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## Machine learning based prediction of perioperative blood loss in orthognathic surgery

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## ABSTRACT

The aim of this study was to evaluate, if and with what accuracy perioperative blood loss can be calculated by a machine learning algorithm prior to orthognathic surgery. The investigators implemented a random forest algorithm to predict perioperative blood loss. 1472 patients who underwent orthognathic surgery from 01/2006 to 06/2017 at our institution were screened and 950 patients were included and separated 80%/20% in a training set - utilized to generate the prediction model - and a testing set - utilized to estimate the accuracy of the model. The outcome variable was the correlation between actual perioperative blood loss and predicted perioperative blood loss in the testing set. Other study variables were the difference of actual and predicted perioperative blood loss and important factors influencing perioperative blood loss using random forest feature importance. Descriptive and bivariate statistics were computed and the P value was set at 0.05. There was a statistically significant correlation between actual perioperative blood loss and predicted perioperative blood loss ( $p < 0.001$ ). The mean difference was 7.4 ml with a standard deviation of 172.3 ml. The results of this study suggest that the application of a machine-learning algorithm allows a prediction of perioperative blood loss prior to orthognathic surgery.

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## 1. Introduction

Besides orthodontic treatment, orthognathic surgery is performed to surgically correct abnormalities of the mandible, maxilla or both after congenital, developmental or traumatic deformities. Although orthognathic surgery can be regarded as a safe procedure nowadays (Kim and Park, 2007), blood loss is still one of the major complications (Pineiro-Aguilar et al., 2011).

Having the knowledge of an expected high blood loss of a patient prior to surgery can be beneficial to the attending surgeon. In such cases, it is even more important to take enough time for optimal preoperative preparation. Expected high blood loss could furthermore influence the method of treatment, for example,

favoring a single jaw over a bimaxillary approach or even considering pure orthodontic treatment over combined surgical and orthodontic treatment where possible. In addition expected high blood loss can influence the decision of preparing RBC transfusions for surgery in the rare cases where needed.

There are numerous papers focusing on analyzing the influencing factors on bleeding and using them to predict blood loss in orthognathic surgery, but none of them providing the ability to calculate an exact number of expected blood loss for a patient prior to orthognathic surgery (Ueki et al., 2005; Kretschmer et al., 2008; Rummasak et al., 2011; Madsen et al., 2012; Al-Sebaei, 2014; Schneider et al., 2015; Olsen et al., 2016; Thastum et al., 2016; Salma et al., 2017).

In the last few years a branch of artificial intelligence (the so-called “machine learning”) evolved, enabling computers to make predictions based on labeled data from previous examples by pattern recognition. Different machine learning algorithms have since been used in several medical fields, e.g. cancer diagnosis (Cruz

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and Wishart, 2007), sepsis prediction (Islam et al., 2019), and prediction of bisphosphonate-related osteonecrosis of the jaw after tooth extraction in patients receiving bisphosphonate treatment (Kim et al., 2018).

We now use this technique to introduce a new way of predicting blood loss for a patient to an exact number by applying a machine learning algorithm – random forest – and evaluate in this study whether and to what accuracy perioperative blood loss can be predicted prior to orthognathic surgery using our model.

## 2. Material and methods

This study was conducted on a retrospective patient group which included patients who underwent orthognathic surgery due to dysgnathia. Five types of orthognathic surgical procedures were included: bilateral sagittal split osteotomy with or without genioplasty (BSSO, BSSO + CHIN), surgical assisted rapid palatal expansion (SARPE), Le Fort 1 Osteotomy (LF1) or a combination of bilateral sagittal split osteotomy with Le Fort 1 (BIMAXILLARY). All successive patients who underwent surgery at the Department of Cranio-Maxillofacial Surgery of the Kepler University Clinic Linz, Austria, between January 2006 and June 2017 were screened for enrollment. A total of 1472 patients were screened. Patients who suffered from bleeding diathesis, clotting abnormalities or patients who underwent previous operations because of a cleft lip and palate were excluded as these patients are known to have increased perioperative blood loss. Patients who received RBC transfusions during or after the surgery were also excluded from the study, as the perioperative blood loss was calculated and RBC transfusions would have falsified the result. As postoperative coagulation parameters were not taken by default and therefore missing in over 90% of patients who underwent SARPE procedure, we then excluded patients who underwent SARPE. Patients with missing weight or height values and patients <18 years were excluded as the used formula for blood volume can only be applied to adults, leaving a total of 950 patients included in the study. The trial was approved by the Ethics Committee of Upper Austria (K-143-17).

Based on height and weight, blood volume was calculated using the Nadler Formula (Nadler et al., 1962). Perioperative blood-loss was calculated according to blood volume, preoperative and postoperative hemoglobin values by the hemoglobin balance method (Gao et al., 2015).

Every patient was treated according to an individual treatment plan which was compiled by an orthodontist and a craniomaxillofacial surgeon in cooperation. All surgical procedures were performed by experienced craniomaxillofacial consultants. The BSSO was performed according to the Obwegeser-Dal Pont technique with the Hunsuck modification (Hunsuck, 1968). In cases where needed the BSSO was combined with a sliding genioplasty. The Le Fort 1 Osteotomy was performed according to the Bell technique (Bell et al., 1988).

All patients underwent standard monitoring according to standard operating procedures established at our institution. Intravenous antibiotic prophylaxis with 1 g Sulbactam and 2 g Ampicillin was performed preoperatively and patients received clonidine 0,3 mg and midazolam 3,75 mg 30 min before surgery. After the induction of anaesthesia the surgeon applied local anesthesia with epinephrine in the surgical field in order to minimize bleeding; in a single jaw procedure 10 ml was used, and 20 ml in double jaw procedures.

General anesthesia was induced intravenously by a combination of remifentanyl, propofol and rocuroniumbromid, or a balanced anesthesia using sevoflurane and remifentanyl was applied according to the assessment of the attending anesthesiologist. Patients were intubated tracheally and mechanically ventilated. Tidal volume and

respiration rate were set to maintain normocapnia. Fluid losses were substituted by the infusion of crystalloids or colloids according to the assessment of the attending anesthesiologist. The transfusion of blood products was conducted according to the “Cross-Sectional Guidelines for Therapy with Blood Components and Plasma Derivatives”, published by the board of the German Medical Association (Bundesärztekammer). PRBCs were always transfused to patients with a lower hemoglobin level of 6 g/dl, and never with a higher hemoglobin level of 10 g/dl. Between a hemoglobin level of 6–10 g/dl, transfusion was or was not conducted due to the capacity of compensation, symptoms of anemic hypoxia (e.g. tachycardia, hypotension, ECG ischemia, lactic acidosis) or ongoing blood loss.

All patients were extubated at the end of surgery and monitored after surgery. Prophylactic anticoagulant enoxaparin-natrium was given 6 h after surgery according to the assessment of the surgeon and postoperatively the administration of intravenous antibiotic and pain medication was conducted according to the standard operating procedures of our institution.

Data were obtained retrospectively using medical records such as operative reports, nursing reports, anesthesia logs, and laboratory findings. The following data set was collected: demographic data such as age, weight, sex, type of operation, American Society of Anesthesiologists (ASA) status, preoperative laboratory findings, administered blood products, surgical time, anesthesia time and type of anesthesia.

The applied machine learning algorithm is called random forest (RF), which is a tree-based algorithm that creates subsets of decision trees that are used for the improvement of the algorithm performance (Breiman, 2001). The general idea is that the combination of weak decision tree outputs yields highly accurate results. The creation of the subsets follows a random process which is known as bagging. Bagging stands for bootstrapping the data plus using the aggregate to make a decision.

The original data set was split according to the holdout method into a training set (80% of data), which was utilized to generate the prediction model, and a testing set (20% of data), which was utilized to estimate the accuracy of the model. Data imputation was performed according to the following: If a variable was missing in more than 25% of cases, the variable was excluded from the study. If a variable was missing in less than 25% of the cases, the mean of the existing variables was used for missing metric variables, and for missing categorical variables, the category which was most common in the existing data of this variable was used.

Therefore, after generating the prediction model using the training set, our model was used to predict perioperative blood loss for the patients in the test set. Then we compared the predicted blood loss values and the actual values for perioperative blood loss in our test set using a linear regression model.

We then calculated the difference between the predicted perioperative blood loss and the actual perioperative blood loss in our testing set to measure the accuracy of the prediction. Using feature importance, we analyzed important factors influencing perioperative blood loss.

Statistical analysis was performed using the R programming language (R Core Team, Vienna, Austria). A significance threshold of  $p < 0.05$  was defined.

## 3. Results

### 3.1. Baseline characteristics and perioperative blood loss

A total of 950 patients were included of the 1472 patients who were initially screened. Detailed baseline characteristics and perioperative blood loss values of the included patients are listed in Table 1.

**Table 1**  
Baseline characteristics and perioperative blood loss. Imaged are important baseline characteristics and perioperative blood loss divided among the different groups of operations and sex.

Type of Operation/Sex	n	Age in years m (SD)	BMI m (SD)	ASA in % I/II/III	Surgical Time in min m (SD)	Blood loss in ml m (SD)
<b>TOTAL</b>	950	28,1 (±9,3)	22,9 (±3,8)	87/13/-	108,1 (±42,3)	421,5 (±229,4)
Female	574	28,1 (±8,8)	22,1 (±3,6)	88/12/-	105,3 (±41,5)	370,6 (±187,4)
Male	376	28,2 (±9,9)	24,1 (±3,7)	85/15/-	112,4 (±43,1)	499,1 (±263,5)
<b>BIMAXILLARY</b>	598	27,7 (±8,6)	23,0 (±3,9)	87/13/-	124,7 (±40,5)	494,1 (±223,4)
Female	369	27,9 (±8,4)	22,2 (±3,8)	88/12/-	122,6 (±39,1)	435,7 (±179,8)
Male	229	27,3 (±9,0)	24,2 (±3,8)	87/13/-	128,1 (±42,6)	588,2 (±253,1)
<b>BSSO</b>	264	28,1 (±9,4)	22,8 (±3,5)	87/13/-	78,2 (±27,6)	291,6 (±167,7)
Female	152	28,0 (±8,9)	22,2 (±3,4)	89/11/-	70,9 (±22,3)	246,6 (±135,9)
Male	112	28,1 (±10,0)	23,6 (±3,5)	83/17/-	88,2 (±31,0)	352,6 (±187,1)
<b>BSSO + CHIN</b>	57	29,7 (±10,9)	22,0 (±3,0)	87/13/-	92,0 (±27,4)	284,5 (±151,4)
Female	37	29,6 (±11,2)	21,3 (±2,7)	94/6/-	89,4 (±27,4)	264,4 (±145,8)
Male	20	30,0 (±10,8)	23,3 (±3,1)	75/25/-	96,9 (±27,4)	321,6 (±158,3)
<b>LF 1</b>	31	34,7 (±13,7)	24,5 (±4,4)	75/25/-	71,3 (±24,0)	378,7 (±300,5)
Female	16	31,4 (±9,9)	22,8 (±4,3)	73/27/-	69,0 (±15,0)	294,5 (±131,0)
Male	15	38,3 (±16,5)	26,5 (±3,8)	79/21/-	73,8 (±31,4)	468,5 (±397,9)

*n* = number of patients, *m* = mean, *SD* = standard deviation.

### 3.2. Machine learning based prediction

A plot comparing the predicted blood loss values versus the actual values for perioperative blood loss in our test set is shown in Fig. 1. The linear regression showed a highly significant correlation between the predicted and the actual blood loss values ( $p < 0.001$ ).

The frequency of the calculated difference of the predicted and the actual blood loss values for our test set are plotted using a histogram (see Fig. 2). The mean difference was 7.4 ml with a standard deviation of 172.3 ml.

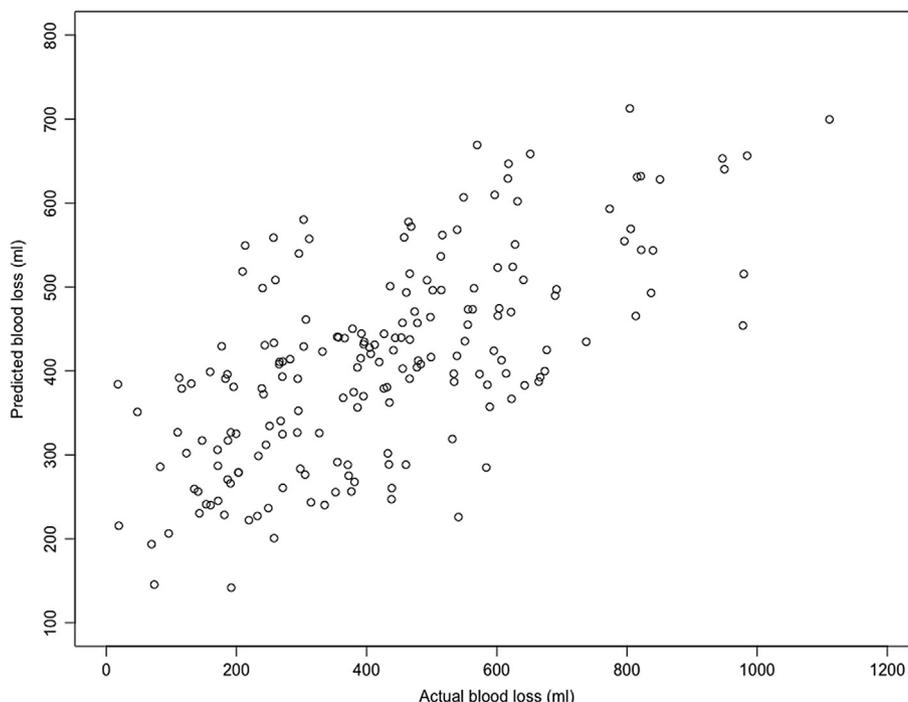
### 3.3. Factors influencing perioperative blood loss - importance

The factor with the highest feature importance was “bimaxillary surgery” with a feature importance of 9192. Table 2 shows factors

influencing perioperative blood loss and the respective feature importance values.

## 4. Discussion

This study aimed to evaluate whether perioperative blood loss in orthognathic surgery can be predicted by the random forest algorithm. Our key finding was that there was a statistically highly significant ( $p < 0.001$ ) correlation in our test set between our machine learning based predicted blood loss and the actual perioperative blood loss. The predicted perioperative blood loss deviated on average only 7.4 ml from the actual blood loss with a standard deviation of 172.3 ml, meaning that with our model the perioperative blood loss in orthognathic surgery can be predicted accurately prior to surgery.



**Fig. 1.** Actual perioperative blood loss in ml of the patients in the test set plotted against the machine-learning based predicted blood loss in ml of the same patients.

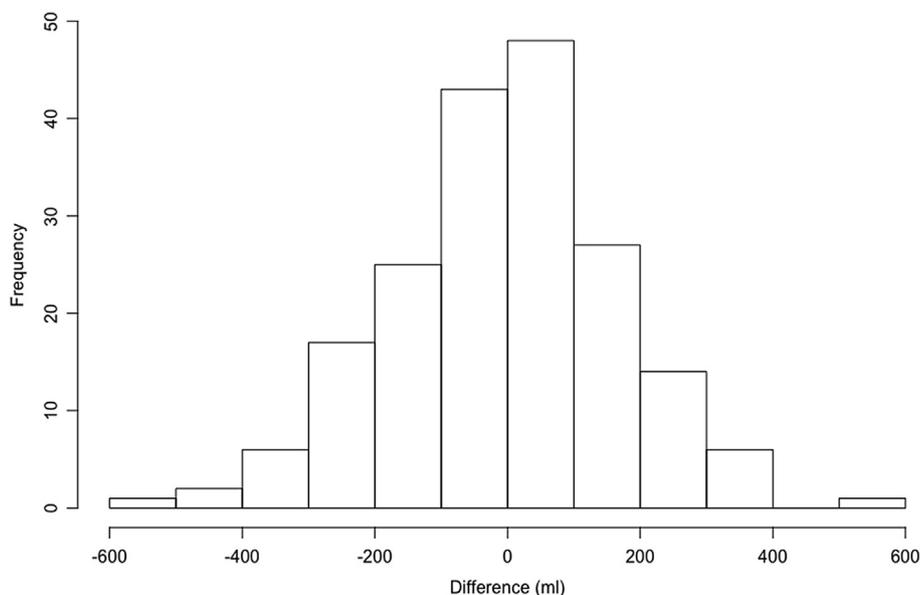


Fig. 2. Histogram of the frequency (in total patients) of the difference in ml between predicted and actual perioperative blood loss of the test set.

Table 2

Feature importance of factors predicting perioperative blood loss. Imaged are the random forest feature importance of factors predicting the perioperative blood loss sorted from high to low.

Factor	Feature importance
Bimaxillary surgery	9192
Preoperative hematocrit	5049
Preoperative hemoglobin	4867
Preoperative erythrocytes	4676
Surgical time	3838
Blood volume	3472
BSSO	2723
Sex	1972
BMI	1043
BSSO + CHIN	149
Age	123
LF 1	-70

Nowadays orthognathic surgery can be described as a safe surgical procedure (Kim and Park, 2007), however, despite these advances perioperative blood loss still has to be considered a major complication, resulting in RBC transfusions (Pineiro-Aguilar et al., 2011). In the literature, the frequency for RBC transfusions in orthognathic surgery is generally described to be quite low (Moening et al., 1995; Panula et al., 2001; Kretschmer et al., 2008; Pineiro-Aguilar et al., 2011; Faverani et al., 2014), but there are also studies with higher transfusion requirements (Al-Sebaei, 2014; Salma et al., 2017).

Pronounced regional blood flow of the surgical area may be one of the most important reasons for blood loss in orthognathic surgery. In the upper jaw, the A. sphenopalatina, A. palatina descendens, the Plexus pterygoideus, the A. maxillaris interna and their lateral branches run near the operating area. Especially when detaching the maxilla from the pterygoid, these blood vessels can be injured and can lead to massive perioperative bleeding. In the lower jaw, the A. alveolaris inferior and the A. facialis run in the operating area. If these arteries are injured, there may be significant perioperative bleeding just as in the upper jaw. Hemostasis in the sense of ligatures and cauterization is difficult due to limited vision and limited access to the surgical site and the respective vessels, some of them having an intraosseous course.

In order to better understand blood loss in orthognathic surgery, attempts to identify predictors of blood loss have been made by many authors in previous research (Madsen et al., 2012; Al-Sebaei, 2014; Schneider et al., 2015; Olsen et al., 2016).

The study presented introduces the prediction of perioperative blood loss in orthognathic surgery by a machine learning algorithm, which to our knowledge has never been done before.

Since orthognathic surgery is an elective procedure, it is of particular importance to anticipate possible complications before onset of the surgical procedure. With our model, one can calculate the perioperative blood loss prior to surgery with a mean difference from actual blood loss of 7.4 ml (SD 172.3 ml), enabling enhanced perioperative management.

Having the knowledge of high intraoperative blood loss, it is even more important to take enough time for optimal preoperative preparation. In such cases, operations should only be performed after achieving an optimal initial state. Furthermore, anticipation of high perioperative blood loss may influence the method of treatment, favoring a single jaw over a bimaxillary approach or favoring pure orthodontic treatment over combined surgical and orthodontic treatment in rare cases where possible.

When surgical treatment is needed and - despite optimal preoperative preparation - high perioperative blood loss can be expected, the knowledge of the expected amount of perioperative blood loss can influence the decision of preparing RBC transfusions for surgery. This is also of economic interest, as the cost of testing and preparing blood components is up to 30% of the total cost of blood products (Shander et al., 2010). It is therefore necessary to keep the ratio of prepared to transfused blood components as small as possible. Alarmingly, a study of Austrian hospitals showed that 60.3% of the RBC transfusions prepared for a possible administration during surgery are not administered (Gombotz et al., 2011).

There are already systems such as the Patient Specific Blood Ordering System (PSBOS), which addresses relevant parameters of the individual patient in order to optimize the ordering practice significantly (Palmer et al., 2003). The Mercuriali algorithm contributes to this, which can be used to determine the patient specific need for transfusion with the aid of the preoperative hemoglobin value, the retrospectively calculated perioperative blood loss and certain transfusion triggers (Mercuriali and Inghilleri, 1996).

Interestingly, Hayn et al. showed in their study that a random forest based predictive modeling applied prior to surgery can predict the transfused volume of red blood cells more accurately than the state of the art Mercuriali algorithm (Hayn et al., 2017).

The mean amount of perioperative blood loss in our study was 421.5 ml (SD 229.4 ml) in all operation groups combined. The operation group with the highest perioperative blood loss in our study was the bimaxillary group with 494.1 ml. A review from Pineiro-Aguilar et al., which found the mean intraoperative blood loss from orthognathic surgery on the basis of 7 included studies out of 90 publications examined, showed a comparable value of 436.1 ml (SD 207.9 ml) (Pineiro-Aguilar et al., 2011). The highest perioperative blood loss being in the bimaxillary group can be explained by the fact that in bimaxillary surgery both jaws are operated on and therefore the intervention is more complex and the risk is larger to hurt more blood vessels (Thastum et al., 2016). In addition, the duration of surgery is longer and therefore blood loss could also increase and the nasal mucosa is located in the operating area, which is very well vascularized and can promote perioperative bleeding.

Other factors, such as BMI (Al-Sebaei, 2014; Thastum et al., 2016), age (Kretschmer et al., 2008; Rummasak et al., 2011; Faverani et al., 2014), sex (Ueki et al., 2005; Pineiro-Aguilar et al., 2011; Rummasak et al., 2011; Faverani et al., 2014; Olsen et al., 2016; Thastum et al., 2016; Salma et al., 2017) or surgical time (Moening et al., 1995; Ueki et al., 2005; Kretschmer et al., 2008; Rummasak et al., 2011; Thastum et al., 2016), that may possibly influence blood loss in orthognathic surgery are the subject of current clinical investigations. Using feature importance, we evaluated important factors in our model for predicting perioperative blood loss (see Fig. 2). The factor with the highest feature importance (9192) was bimaxillary surgery, followed by preoperative hematocrit (5049). Feature importance indicates how important a specific variable has been for our model in order to predict blood loss. This means that the factors with high feature importance such as bimaxillary surgery or preoperative hematocrit were important for the model to predict perioperative blood loss accurately. However, this does not elucidate whether there is a positive or a negative correlation between the factors and predicted blood loss. By comparing the feature importance values, conclusions about the importance of the factors can be drawn. For example, one can deduce that the factor bimaxillary surgery was nearly twice as important as the following variable preoperative hematocrit or more than twice as important as surgical time. Le Fort 1 osteotomy, for instance, was with a negative feature importance not helpful for our model in order to predict blood loss. Our findings on the factors are widely consistent with the literature presented above, being the same factors influencing blood loss the most, as are already known. However, with feature importance we offer a way to weight the influence of each individual factor by the effect they have on perioperative blood loss.

Of course, the influence of confounders is possible. For example, although the feature importance of a bimaxillary surgery was much higher than that of the operation time, the higher operation time associated with a bimaxillary surgery may itself influence the higher feature importance of the bimaxillary surgery acting as a confounder.

Bleeding may also be dependent on the skill and experience of the single surgeon, although Kretschmer et al. stated in their paper that the experience of the surgeon had no influence on blood loss in 127 patients undergoing bimaxillary surgery (Kretschmer et al., 2008). Due to the unfortunately very strict regulations of our works council, it was not possible for us to include the variable “surgeon” in the analysis. As mentioned in the Material and Methods section, however, “all surgical procedures were performed

by experienced craniomaxillofacial consultants”. Even without the variable “surgeon” being included in our algorithm, we could still accurately predict blood loss to 7.4 ml on mean average prior to orthognathic surgery.

Another limitation of our study may be the potentially limited general validity of our model for other datasets. Since the model was created with our data, if the model is applied to another clinic that has other surgical methods, other structures or another patient population, it may result in erroneous prediction values.

Another limitation may be the fact that perioperative blood loss was calculated using the hemoglobin balance method (Gao et al., 2015) and not determined intraoperatively by measuring rinsing saline and the total volume of blood and rinsing saline in the suction device, and therefore may not represent the correct blood loss. However, the hemoglobin balance method, being a scientifically logical and well-known method for calculating blood loss, was shown to provide relatively accurate results (Gao et al., 2015), is used by many scholars in other fields of medicine (Good et al., 2003; Foss and Kehlet, 2006) and also takes into account the occurrence of hematomas, since the perioperative blood loss is greater than the intraoperative measured blood loss alone anyway (Gombotz et al., 2011). Hence we calculated blood loss; patients who underwent RBC transfusions were excluded. Therefore as another possible limitation, our model only gives a view to the identification of patients at risk for a transfusion if a high blood loss is expected, but cannot directly predict RBC transfusion requirements.

## 5. Conclusion

In this study we have shown that the application of a machine-learning algorithm (random forest) allows a prediction of perioperative blood loss prior to orthognathic surgery. Having the knowledge of an expected high blood loss even before orthognathic surgery may influence the method of treatment or may give a view to the identification of patients at risk for RBC transfusion; however actual RBC transfusion requirements cannot be calculated using our model.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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All authors have viewed and approved the final version of this study and agreed to the submission to JCMFS.

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