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Predicting blood loss in burn excisional surgery

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Background: Blood loss during burn excisional surgery remains an important factor as it is associated with significant comorbidity, mortality and longer length of stay. Blood loss is, among others, influenced by length of surgery, burn size, excision size and age. Most literature available is aimed at large burns and little research is available for small burns. Therefore, the goal of this study is to investigate blood loss and develop a prediction model to identify patient at risk for blood loss during burn excisional surgery ≤ 10% body surface area.

Study design and methods: This retrospective study included adult patients who underwent burn excisional surgery of ≤ 10% body surface area in the period 2013–2018. Duplicates, patients with missing data and delayed surgeries were excluded. Primary outcome was blood loss. A prediction model for per-operative blood loss (> 250 ml) was built using a multivariable logistic regression analysis with stepwise backward elimination. Discriminative ability was assessed by the area under the ROC-curve in conjunction with optimism and calibration.

Results: In total 269 patients were included for analysis. Median blood loss was 50 ml (0–150) / % body surface area (BSA) excised and 0.28 (0–0.81) ml / cm^2. Median burn size was 4% BSA and median excision size was 2% BSA. Blood loss of > 250 ml was present in 39% of patients. The model can predict blood loss > 250 ml based on %BSA excised, length of surgery and ASA-score with an AUC of 0.922 (95% CI 0.883 – 0.949) and an AUC after optimism correction of 0.915. The calibration curve showed an intercept of 0.0 (95% CI –0.36 to 0.36) with a slope of 1.0 (95% CI 0.78–1.22).

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Conclusion: Median blood loss during burn excisional surgery of ≤ 10% BSA is 50 ml / % BSA excised and 0.28 ml / cm^2 excised. However, a substantial part of patients is at risk for higher blood loss. The prediction model can predict P(blood loss > 250 ml) with an AUC of 0.922, based on expected length of surgery, ASA-score and size of excision. The model can be used to identify patients at risk for significant blood loss (> 250 ml).

1. Introduction

Blood loss during excisional surgery remains common despite advances in blood sparing techniques. Blood sparing techniques include adrenaline-soaked gauzes, topical tranexamic acid, tourniquet, and cell salvage [1–3]. Reported blood loss ranged between 0.47 and 0.8 ml/cm^2 excised [4–6]. Blood loss and erythrocyte transfusions were associated with more comorbidity, mortality, and longer hospital length of stay in burn patients [7–9].

Several factors influenced the volume of blood loss. Length of surgery, initial full thickness burn size, area of excision and age have been described as contributing factors [4,10]. Furthermore, timing of surgery after initial trauma influenced blood loss, with early excision leading to more blood loss [11,12]. Predicting blood loss is difficult. However, it can help the clinical decision for the safe size of excision with respect to blood loss and the need for perioperative erythrocyte transfusion. Unfortunately, most literature available was aimed at large burns and little research is available to investigate blood loss in burns ≤ 10% body surface area (BSA). Therefore, the aim of this study is to investigate the volume of blood loss and to develop a predictive model to identify patient at risk for blood loss during small burn excisional surgery.

2. Methods

This retrospective study was conducted in the Maasstad Hospital, one of three burn centers in the Netherlands. The Maasstad hospital treats approximately 300 burn patients annually. The medical ethical committee of the Maasstad Hospital Rotterdam assessed the study (L2018046) and waived the need for written consent.

Primary outcome was volume of blood loss per area excised (ml/cm^2 or ml/% BSA). Secondary outcomes were the influence of time between burn trauma and surgery on blood loss and ability to predict blood loss > 250 ml. The threshold of 250 ml was chosen because of possible clinical significance in burn patient who are often anemic [8].

2.1. *Patients*

All adult patients (≥18 years), who underwent excisional surgery up to and including 10% TBSA, in the period from 2013 to 2018 were eligible for inclusion. Duplicates of the same procedure, patients with missing data (i.e., blood loss, size of excision or transfusion data) and delayed surgery (time to surgery > 1 month after initial burn) were excluded. Patients were identified using a prospectively collected database, which contains all data regarding burn trauma, treatment, and length of stay. Additional data regarding blood loss, transfusion, surgery characteristics and laboratory results were manually extracted from the electronic patient records.

2.2. *Surgical procedure*

All patients were treated with standard care. A dedicated team of burn professionals performed excisional surgery either using sharp instruments or VERSAJET (Smit & Nephew). Based on clinical expertise (i.e., based on full-thickness-/deep dermal burns) and assisted by Laser Doppler imaging the team decided the extend of excision and timing of surgery. During surgery, epinephrine-soaked gauzes were used to reduce blood loss. After full excision, wound surface was covered using autologous split skin graft. General anesthesia was administered at the discretion of the attending anesthesiologist. The anesthesiologist based the decision of erythrocyte transfusion on a standardized nationwide protocol [13]. During surgery, blood loss was monitored by weighing gauzes and surgical drapes (standard care). Blood loss and extend of excision were reported in the operative report (standardized measurements).

2.3. *Statistical analysis*

Analyses were conducted using R version 3.6.1 (The Comprehensive R Archive Network) [14]. Figures were produced using GraphPad Prism version 9.1.0 and the ROC curve and calibration plots were produced by R version 3.6.1. Depending on the normal distribution of continuous parameters, baseline characteristics were either described using medians and interquartile range and tested using Mann Whitney U tests or using means and standard deviations and using Student's t-tests. A clinical prediction model for peroperative high blood loss (> 250 ml) was built. Firstly, a multivariable logistic regression analysis was performed including all candidate predictors (age, gender, total burn size area excised, superficial burns, operation duration, timing of surgery and ASA-score. Secondly, stepwise backward elimination was conducted until the remaining variables in the model were all statistically significant ($p < 0.05$). Calibration of the model was assessed by visual inspection of calibration plots, upon which it was decided to include an interaction term between operation duration and the total burn size area excised to improve model fit. Discriminative ability was assessed by calculating the area under the receiver operating characteristic (ROC) curve (AUC) using the *pROC* package (version 1.16.2) [15]. Calibration curves were generated in R using the using the *rms* package (version 6.1–1) [16] and *CalibrationCurves* package [17]. Optimism in the AUC due to overfitting was assessed by bootstrap analysis using b= 1000 bootstrap samples, following the approach described by Steyerberg et al.[18].

3. Results

3.1. Patients

During the inclusion period, 347 burn excisional surgeries were performed ≤ 10% BSA, 78 patients were excluded: 41 patients were operated > 31 days after burn trauma, 12 patients were operated twice and in 25 patients' blood loss was missing (Fig. 1). In total 269 patients were included for analysis with a median BSA burned of 4% (1–7%) and a BSA excised of 2% (1–4%). Fig. 2 shows the trend in blood loss during surgery and the parameters used in the prediction model. During the first week after burn trauma the minority of patients is operated. Fig. 3.

3.2. Blood loss and transfusion

Median blood loss was 50 ml (0–150) / % BSA and 0.28 (0–0.81) ml/cm^2 (Table 1). Blood loss of > 100 ml was present in 48% of patients, and blood loss of > 250 ml was present in 39% of patients. Blood loss in patient undergoing larger excision (> 5% BSA) was 0.76 (0.53–1) ml/cm^2. Blood transfusion was uncommon, only 17 patients were transfused (6%; Table 1), all patients after transfusion had a hemoglobin level of > 7.0 g/dl.

3.3. Prediction model

After stepwise backwards elimination, %BSA excised, length of surgery and ASA-score showed a significant effect on blood

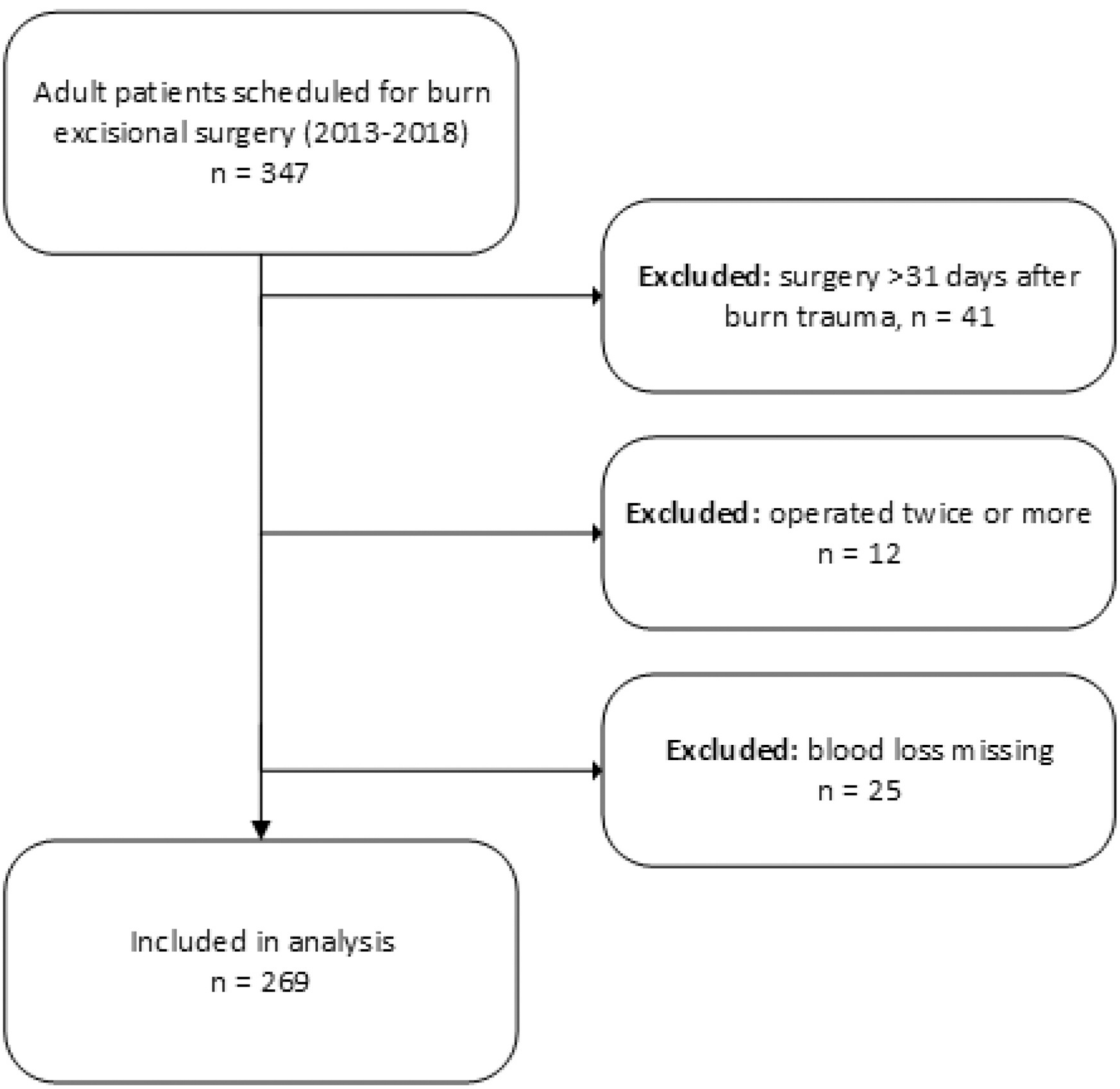

Fig. 1 – Flowchart of inclusion.

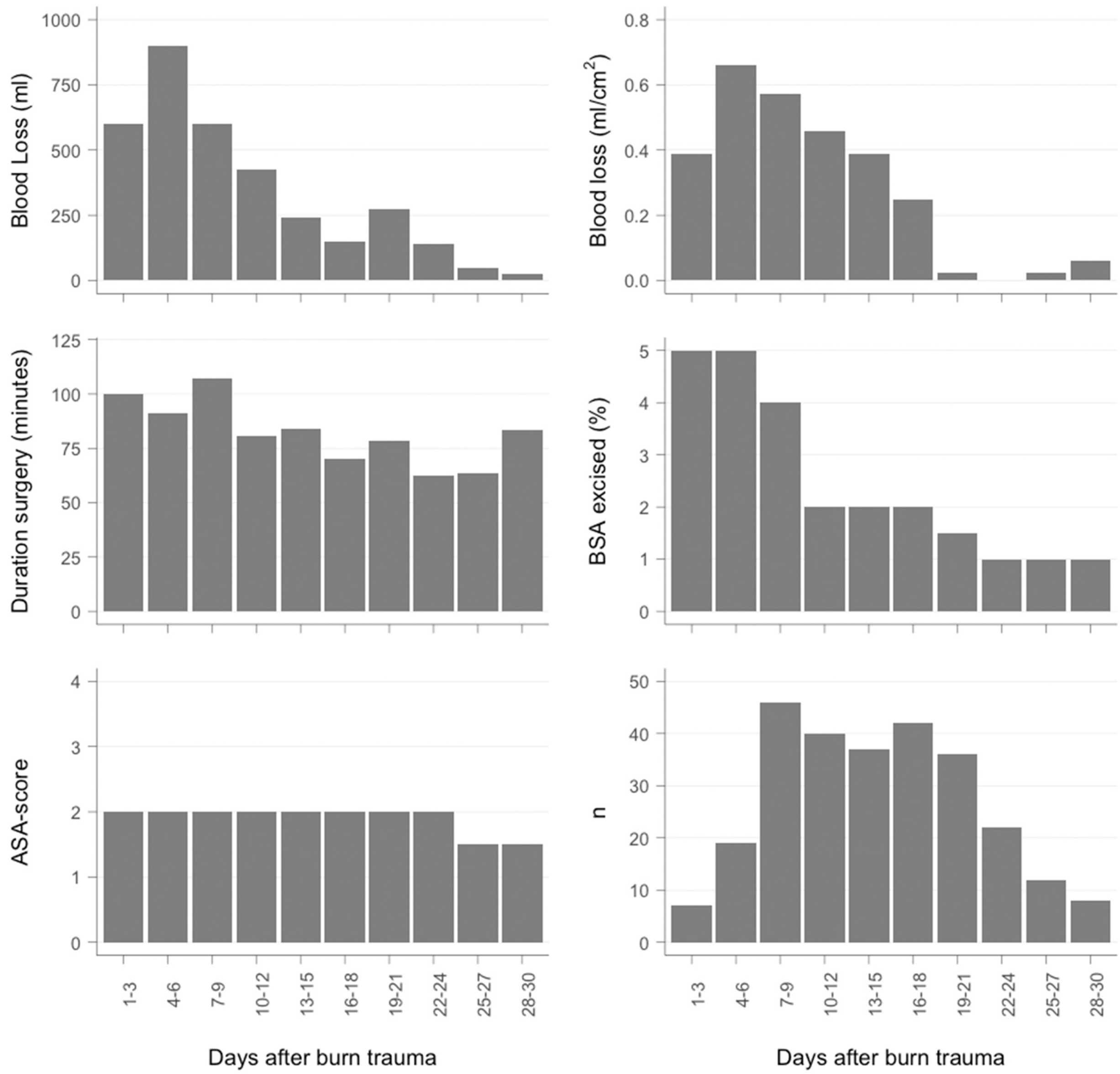

Fig. 2 – . Trends of blood loss and parameters used in the model. All panels represent the median of the respective parameters except for the lower right panel, which represents the number of patients operated at each timepoint. Abbreviations: BSA, body surface area; %, percentage excised of the total body surface area; ASA-score, American Society of Anesthesiologists Physical Status Classification System.

loss in our model. For prediction of P(blood loss > 250 ml), the model has an AUC of 0.992 (95% CI 0.883 – 0.949). The optimal corrected AUC is 0.915. The calibration curve shows a calibration intercept of 0.0 (95% CI −0.36 to 0.36) and slope of 1 (95% CI 0.78–1.22), the discrimination c-statistic was 0.92 (95% CI 0.88–0.95). Tables 2 and 3.

Using the following formulas P(blood loss > 250 ml) can be predicted (table 4).

$$x = -7.87 + 2.11{*}\%BSAexcised + 0.06{*}lengthsurgery - 0.01{*}\%BSAexcised{*}lengthsurgery - ASA2{*}1.02 - ASA3or4{*}0.66$$

Using the logistic function P(blood loss > 250 ml) can be calculated.

$$P(bloodloss > 250ml) = \frac{e^x}{(1 + e^x)}$$

As an example, when planning an excision of 5% BSA, in an ASA 4 patient and an expected surgery time of 100 min:

$$3.02 = -7.87 + 2.11{*}5 + 0.06{*}100 - 0.01{*}5{*}100 - 0{*}1.02 - 1{*}0.66$$

Followed by:

$$0.953 = \frac{e^{3.02}}{(1 + e^{3.02})}$$

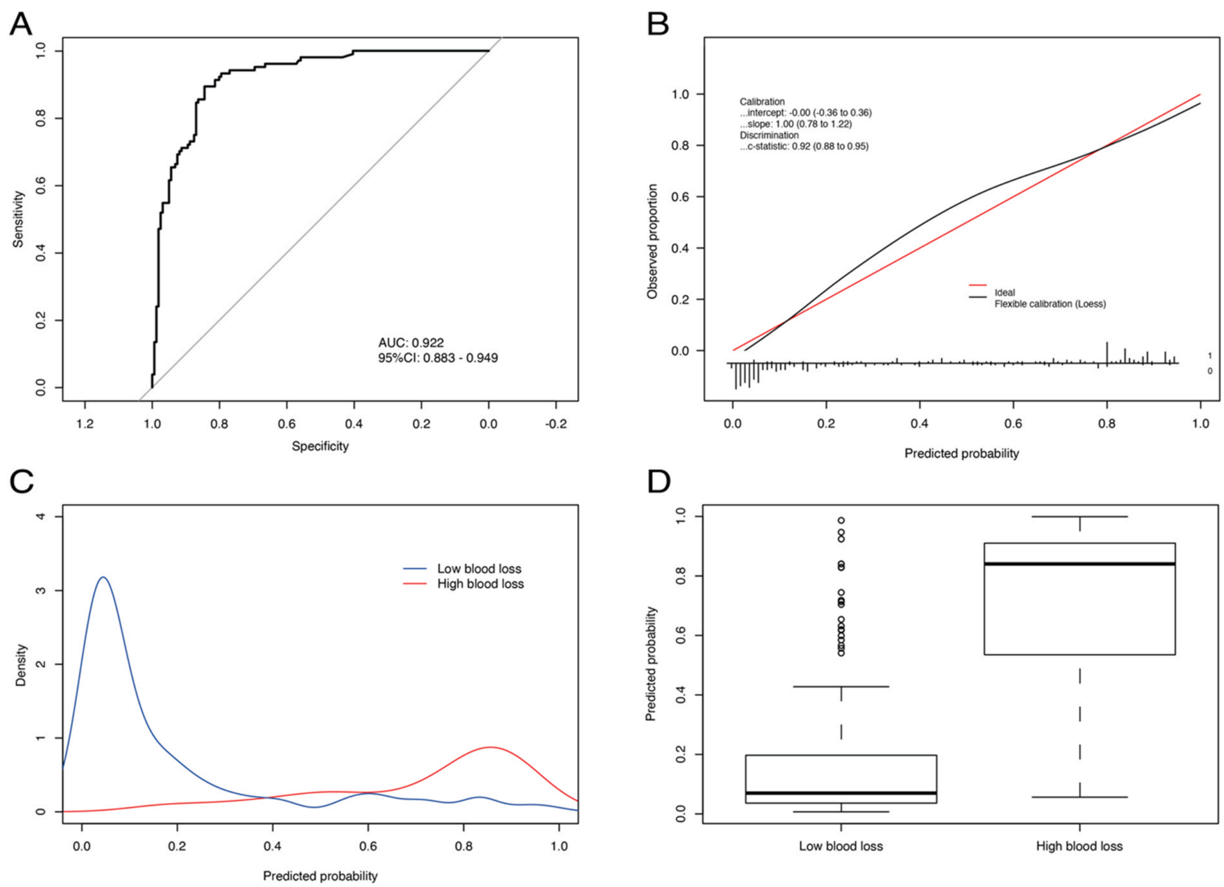

Fig. 3 – . overview of metrics of the predictive model. A: ROC curve of the predictive model.B: Calibration plot of the predictive model C: Density plots showing the distribution of the predicted probabilities for patients with low blood loss (< 250 ml, blue line) and high blood loss (> 250 ml, red line). D: Boxplots of the predicted probabilities for patients with high and low blood loss.

So, a 5% BSA excision in an ASA 4 patient with an expected surgery time of 100 min had a chance of blood loss of > 250 ml of 95.3%. An automated calculator (excel) is included in the appendix to ease the calculation of the risk.

4. Discussion

In this retrospective observational study, median blood loss was 50 ml / % BSA excised and 0.28 ml / cm^2 excised. A substantial part of patients (39%) had significant blood loss of > 250 ml. The median burn size was 4% BSA and median excision size of 2% BSA. A prediction model was developed for predicting the risk for patients of having > 250 ml blood loss during surgery with an AUC of 0.992 (95% CI 0.883 – 0.949) and optimism corrected AUC of 0.915 based on: %BSA excised, length of surgery and patient's ASA-score.

Reported blood loss (0.28 ml/cm^2) is lower compared to recent trials, which reported a blood loss of 0.47–0.8 ml/cm^2 excised [4–6]. Several factors might explain the difference. For example, subtle differences in operation techniques and smaller burns (4% vs. 6–7%) and excision size (2% vs. 3–40%) in our population. Indeed, in the larger excision (> 5% BSA) from our population, blood loss (0.76 (0.53–1)) is more in line with literature (0.47–0.8 ml/cm^2). Furthermore, as described previously, larger burn trauma is an independent risk of blood transfusion and coagulopathy which could contribute to larger blood loss [10,19,20]. While blood sparing techniques were similar, depth and technique of excision were at the discretion of the attending surgeon. As for example, fascial techniques are associated with lower blood loss when compared to tangential excision [21].

To our knowledge this the first model to predict the risk for > 250 ml blood loss during surgery. Identifying burn excisional patients at risk for > 250 ml blood loss is important, as burn patient are often anemic and can therefore drop below the transfusion trigger of 7 g/dl. By identifying these patients, the correct measures can be taken to reduce the perioperative risk. For example, intensive measurement of preoperative and intraoperative hemoglobin, delayed surgery or limit the size of excision. Furthermore, the model can assist the anesthesiologist in pre-emptive blood ordering.

Similar to our model, Farny et al. reported a correlation between ASA-score and length of surgery on the volume of blood loss [4]. Other models have been suggested. Rizzo et al. developed a model to preoperatively predict the number of red blood cell concentrates and fresh frozen plasma needed based on the size of excision [22]. Furthermore, Farny et al.

Table 1 – Patients' characteristics.

Characteristic	n = 269
Male – n (%)	171 (64%)
Female – n (%)	98 (46%)
Age (years) – mean ± SD	48 ± 19
TBSA burned (%) – median (IQR)	4 (1–7)
TBSA excised (%) – median (IQR)	2 (1–4)
ABSI – median (IQR)	6 (6–7)
BAUX – mean ± SD	53 ± 19
Revised-BAUX – mean ± SD	54 ± 20
Inhalation injury – n (%)	16 (6%)
Time after trauma (days) – mean ± SD	15 ± 7
Surgery time (minutes) – median (IQR)	81 (60–108)
Patients receiving transfusion – n (%)	17 (6%)
Postoperative Hb transfused patients (g/dl) – median (IQR)	10.6 ± 2.4
Length of stay hospital (days) – median (IQR)	15 (1–23)
Length of stay ICU (days) (n = 50) – median (IQR)	5 (2–6)
Mechanical ventilation (days) (n = 24) – median (IQR)	4 (2–7)
Mortality – n (%)	1 (< 1%)
Blood loss (ml) – median (IQR)	100 (0–500)
Blood loss / % BSA excised (ml) – median (IQR)	50 (0–150)
Blood loss / cm^2 (ml) – median (IQR)	0.28 (0–0.81)

Abbreviations: TBSA, total body surface area; BSA, body surface area; ABSI, Abbreviated Burn Severity Index; ICU, intensive care unit; IQR, interquartile range 25–75%; SD, standard deviation; Hb, hemoglobin.

Table 3 – Predictive values model for blood loss.

	Coefficient	Odds Ratio (95% CI)	p-value
(intercept)	-7.87		
% BSA excised	2.11	8.24 (4.25–15.90)	< 0.001
Surgery time (min)	0.06	1.06 (1.04–1.09)	< 0.001
ASA-score 2	- 1.02	0.36 (0.15–0.85)	0.019
ASA-score 3 or 4	- 0.66	0.52 (0.15–1.77)	0.293

Abbreviations: BSA, body surface area; min, minutes; ASA-score, American Society of Anesthesiologists Physical Status Classification System. The ASA-score assesses the medical co-morbidities of an individual patients from 1 to 4, a score of 1 represent a normal healthy patient and a score of 4 represent a patient with severe systemic disease.

developed a formula in which the safe excision size without transfusion could be determined based on the preoperative hemoglobin level [4]. Both models of are lacking strategies to evaluate overfitting and internal validation, unlike the model from this study which was corrected for optimism and analyzed for calibration.

The next step for the prediction model is currently being prepared, which is to perform an external validation on data from another burn center to evaluate external validity and generalizability. Hereafter, implementation in practice is feasible as shown by the calculator in the appendix.

In this study, the percentage of patients receiving transfusion is comparable to literature (6 vs 5.7%) in patient with a burn size of < 10% BSA. An interesting detail is that the mean postoperative hemoglobin level in transfused patients was 10.6 ± 2.4 and all were > 7 g/dl which could indicate a too liberal transfusion strategy. The need for reducing the number of erythrocyte transfusions is currently undebated as there is sufficient evidence that a restrictive strategy (threshold > 7 g/dl mmol/L) is safe and beneficial for patients [8,9]. Furthermore, according to a recent study blood transfusions were related to line-/wound infections, sepsis, pneumonia, thrombosis and prolonged hospital and ICU stay [7]. Reducing the number of erythrocyte transfusions during burn excisional surgery can be challenging as seen in our study.

5. Limitations

Limitations of a prediction model are generalizability, and overfitting in which the model performs well on the data provided for training but loses effectiveness on external data. External validation was not performed. However, to reduce the risk of overfitting an optimism correct AUC was calculated and a calibration of the model was performed. The optimism corrected AUC was similar to the unadjusted AUC and the calibration curve showed an intercept of 0.00 and a slope of 1.00. Generalizability will be analyzed in the next step for our model, in which the data will be externally validated on a dataset from another burn center. Due to the retrospective nature of this study, 25 patients were excluded due to missing blood loss in the operation report. Blood loss was missing completely as random. Finally, blood loss is notoriously difficult to measure and to use as primary endpoint. However, the measurement of blood loss was standardized, and the surgical team remained similar during the study period.

Table 2 – Laboratory results.

	n	preoperative	postoperative	p-value
Hemoglobin (mmol/L) – mean ± SD	195 / 84	8.2 ± 1.1	6.6 ± 1.4	**< 0.01**
Hematocrit (L/L) – mean ± SD	193 / 77	0.39 ± 0.05	0.33 ± 0.04	**< 0.01**
Leucocytes (x10e9/L) – median (IQR)	135 / 62	11 (9–14)	10 (8–15)	0.42
INR – median (IQR)	33 / 12	1.1 (1.0–1.2)	1.1(1.0–1.2)	0.70
APTT (s) – median (IQR)	33 / 12	30 (28–35)	30 (26–33)	0.62
Thrombocytes (x10e9/L) – median (IQR)	142 / 62	360 (260–555)	410 (294–537)	0.75

Abbreviations: INR, International Normalized Ratio; APTT, activated partial thromboplastin time; IQR, interquartile range 25–75%; SD, standard deviation.

6. Conclusion

To our knowledge this is the first model developed to predict the chance of blood loss (> 250 ml). Based on %BSA excised, length of surgery and the ASA-score the model can identify patient at risk for > 250 ml blood loss during small burn excisional surgery with an AUC of 0.992. Our model is a step towards improving perioperative care and blood management during burn excisional surgery. Future research will include validation on an external cohort to evaluate the validity and generalizability of our findings.

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Ethics approval

The medical ethical committee of the Maasstad Hospital Rotterdam assessed the study (L2018046) and waived the need for written consent.

CRediT authorship contribution statement

RG was responsible for the manuscript, design, performing statistical analysis and finalization. DT was responsible for design, data gathering and review of the manuscript. MK was responsible for statistical analysis, model development and review of the manuscript. GR and JD were responsible for data gathering and reviewed the manuscript. SK and CV were responsible for the design and reviewed the manuscript.

Competing interest

The authors declare that they have no competing interests.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.burns.2023.01.003.

REFERENCES

[1] Gigengack RK, Verhees V, Koopman-van Gemert AWMM, Oen IMMH, Ossewaarde TM, Koopman SSHA, et al. Cell salvage in burn excisional surgery. Burns 2020. https://doi.org/10.1016/j.burns.2020.06.030
[2] Cartotto R, Musgrave MA, Beveridge M, Fish J, Gomez M. Minimizing blood loss in burn surgery. J Trauma - Inj, Infect Crit Care 2000;49:1034–9. https://doi.org/10.1097/00005373-200012000-00010
[3] Tang YMJ, Chapman TWL, Brooks P. Use of tranexamic acid to reduce bleeding in burns surgery. J Plast, Reconstr Aesthetic Surg 2012;65:684–6. https://doi.org/10.1016/j.bjps.2011.09.028
[4] Farny B, Fontaine M, Latarjet J, Poupelin JC, Voulliaume D, Ravat F. Estimation of blood loss during adult burn surgery. Burns 2018;44:1496–501. https://doi.org/10.1016/j.burns.2018.04.019
[5] Butts CC, Bose K, Frotan MA, Hodge J, Gulati S. Controlling intraoperative hemorrhage during burn surgery: a prospective, randomized trial comparing NuStat® hemostatic dressing to the historic standard of care. Burns 2017;43:374–8. https://doi.org/10.1016/j.burns.2016.08.026
[6] Luo G, Fan H, Sun W, Peng Y, Chen L, Tao J, et al. Blood loss during extensive escharectomy and auto-microskin grafting in adult male major burn patients. Burns 2011;37:790–3. https://doi.org/10.1016/j.burns.2011.01.021
[7] Kaserer A, Rössler J, Slankamenac K, Arvanitakis M, Spahn DR, Giovanoli P, et al. Impact of allogeneic blood transfusions on clinical outcomes in severely burned patients. Burns 2020;46:1083–90. https://doi.org/10.1016/j.burns.2019.11.005
[8] Palmieri TL, Holmes JH, Arnoldo B, Peck M, Potenza B, Cochran A, et al. Transfusion Requirement in Burn Care Evaluation (TRIBE). Ann Surg 2017;266:595–602. https://doi.org/10.1097/SLA.0000000000002408
[9] Palmieri TL. Burn injury and blood transfusion. Curr Opin Anaesthesiol 2019;32:247–51. https://doi.org/10.1097/ACO.0000000000000701
[10] Wu G, Zhuang M, Fan X, Hong X, Wang K, Wang H, et al. Blood transfusions in severe burn patients: Epidemiology and predictive factors. Burns 2016;42:1721–7. https://doi.org/10.1016/j.burns.2016.06.002
[11] Miroshnychenko A, Kim K, Rochwerg B, Voineskos S. Comparison of early surgical intervention to delayed surgical intervention for treatment of thermal burns in adults: a systematic review and meta-analysis. Burns Open 2021;5:67–77. https://doi.org/10.1016/j.burnso.2021.02.003
[12] Ong YS, Samuel M, Song C. Meta-analysis of early excision of burns. Burns 2006;32:145–50. https://doi.org/10.1016/j.burns.2005.09.005
[13] CBO. Richtlijn Bloedtransfusie 2011.
[14] R Core Team. R: A Language And Environment For Statistical Computing. R Foundation for Statistical Computing; 2020.
[15] Robin X, Turck N, Hainard A, Tiberti N, Lisacek F, Sanchez J-C, et al. pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinforma 2011;12:77. https://doi.org/10.1186/1471-2105-12-77
[16] Frank E.Harrel Jr. rms: Regression Modeling Strategies (R Package) 2021.
[17] Cock B. de, Nieboer D., Calster B. van, Steyerberg E., Vergouwe Y. CalibrationCurves (R package) 2018.
[18] Steyerberg EW. Clinical Prediction Models. Cham: Springer International Publishing; 2019. https://doi.org/10.1007/978-3-030-16399-0
[19] Hahn RG. Adverse effects of crystalloid and colloid fluids. Anestezjol Intensywna Ter 2014;49:303–8. https://doi.org/10.5603/AIT.a2017.0045
[20] Glas GJ, Levi M, Schultz MJ. Coagulopathy and its management in patients with severe burns. J Thromb Haemost 2016;14:865–74. https://doi.org/10.1111/jth.13283
[21] Saffle JR. Critical Care Management of the Severely Burned Patient. Critical Care Medicine. Elsevier; 2008. p. 1425–52. https://doi.org/10.1016/B978-032304841-5.50070-4
[22] Rizzo JA, Ross E, Ostrowski ML, Gomez BG, Aden JK, Cap AP. Intraoperative blood transfusions in burn patients. Transfus 2021;61:S183–7. https://doi.org/10.1111/trf.16505