HUE UNIVERSITY
UNIVERSITY OF MEDICINE AND PHARMACY

NGUYEN HAI CUONG

PREDICTIVE PERFORMANCE OF NCDR CathPCI AND CRUSADE RISK SCORES FOR IN-HOSPITAL AND ONE YEAR BLEEDING IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

Major: Internal medicine
Code: 9720107

SUMMARY OF MEDICAL DOCTORAL DISSERTATION

HUE - 2023

The project was completed at:

University of Medicine and Pharmacy, Hue University

Scientific instructor:

Dr. NGUYEN CUU LOI

Assoc. Prof. Dr. LE THI BICH THUAN

Review 1:

Review 2:

Review 3:

Thesis defended at

At …. Hours … on … day … month … year

The thesis can be found at:

1. Library of University of Medicine and Pharmacy, Hue University

2. National Library of Vietnam

HUE UNIVERSITY
UNIVERSITY OF MEDICINE AND PHARMACY

NGUYEN HAI CUONG

PREDICTIVE PERFORMANCE OF NCDR CathPCI AND CRUSADE RISK SCORES FOR IN-HOSPITAL AND ONE YEAR BLEEDING IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

Major: Internal medicine
Code: 9720107

SUMMARY OF MEDICAL DOCTORAL DISSERTATION

HUE – 2023

INTRODUCTION

1. Rationale for the study

Coronary revascularization by percutaneous coronary intervention (PCI) is the optimal technique for treating coronary artery disease, with the advantage of reducing major cardiovascular events and mortality. However, bleeding remains one of the serious complications due to the invasive nature of PCI and the use of antithrombotic drugs. PCI-related bleeding causes significant short- and long-term adverse events. To prevent bleeding risk and improve the quality of treatment, pre-interventional bleeding risk stratification based on available scales is considered the simplest and most important step.

In Vietnam, PCI has been conducted routinely, but there is no domestic study investigating bleeding complications in all groups of patients undergoing PCI with long follow-up to identify risk factors and influence of bleeding on the overall outcome. Therefore, we conducted the study entitled "Predictive performance of NCDR CathPCI and CRUSADE risk scores for in-hospital and one year bleeding in patients undergoing percutaneous coronary intervention" to address these gaps in knowledge.

2. Research objectives

(1) To estimate the rate of bleeding, risk factors for bleeding, and the effect of bleeding on the study group's prognosis of mortality.

(2) To estimate the risk factors for bleeding and evaluate the predictive performance of the NCDR CathPCI and CRUSADE risk scores for bleeding in the study subjects.

3. Scientific and practical significance

3.1. Scientific significance

Bleeding complications may occur early or late after PCI, during the period of antithrombotic therapy to prevent secondary complications. Early identification of risk factors for bleeding and an

appropriate risk assessment scale for Vietnamese patients can lead to important conclusions about the effectiveness of the tool and strategic directions.

3.2. Practical significance

The study's findings help in the early identification of bleeding risk factors, selection of a risk stratification tool, and prophylactic strategy to reduce the risk of bleeding for patients undergoing PCI while optimizing targeted therapy.

4. Contributions of the dissertation

This is the first study in Vietnam to use two combined bleeding risk scales to evaluate all subjects with acute and chronic coronary syndromes undergoing PCI, with a follow-up period of 12 months. The study determined that the overall rate of bleeding complications in the study population was 3.8%, with major bleeding complications occurring during hospital stay. Additionally, the study showed that both the NCDR CathPCI and CRUSADE scores could predict the risk of bleeding and mortality in patients undergoing PCI with a separate optimal cutoff for each scale.

Chapter 1
LITERATURE REVIEW

1.1. OVERVIEW OF CORONARY ARTERY DISEASE

1.1.1. Pathophysiology of coronary artery disease

Coronary artery disease (CAD) is a progressive process that involves different stages. The beginning is atherosclerotic lesion due to a chronic and complex inflammatory process causing endothelium hyperplasia; atherosclerotic plaque continues to progress with repeated episodes of plaque rupture and self-healing, when the atherosclerotic lesions increase in size, they will invade into the

lumen, causing a decrease in coronary flow; atheroma can be stable or unstable. Unstable atherosclerotic plaques are characterized by thin shells that are prone to rupture and erosion, which can lead to thrombus formation in the vessel lumen, causing acute coronary syndromes.

1.1.2. Classification of coronary artery disease

CAD due to atherosclerotic includes two clinical syndromes:

- Acute coronary syndromes, including ST-elevation myocardial infarction (STEMI), non-STEMI, and unstable angina are associated with atherosclerotic plaque rupture, thrombosis, and narrowing or occlusion of the arterial lumen.

- Chronic coronary syndrome, which replaces the previous names of stable angina, stable CAD, ischemic cardiomyopathy or coronary insufficiency. This pathology is related to the relative stability of atherosclerotic plaque in the absence of sudden rupture after the acute phase or after intervention/surgery.

Due to the dynamic process and physiological mechanism, CAD is not only the epicardial coronary artery injury but also the coronary microcirculation damage mechanism, coronary artery vasospasm.

1.2. TREATMENT OF CORONARY ARTERY DISEASE WITH PERCUTANEOUS CORONARY INTERVENTION

Percutaneous coronary intervention (PCI) is a minimally invasive procedure performed to improve blood flow at one or more sites of the coronary circulation. PCI involves inserting a small catheter into the lumen of a narrowed or blocked coronary artery through the brachial or femoral artery and then dilating and placing a drug-coated stent or drug-free. Depending on the condition of the acute or chronic coronary syndrome, there will be indications for first aid, rescue or program.

PCI procedures include following steps:

(1) Selection of arterial access: While the femoral artery was previously the most commonly used access site, the radial approach is now preferred due to its advantages.

(2) Inserting the interventional catheter into the coronary artery ostium: A guide wire is used to slide the interventional catheter with the appropriate size and shape into the aortic arch, then adjusted into the left or right of the coronary artery that required intervened.

(3) Guiding the guidewire through the lesion: The interventional lead is selected based on the coronary artery anatomy, lesion morphology, and interventionist experience. The lead tip is curved according to the morphology of the target artery. Insert the guidewire gently through the lesion, all the way to the distal part of the coronary artery that needs intervention.

(4) Balloon angioplasty: A balloon is used to pre-expand the narrow lesion to minimize the risk of dissection of the coronary artery wall. The size and type of balloon used are selected according to the characteristics of the lesion. The narrow lesion is pre-expanded with a balloon to minimize the risk of dissection of the coronary artery wall. Select the size and type of balloon (normal pressure, high pressure, cutting balloon) according to the lesion characteristics.

(5) Intra-coronary stent placement at the stenosis site: Select the type of stent suitable for the reference length and diameter of the lesion that has just been ballooned.

PCI is an invasive interventional procedure, with the use of antithrombotic drugs. While PCI significantly reduces short- and long-term ischemic complications, it is associated with bleeding.

1.2.1. Bleeding Definitions

There are several bleeding grades used in clinical trials and registries, but there is no universally agreed definition. Prior to the

PCI era, the most widely used major bleeding classifications were TIMI (Thrombolysis in Myocardial Infarction) and GUSTO (The Global Use of Strategies to Open Occluded Arteries), although these two definitions are no longer relevant since they are designed only for patients treated with thrombolytics. In 2011, the Bleeding Academic Research Consortium (BARC) released a classification of bleeding events from non-bleeding (type 0) to fatal bleeding (type 5). BARC is considered as a temporary standard and is commonly used in clinical studies since 2013.

1.2.2. Bleeding after PCI and prognosis

The rates of major bleeding ranged from 1% to 10% in studies reported prior to 2008, depending on the study population, study design, and bleeding classification used. Studies after 2008 recorded a narrower margin with a rate of 2% - 5%. Bleeding after PCI increases the risk of mortality, major cardiovascular events, and rehospitalization. The mortality rate during hospital stay and the first 30 days of the group of patients with bleeding increased from 3 to 10 times compared with the group without bleeding.

1.2.3. Risk factors and predictors of bleeding

Risk factors

The most common risk factors for bleeding early during and immediately after intervention were femoral artery access, sheath size, length of intervention, and use of mechanical circulatory assist devices such as intra-aortic balloon counterpulsation, intra-coronary atherectomy device, complexity of coronary injury (type C), and use of strong and complex anticoagulation. Other factors included main artery or three vessel artery disease, smoking, and INR >2.6 in patients taking warfarin.

Independent predictors of late bleeding after coronary stenting were older age, history of bleeding, chronic kidney disease, dual antiplatelet therapy and warfarin.

Prognosis of bleeding

The development of models to identify bleeding risk in patients undergoing PCI has become increasingly important as the impact of bleeding on prognosis has become more apparent. These models take into account various clinical, subclinical, interventional, and antithrombotic factors to help stratify patients based on their risk of bleeding post-PCI.

Table 1.1. Summary of two predictive scales for bleeding risk for patients receiving PCI in the study

Score	Subjects	Bleeding time	Variables
CRUSADE (2009)	Non-ST elevation acute coronary syndrome	In-hospital	Baseline hematocrit <36% Creatinine clearance Heart rate Female Congestive heart failure Systolic blood pressure <110 mmHg or >180 mmHg Peripheral vascular disease Diabetes mellitus
NCDR-CathPCI (2013)	PCI	Within 72 hours after the intervention	ST elevation MI Age BMI Previous PCI Chronic kidney disease Heart Shock Cardiac arrest within 24 hours Female Baseline Hemoglobin PCI status

1.3. INTERNATIONAL AND DOMESTIC RESEARCH

1.3.1. International research

Applied CRUSADE score: Ran Liu (2017) in China, Tien Yu Chen (2019) in Taiwan, Sun Young Choi (2018) in Korea, Jarrah Mohamad (2017) in Jordani.

Applied NCDR CathPCI score: David R. Dobies et al (2014) in the US, Michael J Thibert et al (2019) in Canada, Georg Wolff et al (2020) in Germany.

1.3.2. Domestic research

In Vietnam, studies that assessed pre-PCI bleeding risk have been got more attention.

Chapter 2
METHODOLOGY

2.1. STUDY SUBJECTS

All patients diagnosed with coronary artery disease, including acute and chronic coronary syndromes, were admitted to the Cardiovascular Emergency Center of Hue Central Hospital and the Interventional Cardiology Department of Lam Dong General Hospital during the period from January 2017 to January 2020; underwent PCI, had normal coagulation function and agreed to participate in the study. Exclusion criteria included patients with autoimmune disease, malignancy, cyanotic congenital heart disease, pulmonary embolism, severe infection, liver failure, cirrhosis, and musculoskeletal injury.

2.2. RESEARCH METHODOLOGY

2.2.1. Study design

This was a prospective cohort study with 12 months of follow-up.

2.2.2. Sample size

The minimum required sample size was calculated using the formula:

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

In which:

n: minimum required sample size

z(1- α/2): critical value of the Normal distribution at α/2; with α = 0.05, z=1.96

p: sample proportion; p=0.05 (the rate of bleeding after PCI in recent study).

d: margin of error (1.5%).

For this study, the minimum required sample size was 811 patients, with an estimated 20% dropout rate, an expected study sample size was 911 patients. The actual sample size collected in this study was 1,096 patients.

2.2.3. Research procedure

The research procedure involved selecting patients who met the selection criteria, conducting the process of asking, clinical examination, paraclinical examination, diagnosis, treatment, and monitoring of patients with coronary artery disease who were assigned PCI. Information was recorded in a research sheet that included administrative information, history of cardiovascular diseases, other comorbidities and drugs being treated, clinical symptoms, laboratory tests, diagnosis pre-PCI, pre- and post-procedural medication, pre-procedural bleeding risk stratification score, information related to PCI, bleeding events, and mortality after PCI during hospital stay and 12 months after discharge.

2.2.4. CRUSADE and NCDR CathPCI Score for predicting bleeding events

* CRUSADE score

The CRUSADE scale consists of 8 parameters, each parameter's value corresponds to a different score with a total score from 0 to 100, classified into five categories: very low (< 21 points), low (21-30 points), average (31-40 points), high (41-50 points) and very high risk (> 50 points).

* NCDR CathPCI score

The NCDR Cath PCI score is based on 10 parameters, with a total score of 0-210, divided into low-risk (<25 points), moderate (25-65 points), and high-risk groups (>65 points).

2.2.5. Bleeding Definitions

Used BARC score, along with the 2 bleeding risk scales, as the primary score to evaluate when a bleeding event occurs.

2.3. Data analysis

Data were entered and analyzed using SPSS statistical software version 20.0.

Qualitative data were described as frequency (n) and percentage (%). Quantitative variables were tested for normal distribution (by Kolmogorov-Smirnov or Shapiro-Wilk test) and described as mean and standard deviation if normally distributed or median, Q1, Q3, minimum, and maximum if non-normally distributed.

The ROC curve was analyzed to evaluate the predictive value of bleeding risk scores for bleeding and mortality using the area under the ROC curve (AUC). An AUC value of ≥0.7 was considered to have adequate diagnostic accuracy. Univariate and multivariable logistic regression were used to calculate the OR and 95% CI to examine some factors related to bleeding and mortality in the study group.

The Kaplan Meier method was used to describe the survival time of study subjects to 12 months after admission in the group with bleeding and without bleeding events.

The tests were statistically significant when $p < 0.05$.

2.4. Research ethics

The study protocol was approved by the ethics committee of Hue University of Medicine and Pharmacy No. 918/QĐ-ĐYH on April 28, 2017. Patients voluntarily participated in the study and had the right to withdraw at any stage. The identities of all study subjects were kept confidential. The tests performed in this study did not adversely affect the health of the patients participating in the study.

CHAPTER 3
RESULTS

3.1. GENERAL CHARACTERISTICS OF STUDY POPULATION

3.1.1. Demographic and anthropometric characteristics

Our study included subjects aged 36 to 96, with an average age of 68.5 ± 10.7. The female group was statistically significantly older than the male group ($p < 0.001$). The male group had a significantly higher BMI than the female group ($p < 0.001$).

3.1.2. History of smoking, comorbidities and coronary artery disease

Hypertension was the most common comorbidity in our study (52.1%), while chronic kidney disease and peripheral artery disease were the least prevalent (1.3% and 1.4% respectively). The majority of patients had a history of PCI (28.5%), while only 0.5% had a history of coronary artery bypass grafting.

3.1.3. Clinical features

The majority of patients in our study had heart failure NYHA II and III (81.6%). The number of patients who experienced cardiac arrest and within 24-hour and cardiogenic shock was 0.5% and 3.5%, respectively.

3.1.4. Subclinical features

In our study, LVEF, Hct, HgB, platelet count, and glomerular filtration rates were within normal limits.

3.1.5. Diagnostic features

Most patients in our study were diagnosed with stable angina (60.5%) before intervention, followed by STEMI (23.7%). The rate of unstable angina was the lowest (6.3%). 60.6% of patients were diagnosed with chronic coronary syndrome before the intervention, and 51.9% of subjects suffered one injured coronary branch on coronary angiography.

3.1.6. Features of percutaneous coronary intervention

In this study, 72.2% of patients received elective PCI. In the group of patients with acute coronary syndrome, the majority of patients receiving primary emergency intervention (45.1%), while most patients with chronic coronary syndrome were scheduled (99.2%). The rate of complete PCI during hospital stay of patients with 1, 2, and 3 coronary artery stenosis was 100%, 59.3%, and 24.5%, respectively.

Assist devices were only used in STEMI patients, with a proportion of 3.1%. The rate of patients using support devices in the group with cardiogenic shock was 13.2%, which was higher than the group without cardiogenic shock (0.3%). The most commonly used catheter size for intervention was 6F.

3.1.7. Characteristics of medical treatment before and after intervention

Only 0.5% of patients used thrombolytic drugs before the intervention, and all cases belonged to the STEMI group. Aspirin and clopidogrel were the two most commonly used preprocedural antithrombotic drugs, with rates of 99.5% and 65.5%, respectively. Dual antiplatelet therapy with aspirin and clopidogrel were used most commonly in both sexes, with rates of 63% in women and 57% in men, respectively.

3.2. BLEEDING EVENTS AND ASSOCIATION BETWEEN BLEEDING AND MORTALITY

3.2.1. Bleeding events

Out of the 1096 patients in the study, 42 patients experienced bleeding events after the intervention, accounting for 3.8%. The site of bleeding accounted for the highest percentage was at the needle puncture site (42.9%) and in the digestive tract (40.5%). Bleeding occurring during hospital stay was more common (73.8%) than bleeding occurring after hospital discharge.

3.2.2. Association between bleeding events and mortality

There was a statistically significant association between bleeding events and mortality within 1 year after PCI ($p < 0.001$). Multivariable logistic regression analysis showed that bleeding increased the risk of mortality 11.5 times (p=0.002).

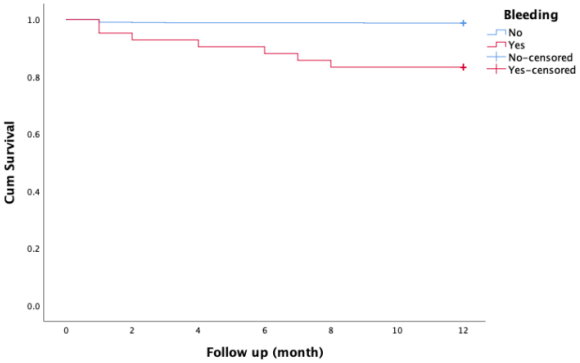

Figure 3.1. Kaplan-Meier survival curves for PCI patients with and without bleeding events

The group of patients who experienced bleeding had a lower cumulative survival rate at the 12-month follow-up compared to the group without bleeding. This difference was found to be statistically significant with a p-value of less than 0.001.

3.3. RISK FACTOR OF BLEEDING AND PREDICTIVE PERFORMANCE OF CRUSADE AND NCDR CathPCI SCORES FOR BLEEDING RISK

3.3.1. Risk factors associated with bleeding events

Table 3.1. The association between bleeding events and risk factors in study subjects (n=1096)

Variable		**Crude OR (95%CI)**	**p**	**Adjusted OR (95%CI)**	**p**
CRUSADE		1.09 (1.06-1.12)	<0.001	1.07 1.03 – 1.11)	<0.001
Hypertension	No	1		1	
	Yes	3.5 (1.7 – 7.4)	0.001	2.7 (1.01 - 7)	0.048
Previous bleeding	No	1		1	
	Yes	15.7 (4.4 – 56.1)	<0.001	7.4 (1.2 – 46.5)	0.032
Use of clopidogrel	No	1		1	
	Preprocedural	1.4 (0.1 – 13.3)	0.787	0.3 (0.02 - 7)	0.475
	Postprocedural	14.9 (2.3 – 95.4)	0.004	18.6 (1.3 – 265.1)	0.031
	Pre- and post-procedural	7.2 (2.2 – 23.6)	0.001	4.6 (1.04 – 20.6)	0.045
Preprocedural fibrinolytics	No	1		1	
	Yes	55.4 (9.8 – 311.7)	<0.001	37 (3.3 – 417.4)	0.004

Comment: The multivariable logistic regression model reported the association between bleeding events and variables including CRUSADE, hypertension, history of bleeding, use of clopidogrel and fibrinolytics.

Table 3.2. Association between bleeding events and NCDR CathPCI risk scores and some other factors in study subjects (n=1096)

Variable		**Crude OR (95%CI)**	**p**	**Adjusted OR (95%CI)**	**p**
NCDR CathPCI		1.03 (1.02 - 1.034)	<0.001	1.01 (0.99 - 1.03)	0.109
Sex	Male	1		1	
	Female	3.2 (1.7 – 6)	<0.001	3.4 (1.5 - 8)	0.004
Chronic kidney disease	No	1		1	
	Yes	7.3 (2 – 27.2)	0.003	10.1 (1.8 - 58	0.009
Previous bleeding	No	1		1	
	Yes	15.7 (4.4 – 56.1)	<0.001	9.5 (1.6 - 56.4	0.013
Use of clopidogrel	No	1		1	
	Preprocedural	1.4 (0.1 - 13.3)	0.787	0.5 (0.03 - 8.3	0.635
	Postprocedural	14.9 (2.3 - 95.4)	0.004	13.9 (1.1 - 183.5)	0.045
	Pre- and post-procedural	7.2 (2.2 - 23.6)	0.001	4.4 (1.02 - 19.1)	0.047
Preprocedural fibrinolytic	No	1		1	
	Yes	55.4 (9.8 - 311.7)	<0.001	29.7 (2.8 - 311.1)	0.005

Multivariable logistic regression model emphasized the statistically significant association between bleeding events and use of clopidogrel, fibrinolytics therapy before intervention.

3.3.2. Predictive performance of CRUSADE and NCDR CathPCI for bleeding events

3.3.2.1 In whole group of PCI

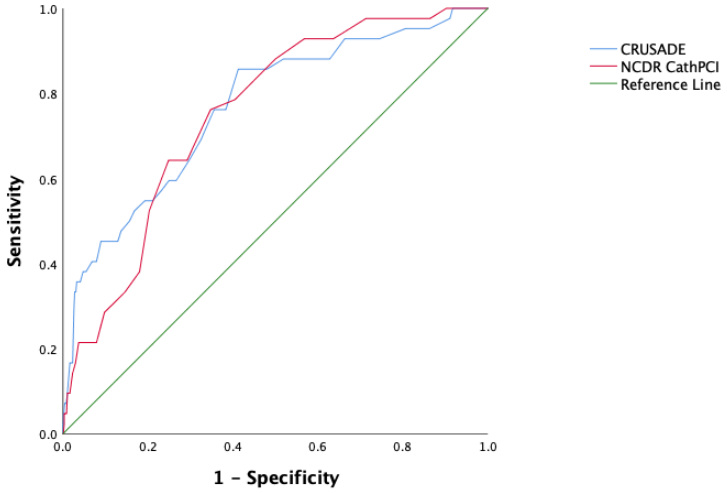

Figure 3.2. ROC curves of CRUSADE and NCDR CathPCI scores for predicting bleeding events

The optimal cut-off point of the CRUSADE in predicting bleeding after PCI was ≥31.5; corresponding to a sensitivity of 85.7% (79.5% - 91.9%) and specificity of 58.7% (50% - 67.4%); AUC=0.77 (95%CI: 0.69-0.84) ($p<0.05$).

The optimal cut-off point of the NCDR CathPCI in predicting bleeding after intervention was ≥57.5; corresponding to sensitivity of 76.2% (68.7% - 83.7%) and specificity of 65.3% (56.9% - 73.7%); AUC=0.75 (95%CI: 0.69-0.82) ($p<0.05$).

3.3.2.2. In patients with acute coronary syndromes

In patients with acute coronary syndromes, the optimal cut-off point for the CRUSADE was ≥33.5 with a sensitivity of 82.8% (76.2% - 89.4%) and specificity of 60.8% (52.2% - 69.4%), area under the ROC curve: 0.77 (95% CI: 0.68-0.85, p<0.05). For the NCDR CathPCI, it was ≥72.5, with a sensitivity of 75.9% (68.4% - 83.4%) and specificity of 50.9% (42.1% - 59.7%), area under the ROC curve: 0.66 (95% CI: 0.57 - 0.75, p<0.05).

3.3.2.3. In patients with chronic coronary syndromes

In patients with chronic coronary syndromes, the optimal cut-off point for the CRUSADE scale was ≥31.5, with a sensitivity of 84.6% (78.2% - 91%) and specificity of 59.9% (51.3% - 68.5%), and for the NCDR CathPCI scale it was ≥42.5, with a sensitivity of 76.9% (69.5% - 84.3%) and specificity of 57.8% (49.1% - 66.5%). The area under the ROC curve of CRUSADE and NCDR CathPCI was 0.74 (95% CI: 0.59-0.9) and 0.72 (95% CI: 0.58-0.85), respectively.

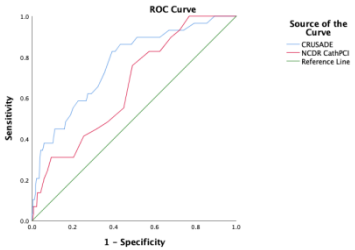

Figure 3.3. ROC curves of CRUSADE and NCDR CathPCI scores for predicting bleeding in patients with acute coronary syndromes

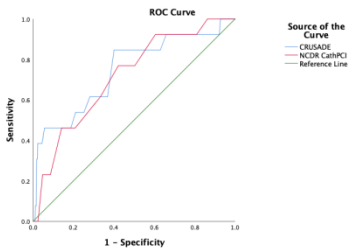

Figure 3.4. ROC curves of CRUSADE and NCDR CathPCI scores for predicting bleeding in patients with chronic coronary syndromes

Chapter 4
DISCUSSION

4.1. GENERAL CHARACTERISTICS OF STUDY POPULATION

4.1.1. Demographic and anthropometric characteristics

The study sample had a mean age of 68.5 ± 10.7, with a median age of 69. Females had a higher median age (72) than males (67), consistent with findings by Vu Thi Thanh Hoa (2020).

The study sample had a mean BMI of 21.9 ± 2.9, which was similar to findings by Nguyen Thi Thanh (2018) and lower than other studies in Asia, such as Japan (24.2 ± 3.6), China (26.0 ± 3.2), and Korea (24.6 ± 3.1).

4.1.2. Smoking, comorbidities, and coronary artery disease history

In this study, 14.7% of patients were current smokers, which was higher than in Vu Thi Thanh Hoa's study (10.8%). However, this percentage was lower than in other studies, such as Numasawa's study in Japan (34.12%), Xue Yan Zhao's study in China (57.15%), Wlodarczyk's study in Australia (23.6%), and Vijay Kunadian's study in the United Kingdom (57.33%).

The most common comorbidities found were hypertension (52.1%), diabetes (12.7%), and hyperlipidemia (5.4%). The rates of peripheral artery disease and chronic kidney disease were the lowest, (1.4% and 1.3%, respectively).

Among the patients, 28.5% had a history of PCI, 4.2% had a history of myocardial infarction, and 0.5% had a history of CABG.

4.1.3. Clinical Characteristics

In this study, approximately 30.2% of patients presented with heart failure, which differs from findings in other countries due to the unique characteristics of the patient population and research objectives. The median LVEF was 60, consistent with results from a study conducted by Vu Thi Thanh Hoa in Vietnam.

The incidence of cardiac arrest within the first 24 hours of admission was 0.5%, which was similar to the rate reported by Vu Thi Thanh Hoa (0.6%) and lower than that reported in foreign studies. In addition, a higher proportion of patients in our study

presented with cardiogenic shock (3.5%), compared to Vu Thi Thanh Hoa's study (1.1%).

4.1.4. Clinical diagnostic features

Our sample was composed mainly of subjects with chronic coronary syndrome, with the majority of stable angina (60.5%). This contrasted with larger studies assessing the risk of bleeding in all subjects undergoing PCI, where those with acute coronary syndrome were more prevalent.

4.1.5. Features related to coronary intervention

The majority (72.2%) of interventions were planned, while 18.1% were primary emergency intervention, and 9.7% were rescue PCI. In this study, the rates of emergency and rescue PCI were much lower compared to data from the NCDR CathPCI Registry from February 2008 to April 2011, which indicated the rates of to be 17% and 37.5%, respectively.

Most patients (95.3%) received PCI via the radial artery access and only 4.7% through the femoral artery. This was consistent with recent studies that show radial access was associated with a reduction in postprocedural bleeding and acute kidney injury compared with femoral arterial access.

In this study, the proportion of one branch damage was more prevalent (51.9%). This result was similar to studies conducted in Jordan and Italy.

Only eight patients used assist devices during the intervention, and all o them were in the STEMI group, five of which had cardiogenic shock.

The study mainly used a 6F sheath (97.9%), reserving the use of the 7F device for complex trauma, main coronary artery injury, and transfemoral access for PCI.

4.1.6. Characteristics of medical treatment before and after intervention

In this study, prior to intervention, the rate of patients using fibrinolysis was 0.5%, and among 260 patients uith STEMI, this proportion was 2.3%. This figure was lower compared to a previous study using data from CathPCI Registry by Sunil Rao, which reported a rate of 8.1%.

Aspirin and Clopidogrel were the two most commonly used drugs prior to intervention, with usage rates of 99.5% and 65.5% respectively. Dual antiplatelet therapy with aspirin and clopidogrel was the most commonly used in clinical settings, followed by dual antiplatelet therapy with aspirin and ticagrelor.

The use of aspirin and clopidogrel compared with aspirin and ticagrelor were similar before and after intervention. However, the rate of using ticagrelor after intervention was 38.9%, higher than before intervention (33.7%). Comparing the current study with previous foreign studies, dual antiplatelet therapy using aspirin and clopidogrel is still mainly used before and after PCI.

4.2. BLEEDING EVENT RATE AND ASSOCIATION BETWEEN BLEEDING AND MORTALITY

4.2.1. Proportion of bleeding events

After 12 months of follow-up, the cumulative bleeding rate, including in-hospital and post-discharge bleeding, was 3.8%. In-hospital bleeding accounted for the majority of this rate (2.8% compared to 1% after 12 months of follow-up). It was difficult to compare bleeding rates with other studies due to heterogeneity among studies, but our rate was lower than in randomized clinical studies or some large registry studies.

There are two main reasons for this. First, the group prone to bleeding after intervention, acute coronary syndrome group, has a lower rate than the group with chronic coronary syndrome (39.4% versus 60.6%). Additionally, the proportion of elderly patients, patients with heart failure or chronic kidney failure, and those requiring intervention for complicated lesions such as chronic occlusion or calcifications requiring the use of assistive devices was relatively low. Second, the intervention technique and pharmacology before and after coronary intervention in our study differed from studies that enrolled patients before 2015, especially regarding the radial access artery in PCI intervention, which is considered to reduce significant bleeding events. In our study, most cases used PCI via radial artery access (95.2%).

4.2.2. Association between bleeding and mortality

The study found that the mortality rate was higher in the group with bleeding (16.7%) compared to the group without bleeding

(1.2%). After adjusting for variables such as age, sex, history of myocardial infarction, hyperlipidemia, use of fibrinolysis, and enoxaparin, a multivariable logistic regression model showed that patients with bleeding were associated with an increased risk of death 11.5 times higher than the group without bleeding (95%CI: 2.5-53.5; p=0.002). This result was consistent with other studies such as a meta-analysis of Kwok et al. including 42 studies, which showed that bleeding after PCI increased the risk of mortality 3 times, and study of Hirono which showed a 5.97 times higher risk of death.

Furthermore, the study found that the survival time of the group with bleeding was shorter compared to the group without bleeding. The Kaplan Meier curve also showed that survival rates began to diverge from the first month after PCI and became increasingly distinct over time.

4.3. RISK FACTORS OF BLEEDING AND THE PREDICTIVE PERFORMANCE OF CRUSADE AND NCDR CathPCI SCORES

4.3.1. Risk factors associated with bleeding events

4.3.1.1. Bleeding and Patient's demographic, anthropometric characteristics

In terms of demographic characteristics, patients who experienced bleeding events were on average 76.5 years old, which was statistically significantly higher than the non-bleeding group who were on average 68.0 years old ($p < 0.001$). Female patients had 3.2 times higher risk of bleeding than male patients (95% CI: 1.7 - 6), which was statistically significant ($p < 0.001$).

The multivariable logistic regression model identified two good predictors of bleeding including history of previous bleeding and hypertension. Compared with patients with no previous bleeding history, the group of patients with a history of bleeding had a 7.4 times higher probability of bleeding (95% CI: 1.2-46.5). Compared with patients without hypertension, the group of hypertensive patients was 2.7 times more likely to bleed (95% CI: 1.01-7).

It should be noted that the relationship between demographic characteristics, disease characteristics, and bleeding risk may vary across studies due to different patient selection criteria, drug regimens, and follow-up duration.

4.3.1.2. Bleeding and factors related to interventional procedures

There was a statistically significant relationship between bleeding status and intervention status in study subjects (p=0.001). The diagnosed clinical disease and PCI status were also factors related to bleeding events.

The bleeding rate was highest when using femoral artery access (17.3%), followed by radial artery access (3.2%), and the difference was statistically significant (p<0.001). This result was consistent with a meta-analysis of 24 studies by Ferrante et al. that found percutaneous femoral artery intervention increased the risk of major bleeding compared with radial artery intervention.

The size of the catheter used was also a factor associated with bleeding events. The bleeding rate in the group using the 7F catheter was 21.7%, which was statistically significantly higher than the group using the 6F catheter (3.4%) (p = 0.001).

In our study, we did not find an association between assist device use and bleeding. However, this differed from the finding of a study conducted in Japan by Numasawa et al., one explanation might be due to just a small number of patients using interventional aids in our study.

4.3.1.3. Bleeding and antithrombotic drugs used before and after intervention

Our study found that there was a statistically significant association between bleeding events and the use of clopidogrel, ticagrelor, fibrinolysis, heparin, and enoxaparin in pretreatment intervention (p<0.05). However, the multivariable logistic regression model only confirmed a significant association between bleeding and the use of fibrinolysis before intervention. Similar results were found in other studies, which also identified fibrinolytics as a predictor of the risk of major cardiovascular events and in-hospital bleeding up to the first 30 days, independent of other important clinical variables.

Furthermore, our study revealed a statistically significant relationship between bleeding events and the use of clopidogrel and ticagrelor after intervention (p<0.001). The multivariable logistic regression model only confirmed the role of clopidogrel, indicating that the group that used clopidogrel before and after the intervention

or after the intervention had a higher risk of bleeding than the non-users.

4.3.1.4. Bleeding events and clinical diagnosis, bleeding risk score

The bleeding rate in the acute coronary syndrome group was 6.7%, which was significantly higher than the chronic coronary syndrome group (2%). Multivariable logistics regression model found that the CRUSADE bleeding risk score was associated with the risk of bleeding, whereas this association was not observed for NCDR CathPCI bleeding risk score.

In summary, the multivariable logistic regression model highlighted factors associated with an increased risk of bleeding, including hypertension, history of bleeding, clopidogrel use, fibrinolysis, and CRUSADE bleeding risk score.

4.3.2. The predictive performance of crusade and ncdr cathpci scores

Both CRUSADE and NCDR CathPCI scores had good value for predicting bleeding in patients after PCI and subgroups of acute and chronic coronary syndromes.

4.3.2.1. CRUSADE Score

In our study, the median CRUSADE score was 29 (Q1-Q3: 22-38). Using a cutoff point of 31.5, the CRUSADE scale was able to predict general bleeding events with an 85.7% sensitivity (95%CI: 79.5% - 91.9%) and a 58.7% specificity (95%CI: 50% - 67.4%), with an area under the ROC curve of 0.77 (95%CI: 0.69 – 0.84, $p<0.001$). Study conducted by Flores-Rios showed a comparable predictive value of CRUSADE to predict bleeding with a C-statistic of 0.77 (95% CI: 0.75 - 0.79).

The CRUSADE score was a good prognostic value in predicting bleeding in acute coronary syndromes with a cutoff point of ≥33.5, and in chronic coronary syndromes with a cutoff point of ≥31.5, corresponding to an area under the ROC curve of 0.77 (95%CI: 0.68-0.85) and 0.74 (95%CI: 0.59-0.9), respectively, which was consistent with Bento Dina's study in 2018.

4.3.2.2. NCDR CathPCI Score

The median of the NCDR CathPCI scale of our sample was 50 (Q1-Q3: 30-70). Using a cutoff point of ≥57.5, the NCDR CathPCI score was significant in predicting overall bleeding events in our

study sample with a 76.2% sensitivity (68.7% - 83.7%) and a 65.3% specificity (56.9% - 73.7%), with an area under the ROC curve of 0.75 (95%CI: 0.69-0.82, p<0.01).

The NCDR CathPCI score was a good predictor of bleeding in patients with acute and chronic coronary syndromes with a cutoff point of ≥72.5, and ≥42.5, corresponding to an area under the ROC curve of 0.66 (95% CI: 0.57 - 0.75; p<0.05) and 0.72 (95% CI: 0.58-0.85), respectively. Our study found a lower ability to distinguish bleeding risk in subjects with acute coronary syndromes compared to Wolff Georg's study (AUC=0.82; 95% CI: 0.78-0.86) and Michael J Thibert's study (AUC=0.73; 95% CI: 0.69 – 0.76).

CONCLUSION

Through the study of bleeding risk in 1,096 patients undergoing percutaneous coronary intervention using the NCDR CathPCI and CRUSADE scores, we have reached the following conclusions:

1. Bleeding rate and influence of bleeding on mortality prognosis

The overall bleeding rate in the study sample was 3.8%, with most complications occurring in the hospital.

The mortality rate was higher in the bleeding group than in the non- bleeding group. There was a statistically significant association between bleeding events and mortality within 12 months after PCI, with an adjusted odds ratio of 11.5 (95% CI: 2.5 – 53.5, p=0.002).

2. Risk factors of bleeding and bredictability of bleeding risk of CRUSADE and NCDR CathPCI scores

Factors associated with bleeding events recorded in this study included age, female, hypertension, diabetes, hyperlipidemia, chronic kidney disease, history of stroke, history of bleeding, arterial access, intervention status, catheter size, use of thrombolytics, use of clopidogrel, ticagrelor, enoxaparin, and clinical characteristics. The multivariable logistic regression model highlighted factors associated with an increased risk of bleeding, including hypertension, bleeding history, clopidogrel use, pre-interventional fibrinolysis, and CRUSADE bleeding risk score.

The optimal cut-off point of the CRUSADE score in the prognosis of bleeding within 12 months of admission was ≥31.5,

corresponding to a sensitivity of 85.7% (95%CI: 79.5% - 91.9%) and specificity of 58.7% (95%CI: 50% - 67.4%), AUC=0.77 (95%CI: 0.69-0.84, $p<0.05$).

The optimal cutoff score of the NCDR CathPCI scale in the prognosis of bleeding within 12 months of admission is ≥57.5, corresponding to a sensitivity of 76.2% (68.7% - 83.7%) and specificity of 65.3% (56.9% - 73.7%); which gave an AUC of 0.75 (95%CI: 0.69-0.82, $p<0.05$).

Both tools are capable of predicting bleeding events after PCI in general population as well as acute and chronic coronary syndrome patients.

RECOMMENDATION

Based on study's findings, we would like to suggest the following recommendations:

Bleeding events after percutaneous coronary intervention increase risk of mortality within one year of the procedure. Therefore, early prediction of bleeding in all patients undergoing percutaneous coronary intervention is crucial. The CRUSADE and NCDR CathPCI scores are useful, inexpensive tools and high practical value. Therefore, CRUSADE and NCDR CathPCI scores should be incorporated into routine clinical practice to identify patients at risk for bleeding and mortality following percutaneous coronary intervention and hence select effective strategies and techniques, interventional equipment, treatment and duration of anticoagulant therapy, as well as orientation of appropriate prophylactic strategies to improve overall outcomes.

LIST OF RELATED SCIENTIFIC WORKS
THAT HAD BEEN PUBLISHED

1. Nguyen Hai Cuong, Nguyen Cuu Loi, Le Thi Bich Thuan. Predictive performance of CRUSADE and NCDR CathPCI scores for bleeding risk after percutaneous coronary intervention (2021). *Journal of Medicine and Pharmacy*, 4 (11), p. 105–109.

2. Nguyen Hai Cuong, Nguyen Cuu Loi, Le Thi Bich Thuan (2020), Characteristics of bleeding complications after percutaneous coronary intervention. *Vietnam Journal of Diabetes and Endocrinology*, (43), p. 55–56.