardiovascular outcome

Along with acute coronary syndrome, Figure 2 firstly illustrates the insignificant difference of cumulative hazard ratio between two groups, focusing on the period from 5 to 7 years after exposed to the ABI reveals the significant difference of hazard rate. The log-rank test reveals the significance (p-value=0.04). Additionally, the covariate analyses found significant correlations of ACS among male, duration of diabetes and CKD [adjusted hazard ratio (AHR) 2.05 (95% confidence interval (CI)=1.11-3.79), 1.09 (95% CI=1.05-1.13) and 2.07 (95% CI=1.07-3.98) respectively].

According to the acute myocardial infarction data, Figure 3 shows a significantly higher cumulative hazard ratio in the low-ABI group which was found to be prominent over a period of 0-3 years and 4-7 years. The log-rank test also reveals the significance (p-value<0.01). The significantly associated covariates are male, duration of diabetes and CKD [AHR 2.67 (95% CI=1.26-5.62), 1.11 (95% CI=1.07-1.16) and 2.77 (95% CI=1.33-5.77) respectively].

The coronary revascularization data in Figure 4 reveals a significant hazard over a period of 4-7 years after exposure to low-ABI. The log-rank test shows a significant hazard (p-value=0.01). The significantly affected factors are male, and duration of diabetes [AHR 2.41 (95% CI=1.14-5.10) and 1.13 (95% CI=1.08-1.18) respectively].

The analyzed data of the rest outcomes cumulative hazard including limb amputation, leg revascularization, stroke and renal replacement therapy between low-ABI and normal-ABI group were insignificantly different along the study period. However, the data revealed significant correlation between the outcomes and distinctive factors including limb amputation among duration of diabetes, CKD and smoking [AHR 1.08 (95% CI=1.04-1.11), 2.40 (95% CI=1.27-4.54) and 2.16 (95% CI=1.27-3.68) respectively], leg revascularization and CKD [AHR 2.48 (95% CI= 1.26-4.87)], stroke among male and hypertension [AHR 2.36 (95% CI=1.08-5.16) and 2.38 (95% CI=1.00-5.66) respectively], renal replacement therapy (RRT) and CKD [AHR 4.50 (95% CI=1.93-10.48)].

Table 1 Baseline characteristics of the individuals in normal-ankle-brachail index group and low-ankle-brachail index group

Variables	Normal-ABI# (406)	Low-ABI# (142)	P-value*
Age, year (median±IQR)	61.0±13.0	71.0±15.0	<0.01
Male, n (%)	184 (45.3)	65 (45.8)	0.90
BMI, kg/m^2 (median±IQR)	25.5±5.7	24.5±4.9	0.01
History of amputation, n (%)	14 (3.4)	21 (14.8)	0.01
Smoking status			0.01
Current, n (%)	6 (1.4)	7 (4.9)	
Ex, n (%)	7 (1.7)	6 (4.2)	
Fasting plasma glucose, mg/dL (median±IQR)	134.0±63.0	136.0±67.0	0.93
Glomerular filtration rate, mL/min/1.73 m^2 (median±IQR)	70.0±46.0	37.0±40.2	<0.01
Duration of diabetes, year (median±IQR)	7.0±7.0	8.5±7.75	<0.01
Past medical conditions			
Previous myocardial infarction, n (%)	19 (4.7)	33 (23.2)	<0.01
Previous stroke, n (%)	17 (4.2)	24 (16.9)	0.05
Peripheral vascular disease, n (%)	24 (5.9)	24 (16.9)	<0.01
Dyslipidemia, n (%)	276 (68.0)	81 (57.0)	0.02
Hypertension, n (%)	208 (51.2)	92 (64.8)	<0.01
Chronic kidney disease, n (%)	53 (13.0)	37 (26.0)	<0.01

*Statistical significant at p-value<0.05 #ABI measured by Omron Collin VP-1000

ABI=ankle-brachial index, IQR=interquartile range, BMI=body mass index

Table 2 Medication uses of the individuals in normal-ankle-brachail index group and low-ankle-brachail index group

Variables	Normal-ABI[#] Number (%)	Low-ABI[#] Number (%)	P-value*
Antihypertensive agent			
Beta-blocker	117 (28.8)	71 (50.0)	0.02
Angiotensin-converting enzyme inhibitor	84 (20.6)	25 (17.6)	0.50
Angiotensin receptor blocker	52 (12.8)	18 (12.6)	0.90
Calcium channel blocker	130 (32.0)	79 (55.6)	<0.01
Nitrates	13 (3.2)	17 (12.0)	<0.01
Thiazides	68 (16.7)	29 (20.4)	0.39
Other	6 (1.5)	6 (4.2)	0.09
Glucose lowering agent			
Metformin	247 (60.8)	68 (47.9)	<0.01
Sulfonylurea	152 (37.4)	61 (43.0)	0.29
Insulin	94 (23.1)	51 (35.9)	<0.01
Other	25 (6.2)	6 (4.2)	0.51
Lipid lowering agent			
Simvastatin	271 (66.7)	102 (71.8)	0.31
Fibrate	5 (1.2)	5 (3.5)	0.13
Other	6 (1.4)	3 (2.1)	0.70
Antiplatelet			
Aspirin	112 (27.6)	81 (57.0)	<0.01
Non-aspirin	15 (36.9)	16 (11.2)	<0.01

*Statistical significant at p-value<0.05 [#]ABI measured by Omron Collin VP-1000

ABI=ankle-brachial index

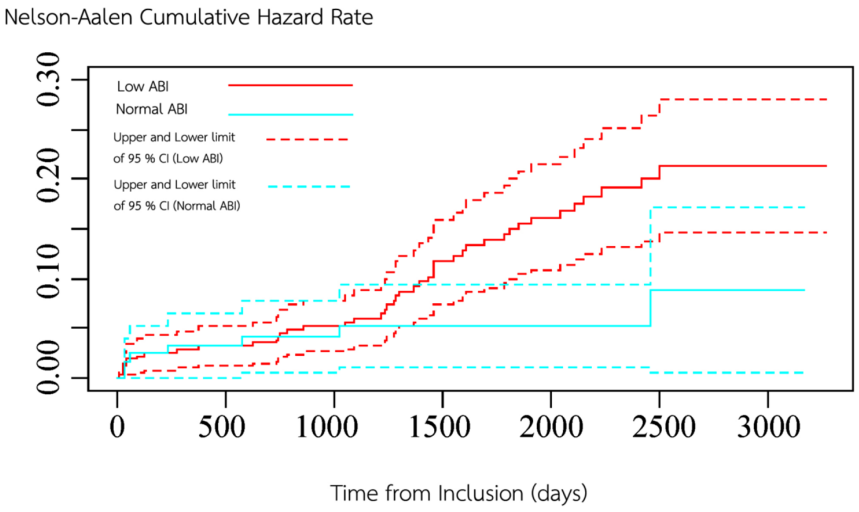

Figure 2 Time to acute coronary syndrome in patients with low-ankle-brachail index and normal-ankle-brachail index

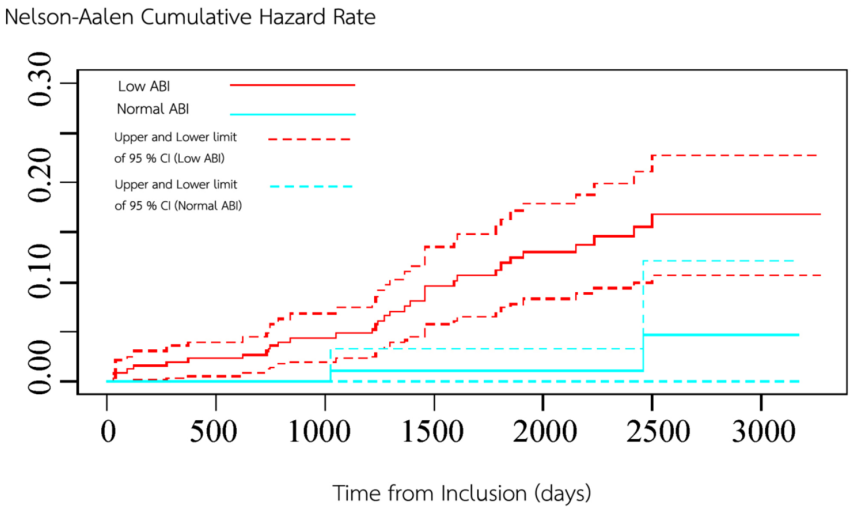

Figure 3 Time to acute myocardial infarction in patients with low-ankle-brachail index and normal-ankle-brachail index

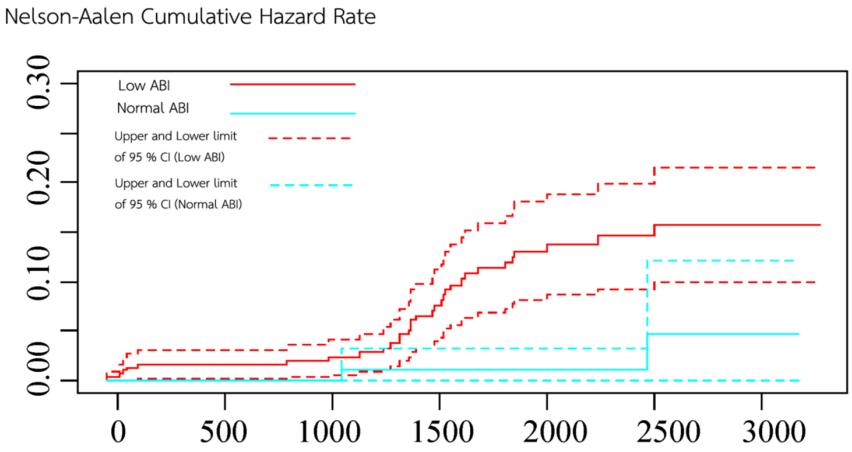

Figure 4 Time to acute coronary revascularization in patients with low-ankle-brachail index and normal-ankle-brachail index

Discussion

This is an observational retrospective cohort study gathering data from hospital information system of Songklanagarind Hospital. There are many previous cohort studies about ABI in Europe. This study aims to find correlations between having abnormal ABI and associated factor in Songklanagarind's patients. The descriptive study reveals the statistically difference among baseline characteristics. Individuals with low-ABI tend to be significantly older and having more complicated disease that are the same trends of Dormandy and Selvin study.[4,5] This study also found a higher rate of history of limb amputation, history of smoking, history of MI, history of stroke and underlying diseases including hypertension, CKD and PAD. In addition, glomerular filtration rate (GFR), duration of diabetes and fasting plasma glucose (FPG) were found higher in low-ABI group that

could indicate poorer and longer disease status following the trend of Jessadapattarakun's study.[6] The study of Ix[7] reported a positive correlation between higher BMI and lower ABI in non-smokers. However, the direction of this association differed in persons who are smokers. Those with a higher BMI tended to have a lower PAD prevalence. Following the previously mentioned trend, analyses of BMI and dyslipidemia in this study revealed no significant difference between the two groups.

The study of Dormandy found the significantly higher rate of insulin usage in PAD patients while the rest were insignificant.[4] In addition, there is the data of Muntner[8] that indicates a higher risk of PAD in poorer controlled diabetic patients. This study found that insulin use was also common in low-ABI patients while metformin was common in normal-ABI ones. By considering the usage of hypoglycemic agents and FPG level, it could be assumed that uncontrolled diabetes might be associated with low-ABI. According to the significantly prominent history of MI in low-ABI patients, the data revealed a higher rate of beta blockers usage, which is considerable in individuals with ischemic heart disease. In addition, a higher rate of calcium channel blocker prescriptions in the low-ABI group was also reasonable. Thus, the agent has been the antihypertensive drug of choice for PAD individuals for years.[9] In addition, aspirin found higher in low-ABI group that could be from the higher risk of cardiovascular disease while other antiplatelet were inexplicably found higher in normal-ABI patients. Unaccountably, ratio of lipid-lowering agent uses was insignificant different between the groups whereas Dormandy found it is higher in the PAD group.

Dormandy found the rate of cardiovascular outcome higher in the patients with diabetes and PAD.[4] The onset of diseased appears to be significant around 3 years (with minimum follow-up time of 2.5 years). This study also followed the populations mostly longer than 3 years and the follow-up time between 2 groups were similar. Newman AB. revealed that having low-ABI, especially with diabetes, was a risk for cardiovascular diseases and its predictors.[10] The analyses explicit the higher rate of ACS, MI and coronary revascularization in low-ABI individuals (p-value= 0.05, <0.01 and <0.01 respectively) while other events were insignificantly different. The significance found after around 4-5 years and after 7 years exposed to low-ABI. Furthermore, age, male sex, smoking, hypertension, dyslipidemia, duration of diabetes and CKD played as the risk factor of those explained events. Although the study of Dormandy found the higher rate of limb amputation and leg revascularization, this study did not elucidate the significance.

A previously published study of Mostaza revealed the correlation between CKD and low-ABI.[11] In this research, it is interesting that CKD played a role as the significant risk factor of ACS, MI, limb amputation and leg revascularization. However, the rate of renal replacement therapy was similar between low-ABI and normal-ABI in this study (p-value=0.70). It showed that having low-ABI would not be the risk of future renal replacement therapy.

Conclusion

Songklanagarind's diabetic patients with low-ABI were associated with the significantly higher rate of multiple cardiovascular risk factors including hypertension, CKD, smoking, history of previous MI, history of previous stroke and age. They also tend to significantly experience more ACS, MI and coronary revascularization after 4 years approximately exposed to low-ABI.

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