Prediction of Bleeding After Cardiac Surgery: Comparison of Model Performances: A Prospective Observational Study

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Objectives: **Primary aims were to (1) perform external validation of the Papworth Bleeding Risk Score, and (2) compare the usefulness of the Dyke et al universal definition of perioperative bleeding with that used in the Papworth Bleeding Risk Score. A secondary aim was to use a locally developed logistic prediction model for severe postoperative bleeding to investigate whether prediction could be improved with inclusion of the variable "surgeon" or selected intraoperative variables.**

Design: **Single-center prospective observational study.**

Setting: **University hospital.**

Participants: **7,030 adults undergoing cardiac surgery.**

Interventions: **None.**

Measurements and Main Results: **Papworth Bleeding Risk Score could identify the group of patients with low risk of postoperative bleeding, with negative predictive value of 0.98, when applying the Papworth Score on this population. The positive predictive value was low; only 15% of the patients who were rated high risk actually suffered from increased postoperative bleeding when using the Papworth Score on this population. Using the universal definition of perioperative bleeding proposed by Dyke et al, 28% of patients in the Papworth high-risk group exceeded the threshold of excessive bleeding in this population. The local models showed low ability for discrimination (area under the receiver operating characteristics curve <0.75). Addition of the factor "surgeon" or selected intraoperative variables did not substantially improve the models.**

Conclusion: **Prediction of risk for excessive bleeding after cardiac surgery was not possible using clinical variables only, independent of endpoint definition and inclusion of the variable "surgeon" or of selected intraoperative variables. These findings may be due to incomplete understanding of the causative factors underlying excessive bleeding.**

KEY WORDS: risk score, risk prediction, hemorrhage, cardiac surgery, bleeding endpoint

SEVERE BLEEDING after cardiac surgery is a relatively common complication and may occur in as many as 20% of the patients.[1] Previous studies have tried to identify preoperative predictors for blood loss after coronary artery surgery, mostly without success. Wahba et al[2] found that laboratory testing for hyperfibrinolysis and platelet dysfunction was useful to predict abnormal bleeding after coronary artery bypass grafting (CABG), but except for preoperative platelet count, only the postoperative variables were significant. Point-of-care tests like rotational thromboelastometry (ROTEM) to monitor multiple coagulation parameters represent an interesting alternative, but preoperative ROTEM analysis does not seem useful to predict postoperative hemorrhage in cardiac surgery patients.[3,4]

Identification of patients at the highest risk of excessive blood loss after cardiac surgery could lead to prophylactic interventions, such as termination of antiplatelet therapy preoperatively, meticulous surgical hemostasis, and prophylactic antifibrinolytic drug treatment. It also could lead to early postoperative treatment with platelets and fresh frozen plasma, coagulation factors, and surgical intervention, if relevant. Patients requiring re-exploration for bleeding are at higher risk of adverse outcomes, which increases if time to re-exploration is prolonged.[5]

In 2011, Vuylsteke et al developed the Papworth Bleeding Risk Score from a prospectively created database of patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).[6] The authors included preoperative data from one hospital only, and the score´s external applicability and clinical utility have not been validated. From the field of epidemiology, it is clearly recognized that external validation of any prediction model is of major importance before it is useful in clinical practice.[7] Dyke et al recently proposed a universal definition of perioperative bleeding in adult cardiac surgery,[8] using a different definition from that used for the Papworth Bleeding Risk Score.

The authors hypothesized that, without external validation, neither the Papworth Bleeding Risk Score nor the endpoint suggested by Dyke et al[8] will be used clinically even if their properties seem attractive. The main aims of the present study, therefore, were (1) to perform external validation of the Papworth Bleeding Risk Score, and (2) to compare the usefulness of the definition of increased bleeding proposed by Dyke et al with that used in the Papworth Bleeding Risk Score. As a secondary aim, a local risk prediction model was developed to identify cardiac surgical patients at the highest risk of severe postoperative bleeding, which permitted investigation of whether prediction could be improved if the variable "surgeon" or some selected intraoperative variables were included.

METHODS

The study was based on prospectively collected data from 7,137 adult patients undergoing cardiac surgery from 2000 to 2011 at St. Olav

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University Hospital, Trondheim, Norway. The present study was part of the Cardiac Surgery Outcome Study (CaSOS), and some of the data have been used for development of risk prediction models for mortality, postoperative cardiac dysfunction, prolonged ventilation, prolonged stay in the intensive care unit, acute kidney injury, and prediction of genetic and clinical risk factors for fluid overload after cardiac surgery, as well as for validation of previously published scores for several endpoints.[9–14] The CaSOS study was approved by The Regional Research Ethics Committee in Medicine in Trondheim, Norway, and The Norwegian Data Inspectorate.

All patients registered in the database underwent cardiac surgery with CPB. Patients treated with acetylsalicylic acid (ASA) used 75 or 160 mg. Clopidogrel was not included in the analysis because of incomplete registration. In the database, clopidogrel was registered from 2008. Before CPB, heparin (300 U/kg; Leo, Copenhagen, Denmark) was given to achieve a kaolin activated coagulation time (ACT; Medtronic Blood Management, Parker, CO) of more than 480 seconds. Additional heparin was given when needed. The perfusion circuit was primed with 1,500 mL of Ringer's acetate solution with 7,500 U of heparin. A coated membrane oxygenator was used. After CPB, protamine sulfate (Leo, Copenhagen, Denmark) was given to achieve an ACT within 10% of the baseline value. Blood remaining in the CPB circuit was collected and retransfused to the patient. Tranexamic acid (30 mg/kg) was used routinely in the authors' hospital from 2000 and was given before the start of CPB. High-dose aprotinin was used until 2008 in most patients with postinfarction rupture of the ventricular septum or dissection of the ascending aorta and in some patients with endocarditis, altogether approximately 150 patients (2.1%), but was not registered in the database. The study design is outlined in Figure 1.

Validation of the Papworth Bleeding Risk Score

The Papworth Bleeding Risk Score is based on 5 risk factors: Surgery priority, surgery type (CABG or single valve), aortic valve disease, body mass index (BMI), and age.[6] On the basis of the calculated scores (0-5 points), patients were divided into the 3 defined risk groups for the Papworth Score: low-risk (0 points), medium-risk (1-2 points), and high-risk (3-5 points). Matching definitions was possible in the present population for all variables except aortic valve disease, for which aortic valve surgery was used. In the original publication, blood loss exceeding 2 mL/kg/h during the first 3 hours in the intensive care unit (or during a shorter period if the patient underwent transfusion with fresh-frozen plasma, platelets, or cryoprecipitate, reoperation, or died within 3 hours) was considered an adverse outcome. In the database, postoperative drainage volumes were recorded after 4 hours, so this time frame was used in the external validation. Information about transfusion timing in the intensive care unit was missing. The patients who underwent reoperation within 4 hours exceeded the threshold of 2 mL/kg/h, and no patients died within 4 hours because of bleeding. The endpoint used for excessive postoperative blood loss then was defined as blood loss exceeding 2 mL/kg/h the first 4 hours postoperatively.

The negative predictive value (NPV) in the Papworth low-risk group was calculated (ie, the proportion of patients without severe bleeding in that group). The positive predictive value (PPV) in the Papworth high-risk group also was calculated (ie, the proportion of patients with severe postoperative bleeding in that group).

Alternative Endpoint Definition

The composite bleeding endpoint defined by Dyke et al has 5 bleeding categories based on chest tube drainage during the first 12 postoperative hours: Transfusion of red cells, plasma, and platelets; use of cryoprecipitate, prothrombin complex concentrates, or recombinant activated factor VII; re-exploration or tamponade; and delayed sternal closure.[8] The criteria were partly redundant. Cryoprecipitate or prothrombin were never used during the study period in the present population, and recombinant activated factor VII was used for approximately 10 patients, so these criteria were omitted. As in the original paper, the frequency of patients in each bleeding class was assessed (0 = insignificant, 1 = mild, 2 = moderate, 3 = severe, and 4 = massive). Dyke class 3 and 4 patients were defined as having excessive postoperative bleeding and compared with patients from Dyke class 0 - 2. The NPV and PPV for the Papworth Bleeding Risk Score were calculated using this bleeding endpoint instead of the original Papworth definition.

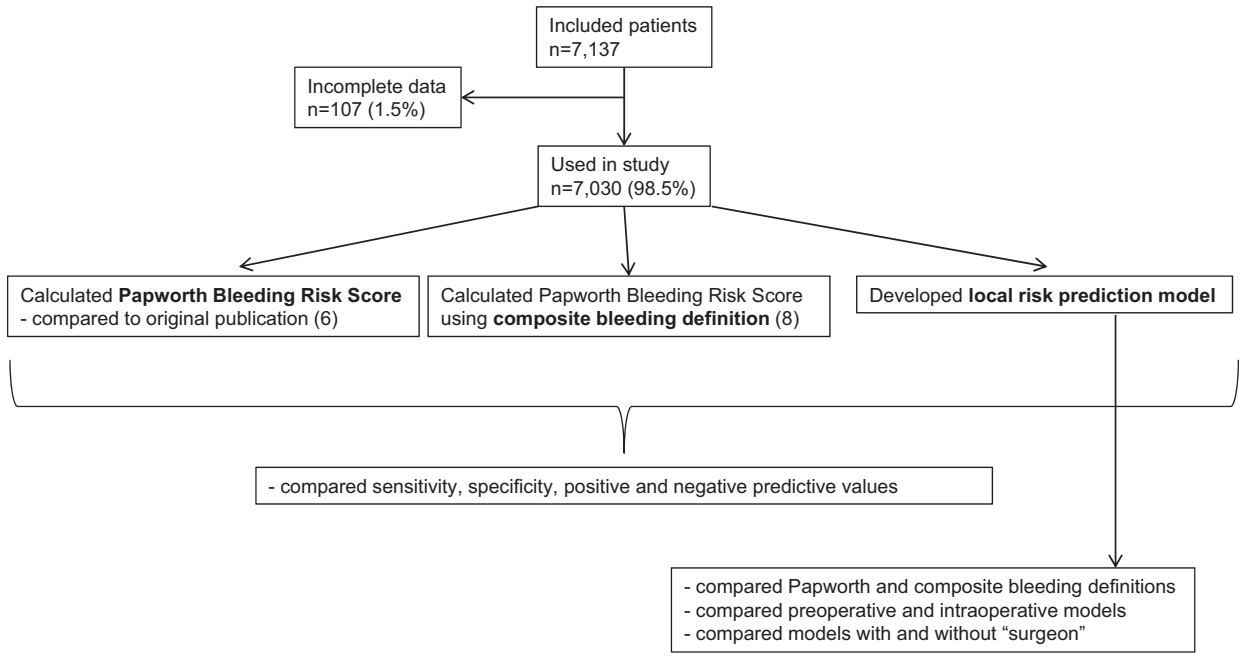

Fig 1. Outline of study design.