Original article

Cardiovascular outcome in patients with high risk cardiovascular events in Nakornping Hospital

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Objectives   Patients with atherosclerosis are at different levels of elevated risk of ischemic events depending on the specific manifestation of the disease and may have varying degrees of future risk for ischemic events. This study evaluated the incidence of composite cardiovascular outcomes of patients with high risk cardiovascular events in Nakornping Hospital.

Methods This prospective observational non-interventional cohort study enrolled patients age 45 years or more who met the inclusion criteria of the Outpatient Department of Medicine, Nakornping Hospital, between January 2008 and December 2009. The follow-up period for each patient was 60 months. The composite cardiovascular outcome of cardiovascular deaths, non-fatal myocardial infarctions, non-fatal strokes and hospitalizations for heart failure was determined.

Results   Of the 387 patients in the Outpatient Department of Medicine of Nakornping Hospital, 103 were in the established atherosclerotic disease group and 284 were in the multiple risk factors group. The rate of overall composite cardiovascular events (cardiovascular death, non-fatal MI, non-fatal stroke, and hospitalization for heart failure) was 3.83%. The rate was higher in the established atherosclerotic disease group than in the multiple risk factors group 6.79% vs. 1.41% (HR = 14.28; 95% CI, 2.26-90.02, p = 0.005) which was driven by hospitalization for heart failure, but the established atherosclerotic disease group had a lower rate of medical treatment for diabetes than the multiple risk factors group. The rate of receipt of anti-diabetic drugs was statistically significantly lower in the established atherosclerotic disease group than in the multiple risk factors group.

Conclusions Patients with established atherosclerotic disease have a higher rate of composite cardiovascular outcomes than patients with multiple risk factors, but they have a lower rate of medical treatment for diabetes. **Chiang Mai Medical Journal 2021;60(1):17-26. doi 10.12982/CMUMEDJ.2021.02**

Introduction

Atherosclerosis is a systemic disease process in which fatty deposits, inflammatory cells and scar tissue build up within the walls of arteries. Individuals who develop atherosclerosis tend to develop it in a number of different types of arteries (1), and it is the underlying cause of the majority of clinical cardiovascular events, e.g., acute myo-cardial infarction, stroke, and peripheral vascular disease (PVD), which are collectively known as cardiovascular disease (CVD), the leading cause of morbidity and mortality.

Coronary artery disease and stroke have been projected to be the first and second leading of death in the world (2,3), and most of these events

occur in developing countries (4,5). The three strategies for the prevention of CVD include the following (1). A population strategy which is critical to reducing the overall incidence of CVD since it aims to reduce risk factors at the population level through lifestyle and environmental changes that affect the whole population without requiring medical examination of individuals and because it can be achieved through the establishment of ad hoc policies and community interventions (2). A high-risk primary prevention strategy which deals with healthy persons and harmonizes the advice that given to primary care and second-line care health professionals (3). A strategy for secondary prevention of established cardiovascular disease. All three strategies are necessary and complement each other (6). Following these three strategies to better treat vascular disease and prevent these events would have significant public health implications as well as reduce the financial impact for patients, health systems and governments. Although lifestyle changes and targeted therapies can reduce vascular disease and vascular events, such interventions are often either under-utilized or are not applied appropriately for some at risk-populations (7-9). A better understanding of how such therapies could be implemented and their potential impact on various populations could significantly influence medical practices toward the goal of preventing vascular events. Additionally, for clinicians the ability to rapidly identify the major determinants of risk among patients with atherosclerosis would facilitate tri-aging preventive therapies for individuals at the high end of the risk spectrum.

The InterAsia study (10) reported that the major cardiovascular risk factors in urban and rural areas of Thailand in individuals age 35 years or older were high blood pressure, high cholesterol, overweight or obesity, and diabetes.

The Comparative Determinants of 4-Year Cardiovascular Event Rates in Stable Outpatients at Risk of or with Atherothrombosis study (REACH study) (11) found that patients with atherothrombosis and those with a prior history of ischemic events at baseline had the highest rate of sub-sequent ischemic events, and patients without established atherothrombosis but who had other risk factors had the lowest risk of ischemic events.

Objectives

The aims of study were to evaluate event rates and incidence rates of composite cardiovascular outcomes and the rate of medical treatment of risk factors in patients with high risk cardiovascular events in the Outpatient Department of Nakornping Hospital

Methods

This was a prospective observation non-interventional cohort study of out-patients of Nakornping Hospital with high atherosclerotic risk. The study was approved by ethics committee of Nakornping Hospital. All patients provided written informed consent before participation in this study.

Patient population

Patients were eligible for enrollment in the study if they signed an informed consent agreement, were at least 45 years old and had at least one of the following inclusion criteria.

Inclusion criteria

1. Risk factors for atherosclerotic disease. (The multiple risk factors group had at least three of the following risk factors.)

1.1 Diabetes mellitus or impaired fasting glucose

1.2 Hypertension (blood pressure more than 140/90 mmHg) or treatment of hypertension

1.3 Dyslipidemia (hypercholesterolemia with total cholesterol ≥ 200 mg/dL or LDL-C ≥ 130 mg/dL, hypertriglyridemia with triglyceride ≥ 150 mg/dL, low high-density lipoprotein cholesterol (HDL-C < 40 mg/dL) or current treatment with lipid-modifying agents).

1.4 Chronic Kidney Disease (proteinuria or estimated glomerular filtration rate < 60 mL/min)

1.5 Current smoking habit of at least 1 cigarette/day

1.6 Male over 55 years old or female over 65 years old

1.7 Family history of premature athero-sclerosis

2. Established symptoms and signs of CVD (the established atherosclerotic disease group had at least 1 of these criteria)

2.1 CVD: transient ischemic attack, ischemic stroke

2.2 CAD: stable angina with evidence of myocardial infarction, history of acute coronary syndrome, history of percutaneous intervention, history of coronary artery bypass graft, coronary stenosis > 50% diagnosed by coronary angiography or coronary CT angiogram

2.3 PVD: symptoms of intermittent claudication with ankle brachial index (ABI) less than 0.9, history of intermittent claudication and peripheral intervention such as angioplasty, vascular bypass graft or amputation

Exclusion criteria

1. Diagnosis or symptoms and signs of acute cerebrovascular disease or acute coronary artery disease within the past 3 months

2. Patients who had participated in a previous blinded clinical trial

3. Patients with limited life expectancy due to non-cardiovascular conditions, e.g., cancer or documented HIV

4. Patients who could not be followed up

5. Patients with a large aortic aneurysm with indications for surgery

6. Patients who declined to sign the informed consent form

Nakornping Hospital was the study site with a cohort of patients at high risk for cardiovascular events (CORE Thailand). A total of 400 patients were enrolled between January 2008 and December 2009. The follow-up period was 60 months. Patients were evaluated at baseline for demographic and medical characteristics, and were scheduled for re-evaluation at 6, 12, 24, 36, 48, 60 months. Patient data collected included height, weight, waist circumference, seated SBP and DBP, ECG (electrocardiography), ankle-brachial index, available laboratory data and medications and cardiovascular event outcomes.

The primary measure was the incidence rate and outcome of events of composite cardiovascular end points (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke (ischemic or hemorrhagic stroke), hospitalization for heart failure (admitted with congestive heart failure) in both the established atherosclerotic disease group and the multiple risk factors group.

The secondary measure was the event and incidence rate of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, and hospitalization for heart failure as well as the rate of medical treatment of risk factors in both the established atherosclerotic disease group and in the multiple risk factors group (endpoint was not adjudicated).

Statistical analysis

Categorical variables are expressed as frequencies and percentages. Continuous variables are expressed as mean ± SD or median (interquartile range 25-75) as appropriate. Group comparisons were analyzed using the Student's t-test or the Wilcoxon rank sum test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables. Multivariable analysis was performed to determine the predictors of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and hospitalization for heart failure using the Cox proportional hazard model to calculate the hazard ratio and a logistic regression model to calculate the odds ratio. Results were considered to be statistically significant if the $p < 0.05$. Statistical analysis was performed using IBM SPSS statistics version 16.0 (IBM Corp., Armonk, New York).

Results
Baseline characteristics

A total of 401 patients were enrolled of whom 14 were excluded due to age less than 45 years and/or having less than 3 risk factors (Figure 1). The 387 patients were all available for 5 year follow-up. The multiple risk factors group (asymptomatic patients) included 284 individuals and the established atherosclerotic disease group
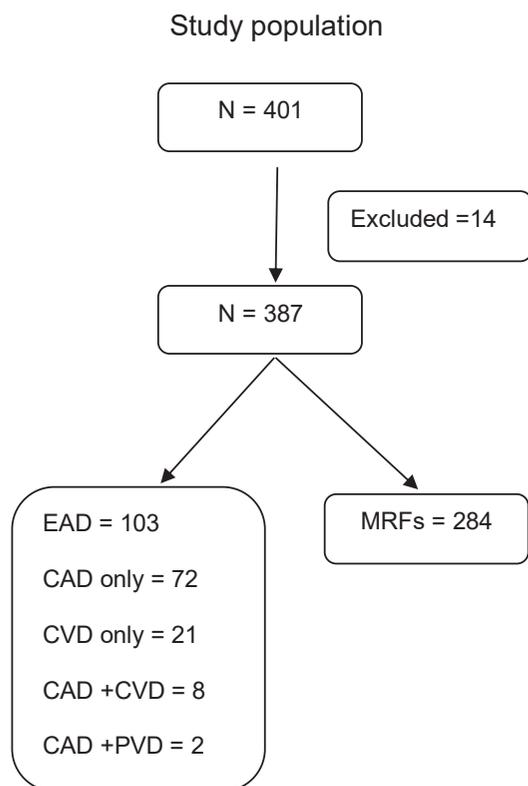
Study population

Figure 1. Profile of the study population
EAD; established atherosclerotic disease, MRFs; multiple risk factors, CAD; coronary artery disease, CVD; cerebrovascular disease, PAD; peripheral arterial disease

(symptomatic patients) had 103: CAD only - 72 (69.9%), CVD only – 21 (20.4%), CAD and CVD – 8 (7.8%), CAD and PVD 2 (1.9%).

The patients' mean age was 65.2 in the established atherosclerotic disease group and 61.5 years in the multiple risk factors group. Males were 57.2% in the established atherosclerotic disease group and 42.2% in the multiple risk factors group. Hypertension, diabetes and dyslipidemia were very common in the multiple risk factors group, while hypertension, diabetes and BMI ≥ 23 were very common in established atherosclerotic disease group.

Antihypertensive drugs were received by 95.1% in the established atherosclerotic disease group and by 96.0% in the multiple risk factors group. The difference was not statistically significant. Receipt of angiotensin-receptor blocker (ARB) and calcium channel blocker was higher in the multiple risk factors group than the established atherosclerotic disease group, while receipt of β-blockers and diuretics was higher in the established atherosclerotic disease group than the multiple risk factors group. Both differences were statistically significant. Stains were received by 88.3% in the established atherosclerotic disease group and 91.9% in multiple risk factors group, a non-statistically significant difference. Receipt of anti-diabetic drugs was higher in the multiple risk factors group (93.6%) than the established atherosclerotic disease group (55.3%), a statistically significant difference (except Thiazolidinedione (TZD) and dipalmitoyl phosphatidic acid (DPPA) inhibitors). Baseline characteristics of the patients and medication use is shown in Table 1.

During the 5 years of follow-up, 11 (3.83%) composite cardiovascular events occurred. In the established atherosclerotic disease group, the composite cardiovascular outcome event rate was 6.79% and the incidence rate was 30.15/10,000/ month (for cardiovascular death, 1.94%, incidence rate 8.24/10,000/month, for non-fatal myocardial infarction, 1.94%, incidence rate 8.46/ 10,000/ month, for hospitalization for heart failure 2.91%, 121.49/10,000/month. The subgroup event rate for CAD was 6.9% and the CVD event rate was 9.5%. Diabetes was a risk factor for all patients in the established atherosclerotic disease group who had had a cardiovascular event.

The multiple risk factors group composite cardiovascular outcome was event rate 1.41%, incidence rate 2.78/10,000/month (0.35%, 13.93/ 10,000/month for non-fatal MI, 0.35%, 13.93/ 10,000/month for non-fatal stroke and 0.70%, 14.09/10,000/month for hospitalization for heart failure). Diabetes was a risk factor for all patients in the multiple risk factors group who had had a cardiovascular event.

Cumulative incidence for the composite cardiovascular outcomes in the established atherosclerotic disease group was higher than in the multiple risk factors group. The difference was statistically significant (HR = 14.28; 95% CI, 2.26-90.02; p = 0.005) and was driven by hospitalization for heart failure (HR 11.52: 95% CI, 1.132-

Table 1. Demographic and baseline characteristics of patients

	Established atherosclerotic disease group (n=103)	Multiple risk factors group (n=284)	*p*-value
Age (year); mean ±SD	65.2±9.0	61.5±8.7	0.05
Male n (%)	59 (57.2)	120 (42.2)	0.009
Cardiovascular risk factors (%)			
Hypertension	94.2	97.5	0.70
Diabetes mellitus	63.1	97.9	0.01
Dyslipidemia	84.5	98.6	0.01
Current smoking ≥ 1 cigarette/day	8.7	4.9	0.16
Body Mass Index ≥ 23	70.3	80.2	0.34
Chronic kidney disease	29.1	28.9	0.96
Family history of premature of atherosclerosis	7.8	4.2	0.16
Vascular disease status (%)			
CAD at baseline	100	0.0	0.00
CVD at baseline	100	0.0	0.00
PVD at baseline	100	0.0	0.00
Medication			
Aspirin	74.8	67.6	0.17
Clopidogrel	39.8	2.5	0.00
Ticlopidine	1.0	4.0	0.45
Warfarin	3.9	0.4	0.01
Statin	88.3	91.9	0.28
Antihypertensive drugs	95.1	96.0	0.6
ACEI	35	42.3	0.19
ARB	22.3	34.9	0.02
β-blocker	60.2	42.6	0.01
Calcium channel blocker	35	47.9	0.02
Diuretics	45.6	35.9	0.08
Nitrates	88.3	91.9	0.01
Anti-diabetic drugs	55.3	93.6	0.001
Insulin	17.5	28.5	0.02
Sulfonylurea	28.2	53.2	0.01
Biguanide	36.9	68.7	0.01
Thiazolidinedione (TZD)	10.7	18.3	0.07
Dipeptidyl Peptidase-4 inhibitor	7.8	14.1	0.09

CAD; coronary artery disease, CVD; cerebrovascular disease, PVD; peripheral vascular disease

116.82; *p* = 0.04).

In the established atherosclerotic disease group, myocardial infarction and CAD were the two variables which best predicted composite cardiovascular outcome (HR 8.66 (95%CI 2.3-32.53, *p* = 0.002), HR 6.33 (95% CI 1.66-24.1, *p* = 0.002), respectively). Table 2 shows the adjusted hazard ratio for composite cardiovascular outcome, and Fig. 2 shows the Kaplan-Meier cumulative inci-dence for composite cardiovascular outcomes in the established atherosclerotic disease group and the multiple risk factors group over the 5 years follow-up period

Discussion

This prospective observational non-interventional cohort registry study with 5 years of follow-up found that the overall rate of composite

Table 2. Adjusted Hazard Ratio for composite cardiovascular outcome

	Established atherosclerotic disease group		Multiple risk factors group		Adjusted Hazard Ratio (aHR) 95% CI	*p*-value
	Event	Incidence rate (/10000/month)	Event	Incidence rate (/10000/month)		
Composite cardiovascular outcome	7	30.149	4	2.785	14.28(2.26-90.02)	0.005
1. CV death	2	8.239	0	0	6.57(0.00-2.90)	0.51
2. Non-fatal MI	2	8.463	1	13.93	7.36(0.65-82.98)	0.10
3. Non-fatal stroke	0	0	1	13.93	0.04(0.00-1.39)	0.77
4. Hospitalization for heart failure	3	121.49	2	14.09	11.52(1.132-116.82)	0.04

Adjusted HR for age, sex, DM, dyslipidemia, clopidogrel, warfarin, ARB, β-blocker, calcium channel blocker, diuretic, nitrate, insulin, sulfonylurea, biguanide, TZD, DPP4-inhibitor
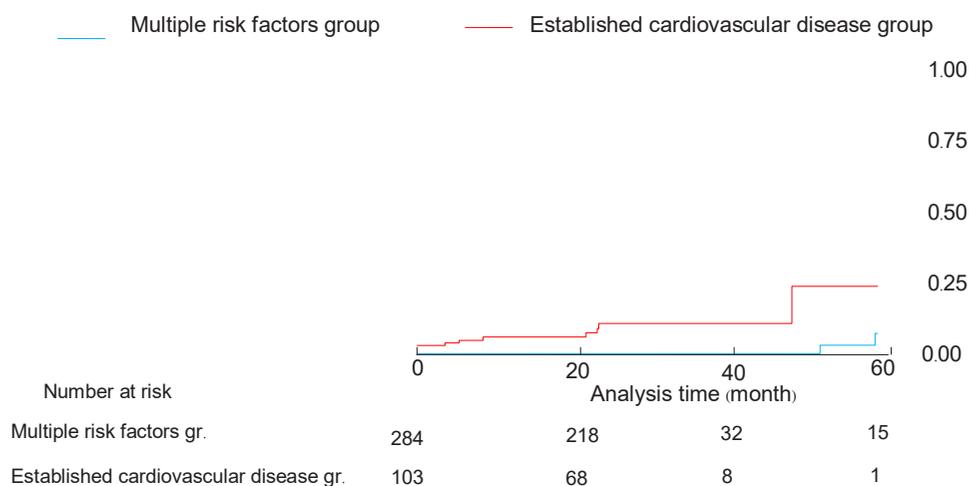
Figure 2. Kaplan-Meier cumulative incidence for composite cardiovascular outcome (%) in the established atherosclerotic disease group and the multiple risk factors group with 5 years follow-up

cardiovascular events, (cardiovascular death, non-fatal myocardial infarction, nonfatal stroke, hospitalization for heart failure) was 3.83%. The incidence of composite cardiovascular events in the established atherosclerotic disease group was 6.79% (1.94% for cardiovascular death, 1.94% for non-fatal myocardial infarction and 2.91% for hospitalization for heart failure). The incidence for subgroup with CAD only and diabetes was 6.9%, and for the subgroup with CVD only and diabetes was 9.5%. The incidence of composite cardiovascular events in the multiple risk factors group was 1.41% (0.35% for non-fatal stroke and non-fatal MI, 0.70% for hospitalization for heart

failure). The cumulative incidence for composite cardiovascular events was higher in the established atherosclerotic disease group than in the multiple risk factors group and reached statistical significance (HR 14. 28: 95% CI, 2.26-90.02; $p = 0.005$). The incidence was driven by hospitalization for heart failure (HR 11.52: 95% CI, 2.26-90.02; $p = 0.04$). The rate of receipt of anti-diabetic drugs was significantly higher in the multiple risk factors group than the established atherosclerotic disease group ($p < 0.05$). The rate of receipt of antihypertensives and statins was high in both groups.

The Comparative Determinants of 4-Year Cardiovascular Event Rates in Stable Outpatients at Risk of or With Atherothrombosis study (REACH study) (11) reported that the overall rate of cardiovascular outcomes (cardiovascular death, myocardial infarction, or stroke) in outpatients was 12.1%: 7% in non-diabetic patients with risk factors for atherothrombosis, 25% in patients with polyvascular disease and prior ischemic events and around 22% in single vascular disease patients with diabetes. These rates are comparable to the present study, showing that established atherosclerotic diseases are a predictor of high risk for developing a cardiovascular event in the future, the highest risk occurs when atherosclerotic disease is combined with diabetes, and the multiple risk factors group had a lower risk for cardiovascular events. In the present study the overall composite cardiovascular event rate in both the multiple risk factors group and the established atherosclerotic group was lower than in the REACH study (11), but rate of cardiovascular events in the present study were comparable with In the InterASAIA study (12) and the Electricity Generating Authority of Thailand Study (EGAT study) (13) (1.8%, 1.2% and 1.94%, respectively), which may be explained by four factors 1) the present study had a small sample size and single center, 2) Differences in the definition of cardiovascular outcome event, 3) Our population was Thais which event rate was lower (10-13) than REACH study, 4) Patients in the present study had a higher incidence of receiving statins than the REACH study (91% vs. 77%).

In the present study, the established atherosclerotic disease group had a higher rate of hospitalization for heart failure than the multiple risk factors group (2.91% vs. 0.70%) and compared with REACH study11 rate for CV hospitalization for established cardiovascular group 20.7% in single vascular, 35.48% in polyvascular and 10.7% in risk factor group. The present study also had a lower rate of hospitalization than the REACH study (11) which may be explained by three factors: 1) the present study had a small sample size; 2) there could be differences in the definition of

hospitalization admission; and 3) The Thai population overall has a lower event rate than other population groups (10-13).

The rate of receipt of antihypertensive drugs and statins by both groups in the present study was comparable with the REACH study (11) and the Management of atherosclerotic risk factors for patients at high cardiovascular risk in real-world practice: a multicenter study (14).

The rate of receipt of anti-diabetic drugs in the established atherosclerotic disease group in the present study was lower than in the REACH study (11) as well as the Management of atherosclerotic risk factors for patients at high cardiovascular risk in real-world practice: a multicenter study (13) (55.3%, 83.8-86.0%, and 73.4%, respectively). Receipt of anti-diabetic drugs in the multiple risk factors group in the present study was comparable with the REACH study (11) and the Management of atherosclerotic risk factors for patients at high cardiovascular risk in real-world practice: a multicenter the study (14).

In this study, the presence of established atherosclerotic disease with diabetes was a stronger predictor of risk of future ischemic events than was multiple risk factors with diabetes, indicating that the risk from diabetes is not equivalent to that from atherosclerosis. The findings of this study should provide clinicians with improved ability to estimate the future cardiovascular risk of their patients and thus enable more effective identification of patients who should be targeted for more intensive follow-up and therapy which is in concurrence with the 2016 European Guideline of cardiovascular disease prevention in clinical practice (15), the 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease (16), and Thai guidelines (17). Those guidelines recommend the assessment of total CVD risk for the prevention of CVD in clinical practice because atherosclerosis is usually the product of a number of risk factors. The guidelines suggest that prevention of CVD in an individual should be adapted to his or her personal CV risk: the higher the risk, the more intense the action should be. The guidelines further suggest

that patients with established cardiovascular disease are at very high risk for CV death. Prevention strategies, including medical therapy and secondary prevention, should be guideline-directed. Diabetes was a common risk factor in both groups in our study, but patients in the established atherosclerotic disease group received anti-diabetic drugs at a lower rate than other studies (11,14). This implies that the patients were under-treated based on existing medical therapy and secondary prevention guidelines. In the future, cardiovascular treatment for patients with established atherosclerotic diseases should include improved treatment of diabetes.

Limitations

This prospective study was a single center study with a small sample size and the endpoints were not adjudicated.

Conclusions

Patients with established atherosclerotic disease have a higher rate of composite cardiovascular outcomes than patients with multiple risk factors, but in practice at Nakornping Hospital they received lower levels of medical treatment for diabetes than the multiple risk factors group.

Patients in a high-risk factor group should be assessed to determine their CVD risk score and a guideline-directed medical therapy and primary prevention strategy should be developed for them.

Acknowledgements

Conflict of interests

All authors declare no conflict of interest relevant to this study.

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ผลลัพธ์ทางคลินิกด้านหัวใจและหลอดเลือดในผู้ป่วยที่มีความเสี่ยงสูงที่จะเกิดเหตุการณ์ทางด้านหัวใจและหลอดเลือดในโรงพยาบาลนครพิงค์

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วัตถุประสงค์   เพื่อศึกษาอัตราการเกิดผลลัพธ์รวมทางคลินิกด้านหัวใจและหลอดเลือดในผู้ป่วยที่มีความเสี่ยงสูงที่จะเกิดเหตุการณ์ทางด้านหัวใจและหลอดเลือดในโรงพยาบาลนครพิงค์

วิธีการ   เป็นการศึกษา prospective cohort, รวบรวมข้อมูลผู้ป่วยโรงพยาบาลนครพิงค์แผนกผู้ป่วยนอกกลุ่มงานอายุรกรรมที่มีอายุตั้งแต่ 45 ปี และเข้าได้กับ inclusion criteria ระหว่างเดือนมกราคม พ.ศ. 2551 ถึงเดือนธันวาคม พ.ศ. 2552 และติดตามไปเป็นระยะเวลา 60 เดือน เพื่อประเมินอัตราการเกิดผลลัพธ์รวมทางคลินิกด้านหัวใจและหลอดเลือด (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and hospitalization for heart failure)

ผลการศึกษา ผู้ป่วยทั้งหมด 387 คน 103 คน อยู่ในกลุ่มผู้ป่วยที่มีโรคทางด้านหัวใจและหลอดเลือด 284 คน อยู่ในกลุ่มผู้ป่วยที่มีแต่ปัจจัยเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือด อัตราการเกิดผลลัพธ์รวมทางคลินิกด้านหัวใจและหลอดเลือดของผู้ป่วยทั้งหมด คือ ร้อยละ 3.83 กลุ่มผู้ป่วยที่เกิดโรคทางด้านหัวใจและหลอดเลือดมีอัตราการเกิดผลลัพธ์รวมทางคลินิกด้านหัวใจและหลอดเลือดสูงกว่ากลุ่มผู้ป่วยที่มีแต่ปัจจัยเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือดที่ร้อยละ 6.79 และร้อยละ 1.41 ตามลำดับ และอัตราการเกิดผลลัพธ์ทางคลินิกด้านหัวใจและหลอดเลือดในผู้ป่วยทั้งสองกลุ่มมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติที่ HR = 14.28; 95% CI, 2.26-90.02; p = 0.005 และกลุ่มผู้ป่วยที่เกิดโรคทางด้านหัวใจและหลอดเลือดได้รับยาในการรักษาเบาหวานน้อยกว่ากว่ากลุ่มผู้ป่วยที่มีแต่ปัจจัยเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือดอย่างมีนัยสำคัญทางสถิติ

สรุป ที่แผนกผู้ป่วยนอก กลุ่มงานอายุรกรรม โรงพยาบาลนครพิงค์กลุ่มผู้ป่วยที่เกิดโรคทางด้านหัวใจและหลอดเลือดมีอัตราการเกิดผลลัพธ์รวมทางคลินิกด้านหัวใจและหลอดเลือดสูงกว่ากลุ่มผู้ป่วยที่มีแต่ปัจจัยเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือดแต่ได้รับยาในการรักษาเบาหวานน้อยกว่ากว่ากลุ่มผู้ป่วยที่มีแต่ปัจจัยเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือดอย่างมีนัยสำคัญทางสถิติ **เชียงใหม่เวชสาร 2564;60(1):17-26. 10.12982/CMUMEDJ.2021.02**

คำสำคัญ: ผลลัพธ์รวมทางคลินิกด้านหัวใจและหลอดเลือด ผู้ป่วยที่มีความเสี่ยงสูงที่จะเกิดเหตุการณ์ทางด้านหัวใจและหลอดเลือด