Can Preoperative Sex-Related Differences in Hemostatic Parameters Predict Bleeding in Orthognathic Surgery?

Jesper Jared Olsen, DDS, [*] *Janne Ingerslev, DDS,* [†] *Jens Jørgen Thorn, DDS, PhD,* [†] *Else Marie Pinholt, DDS, MSci, DrOdont,* [‡] *Jørgen Brodersen Gram, MD, DSi,* [§] *and Johannes Jakobsen Sidelmann, PhD* [‖]

Purpose: Bleeding volume in orthognathic surgery (OS) varies considerably, although OS comprises standardized procedures and the patient population consists of young healthy individuals. The aim of this prospective cohort study was to investigate the influence of preoperative sex-related differences in hemostatic parameters on intraoperative bleeding (IOB) volume in OS.

Materials and Methods: Patients scheduled for routine OS in our department in Esbjerg, Denmark, were included as study patients in this short-term cohort study. The primary predictor variable was patient sex, and the primary outcome variable was IOB volume measured in milliliters. Secondary outcome variables included preoperative measures of hematologic variables, thromboelastography, fibrinogen concentration, D-dimer concentration, prothrombin fragment 1+2 (F1+2) concentration, and type of osteotomy. Data analyses included the χ^2 test, Mann-Whitney *U* test, Pearson product moment correlation analysis, and analysis of covariance for analyses of dichotomous variables, comparison between sex, correlations between IOB volume and secondary predictors, and adjustment for confounders, respectively.

Results: Forty-one consecutive patients undergoing bimaxillary OS were included and subsequently grouped according to sex (26 men and 15 women). The main finding was that male patients bled twice as much as female patients on average (400 mL [interquartile range, 300 to 500 mL] vs 200 mL [interquartile range, 63 to 288 mL]; $P = .001$). Age and preoperative measures of thromboelastography, fibrinogen concentration, D-dimer concentration, and F1+2 concentration were significantly associated with sex ($P = .001$, $P = .002$, $P = .007$, and $P = .014$, respectively). The significant association between sex and IOB volume disappeared when adjusted for these confounders ($P = .18$).

Conclusions: Preoperative sex-related increases in measures of fibrin turnover predict IOB volume in bimaxillary OS, with women displaying a significantly lower IOB volume than men.
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[*]PhD Student, Department of Oral and Maxillofacial Surgery, Hospital of South West Denmark, Esbjerg; Faculty of Health, Institute for Regional Services Sciences, University of Southern Denmark.

[†]Consultant, Department of Oral and Maxillofacial Surgery, Hospital of South West Denmark, Esbjerg, Denmark.

[‡]Professor and Consultant, Department of Oral and Maxillofacial Surgery, Hospital of South West Denmark, Esbjerg; Faculty of Health, Institute for Regional Services Sciences, University of Southern Denmark, Esbjerg.

[§]Professor, Unit for Thrombosis Research, Department of Public Health, University of Southern Denmark, and Department of Clinical Biochemistry, Hospital of South West Denmark, Esbjerg, Denmark.

[‖]Associate Professor and Head of Section, Unit for Thrombosis Research, Department of Public Health, University of Southern Denmark, and Department of Clinical Biochemistry, Hospital of South West Denmark, Esbjerg, Denmark.

Address correspondence and reprint requests to Dr Olsen: Department of Oral and Maxillofacial Surgery, Hospital of South West Denmark, Finsensgade 35, DK-6700 Esbjerg, Denmark; e-mail: jesper.jared.olsen@rsyd.dk

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Orthognathic surgery (OS) is known to induce occasional incidents of excessive bleeding, and although blood transfusions are rare, they may be required from time to time.[1] The patient population undergoing OS is homogeneous concerning age, health status, and surgical procedure, yet intraoperative bleeding (IOB) volume has been shown to vary significantly.[2] Thus prediction of bleeding before surgery is advantageous. A recent study performed by our group showed that thromboelastography (TEG) is a potential method for preoperative prediction of IOB volume.[2]

The effect of sex on bleeding during surgery has been studied on several occasions,[3-6] and it might be considered whether women have a reduced risk, given that the female sex is associated with a more ample hemostatic profile compared with the male sex when evaluated by global hemostatic assays.[7] Studies concerning the influence of patient sex on IOB volume are few and have so far been restricted to isolated fields of surgery with male sex as a predictor of higher IOB volume in hepatectomy and various types of arthroplasty.[8-13] With respect to OS, it remains uncertain whether sex affects the bleeding risk although most observations find no sex-specific effects.[4-6]

The purpose of this study was to investigate the influence of sex on IOB volume through a short-term prospective cohort study, in which we hypothesized that sex does not influence IOB volume. The specific aims were *1)* to investigate the influence of sex on primarily IOB volume measured in milliliters, *2)* to detect correlations between IOB volume and hemostatic quantities (ie, measures associated with the turnover of fibrinogen and fibrin), and *3)* to adjust the possible association between IOB volume and sex for the potential confounding effect of the measures.

Materials and Methods

STUDY DESIGN AND SAMPLE

To address the research purpose, we designed and implemented a prospective short-term cohort study. Approval was obtained from the local ethics committee (S-RRS200610), and the Helsinki Declaration was observed. The study population comprised all patients presenting to the Department of Oral and Maxillofacial Surgery, Hospital of South West Denmark, Esbjerg, for evaluation and management of maxillary and/or mandibular anomaly between November 2006 and 2007. The treatment consisted of a combined orthodontic-surgical treatment to improve occlusion, bite function, and facial symmetry and harmony.

To be included in the study sample, patients had to be diagnosed with maxillary and/or mandibular deficiency, excess, or asymmetry. Patients were excluded as study patients if the following criteria were met: younger than 18 years; pregnancy; history of diabetes, connective tissue disorders, or cancer; use of hormonal contraceptives or hormonal replacement therapy within 3 months preoperatively; or intake of omega-3 fatty acids, garlic, ginseng, and *Ginkgo biloba* up until 10 days preoperatively.

STUDY VARIABLES

The primary predictor variable was patient sex. The primary outcome variable was IOB volume determined by deducting the volume (in milliliters) of saline irrigation fluid used during surgery from the total volume in the suction canister. Secondary outcome variables comprised age and body mass index, as well as perioperative hematologic variables of hemoglobin level and hematocrit level and hemostatic variables of thromboelastography (TEG), activated partial thromboplastin time (APTT), prothrombin time (PT), prothrombin fragment 1+2 (F1+2) concentration, fibrinogen concentration, and D-dimer concentration, determined preoperatively.

SAMPLING AND LABORATORY ASSAYS

Blood samples for determination of the aforementioned variables were collected preoperatively from fasting patients. Blood for determination of hemoglobin and hematocrit levels was additionally collected 48 hours after surgery. Di-potassium (K2)-EDTA–anticoagulated whole blood samples collected in Venosafe VF-053SDK tubes (Terumo Europe, Leuven, Belgium) were used for measurement of hemoglobin level, hematocrit level, and platelet count on an ADVIA 120 analyzer (Siemens, Erlangen, Germany). Citrate-anticoagulated whole blood collected in Venosafe VF-054SBCS07 tubes (Terumo Europe) was subjected to automated TEG (Roteg; Pentapharm, Munich, Germany). Tissue factor–induced activation of coagulation was initiated with Innovin (Dade Behring, Marburg, Germany). TEG parameters of clot formation time (CFT), maximum clot firmness (MCF), and alpha angle were recorded.

Citrate-anticoagulated blood collected in Venosafe VF-054SBCS07 tubes was centrifuged for 20 minutes at 2,000*g*. The plasma was collected and used for determination of APTT and fibrinogen concentration by use of the STA-5 kit (Diagnostica Stago, Asnières-sur-Seine, France), PT by use of the STA-SPA kit (Diagnostica Stago), D-dimer concentration by use of the STALiatest kit with the STA-R Evolution coagulation analyzer (Diagnostica Stago), and F1+2 concentration by use of a commercial enzyme-linked immunosorbent assay, ELISA (Enzygnost-F1+2 monoclonal micro-assay; Siemens, Marburg, Germany) using mouse monoclonal antihuman F1+2.

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