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The Role of Pretest Factors and Cardiovascular Risk Factors in Predicting Obstructive Coronary Artery Disease

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Abstract

Background: How the role of cardiovascular risk factors (hypertension, diabetes, smoking, dyslipidemia, family history of premature cardiovascular disease) affect the prior probability of coronary artery disease? Data on the pretest probability of coronary artery disease and studies evaluating the impact of pretest risk factors and cardiovascular risk factors on the ability to diagnose obstructive chronic coronary artery disease as for the Vietnamese population still very small. So, we did the study: "The role of extended model in predicting obstructive coronary artery disease" to answer this question.

Materials and Methods: There were 198 patients who received invasive coronary angiography at Nguyen Trai Hospital from September 1, 2020 to August 30, 2022. This was a cross-sectional study.

Results: There were 99 cases (50%) with chronic obstructive coronary artery disease and 99 cases (50%) with non chronic obstructive coronary artery disease, median age was 66 (IQR, 57-73), 56% of men, obesity was 34,3%. There were statistically significant independent associations between age, smoking, diabetes, hypertension, history of dyslipidemia, chest pain characteristics, LDL-cholesterol, and ST-T abnormalities and pathological Q waves on electrocardiogram with chronic obstructive coronary artery disease in multivariable logistic regression analysis with $p<0.05$. The area under the ROC curve of the classical model was 0.75 (95% CI 0.67-0.81), the clinical model was 0.82 (95% CI 0.77-0.88). Our extended model had the best predictive value for obstructive coronary artery disease with an area under the ROC curve of 0.86 (95% CI 0.8-0.92, $p < 0.001$).

Conclusions: The value of our extended model is also shown through high AUC, the model had the ability to distinguish well between groups of patients with or without the possibility of obstructive coronary artery disease. The model was built to help clinicians have more consulting tools and plan follow-up for patients.

Keywords: Obstructive Coronary Artery Disease, Pretest Factors, Cardiovascular Risk Factors

1. Introduction

Cardiovascular disease remains the leading cause of death in the world. According to a report by the World Health Organization in September 2020, the biggest "killer" is still coronary artery disease, accounting for up to 16% of global causes of death[1]. Since 2000, the number of deaths due to this disease has increased rapidly from more than 2 million to 8.9 million deaths (2019)[1]. According to the third statistical data on cardiovascular disease in early 2022 of the European Society of Cardiology, cardiovascular disease is still the most common cause of death in the association's member countries, in which cardiovascular disease is still the most common cause of death in the association's member countries. Ischemic heart disease accounts for up to 45% of women and 39% of men[2]. In the United States, according to the latest statistics recently published in 2022 on causes of death, coronary artery disease is still the leading cause, accounting for 41.3%[3]. On the basis of the US National Health and Nutrition Examination Survey data from 2015 to 2018, an estimated 20.1 million Americans ≥ 20 years of age have coronary artery disease, in addition to the prevalence of coronary artery disease. Coronary artery disease is higher in men than in women ≥ 60 years old[3].

Particularly in Vietnam, according to the 2020 report of the Center for Asian Health Research and Education at Stanford University School of Medicine, cardiovascular disease, including stroke and ischemic heart disease, are still the two leading causes. leading cause of death, accounting for 31% of all causes of death, equivalent to about 170,000 cases[4]. Although there

have been significant advances in the diagnosis and treatment of cardiovascular diseases in general and coronary artery disease in particular, mortality and morbidity from cardiovascular disease remain very high worldwide in That includes Vietnam. Therefore, currently, the diagnosis and management of cardiovascular disease, especially coronary artery disease, still remains major challenges for Vietnam's health care system. With efforts to improve the ability to diagnose and classify patients with coronary artery disease, in 2019, for the first time, the European Society of Cardiology proposed the term chronic coronary artery disease and also introduced a pre-probability table. "improved" testing based on age, gender, and symptoms of chest pain or shortness of breath[5]. Then in 2021, cardiovascular experts in the United States also reached a consensus on approaching patients with chest pain. The highlight of this guideline is that the authors also mention the prior probability of obstructive coronary artery disease but are somewhat different from the European Society of Cardiology guideline[6]. However, the remaining problem is that there are many factors that also affect this probability. In particular, the role of cardiovascular risk factors (hypertension, diabetes, smoking, dyslipidemia, family history of premature cardiovascular disease) affects the prior probability of predicting coronary artery disease like? Furthermore, data on the prior probability of coronary artery disease and studies evaluating the impact of pretest factors and cardiovascular risk factors on the ability to diagnose obstructive chronic coronary artery disease as for the Vietnamese population still very small. Therefore, we conducted the study " The role of extended model in predicting obstructive chronic coronary artery disease " with the following objectives:

1. Determine the prevelence and describe the clinical and subclinical characteristics of patients with obstructive coronary artery disease.
2. Identify cardiovascular risk factors in patients with obstructive coronary artery disease.
3. Determine the role of extended model in predicting obstructive coronary artery disease.

2. Materials and Methods

2.1 Research Subjects:

2.1.1 Study population: All patients who received invasive coronary angiography at Nguyen Trai Hospital from September 1, 2020 to August 30, 2022.

2.1.2 Sample selection criteria: all patients ≥ 18 years old with invasive coronary angiography at Nguyen Trai Hospital from September 1, 2020 to August 30, 2022.

2.1.3 Exclusion criteria: Patients did not have complete information on key study variables [such as symptoms of chest pain or shortness of breath, age, gender and five cardiovascular risk factors (hypertension, diabetes, dyslipidemia, smoking), tobacco, family history of premature cardiovascular disease). The patient had a confirmed diagnosis of obstructive chronic coronary artery disease before coronary angiogram. The patient had a history of acute coronary syndrome or coronary artery revascularization before this coronary angiogram.

2.2 Research Methods:

2.2.1 Study design: cross-sectional study.

Sample size: sample size calculation formula according to objective 1: Determine the prevelence patients with obstructive coronary artery disease.

$$n = Z^2_{1-\alpha/2} \frac{p(1-p)}{d^2}$$

In which: p = 30,4% The observed rate of obstructive CAD was in New York at 30.4% (95% CI, 29.7%-31.0%) according to Dennis T. Ko *et al*[7].

d = 0.075 is the marginal error of the estimate. Minimum sample size: $n = 1{,}96^2 \times 0.304 \times 0.696/0.075 = 145$ people.

2.2.2 Data analysis: data are processed using SPSS version 26 software. Quantitative variables are expressed as the mean ± standard deviation if belonging to a normal distribution or median and interquartile range of the value 25-75th percentile if not in normal distribution. Compare the difference between two averages using the unpaired t test, Mann-Whitney U test. Qualitative variables are displayed by frequency (percentage). Compare the difference between 2 proportions using the 2-tailed $\chi 2$ test; Fisher's exact test for 2x2 tables with 20% of cells with expected frequency < 5. The diagnostic performance of classical, clinical and extended models for predicting obstructive chronic coronary artery disease were tested using the receiving operating curve (ROC).Univariate and multivariate binary logistic regression analysis between contrast-induced acute kidney injury and qualitative or non-qualitative variables normal distribution. The differences are statistically significant when $p < 0.05$.

3. Results

During the research period from September 1, 2020 to August 30, 2022 at Nguyen Trai Hospital, we collected 198 patients who met the selection criteria and had no exclusion criteria for the study.

3.1 Characteristics of the study population

The median age was 66 (IQR, 57-73) years old, the youngest patient was 33 years old, the oldest patient was 93 years old. Male/female ratio: 1.27. Obesity was 34,3%.

3.2 Clinical characteristics

We noted that the two common reasons for hospitalization still chest pain and shortness of breath, accounting for more than 2/3 of the patients participating in the study. Regarding the current state of comorbidities in the study population, we noted that hypertension, lipid metabolism disorders, and diabetes are common comorbidities, accounting for 78%, 51%, and 32%, respectively. Patients with two major cardiovascular risk factors accounted for the highest proportion of 44.0%. 7.1% of the study population had no co-morbidities and no patients had five or more co-morbidities.

3.3 Laboratory

Table 1: Laboratory

Variables	Obstructive coronary artery disease		P value
	Yes (n = 99)	No (n = 99)	
White blood cell (K/ul)*	9.2 (9.1; 9.3)	9.3 (8.9; 9.7)	**0.045[a]**
Red blood cell (M/ul)*	4.5 (3.7; 5.3)	4.5 (3.5; 5.5)	0.470[a]
Hemoglobin (g/dl)*	13.2 (10.7; 15.7)	13.3 (11.0; 15.6)	0.680[a]
Anemia (n,%) *	27.0 (27.3%)	24.0 (24.2%)	0.600[c]
Platelet (K/ul)*	254.0 (180.0; 328.0)	249.0 (182.0; 316.0)	0.720[a]
Creatinine (umol/L)*	87.0 (51.0; 123.0)	86.0 (56.0; 116.0)	0.150[a]
eGRF (ml/phút/1,73m^2)*	70.0 (21.0)	75.0 (25.0)	0.120[b]
Natri (mmol/l)*	139.5 (135.7; 143.3)	139.9 (135.9; 143.9)	0.230[a]
Kali (mmol/l)*	4.0 (3.4; 4.6)	3.9 (3.4; 4.3)	0.730[a]
Cholesterol toàn phần (mmol/l)***	4.5 (2.4; 6.6)	4.2 (2.7; 6.7)	0.200[a]
Triglyceride (mmol/l)¶	1,9 (0.6; 3.1)	1,7 (0.5; 2.9)	0.210[a]
HDL-Cholesterol (mmol/l)¥	1.2 (0.7; 1.7)	1.1 (0.5; 1.7)	0.820[a]
LDL-Cholesterol (mmol/l)¶	2.6 (0.9; 4.3)	2.1 (0.9; 3.3)	**0.022[a]**

*n = 196, **n = 197,***n= 148,¥n= 149; ¶n = 150; aWilcoxon rank sum test; bt-test; cPearson's Chi-squared test. Data were expressed as median (IQR 25;75)*, medium (SD)**, n (%).

Comment: when analyzing subclinical variables, we noted a statistically significant difference in white blood cell count and LDL-Cholesterol concentration between the two groups of patients with and without obstructive chronic coronary artery disease with p of 0.045 and 0.022, respectively.

3.4 Identifying pretest factors and cardiovascular risk factors for obstructive coronary artery disease

We performed univariate logistic regression analysis to evaluate the association between factors and obstructive coronary artery disease.

Table 2: Association between pretest factors and obstructive coronary artery disease in univariate logistic regression analysis

Variables	OR	IQR 95%	p Value
Age (year)	Predicting obstructive CAD = -1,212 + 0,019 x age (year)		0,131*
Sex			
Female	1	0,62 – 1,90	0,774**
Male	1,09		
Chest pain characteristics			
Atypica angina or no chest pain	1		**<0,001****
Atyical angina	3,84	1,86 – 7,95	
Typical angina	10,21	4,49 – 23,24	
Hypertension			
Yes	1	1,09 – 4,46	**0,027****
No	2,21		
Diabetes			
No	1	1,15 – 3,90	**0,016****
Yes	2,12		
Dyslipidemia			
No	1	1,87 – 5,99	**<0,001****
Yes	3,35		
Smoking			
No	1	1,52 – 9,26	**0,04****
Yes	3,76		
ST-T			
ST-T normal	1	1,04 – 4,25	**0,039****
ST-T abnormal	2,1		
Pathological Q wave			
No	1	1,24 – 12,34	**0,020****
Yes	3,91		
White blood cell (k/uL)	Predicting obstructive CAD = 10,466 -1,121 x White blood cell		**0,04***
LDL-cholesterol (mmol/l)	Predicting obstructive CAD = -0,962 + 0,0382 x LDL -C		**0,013***
EF (%)	Predicting obstructive CAD = 0,923 - 0,165 x EF		0,128*

*Univariable logistic regression ** cPearson's Chi-squared test. CAD: coronary artery disease

Comment: characteristic factors of chest pain, hypertension, diabetes, history of dyslipidemia, smoking, number of blood vessels, LDL-cholesterol level, abnormal ST-T on electrocardiogram, having pathological Q waves on the electrocardiogram has a univariate association with obstructive chronic coronary artery disease, with $p < 0.05$.

After performing univariate logistic regression analysis, we performed multivariate logistic regression analysis with variables in the clinical model (including factors: age, gender, chest pain characteristics, hypertension, diabetes, history of dyslipidemia and smoking) and other pretest factors from research data (including: LDL-cholesterol, ST-T abnormalities on electrocardiogram and presence of Q waves pathology on electrocardiogram) to evaluate the independent association between pretest factors and cardiovascular risk factors with obstructive chronic coronary artery disease. Our study recorded that factors like age, smoking, diabetes, hypertension, history of dyslipidemia, typical and atypical angina symptoms, and LDL-cholesterol levels were related. Statistically significant independent association with obstructive coronary artery disease ($p<0.05$).

3.5 Determining the role of cardiovascular risk factors and pretest factors in predicting obstructive coronary artery disease between classical, clinical and extended models

Table 3: Prediction models for obstructive coronary artery disease in multivariable logistic regression analysis

Variables	Classical model	Clinical model	Extended model
β coefficient	- 2,945	- 4,326	- 9,162
Age	0,026	0,023	0,059
Male sex	0,181	- 0,059	-0,025
Atypical angina	1,347	1,143	1,523
Typical angina	2,359	2,223	2,105
Hypertension		0,912	1,444
Diabetes		0,958	1,152
Dyslipidemia		0,997	1,237
Smoking		1,952	1,845
LDL-Cholesterol			0,654
AIC	244,53	223,1	161,25

Comment: comparing among the 3 models, the results show that the extended diagnostic model and the clinical diagnostic model both give better results than the classic diagnostic model through improving the AIC value as the following regression equations

- In extended models:
  Risk of obstructive CAD = -9.162 + age (years) x 0.059 - male gender x 0.025 + atypical chest pain x 1.523 + typical chest pain x 2.105 + hypertension x 1.152 + diabetes × 1.237 + history of lipid disorders x 1.237 + smoking x 1.845 + 0.654 x LDL C level.
- In clinical models:
  Risk of obstructive CAD = -4.326 + age (years) x 0.023 – 0.059 x male gender + 1.143 x atypical angina + 2.223 x typical angina + 0.0912 x hypertension + 0.958 x diabetes + 0.097 x history of lipid disorders + 1.952 x smoking.
- In the classic model:
  Risk of obstructive CAD = -2.945 + age (years) x 0.026 + 0.181 x male gender + 1.347 x atypical angina + 2.359 x typical angina.

4. Discussion

4.1 Characteristics of the study population

According to medical literature, age is an unchangeable risk factor for the development of BMV, as well as a factor contributing to increased mortality in the presence of BMV[8]. Our study recorded the median and quartile age as 66 [57; 73], more than half of patients are over 60 years old, of which patients over 70 years old account for the highest proportion (36%) and the age group from 30 to <40 accounts for the lowest proportion (3%). When comparing the group with and without coronary artery disease, our study noted no difference in age between the two groups of patients. This result was quite similar to the study by author Sarah Feger and colleagues (2021) [9] to evaluate the value of Diamond-Forrester's prior probability model performed on 1440 patients, in which the median age of the patient group was invaded by CMV is 64 (57-72)[9]. The age range in our study is quite similar to the research results of author Tarun K. Mittal and colleagues. In this study, the author recorded over 3914 patients, the number of male patients recorded was 50.3%[10]. Our study recorded that the proportion of obese patients accounted for about one-third of the study population, and patients with grade I obesity accounted for the highest proportion (33%), with grade II obesity accounting for the lowest proportion (2%). When comparing the two groups of patients with and without obstructive coronary artery disease, we did not note a significant difference in body mass index.

4.2 Clinical characteristics

Our study noted that the three risk factors with the highest prevalence were hypertension (78%), lipid metabolism disorders (51%), and diabetes (32%), respectively. Meanwhile, chronic kidney disease and chronic obstructive pulmonary disease account for only 1%. In addition, all recorded underlying diseases were significantly different between the two groups of patients with and without obstructive coronary artery disease.

4.3 Laboratory

According to the ESC 2019 recommendations for diagnosis and management of chronic coronary artery disease, biochemical tests are used to assess possible causes of myocardial ischemia, assess cardiovascular risk factors and prognosis of patient[5]. In our study, only white blood cell count and LDL-cholesterol had a significant difference between the two groups of patients, with the median value of LDL-cholesterol concentration being relatively high (2.3 mmol/L). Our study has similar results to the study of author Philippe Gabriel Steg and colleagues. Specifically, the author also noted that among patients who had non-invasive assessment, the median values of LDL and HDL were, fasting triglycerides are 2.3; 1.2; 1.4 (mmol/L). In addition, blood creatinine concentration in this study is similar to our study (88 umol/L)[11]. Unlike our study, author David E. Montgomery and colleagues noted that blood creatinine levels did not have a statistically significant difference between the group without or with obstructive coronary artery disease[12]. This difference may be due to different study population characteristics, or due to random variation.

4.4 Identifying pretest factors and cardiovascular risk factors for obstructive coronary artery disease

We evaluate the risk of obstructive coronary artery disease

based on the prior probability models of AHA (2021), ESC (2019) and the model with risk factors of Simon Winther (2020) and record when using Using the AHA model, 16.1% of patients will be overestimated as high risk compared to the ESC model. Meanwhile, if evaluated using Simon Winther's model, 16.2% of patients will be underestimated as high risk compared to the ESC model. In addition, when analyzing the prior probability based on data of patients who were determined to have obstructive coronary artery disease (n = 99), we also noted the same thing, with an overestimation of the model. AHA, and below the level of the Simon Winther model. In addition, there is still a small percentage of patients who are assessed as having a low probability of a prior history but have obstructed coronary artery disease (4%). Post-hoc analysis study based on data from the SCOT-HEART trial on 4146 patients suspected of having coronary artery disease, of which 1613 patients underwent coronary computed tomography angiography. The study noted that only 22% of patients with coronary artery disease had obstruction on coronary computed tomography angiography. In addition, the rate of coronary artery blockage or stenosis of more than 50% of the diameter in the high-risk group is 57.7%, the medium-risk group is 29.2%, and the low-risk group is 13.2%[13]. There is a difference in the results of the above study with our study possibly due to different population characteristics (the SCOT-HEART trial only excluded patients with acute coronary syndrome within 3 months), and the criteria gold standard in various diagnoses (SCOT-HEART trial defines coronary artery stenosis as >70% narrowing of epicardial coronary artery diameter or >50% narrowing of left main coronary artery.

4.5 Comparison of diagnostic value of obstructive coronary artery disease among classical model, clinical model and extended model

After applying to the study population, we found that the AUC of the classic model (including factors such as age, gender and chest pain characteristics) was 0.75 (95% CI 0.67-0, 81), the clinical model (including: age, gender, chest pain characteristics, hypertension, diabetes, dyslipidemia and smoking) was 0.82 (95% CI 0.77- 0.88). In addition, multivariate analysis we noted that LDL-cholesterol is valuable in predicting obstructive coronary artery disease and after adding LDL-cholesterol to the clinical model as a factor in predicting obstructive coronary artery disease (model extended) we found the AUC of this model to be 0.86 (95% CI 0.8-0.92). Compared with the classical model, the clinical model has a higher AUC with p=0.004. In addition, when comparing our model with the classic model and the clinical model with the Delong test, we note that our extended model has a higher AUC value than the classic model with p = 0. .0006 is also higher than the clinical model with p=0.0202. Our model has a higher AUC value possibly because in addition to considering clinical factors, we also include LDL-c in the prediction model.

Overall, studies show that diagnostic models are relatively similar in terms of AUC between studies around the world and our study, although there may be differences in study population characteristics, differences in the epidemiology of risk factors, or due to the different incidence rates of obstructive coronary artery disease in each study.

5. Conclusion

The area under curve ROC of the classical model was 0.75 (95% CI 0.67-0.81), the clinical model was 0.82 (95% CI 0.77-0.88). Our extended model had the best predictive value for obstructive coronary artery disease with an area under curve ROC of 0.86 (95% CI 0.8-0.92, $p < 0.001$).

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