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Data Driven Methods for Predicting Blood Transfusion Needs in Elective Surgery

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Abstract. Research in blood transfusions mainly focuses on Donor Blood Management, including donation, screening, storage and transport. However, the last years saw an increasing interest in recipient related optimizations, i.e. Patient Blood Management (PBM). Although PBM already aims at reducing transfusion rates by pre- and intra-surgical optimization, there is still a high potential of improvement on an individual level. The present paper investigates the feasibility of predicting blood transfusions needs based on datasets from various treatment phases, using data which have been collected in two previous studies. Results indicate that prediction of blood transfusions can be further improved by predictive modelling including individual pre-surgical parameters. This also allows to identify the main predictors influencing transfusion practice. If confirmed in a prospective dataset, these or similar predictive methods could be a valuable tool to support PBM with the ultimate goal to reduce costs and improve patient outcomes.

Keywords. Predictive Modelling, Ensemble Model, Bagged Trees

1. Introduction

Blood transfusion (BT) is a lifesaving procedure with various indications in surgery, intensive care, cardiac disease and many other fields. However, BT is characterised by a high inter-hospital variability of transfusion rates (TR, number of transfused patients per patient population) and a high variability of the amount of product used per transfused patient. Additionally, BT causes not only substantial direct and indirect costs but it can also lead to several adverse events (infections, immunologic reactions, etc.) [1]. Therefore, an increasing number of clinical trials and observational studies try to re-evaluate current BT practices.

While donor blood management focuses on processes related to donation, such as screening, storage and transport of blood products, Patient Blood Management (PBM) concerns procedures applied *to the potential recipient* with the main focus on reducing the amount of blood products which need to be transfused. PBM builds on three pillars:

- Detection and treatment of anaemia *before* elective surgeries
- Minimization of blood loss *during* surgery
- *Exploitation of individual anaemia tolerance* and rational use of blood products according to relevant guidelines [1,2]

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In Austria, benchmark studies for blood use in elective surgery were commissioned by the Austrian Federal Ministry of Health and were conducted from 2004 to 2005 [2] and from 2009 to 2010 [3]. The aims were to measure the key variables of transfusion practice in elective surgery to chart the current situation, to identify predictors of transfusion, and to use the data for developing strategies to optimise transfusion practices across Austrian hospitals. After completion, the investigators of these studies provided a final report to the contracting authority and individual benchmark reports to the participating hospitals. This report is available online from the public information portal of the Austrian Federal Ministry of Health [4], including detailed and overall findings, as well as all relevant data. In terms of predictive aspects, the data were analysed using logistic regression on all collected variables so as to identify the main BT drivers, which were found to be lost red blood cell volume, relative preoperative haemoglobin, lowest relative postoperative haemoglobin, and sex in all types of surgeries analysed. In some kinds of surgery, also age, regional anaesthesia, American Society of Anaesthesiology (ASA) score, body mass index and platelet aggregation inhibitors were identified as independent predictors of BT [3].

According to current PBM guidelines, prior to elective surgeries with a high risk for significant blood loss, physicians are required to order a reasonable number of units of red blood cells (RBC). Based on the Mercuraili algorithm [5], this number is calculated from a) the individual patient's current erythrocyte volume ($EV_{preoperative}$ [L]), b) the individual lower limit of EV that the patient is expected to tolerate ($EV_{min\ acceptable}$ [L]) and c) the expected loss of erythrocyte volume (LEV) during the surgery ($LEV_{anticipated}$ [L]).

$$TEV_{required} = LEV_{anticipated} - (EV_{preop} - EV_{min\ acceptable}) \quad (1)$$

EV_{preop} is estimated from the individual patient's current blood volume (BV [L]), the preoperative venous haematocrit (Hct [1]) and the empirically determined correction factor 0.91 [1] (not used in original formula but in later studies) according to Equation 2

$$EV_{preop} = BV * Hct * 0.91 \quad (2)$$

where BV [L] is calculated from the patient's body weight (BW [kg]) and body height (BH [m]), using gender dependent empirical factors as shown in Equation 3 and Equation 4.

$$BV_{female} = 0.3561 * BH^3 + 0.03308 * BW + 0.1833 \quad (3)$$

$$BV_{male} = 0.3669 * BH^3 + 0.03219 * BW + 0.6041 \quad (4)$$

$EV_{min\ acceptable}$ is also estimated on an individual level. Based on clinical assessment, the physician evaluates, which EV / which Hct the patient is expected to tolerate without significant symptoms. However, the third input parameter for calculating the required EV according to Equation 1, i.e. $LEV_{anticipated}$, is only estimated from data of previous similar surgeries within the respective hospital, not taking into account any individual parameters of the patient [1].

Various attempts have been made to provide clinicians with estimates and predictions of BT needs [6]. However, when it comes to elective surgeries, less efforts have been made, although information on BT needs for specific surgeries could be of

high value. Recently, following the success in different industries, the application of data driven business intelligence and decision support has gained momentum in healthcare settings in general and in the BT topic as well [7].

The present paper re-evaluated the data from the Austrian Benchmarking Studies by going beyond previous analysis attempting to predict BT related outcomes, with the objective to evaluate statistical models to predict LEV as well as TEV based on different feature sets formed by individual pre-, intra and post-surgical parameters.

2. Methods

2.1. The data set

All analyses were based on the data collected in the course of the two Austrian Benchmarking studies, which were comprised of a total of 6,530 case records from 16 centres (408 ± 222 records per centre, min 164, max 907), obtained for elective surgeries of one of the following procedures: total hip replacement, total knee replacement and coronary artery bypass grafting. PBM guidelines require that for estimation of loss and transfusion of blood, historical data of the respective centre are considered. Since no historical data were available within the dataset, these historical data were estimated from all data available within the dataset (features *Historic mean LEV* and *TEV per centre and type of surgery*). Table 1 shows all features which were included in six feature sets:

- Historical data as recorded for a specific centre and type of surgery (Hist. LEV and Hist. TEV)
- Data available prior to the surgery excluding the amount of blood units ordered (Pre, Pre + ordered)
- Data available prior to the surgery including the amount of blood units ordered
- Data recorded during the surgery (Intra)
- Data recorded post-surgery (Post)

2.2. AIT Predictive Modelling Pipeline

The AIT PM pipeline is based on MATLAB R2015b (The Mathworks, Inc, Natik, NE) and consists of the following main modules:

Feature Set Compiler – an extract, transform, load (ETL) module for importing data from a variety of sources (databases, EXCEL or CSV files, output of preprocessing components e.g. for Biosignal analysis, …) governed by a Source Data Definition File and converting the data into a MATLAB datasets object for memory efficient computing based on a feature set definition.

Model Generator – utilizing the MATLAB Statistics and Machine Learning Toolbox and a modelling definition file, a variety of different models can be generated from the Feature sets, including General Linear Models, Bagged Trees, etc. Observations in the feature set can be arbitrarily divided into subsets for training, testing and validation with corresponding predictions being computed automatically.

Model Evaluator – allows visualising and evaluating model based predictions using methods like Receiver Operating Characteristics (ROC) and a variety of standard key performance indicators.

Table 1. The Feature Set used for the different types of predictions. LEV...Lost Erythrocyte Volume, TEV...Transfused Erythrocyte Volume, Pre, Intra, Post ... data available pre, intra and postoperatively. Features pre surgery are analysed including and excluding the number of blood units ordered. (Hb = Haemoglobin concentration, Hct = Haematocrit)

Description	Hist. LEV	Hist. TEV	Pre	Pre + ordered	Intra	Post
center number	1	1	1	1	1	1
type of surgery	1	1	1	1	1	1
Historic mean LEV per center and type of surgery	1		1	1	1	1
Historic mean TEV per center and type of surgery		1	1	1	1	1
gender			1	1	1	1
aggregation inhibitors			1	1	1	1
type of aggregation inhibitors			1	1	1	1
surgical technique			1	1	1	1
preoperative anemia			1	1	1	1
preoperative Hb > normal value			1	1	1	1
preoperative Hb category			1	1	1	1
preoperative Hb			1	1	1	1
Hbpre as percentage of WHO-anemia limit			1	1	1	1
preoperative Hct			1	1	1	1
preoperative circulating ery-volume			1	1	1	1
age			1	1	1	1
body mass index			1	1	1	1
body weight			1	1	1	1
body surface area			1	1	1	1
blood volume			1	1	1	1
total number of PRBC ordered				1	1	1
tranexamic acid					1	1
ASA-Score					1	1
duration of surgery					1	1
Euroscore					1	1
number of bypasses					1	1
extracorporeal circulation (ECC) used					1	1
duration of ECC					1	1
cell saver volume					1	1
cell saver ery-volume					1	1
cell saver used					1	1
unwashed shed blood					1	1
type of anaesthesia					1	1
regional anaesthesia only					1	1
Hb at the end of surgery					1	1
type&screen					1	1
Hb on postoperative day 3						1
Hb on postoperative day 5						1
min of all documented perioperative Hb-values						1
Hb3 as percentage of WHO anemia limit						1
Hb5 as percentage of WHO anemia limit						1
Hbmin as percentage of WHO anemia limit						1
Hct on postoperative day 3						1
Hct on postoperative day 5						1

This pipeline has a number of additional features useful to process large scale and heterogeneous healthcare data, from clinical codes to bio signals. It has previously been utilised for predictive analytics on different healthcare data sets, e.g. to predict the number of future days in hospital based on health insurance claims [8], to evaluate the utility of groups of features in given models by applying statistical tests on a set of related models build from observational subspaces (leave 10% out) [9] and to predict future events using time series approaches [10].

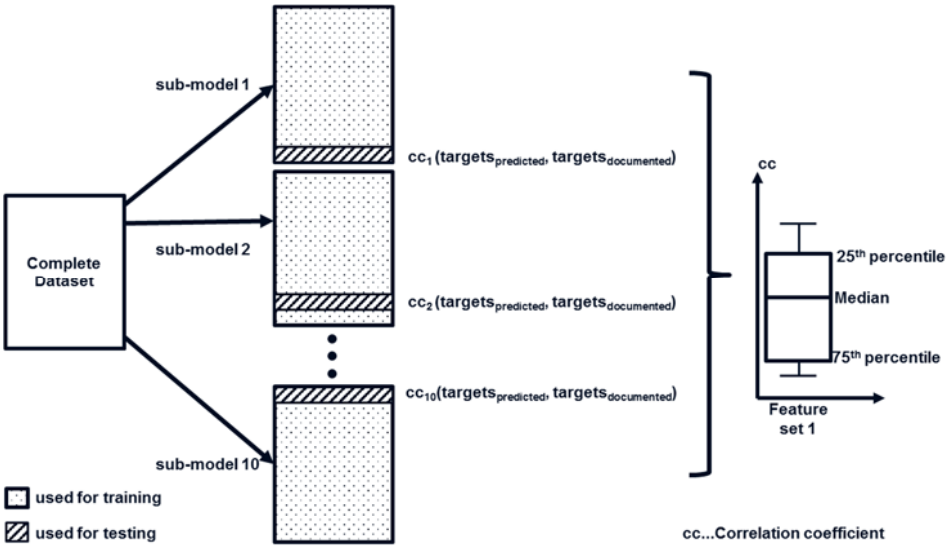

Figure 1. Leave 10% out approach used for training, prediction and statistical evaluation of each model

2.3. Training, Testing and Evaluation

A leave 10 % out approach was used for training and testing our models. This resulted in 10 different sub-models based on a training set of 90 % of the whole data set, which was applied to the remaining 10 % as a test set. Each model was trained with a random forest approach [11] using MATLABs *TreeBagger* functionality with default settings except for *OOBPred = on, NPrint = 1, MinLeaf = 10, Method = regression, Surrogate = off,* and *OOBVarImp = onPrediction.* The modelling result of each sub-model was compared to the actual target parameters and Pearson's correlation coefficient was calculated for each sub-model as a measure of the linear correlation between observed and predicted values. Statistical parameters of the correlation coefficients of the ten sub-models were visualized using boxplots. This approach is illustrated in Figure 1. Results of each feature set were compared to one another and to a baseline / reference model, which comprised of only one single feature representing a single, random number.

3. Results

Models for two prediction targets, i.e. LEV and TEV, with all feature set classes were trained and tested, applying a leave 10 % out approach. On a personal computer with an Intel® Core™ i7-3770 CPU with 3.50 GHz, 8 GB RAM and Windows 7, the overall modelling process, including training, prediction and evaluation for all feature sets and all target parameters took 5 min 11 s. Application of a trained model on an individual patient's dataset took 23 ms for the largest feature set (post-surgery).

Boxplots of the correlation coefficients of the 10 sub-models were drawn for each feature set to compare the respective model performance. The non-parametric Kruskal-Walis test was used to assess the statistical significance differences in performance of each features class, taking the 10 model runs in each group of features as an independent sample (see Figure 2 and Figure 3).

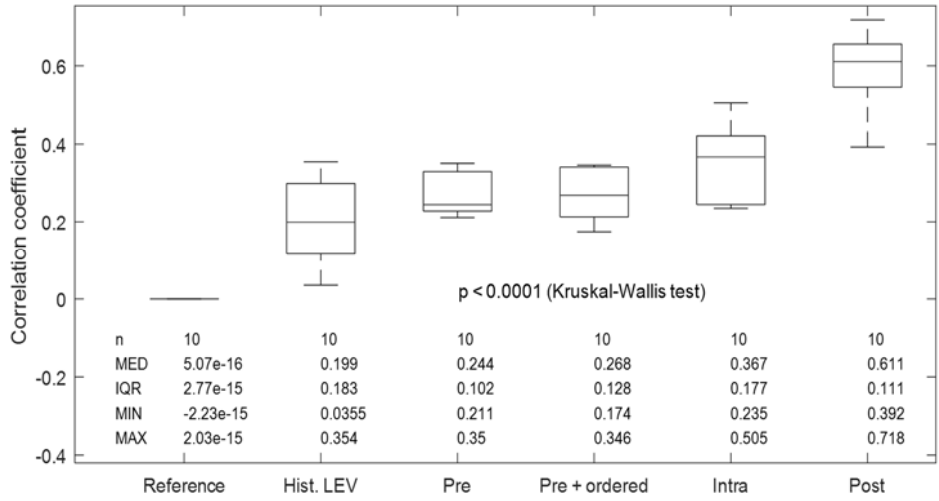

Figure 2. Boxplots of correlation coefficients of predicted loss of erythrocyte volume during surgery (LEV) as compared to actual loss, depending on the class of features used for prediction. Features classes as described for Table 1. Each box represents 10 correlation coefficients as received for different subsets when applying a leave 10 percent out approach for training and testing the respective model.

The correlation coefficient when considering the reference model based on the random feature only was zero for both LEV and TEV. As expected, predictions of LEV as well as TEV increased in precision when historical, pre-, intra- and post-surgical features were included in the model, respectively, resulting in statistically significant differences between the groups. Both parameters showed improved prediction performance even when pre-surgical, individual features were considered as compared to historical data from the respective centre only.

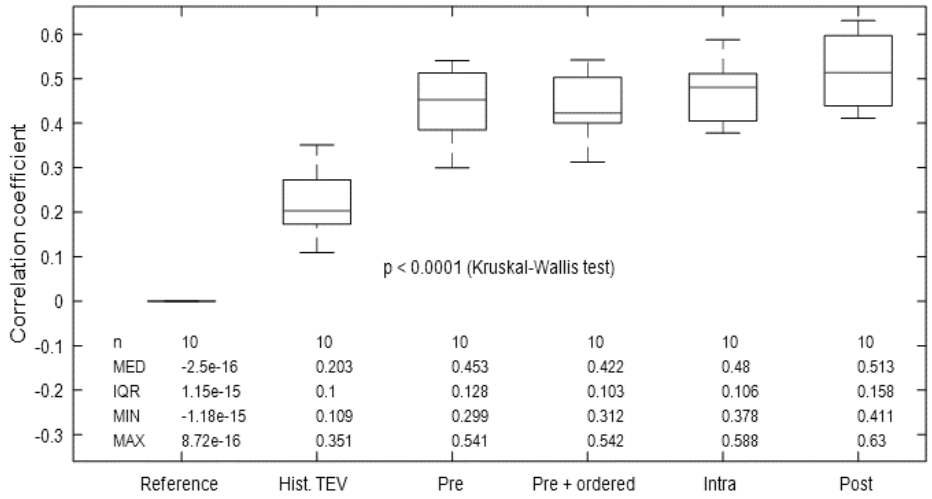

Figure 3. Boxplots of correlation coefficients of predicted transfused erythrocyte volume (TEV) as compared to actual volume, depending on the class of features used for prediction. Features classes as described for Table 1. Each box represents 10 correlation coefficients as received for different subsets when applying a leave 10 percent out approach for training and testing the respective model.

For TEV, the most distinct improvement was found when individual, pre-surgical features were added, while for LEV post-surgical features were most pivotal. Neither for LEV nor for TEV the number of units ordered significantly improved the model performance.

4. Discussion

While individual approaches are already suggested for TEV prediction in current guidelines, LEV is currently predicted without considering individual data. Our results indicate that not only TEV but also LEV can be predicted more precisely when considering individual pre-surgical parameters than when estimating these parameters from historical data of a certain centre only.

As expected, prediction of LEV was significantly more accurate if intra- and post-surgical features were considered. TEV prediction accuracy, on the other hand, already showed good correlation factors when considering pre-surgical data only, but it did not improve that much when adding intra- and post-surgical features. These results can be used to analyse the importance of single features or the performance of certain centres in a retrospective setting. However, in a real world scenario, these data will not be available for predication prior to surgeries.

Murphree et al. applied a large number of different model approaches to a related topic, i.e. the prediction of complications after BT [7]. His results indicate that most models give good results if applied alone and that combining those models with a "majority vote" strategy did not yield a significant improvement. These results have not yet been verified with our dataset.

During the two Austrian benchmarking studies [2, 3] it could be shown that different centres show significantly different blood transfusion patterns and that for some centres significant improvements could be achieved from the first to the second study by applying PBM principles. The present paper, however, did not consider, whether a centre had already applied a PBM program or not. This might have a severe influence on the resulting model which has not yet been investigated. Prediction of LEV are rather independent from PBM programs and therefore we expect that similar results would be achieved if our model would be applied to other centres. TEV prediction and number of ordered blood units, on the other hand, are highly influencing one another, they are dependent on the application of PBM processes, and on centre specific transfusion triggers. These influences could not yet be analysed sufficiently, and, therefore, further analyses are required in the future.

With the end of the EU project *EU-PBM Patient Blood Management* [12] getting closer, there will be a chance to validate these models with an independent, prospectively collected dataset. Also, this data is expected to allow to look at the impact of factors related to the three columns of the PBM strategy. Future work will also focus on aspects of providing prediction results to the physicians in a way which is easy to access and comprehend anywhere in their institution and anytime when decisions need to be made.

5. Conclusion

The results obtained in the present work indicate that predicting BT needs in elective orthopaedic and cardiac surgery is feasible based on a set of parameters which can

expected to be available in most centres. Individual parameters and more features, in particular from time points closer to the respective treatment phase, lead to better results. If these results can be confirmed with independent datasets, an additional tool to support PBM would be available.

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