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Preoperative hypofibrinogenemia is associated with increased intraoperative bleeding in ruptured abdominal aortic aneurysms

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ABSTRACT

Introduction: Ruptured abdominal aortic aneurysm (rAAA) is associated with coagulopathy and intraabdominal hemorrhage. Fibrinogen acts as a key coagulation factor and has previously been suggested as a biomarker for increased perioperative bleeding in other surgical areas. The aim of the present study was to investigate fibrinogen and standard laboratory parameters and their association to preoperative hemodynamic status, intraoperative bleeding (IOB), and outcome in treatment of rAAA.

Methods: This is a single university center retrospective cohort study of 91 consecutive patients with rAAA undergoing open surgery or endovascular aneurysm repair (EVAR) between 2008 and 2013. Patients were analyzed using the Swedish Vascular Registry (Swedvasc), and local hospital medical and laboratory records. Laboratory data analyzed included fibrinogen, hemoglobin, platelet count, prothrombin time ratio, activated partial thrombin time, and creatinine. Odds ratios (OR) with 95% confidence intervals (CI) were calculated in a logistical regression model.

Results: In the study cohort (n = 91), median age was 74 (57-91) years; 80 % men; open surgical repair (n = 72; 77%); EVAR (n = 19; 23%). Median preoperative fibrinogen concentration was 1.8 g/L (IQR = 1.4) and varied significantly across bleeding groups: ≤1999 ml 2.3 g/L, IQR = 1.4 (n = 35); 2000-4999 ml 1.6 g/L, IQR = 1.5 (n = 33); ≥5000 ml 1.4 g/L, IQR = 1.0 (n = 23) (P< 0.001). Preoperative fibrinogen concentration showed a linear relationship with preoperative blood pressure (r = .447, P = 0.01). When analyzing other preoperative laboratory values, only platelets showed a similar linear relationship with preoperative blood pressure (r = .247, P = 0.05). Patients with blood pressure <70 mmHg had an associated median fibrinogen concentration of less than 1.5 g/L (P = 0.001). In the multivariable logistic regression analysis, preoperative fibrinogen <1.5 g/L [OR 10.0, CI (1.8-57.1), P = 0.009] was associated with IOB >2000 ml and preoperative blood pressure <70 mmHg was associated with IOB >2000 ml [OR 3.7, CI (1.1-12.6), P = 0.03] and >5000 ml [OR 5.2, CI (1.3-21.1), P = 0.02]. Low fibrinogen concentration (<1.5 g/L) was associated with 30-day mortality in the univariate analysis but not in the multivariable logistic regression analysis.

Conclusion: Low preoperative fibrinogen concentration was significantly associated with preoperative hypotension and increased intraoperative bleeding in patients with rAAA. Patients in hemodynamic shock with blood pressure <70 mmHg had an associated fibrinogen concentration of less than 1.5 g/L. A fibrinogen concentration less than 1.5 g/L was associated with a ten-fold increased risk of intraoperative hemorrhage of more than 2000 ml.

Introduction

Ruptured abdominal aortic aneurysm (rAAA) is one of the most lethal vascular emergencies with mortality rates ranging from 20% to 50 % [1–3]. Major hemorrhage and hypotension after rAAA are associated with worse outcome [3]. Hemodynamic presentation can differ remarkably depending on the preoperative internal bleeding volume relating to the site and containment of the aortic rupture. To improve outcome immediate efforts must be made to minimize pre- and perioperative blood loss [3]. The coagulation system is activated in patients with rAAA and shock, and the development of coagulopathy predicts poor outcome [4,5]. Preoperative detection of coagulation abnormalities may play a vital role to early correct deficiencies in the emergency surgical situation.

Fibrinogen, acts as one of the key-factors in the coagulation cascade, and has previously been suggested as a biomarker for increased perioperative bleeding in other areas such as cardiac, orthopedic, obstetric, and trauma surgery [6–9]. The aim of the present study was to investigate fibrinogen and standard laboratory parameters and the association

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with preoperative hemodynamic status, intraoperative bleeding (IOB), and outcome in patients with rAAA.

Methods

Data Collection

This was a retrospective cohort study of 91 consecutive patients with rAAA undergoing open surgery or endovascular aneurysm repair (EVAR) at Karolinska University Hospital, Sweden, from May 1 2008 to August 31 2013. Patient data were collected from the Swedish Vascular Registry (Swedvasc) and the hospital's medical records. Laboratory data were collected from the hospital's data bank.

Laboratory Data

Blood samples, including fibrinogen [reference range 2.0-4.0 g/L; 200-400 mg/dL], hemoglobin [female/male 117-153/134-170 g/L], platelet count [165-387/145-348 10^9/L], prothrombin time ratio (PTr) [<1.2], activated partial prothrombin time (APTT) [28-40 s] and s-creatinine [<90/<100 μmol/L], were collected at patients' arrival in the emergency department and directly analyzed by the hospital's clinical chemistry laboratory. Only patients with complete preoperative laboratory status were included in the study cohort.

Outcome Measures

Preoperative laboratory values were analyzed in comparison to lowest preoperative systolic blood pressure, perioperative bleeding volume, and 30-day mortality.

Lowest preoperative blood pressure (mmHg) was captured from ambulance and hospital medical records. Intraoperative blood loss was estimated including intraoperative blood collection, hematocrits, volume of perioperative fluid requirements and transfusion of blood products, and was divided into three groups established in the national vascular registry (Swedvasc): 0-1999, 2000-4999, and ≥5000 ml.

Clinically valid cut-off values for the preoperative parameters were used and related to outcome (fibrinogen ≤1.5 g/L, platelet count <100 [10^9/L], prothrombin time ratio >1.6, age >80 years, s-creatinine >120 μmol/L, and blood pressure <70 mmHg) [9].

Recorded co-morbidities included diabetes mellitus (i.e. treated with oral antidiabetics or insulin), treatment for hypertension (i.e. recorded in medical records as being prescribed antihypertensive medication), renal insufficiency (serum creatinine >150 μmol/l), heart disease (history of previous myocardial infarction, angina pectoris, heart failure or previous coronary intervention), chronic obstructive pulmonary disease (COPD), and smoking.

Ethics

The regional ethics committee at Karolinska Institutet approved the study (reference number 2011/664-31/3).

Statistics

Medians, ranges, interquartile ranges (IQR), and proportions were calculated as appropriate. Chi-square, Mann-Whitney U tests, Kruskal-Wallis Test, Students T test or Fisher's exact tests were used, to compare nominal variables between data. Univariable analysis of binary, nominal and ordinate variables was performed. Variables associated with outcome measures (P <0.05) in univariable analysis were analyzed in a logistical regression model. Significant relationships were expressed as odds ratio (OR) with 95 % confidence interval (CI). P values <0.05 were considered to be statistically significant. Calculations were performed using Statistical Package for Social Sciences (SPSS), version 21.0 (IBM, New York NY, USA).

Results

Demographics and Descriptive Data

During the study period, 568 patients underwent treatment for AAA at our center including 121 (21 %) patients with rAAA. The study cohort included 91 consecutive patients with rAAA (median age 74 years [range: 57-91]; 80 % men) and complete preoperative laboratory data. Demographics, comorbidities and risk factors are presented in Table 1. There were no patients on warfarin or low molecular weight heparin. Thirty rAAA patients were excluded from the analysis because of incomplete data. These patients did not differ from the study cohort in regards to demographics or outcome.

Open surgical repair was performed in 72 patients (79 %) including straight tube grafts (n = 46), aorto bi-iliac (n = 22), and aortobifemoral (n = 4), and there were 19 (21 %) patients that underwent EVAR. None of the EVARs were performed with fenestrated grafts. Resuscitative percutaneous aortic balloon occlusion was used in 5 EVAR and 5 open surgical cases. One patient with rAAA was previously treated with EVAR.

Preoperative Laboratory Data

Preoperative laboratory data in patients arriving in the emergency department with rAAA are presented in Table 2. There was no significant difference in laboratory data related to gender or comorbidities.

Preoperative Laboratory Data Related to Blood Pressure

Preoperative fibrinogen concentration showed a linear relationship with preoperative blood pressure (r = .477, P = 0.01) (Fig. 1). When looking at a cut-off blood pressure value of 70 mmHg, patients with a blood pressure <70 mmHg had a median fibrinogen concentration of 1.4 g/L (IQR 1.0) compared to patients with blood pressures ≥70 mmHg with median fibrinogen concentration of 2.5 g/L (IQR 1.9) (P = 0.001) (Fig. 2). When analyzing the other preoperative laboratory values, only platelets showed a similar linear relationship with preoperative blood pressure (r = .247, P = 0.05) (Fig. 3).

Table 1
Patient demographics and procedure related data.
COPD = Chronic Obstructive Pulmonary Disease. * = Ongoing or abstain <5 years ago. Percentages in brackets refer to distribution within each comorbidity/risk factor.

	N = 91
Age (years)	74 y (57-91)
Male	73 (80 %)
Comorbidities & risk factors:	
COPD	18/85 (22 %)
Diabetes	12/88 (14 %)
Hypertension	59/85 (69 %)
Heart disease	30/81 (37 %)
Previous stroke	9/84 (11 %)
Smoker*	31/53 (58 %)
Aneurysm diameter	75 mm (IQR 29)
EVAR	19 (21 %)
Open repair	72 (79 %)
Lowest preoperative BP (median)	60 mmHg (IQR 40)
Intraoperative bleeding	
≤1999 ml	35 (39 %)
2000-4999 ml	33 (36 %)
≥5000 ml	23 (25 %)