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ORIGINAL ARTICLE

Use of the CRUSADE Bleeding Risk Score in the Prediction of Major Bleeding for Patients with Acute Coronary Syndrome Receiving Enoxaparin in Thailand

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Background CRUSADE risk score stands out as a simple-to-use bleeding risk model. However, its use is still doubtful for Thai population. The aim of this study was to assess the prognostic value of CRUSADE in predicting risk of major bleeding among Thai patients with acute coronary syndrome (ACS) receiving enoxaparin.

Methods A retrospective cohort study was performed using patients with ACS who were hospitalised at a university hospital in Bangkok between 2006 and 2009 and had received enoxaparin. The CRUSADE risk score was calculated. The model validation was tested by using C statistic and Hosmer-Lemeshow goodness-of-fit.

Results The overall incidence of major bleeding was 18.3%. Median CRUSADE score for entire study population, unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI) were 49, 47, 53, and 39, respectively. Hosmer-Lemeshow goodness of fit revealed no statistical significance in all groups. The CRUSADE model demonstrated a satisfactory discriminatory capacity for the entire study population (C = 0.688), UA (C = 0.591), NSTEMI (C = 0.693), and STEMI groups (C = 0.736).

Conclusions Across the ACS spectrum, CRUSADE risk score was able to estimate in-hospital major bleeding of Thai patients with ACS who received treatment with enoxaparin. The application of these results in Thailand may be helpful in the identification of patients at high bleeding risk and also may lead to implementation of appropriate prevention.

Keywords CRUSADE risk score • Enoxaparin • Major bleeding • Acute coronary syndrome • Thailand

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Introduction

Ischaemic heart disease (IHD) is the leading cause of death from cardiovascular diseases in the world. Data from the World Health Organization (WHO) indicated about 41.2% of patients died from IHD compared to cause of death from other cardiovascular diseases [1]. In Thailand, the rates of mortality and hospital admissions are increasing every year, leading to increased costs of care, especially in terms of the national consumption of cardiovascular drugs [2,3]. Anticoagulants are one of the recommendations for a patient who presents with angina symptoms likely to be caused by coronary heart disease [4–7]. Although the morbidity and mortality benefits of anticoagulants have been proved, bleeding complications may adversely affect patients' outcomes.

Enoxaparin, a low molecular weight heparin (LMWH), has several advantages over unfractionated heparin (UFH) in the treatment of Acute Coronary Syndrome (ACS). These include predictable dose response of anticoagulation effect, better subcutaneous bioavailability, longer half-life, and minimised need for routine laboratory monitoring [8]. A number of clinical trials showed that enoxaparin leads to improved morbidity and mortality rates compared to UFH in ACS settings. Through these favourable profiles, enoxaparin is recognised as class I recommendation from current practice guidelines in the treatment of ACS, and class IIb recommendation in percutaneous coronary intervention setting [4–7]. In Thailand, enoxaparin is included in the National Lists of Essential Drugs with full reimbursement scheme and it has become the most commonly used LMWH for ACS setting.

Similar to other anticoagulants, bleeding complications are the most important side effect of enoxaparin. Accurate assessment of bleeding risk is the key to maximise benefits and minimise risks of such complications. There are several risk prediction models available in the literature [9,10], but all were developed from Western populations. These models have not been evaluated for the prediction of such risks in an Asian situation with different characteristics and treatment patterns. In addition, some bleeding risk models arose from clinical trials of certain anti-thrombotic therapies that are not available in Thailand and most other Asian countries [10]. CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) risk score stands out as a simple-to-use model derived from a registry of over 80,000 patients with ACS from 485 American hospitals reflecting real-world practice [11]. The score from the model showed a consistent increase between the rate of major bleeding and bleeding risk score quintiles with a good ability to discriminate between patients who did and did not have a major bleeding episode (C statistics 0.71). In addition, the CRUSADE scoring system was found to perform well in European populations despite differences in patient demographics and treatment patterns of these countries compared to the United States [12–14]. The aim of this study is to assess the prognostic value of CRUSADE in predicting the risk of major bleeding among a wide range of Thai patients with ACS receiving enoxaparin.

Material and Methods

Study Population

This cohort contained patients of ≥18 years of age who were hospitalised at the Ramathibodi Hospital, a tertiary care university hospital, Bangkok, Thailand, based on a diagnosis of ACS by The International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) during 1 January 2006 to 1 February 2009. All patients had received one or more doses of enoxaparin. For patients who had more than one admission, only the most recent admission was included in the analysis. Patients were excluded if one of the following conditions was met: platelet count below or equal to 50,000 cells/mL; pregnancy; burn condition; haemophilia A or B; von Willebrand' s disease, hereditary haemorrhagic telangiectasis; idiopathic thrombocytopenic purpura; thrombocytopaenia; dengue haemorrhagic fever; antithrombin III deficiency; incomplete enoxaparin dosage regimen; missing value in date of birth, serum creatinine or weight. All inpatient medical records meeting the above criteria were retrospectively reviewed using a standardised data collection form, including demographic, medication data, and signs and symptoms related to bleeding complication. The study protocol was approved by the Committee on Human Rights Related to Researches Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital in March 2009.

Variable Definition

Major bleeding was defined according to CRUSADE major bleeding (intracranial bleeding, documented retroperitoneal bleed, haematocrit drop ≥12% (baseline to nadir), any red blood cell transfusion when baseline haematocrit was ≥28%, or any red blood cell transfusion when baseline haematocrit was <28%with witness bleed). For patients who experienced more than one bleeding episode, only the most severe bleeding episode was considered.

On the basis of package inserts, the recommended initial daily dose of enoxaparin is 2 mg/kg (based on 1 mg/kg every 12 hours) for patients with a creatinine clearance (CrCl) of ≥30 mL/min and 1 mg/kg (based on 1 mg/kg every 24 hours) for patients with a CrCl <30 mL/min. CrCl was estimated by using the formula of Cockcroft-Gault. Initial daily doses of enoxaparin were categorised into three sub-groups, excess, lower than recommended, and recommended doses based on renal function and body weight. A recommended dose of enoxaparin was defined as an initial prescribing daily dose that did not vary from the recommended dose by more than 10 mg/day [15]. Excess dose was defined as an initial prescribing daily dose that was more than 10 mg above the recommended dose. Lower than recommended dose was defined as a prescribing daily