Thrombosis Research 134 (2014) 360–368

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Plasma fibrinogen level on admission to the intensive care unit is a powerful predictor of postoperative bleeding after cardiac surgery with cardiopulmonary bypass

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ARTICLE INFO

Article history:
Received 3 April 2014
Received in revised form 23 April 2014
Accepted 7 May 2014
Available online 13 May 2014

Keywords:
Postoperative blood loss
Hemostasis, Surgical
Fibrinogen
Cardiopulmonary Bypass
Coronary Disease
Heart Valve Diseases

ABSTRACT

Introduction: Evidence regarding the behavior of fibrinogen levels and the relation between fibrinogen levels and postoperative bleeding is limited in cardiac surgery under cardiopulmonary bypass (CPB). To evaluate perioperative fibrinogen levels as a predictor of postoperative bleeding in patients undergoing cardiac surgery with CPB.
Materials and Methods: In this prospective, single-center, observational cohort study of 1956 patients following cardiac surgery with CPB, fibrinogen level was measured perioperatively. Excessive bleeding group was defined as patients with a 24-h chest tube output (CTO) exceeded the 90th percentile of distribution.
Results: The median 24-h CTO was 728.6 ± 431.1 ml. A total of 189 patients (9.7%) were identified as having excessive bleeding. At admission to the intensive care (Day 0), the fibrinogen levels were 2.5 ± 0.8 g/l and 2.1 ± 0.8 g/l in the control and excessive bleeding groups, respectively ($P < 0.0001$). The fibrinogen level on Day 0 was significantly correlated with the 24-h CTO (rho = -0.237; $P < 0.0001$). Multivariate analysis demonstrated that the fibrinogen level at Day 0 was the best perioperative standard laboratory test to predict excessive bleeding (P = 0.0001; odds ratio, 0.5), whereas preoperative fibrinogen level was not a predictor. Using receiver operating characteristics curve analyses, the best Day 0 fibrinogen level cutoff to predict postoperative bleeding was 2.2 g/l.
Conclusions: In this large prospective study, the fibrinogen level upon admission to the intensive care unit after CPB predicted the risk of postoperative bleeding. Our data add to the concern regarding the fibrinogen level threshold that might require fibrinogen concentrate infusion to reduce postoperative blood loss.

Introduction

Cardiac surgery under cardiopulmonary bypass (CPB) can be associated with excessive perioperative bleeding that requires allogeneic blood product transfusion [1]. Perioperative red blood cell (RBC) transfusion ranging from 17% to 69% has been reported during cardiac surgery [1–3]. The need for transfusion is increasing worldwide [1]. The extent of perioperative blood loss and the number of RBC units transfused are predictors of higher postoperative morbidity and mortality [2–4]; consequently, there is a need to optimize perioperative hemostasis. Hemostasis is clinically defined as bleeding control without the induction of pathologic thrombotic events [5]. The perioperative management of hemostasis is a challenge. The inflammatory, hemostatic and fibrinolytic pathways are activated during CPB. In association with heparin-protamine use, hemodilution and eventually hypothermia, CPB leads to severe hemostasis impairment [1,5]. Others factors (e.g., advanced age, low RBC volume, preoperative antiplatelet and anticoagulant therapies and the type of surgery) may exacerbate postoperative blood loss [1,5].

Prothrombin time, activated partial thromboplastin time, platelet count and fibrinogen level are the standard perioperative laboratory tests most often used to explore hemostasis during cardiac surgery under CPB. Among these tests, recent studies pay particular attention to the perioperative plasma fibrinogen levels [6–15]. Fibrinogen plays a major role in hemostasis and effective clot formation, and fibrinogen

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http://dx.doi.org/10.1016/j.thromres.2014.05.008
0049-3848/

may be easily, quickly and safely substituted with fibrinogen concentrate [7]. Point-of-care coagulation testing can allow effective and rapid exploration of hemostatic function, specifically fibrinogen function [16]. Studies on the fibrinogen level during cardiac surgery under CPB were performed on small samples of selected patients, and limited perioperative variables were included for analysis. The variation in perioperative plasma fibrinogen levels and the effect on postoperative blood loss require further exploration. There is a considerable body of evidence indicating that the fibrinogen concentration threshold that provided effective clot formation might be higher than the threshold indicated in the actual guidelines (1.5-2 g/l) [9,17–19].

Our study was designed to determine whether perioperative fibrinogen levels were a predictor of excessive perioperative bleeding in patients undergoing cardiac surgery with CPB.

Materials and Methods

Patients

This prospective, observational study included 1956 consecutive patients admitted to the department of cardiovascular surgery of the University Hospitals of Strasbourg from November 2008 through April 2011. The inclusion criteria were age ≥ 18 years, coronary artery bypass graft and/or valve and/or thoracic aorta surgeries with CPB. Exclusion criteria were postoperative need of ventricular assist device or extracorporeal life support. Patients with abdominal aneurysm were not excluded from this study. The baseline demographic, clinical and biological characteristics are reported in Tables 1 and 2.

Study Design

Consecutive patients who met the inclusion and exclusion criteria were enrolled in a prospective, single-center, observational study. The perioperative data and outcomes were prospectively collected and validated. The study procedures were approved by the Institutional Review Board of our institution. Cardiopulmonary bypass (CPB) was performed using unfractionated heparin anticoagulation to maintain an activated coagulation time above 400 seconds. All of the patients received an intraoperative tranexamic acid infusion. Tranexamic acid was given with a bolus of 12.5 mg/kg for the patient and 1 mg/kg for the CPB priming followed by a continuous infusion of 6.5 mg/kg/h during surgery. A dose adjustment for patients on dialysis or with a preoperative glomerular filtration rate <40 ml/min/1.73 m^2 was not done due to the use of intraoperative hemofiltration. When the CPB was stopped, protamine sulfate (dose/dose) was given to reverse the anticoagulation. Small surgical chest drains (8 to 14 drains, each 9 mm in diameter, Peters Surgical, France) were placed around the heart and, if necessary, in the pleural cavity. Intraoperative blood loss was not recorded in our database. No institutional intraoperative transfusion algorithms for allogeneic blood products or factor concentrates have been used. Those products were administrated depending on the results of standard preoperative laboratory tests, the type of surgery, the CPB time, the presence of a significant bleeding after the administration of protamine sulfate and completion of surgical hemostasis and, in some cases, the results of standard intraoperative laboratory tests. In case of suspected or confirmed low fibrinogen level, fresh frozen plasma or fibrinogen concentrate were administrated depending on the anesthesiologist. The surgical procedures and the intraoperative allogeneic blood products or factor concentrates administrated are reported in Table 3.

Upon arrival in the intensive care unit (ICU; Day 0) and on the first postoperative day (Day 1), blood samples were drawn from the arterial catheter for routine laboratory tests. The chest tube output (CTO) was monitored continuously and recorded in our database at 6 h and 24 h. In the majority of the cases, regarding the CTO, the surgical drains were removed on the second postoperative day.

Study Endpoints

The primary endpoint of this study was significant postoperative bleeding during the first 24 h, characterized by a 24-h CTO that

Table 1
Preoperative characteristics of the patients.

Variable	Overall n = 1956	Control group n = 1681	Excessive bleeding group n = 189	P
Age (years)	66.9 ± 12.0	66.8 ± 12.0	67.3 ± 11.1	0.621
Body mass index (kg/m^2)	27.5 ± 4.8	27.6 ± 4.8	26.4 ± 4.2	**0.002**
Females	596 (30.5)	529 (31.5)	37 (19.6)	**0.001**
Current smoker	880 (45.0)	747 (44.4)	95 (50.3)	0.127
Hypertension	1281 (65.5)	1113 (66.2)	116 (61.4)	0.184
Dyslipidemia	1197 (61.2)	1030 (61.3)	120 (63.5)	0.552
Diabetes	543 (27.8)	466 (27.7)	56 (29.6)	0.579
Chronic obstructive pulmonary disease	144 (7.4)	119 (7.1)	16 (8.5)	0.485
Cerebral vascular disease	142 (7.3)	124 (7.4)	14 (7.4)	0.989
Previous cardiac surgery	125 (6.4)	99 (5.9)	15 (7.9)	0.265
Percutaneous coronary intervention	330 (16.9)	275 (16.4)	44 (23.3)	**0.016**
Prior myocardial infarction	286 (14.6)	233 (13.9)	40 (21.2)	**0.007**
Prior heart failure	232 (11.9)	200 (11.9)	21 (11.1)	0.751
Preoperative dialysis	31 (1.6)	19 (1.1)	6 (3.2)	**0.020**
Atrial fibrillation	188 (9.6)	171 (10.2)	11 (5.8)	0.056
Extracardiac arteriopathy	318 (16.3)	262 (15.6)	37 (19.6)	0.156
Active endocarditis	52 (2.7)	43 (2.6)	6 (3.2)	0.615
Emergency surgery	216 (11.0)	172 (10.6)	26 (13.8)	0.135
Intraaortic balloon counterpulsation	58 (3.0)	40 (2.4)	9 (4.8)	0.052
Preoperative aspirin	1138 (58.2)	958 (57.0)	130 (68.8)	**0.002**
Preoperative clopidogrel	485 (24.8)	391 (23.3)	76 (40.2)	<**0.0001**
Echocardiography LVEF (%)	59.2 (11.9)	59.6 ± 11.6	58.6 ± 12.2	0.113
Logistic EuroSCORE (%)	7.0 (8.7)	6.9 ± 8.3	6.8 ± 9.0	0.944
Diagnosis				
Coronary artery disease	1082 (55.3)	901 (53.6)	135 (71.4)	<**0.0001**
Valve disease	1070 (54.7)	938 (55.8)	89 (47.1)	**0.023**
Thoracic aorta disease	130 (6.6)	117 (7.0)	5 (2.6)	**0.019**

The plus-minus values are the mean ± SD, and the others are no. (%). *P*-value, control group versus excessive bleeding group.
LVEF, left ventricular ejection fraction; Logistic EuroSCORE, clinical model for calculating the 30-day mortality after cardiac surgery on the basis of patient, cardiac and operative factors.