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Intraoperative transfusion practices in Europe

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Abstract

Background: Transfusion of allogeneic blood influences outcome after surgery. Despite widespread availability of transfusion guidelines, transfusion practices might vary among physicians, departments, hospitals and countries. Our aim was to determine the amount of packed red blood cells (pRBC) and blood products transfused intraoperatively, and to describe factors determining transfusion throughout Europe.

Methods: We did a prospective observational cohort study enrolling 5803 patients in 126 European centres that received at least one pRBC unit intraoperatively, during a continuous three month period in 2013.

Results: The overall intraoperative transfusion rate was 1.8%; 59% of transfusions were at least partially initiated as a result of a physiological transfusion trigger- mostly because of hypotension (55.4%) and/or tachycardia (30.7%). Haemoglobin (Hb)- based transfusion trigger alone initiated only 8.5% of transfusions. The Hb concentration [mean (SD)] just before transfusion was 8.1 (1.7) g dl⁻¹ and increased to 9.8 (1.8) g dl⁻¹ after transfusion. The mean number of intraoperatively transfused pRBC units was 2.5 (2.7) units (median 2).

Conclusions: Although European Society of Anaesthesiology transfusion guidelines are moderately implemented in Europe with respect to Hb threshold for transfusion (7–9 g dl⁻¹), there is still an urgent need for further educational efforts that focus on the number of pRBC units to be transfused at this threshold.

Clinical trial registration: NCT 01604083.

Key words: anaemia; anesthesia; blood transfusion; surgery; transfusion trigger

It is now considered good clinical practice to use a restrictive transfusion regimen into clinical pathways in order to minimize unnecessary use of allogeneic blood.^{1–3} This is consistent with the current ‘patient blood management’ (PBM) paradigm, a

multidisciplinary, multimodal approach to best transfusion practice.^{4–6} However, despite the general belief that PBM is useful and improves outcome, implementation of all measures of this package is difficult, time consuming, and as a consequence

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Editor's key points

- There is marked variation in blood transfusion practices.
- Most transfusions given intraoperatively are for hypotension or other indicators of tissue hypoperfusion.
- A transfusion threshold or trigger is less relevant in the intraoperative setting.
- Single unit red cell transfusions should be used more often.

is seldom performed completely.^{6–8} The degree to which guidelines have resulted in consensus in community transfusion practice is unknown. Previous European studies evaluating transfusion practices were limited in size and pertained to a single country.^{9–11} Little is known about the intraoperative transfusion triggers used and the transfusion strategy applied in clinical practice across Europe.¹² Therefore, the primary goal of our study was to assess transfusion triggers and existing transfusion practices and the use of packed red blood cell (pRBC), fresh frozen plasma (FFP), and platelet transfusions in a large sample of European centres.

Methods**Study design and participants**

The ETPOS (European Transfusion Practice and Outcome Study) protocol was designed as a prospective, observational, multicentre European study. Centres volunteered to participate in the study via the homepage of the European Society of Anaesthesiology (ESA). Each centre had to contact the local ethics committee and/or the relevant regulatory approving body in order to determine whether obtaining informed consent was necessary or could be waived. If informed consent was required, only patients that agreed to participate and signed a consent form were included in the study. The inclusion procedure stipulated postoperative informed consent for the usage of data obtained. If a patient died before consent could be obtained, data were not used. No centre started without all mandatory local ethical or regulatory requirements being fulfilled.

All patients undergoing an elective noncardiac surgical procedure at each of the participating hospitals were screened for inclusion. Only patients that received intraoperatively at least one pRBC unit during the study period (April 1st – December 31st, 2013) were included in the analysis. Data acquisition time was three consecutive months for each centre. There were no further specific inclusion criteria. The only exclusion criteria was age <18 yr and cardiothoracic, emergency, or trauma surgery.

Pre-study survey

Each centre participating in the study was asked to fill in a pre-study survey. The main characteristics requested were the size of the hospital (beds), specialities provided, and several aspects of the transfusion regimen and blood management of the hospital.

Data collection

Data were collected on patient characteristics (sex, age, body weight and height); ASA physical status; duration of anaesthesia; type of surgery; usage of point of care coagulation monitoring; laboratory values (Hb, INR, aPTT, platelets, fibrinogen) at beginning of surgery, just before transfusion of first pRBC, and at the end of surgery; reason for the transfusion of the first pRBC (Hb threshold, physiological transfusion triggers, transfusion relevant comorbidities, massive acute bleeding); fluid volume,

blood products, and procoagulant drugs administered until end of surgery [pRBC, crystalloids, colloids, cell saver, FFP, platelet concentrates, tranexamic acid, prothrombin complex concentrate (PCC), fibrinogen, recombinant factor VIIa, cryoprecipitate, factor XIII]; estimated volume loss until end of surgery (blood loss, urine output, other fluids). An overview of the protocol is provided in the appendix.

Primary endpoints were: (i) amount of pRBC and blood products and coagulation factors transfused, and (ii) factors determining transfusion of pRBC and blood products in different regions of Europe.

Data acquisition and quality management

The data collection and management was done using the OpenClinica open source software, version 3.2. (Copyright® OpenClinica LLC and collaborators, Waltham, MA, USA, www.OpenClinica.com). Data were collected on paper by the physician providing anaesthesia and recorded afterwards into the study database. The login names and passwords were provided for registration of patients, monitoring of recruiting progress, query management, and source data verification and an internal communication platform. Automatic data entry plausibility checks and mandatory data items enforced high data quality. Furthermore three different data cleaning runs were done with several checks ensuring high data quality.

Statistical analysis

Our aim was to recruit as many participating hospitals as possible and to recruit every eligible patient receiving at least one pRBC during surgery in those hospitals. We anticipated that a minimum sample size of 10 000 patients would enable a precise estimate of current transfusion triggers throughout Europe. Therefore we aimed at 100 participating centres providing 100 patients each. This sample size was also expected to provide sufficient data to be able to describe transfusion practices in different settings.

We used SPSS (version 21.0) for data analysis. Categorical variables are presented as number (%) and continuous variables as mean (SD) when normally distributed or median (IQR) when not.

This study is registered with ClinicalTrials.gov, number NCT01604083.

Role of the funding source

The study was funded by a grant of the ESA Clinical Trial Network. An independent steering committee was responsible for study design, conduct, and data analysis. Members of the steering committee had full access to the study data and were solely responsible for interpretation of the data, drafting and critical revision of the report, and the decision to submit for publication.

Results

One hundred and twenty six hospitals of 30 European countries participated in the study (overview is given in the appendix).

Pre-study survey

An overview of the parameters included in the pre-study survey is given in Table 1.

Of the 126 centres with valid patients all 126 filled in the pre-study survey (with one being incomplete). Approximately a third of the centres ($n=40$) had less than 500 beds, 50 (40%) had between 500 and 1000 beds and 36 (28%) had more than 1000 beds.

Table 1 Prestudy survey of participating hospitals (n=126): casemix, haemostasis and transfusion practices. Values are given as median (IQR) or %. INR, international normalized ratio, apTT, partial thromboplastin time, ACT, activated clotting time, TEG, thrombelastography, TEM, thrombelastometry; percentage values do not necessarily add up to 100% as multiple selections were possible

| Hospital characteristics | |
|--|----------------------------------|
| Beds | |
| <500 | 40 |
| 501–999 | 50 |
| >1000 | 36 |
| no. of operating theatres | 18 (10–26) |
| no. of surgical procedures per yr (estimation) | 15 000 (7050–25 000) |
| no. of board certified anaesthetists | 26 (13–47) |
| no. of anaesthetists in training | 17 (7–30) |
| Hospital specialities | |
| Orthopaedics | 88% |
| Visceral surgery | 89% |
| Urology | 86% |
| Gynaecology | 90% |
| Vascular Surgery | 79% |
| Trauma | 80% |
| Ear Nose Throat | 84% |
| Thoracic Surgery | 63% |
| Cardiac Surgery | 51% |
| Neurosurgery | 67% |
| Hepato – biliary surgery | 83% |
| Dental surgery | 64% |
| Plastics | 74% |
| Ophthalmology | 73% |
| Estimated % of patients prepared with . . . | |
| Oral iron | 1 (0–5) |
| i.v. iron | 1 (0–2) |
| Erythropoietin | 0 (0–1) |
| Perioperative haemostasis monitoring | |
| - conventional monitoring | 90% |
| - INR | 90% |
| - apTT | 85% |
| - fibrinogen | 80% |
| - platelets | 90% |
| - ACT | 24% |
| Point of care monitoring | |
| - INR/apTT | 18% |
| - TEG | 16% |
| - ROTEM | 30% |
| - Multiplate, Verify Now, Platelet Mapping | 14% |
| Massive transfusion | |
| % of hospitals with transfusion protocols | |
| - based on packages | 21% |
| - based on ratios | 27% |
| - based on conventional coagulation tests | 50% |
| - based on POC testing | 31% |
| - based on experience | 37% |
| Transfusion regimen | |
| - for pRBCs | liberal: 30% restrictive: 63% |
| - for FFPs | liberal: 31% restrictive: 63% |

Continued

Table 1 Continued

| | |
|------------------------------------|----------------------------------|
| - for coagulation factors | liberal: 12% restrictive: 82% |
| - for platelets | liberal: 13% restrictive: 80% |
| Transfusion practice | |
| - leukocyte reduced pRBCs used | 54% |
| - non-leukocyte reduced pRBCs used | 46% |
| - cryoprecipitates used | 48% |

Table 2 Patient and perioperative characteristics (n=5803)

| Variable | |
|----------------------------------|-------------|
| Age (yr) | 63.7 (16.1) |
| Male | 49% |
| BMI | 26.2 (5.3) |
| ASA physical status | |
| I | 5.5% |
| II | 31.0% |
| III | 45.9% |
| IV | 16.5% |
| V | 1.1% |
| Type of surgery | |
| Orthopaedic | 21.6% |
| Lower gastrointestinal | 12.4% |
| Vascular | 9.9% |
| Upper gastrointestinal | 9.3% |
| Hepatobiliary | 7.9% |
| Gynaecological | 7.5% |
| Urological | 6.7% |
| Others | 24.7% |
| Cancer Surgery | 36.8% |
| Duration of Surgery (h) | 4.1 (2.7) |
| Point of Care Device used | 15.6% |

The median number of operating theatres in each hospital was 18 (10–20). Most centres reported a higher number of board certified anaesthetists than anaesthetists in training. All relevant specialities were covered by the participating hospitals. A negligible amount of centres reported that they used measures to pre-optimize their patients before surgery with either iron or erythropoietin. Conventional coagulation tests were used by more than 90% of the centres, whereas point of care monitoring systems were implemented only by 14–30% of the centres depending on the specific monitoring device. Fifty seven percent of the hospitals use transfusion protocols, the majority of them based on conventional (laboratory) coagulation tests. Sixty three percent of the hospitals reported having a restrictive transfusion protocol implemented for pRBC, 63% for FFP, 82% for platelets and 80% for coagulation factors.

General data

In total 373 732 patients were screened (Table 2). The first patient was enrolled on April 1st, 2013, and the last patient December 31st, 2013. Data were obtained for 5929 patients for whom informed consent was obtained or waived, of which 126 were excluded, having been identified as duplicates or having missing transfusion data, leaving 5803 subjects for analysis (Table 1). A mean number of 45 (range: 1–165) patients were included per

Table 3 Transfusion data (n=5803). Values are reported as mean (sd). Hb, haemoglobin. INR, international normalized ratio, aPTT, activated partial thromboplastin time

| Variable | No. | Value |
|-------------------------------------|------|-------------|
| Estimated blood loss (ml) | | 1392 (2040) |
| Begin of surgery | | |
| Hb (g dl ⁻¹) | 5674 | 10.6 (2.4) |
| INR (%) | 4500 | 1.2 (0.5) |
| aPTT (sec) | 4004 | 33 (17) |
| Platelets (n microl ⁻¹) | 5180 | 265 (132) |
| Fibrinogen (mg dl ⁻¹) | 1838 | 400 (177) |
| Just before transfusion | | |
| Hb (g dl ⁻¹) | 3977 | 8.1 (1.7) |
| INR (%) | 630 | 1.4 (0.9) |
| aPTT (s) | 570 | 43 (38) |
| Platelets (n microl ⁻¹) | 844 | 209 (127) |
| Fibrinogen (mg dl ⁻¹) | 481 | 297 (174) |
| End of surgery | | |
| Hb (g dl ⁻¹) | 4352 | 9.8 (1.8) |
| INR (%) | 1985 | 1.4 (4.7) |
| aPTT (s) | 1944 | 38 (27) |
| Platelets (n microl ⁻¹) | 2639 | 202 (119) |
| Fibrinogen (mg dl ⁻¹) | 1402 | 307 (163) |

Table 4 Blood product volume administered. pRBC, packed red blood cells, FFP, fresh frozen plasma, PCC, prothrombin complex concentrates

| Blood product | Patients | Amount administered |
|------------------------|----------|---------------------|
| pRBC –intraoperative | 100% | 2.5 (2.7) units |
| Crystalloids | 99% | 2434 (1784) ml |
| Colloids | 65% | 907 (711) ml |
| Cell Saver blood | 6% | 1116 (1388) ml |
| FFP | 31% | 4.5 (5.9) units |
| Platelet concentrate | 7% | 3.0 (4.1) units |
| Tranexamic acid | 13% | 1.4 (1.0) g |
| PCC | 2% | 1846 (1476) I.U. |
| Fibrinogen concentrate | 5% | 3.2 (2.4) g |
| Cryoprecipitate | 1% | 7.2 (5.8) units |
| Factor XIII | <1% | 2119 (1338) I.U. |
| pRBC –postoperative | 56% | 3.7 (4.1) units |

hospital and 193 (range: 5–783) per country. The study included almost equal numbers of females and males, with a mean age of 64 (13; range 18–100) yr, approximately half of whom were categorized into ASA class III. Orthopaedic and lower gastrointestinal surgery were performed most frequently and around third of the operations were for cancer. A point of care device for monitoring of blood coagulation was used in 15.6% of patients.

Course of transfusion

The mean reported blood loss was 1392 (2040) ml (Table 3). In general, 82% of the patients were anaemic as defined by the WHO criteria (male <13 g dl⁻¹, female <12 g dl⁻¹) preoperatively with baseline (pre-surgery) Hb concentration of 10.6 (2.4) g dl⁻¹. Before transfusion of the first pRBC, measured Hb concentration was 8.1 (1.7) g dl⁻¹ and increased to 9.8 (1.8) g dl⁻¹ at the end of surgery. The mean number of transfused pRBC was 2.5 (2.7) units (Median

Table 5 Reasons for transfusion of first packed red blood cell unit. Hb, haemoglobin; SvO₂, mixed venous oxygen saturation, ScvO₂, central venous oxygen saturation

| | |
|---|-------|
| Hb alone | 8.5% |
| Hb & physiological trigger | 8.2% |
| Hb & comorbidity | 8.7% |
| Hb & physiological trigger & comorbidity | 11.4% |
| physiological trigger irrespective of Hb | 14.3% |
| physiological trigger & comorbidity | 12.5% |
| physiological trigger & blood loss | 7.1% |
| physiological trigger & blood loss & comorbidity | 5.4% |
| Comorbidity alone | 5.3% |
| Hb & physiological trigger & blood loss & comorbidity | 4.6% |
| other combinations | 14% |
| Physiological transfusion triggers | |
| Hypotension | 55.4% |
| Tachycardia | 30.7% |
| Acidosis | 7.8% |
| Lactate | 7.3% |
| Arrhythmia | 5.1% |
| ECG | 2.7% |
| ScvO ₂ or SvO ₂ | 3.4% |
| Other | 10.2% |
| Comorbidity | |
| Cardiovascular | 35.7% |
| Renal | 8.1% |
| Pulmonary | 7.7% |
| Haematological | 6.9% |
| Gastrointestinal | 6.4% |
| Others | 8.6% |

2 [IQR 2–2]). One third of patients received 1 pRBC and 41% of patients received 2 pRBC. There was no correlation between the Hb concentration before transfusion or at the end of surgery and the amount of pRBC units administered (correlation coefficient –0.1 and –0.2, respectively). Conventional coagulation tests varied only slightly over time.

Thirty one percent of patients received FFP and 7% of patients received platelets. In patients receiving FFP the mean amount administered was 4.5 (5.9) units and with platelets the mean amount was 3.0 (4.1) units. An overview for all other fluids administered is given in Table 4.

Reason for transfusion

An overview of the rationales for transfusion is given in Table 5. The most prevalent basis for transfusion of the first pRBC was the occurrence of a physiological transfusion trigger (14.3%). The second most important reason was the combination of a physiological transfusion trigger with a suspected or known comorbidity (12.5%). In total 58.9% were transfused at least in part as a result of a physiological transfusion trigger. Only 8.5% of transfusions have been administered solely because of an Hb-based transfusion trigger. If an Hb based transfusion trigger was used, the physician chose an Hb value of 8.1 (1.3) g dl⁻¹. Notably, most of the physiological transfusion triggers were not lactic acidosis (7.3%) or a decline of ScvO₂ (1.3%) but hypotension (55.4%) and tachycardia (30.7%). The most important comorbidity resulting in transfusion was cardiovascular (35.7%), whereas all other comorbidities were uncommon (<9%). Regression analysis found that the amount of pRBC administered decreased with age of patients, and was also not affected by the type of surgery.

Table 6 Perioperative characteristics according to self-reported restrictive or liberal red cell transfusion strategy. pRBC, packed red blood cells, FFP, fresh frozen plasma

| | Restrictive (n=3738) | Liberal (n=2065) | P value |
|--|----------------------|------------------|---------|
| Haemoglobin value (g dl⁻¹) | | | |
| Beginning of surgery | 10.6 (2.5) | 10.8 (2.4) | 0.0004 |
| Just before transfusion | 8.0 (1.7) | 8.4 (1.6) | 0.0000 |
| End of surgery | 9.6 (1.7) | 10.1 (1.8) | 0.0000 |
| Units administered | | | |
| pRBC –intraoperative | 2.4 (2.5) | 2.7 (2.5) | 0.0000 |
| FFP | 4.1 (5.3) | 5.2 (6.7) | 0.0003 |
| Platelet concentrate | 3.1 (4.4) | 2.9 (3.7) | 0.89 |
| pRBC –postoperative | 1.9 (3.4) | 2.3 (3.9) | 0.0008 |
| Estimated blood loss | 1382 (2060) ml | 1408 (2006) ml | 0.22 |

Furthermore, the country had a minimal role, with only two pairwise comparisons between countries being statistically significant although of arguable clinical relevance. The size of the hospital and academic degree did not influence transfusion practice. Differences between single hospitals have were not analysed because of insufficient sample sizes.

Hospitals with different transfusion strategies

Sixty three percent of all hospitals stated to have a restrictive transfusion strategy in the pre-study survey, in contrast to the 37% with a liberal transfusion strategy. Hospitals with a restrictive strategy treated 64% of patients. Indeed, hospitals claiming a more restrictive strategy tended to transfuse at lower Hb concentrations and accept a lower Hb value post-transfusion. As a consequence, in these hospitals significantly less transfusions were needed despite comparable blood loss in both groups. Furthermore less postoperative transfusions and less substitution of FFP coagulation factors were necessary in the restrictive group (Table 6).

Discussion

It has been previously demonstrated that transfusion practice differs between different physicians, centres, and countries.^{9–11 13} For elective surgery, the hospital might therefore be the most important determinant of the number of administered transfusions, with some adopting programmes to reduce transfusions, while others negating the importance of PBM measures on perioperative outcome.¹⁴ There is growing evidence that a restrictive transfusion strategy can be used in most clinical settings, with published guidelines focusing on PBM of the surgical patient.^{2 4}

We found that blood transfusions are rarely used in most surgical procedures, with only 1.8% transfused intraoperatively with pRBC. The intraoperative transfusion rate will depend, among other things, on a hospital's surgical casemix and transfusion practices. In the current study the pre-transfusion Hb concentration averaged 8.1 (1.7) g dl⁻¹. A Hb trigger of 7–9 g dl⁻¹ has been recommended during active bleeding by ESA guidelines.¹⁵ Thus, the old commonly used Hb threshold of 10 g dl⁻¹ is no longer the 'magic number' for transfusion, with European centres now practicing according to current transfusion guidelines, at least in the intraoperative period. The post-transfusion Hb, though, was unnecessarily high (9.8 (1.8) g dl⁻¹), suggesting that the decision to transfuse led to more than 1 pRBC unit at a time. Some hospitals that claimed to have a restrictive transfusion strategy transfused at rather high Hb concentrations. There is thus still

a need for further educational efforts that focus restrictive transfusion approach and on the number of pRBC units to be transfused at this threshold.

The primary rationale for pRBC transfusion has not been previously studied in depth. The current study found that the most frequent triggers for pRBC administration are physiological parameters; 8.5% of transfusions were initiated based only on Hb value. It is worth noticing that if a physiological transfusion trigger had been used, the Hb value chosen for transfusion was 8.1 (1.3) g dl⁻¹, a level very close to the Hb value just before transfusion of the first pRBC in all patients. This fact suggests that in reality many clinicians use the Hb value as an adjunctive ('hidden') transfusion trigger, even if physiological triggers are believed to be the primary trigger. The physiological parameters used to trigger transfusion in the majority of patients were hypotension and tachycardia. The triggers with the highest discriminatory power to manifest tissue hypoxia (e.g. lactate and mixed venous central or central venous saturation) played only a secondary role. This may reflect the tendency of many anaesthetists to use the most easily accessible parameters (heart rate and bp) rather than those that require additional invasive catheters. It may also reflect the emphasis anaesthetists give to maintenance of haemodynamic stability, with less focus on tissue oxygenation.

Preoperative anaemia is one of the most important determinants of intraoperative transfusion, and therefore it had been recommended that elective surgery of anaemic patients should be postponed to enable adequate patient preparation.¹⁶ Furthermore, it has been demonstrated, that even mild or moderate preoperative anaemia is associated with significant morbidity and mortality.¹⁷ Therefore, PBM guidelines state that preoperative optimization of Hb is recommended to avoid unnecessary transfusions.^{1 2 4 6 18 19} The present study found that the majority of centres have not adopted this recommendation. Only 1% of centres prepared their patients with oral/i.v. iron and/or erythropoietin. As 82% of transfused patients in the current study were anaemic at the beginning of the surgery, it may be hypothesized that preoperative Hb optimization could have avoided transfusion to a certain extent. Because of the small number of patients that were pre-treated for their anaemia, we cannot determine whether those patients were less likely to be transfused.

Previous studies suggest that often more than 1 unit of pRBC are transfused once a decision to administer blood has been made, in part because of blood allocation strategies.²⁰ In our study more than 40% of patients had two pRBC units transfused; as less than 25% of patients received three or more units of pRBC it can be speculated that because two pRBC units is often ordered

initially, they were given as package. To overcome this problem Australia initiated a campaign, known as the 'one unit policy' where Hb levels are measured after each pRBC administered to determine the necessity for further transfusion. The results of the present study suggest that a similar campaign should be implemented across Europe.

In our study the mean estimated blood loss was 1392 (2040) ml, reflecting a high variability in blood loss, which warrants cautious interpretation of our data. Unlike in trauma, where massive transfusion protocols have been developed and shown to improve outcome,²¹ protocols for the administration of blood products in the actively bleeding patient in the operating room are missing. Modern guidelines promote use of a point of care monitoring and coagulation factor-based bleeding management.¹⁵ This was not the case in the present study. Almost half of the patients received FFP, platelet concentrates or coagulation factor concentrates. FFP, despite several adverse effects and poor efficacy²² is still the most commonly used agent during intraoperative bleeding, whereas in five percent and two percent of patients fibrinogen concentrate and PCC were used, respectively. Parameters of routine coagulation tests did not reveal coagulopathy either preoperatively and at the end of surgery. However, as immediate pre-transfusion coagulation tests were not documented for participating patients, conclusion regarding the appropriateness of the administration of FFP, platelets or coagulation factors cannot be made.

Our study has some limitations. We recorded selected data and might therefore miss some of the factors that might influence transfusion habits. We did not collect data on those not transfused intraoperatively, not in those transfused before or after surgery. We did not find clinically relevant differences between countries. As centres participating and procedures included varied essentially from country to country, differences in transfusion habits might be more centre-specific than country-specific.

Conclusion

Across Europe, the vast majority of elective surgical patients receiving one or more units of RBC intraoperatively are anaemic at the commencement of surgery (Hb 10.6 g dl⁻¹), and correction of anaemia before surgery deserves further study. Although the transfusion trigger (Hb 8.1 g dl⁻¹) is probably appropriate intraoperatively, post-transfusion Hb values were uniformly high (Hb 9.8 g dl⁻¹) suggesting opportunity to use a single unit transfusion stratagem. Physiological transfusion triggers seem to be the most important catalyst for transfusion intraoperatively. But the physiological triggers mainly used (hypotension and tachycardia) might have a low discriminative power for tissue hypoperfusion and often occur at Hb values that are considered safe for tissue oxygenation in most patients.

Authors' contributions

Study design/planning: all authors
 Study conduct: all authors and collaborators
 Data analysis: all authors
 Writing paper: all authors
 Revising paper: all authors

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Declaration of interest

None declared.

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| Serrano | Helena | Hospital Vall d Hebron | Spain |
| Shmigelsky | Alexander | Burdenko Neurosurgery Institute | Russia |
| Silva | Luisa | Hospital da Universidade de Coimbra | Portugal |
| Simeson | Karen | Mid Yorkshire Hospitals NHS Trust; Pinderfields Hospital | United Kingdom |
| Singh | Rita | Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton | United Kingdom |
| Sipylaite | Jurate | Vilnius University Hospital - Santariskiu Clinics | Lithuania |
| Skitek | Kornel | Carl – Thiem Klinikum Cottbus | Germany |
| Skok | Ira | University Hospital "Sveti Duh" | Croatia |

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|---------------------------|---------------------|--|---------------------------|
| Smékalová | Olga | Faculty Hospital Brno | Czech Republic |
| Smirnova | Nadezda | North Estonian Center | Estonia |
| Sofia | Machado | Hospital Clínico Universitario de Valencia | Spain |
| Soler Pedrola: | Maria | Hospital Son Llatzer | Spain |
| Söndergaard | Sören | Sahlgrenska University Hospital | Sweden |
| Sörmus | Alar | Tartu University Hospital | Estonia |
| Sørvoll | Ingvild Hausberg | University Hospital of North Norway, Tromsø | Norway |
| Soumelidis | Christos | Ippokrateio Hippokrateion General Hospital of Thessaloniki | Greece |
| Spindler Yesel | Alenka | University Medicine Centre Ljubljana | Slovenia |
| Stefan | Mihai | Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu" | Romania |
| Stevanovic | Ana | University Hospital Aachen | Germany |
| Stevikova | Jordana | Faculty hospital, Nitra , Slovak republic | Slovakia |
| Stivan | Sabina | University Medicine Centre Ljubljana | Slovenia |
| Štourač | Petr | Faculty Hospital Brno | Czech Republic |
| Striteska | Jana | University Hospital Hradec Kralove | Czech Republic |
| Strys | Lydia | University Medical Center Johannes Gutenberg Mainz | Germany |
| Suljevic | Ismet | University Clinical Center Sarajevo | Bosnia and Herzegovina |
| Tania | Moreno | Hospital Clínico Universitario de Valencia | Spain |
| Tareco | Gloria | Hospital do Espirito Santo - Évora, E.P.E. | Portugal |
| Tena | Beatriz | Hospital Clinic Barcelona | Spain |
| Theodoraki | Kassiani | Aretaieion University Hospital | Greece |
| Tifrea | Marius | Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu" | Romania |
| Tikuisis | Renatas | Vilnius University Hospital - Institute of Oncology | Lithuania |
| Tolós | Raquel | Hospital Universitari Germans Trias I Pujol | Spain |
| Tomasi | Roland | University Hospital Munich | Germany |
| Tomescu | Dana | Fundeni Clinical institute - Intensive Care Unit | Romania |
| Tomkute | Gabija | Vilnius University Hospital - Santariskiu Clinics | Lithuania |
| Tormos | Pilar | Hospital Vall d Hebron | Spain |
| Trepenaitis | Darius | Kaunas Medical University Hospital, Hospital of Lithuanian University of Health Sciences | Lithuania |
| Troyan | Galina | Zaporizhzhia State Medical University | Ukraine |
| Unic-Stojanovic | Dragana | Cardiovascular Institute Dedinje Belgrade | Serbia |
| Unterrainer | Axel | Christian-Doppler-Klinik | Austria |
| Uranjek | Jasna | General Hospital Slovenj Gradec | Slovenia |
| Valsamidis | Dimitrios | "Alexandra" General Hospital of Athens | Greece |
| van Dasselaaar | Nick | Reinier De Graaf Gasthuis Delft | Netherlands |
| Van Limmen | Jurgen | Ghent University Hospital | Belgium |
| van Noord | Peter | Maastricht University Medical Center | Netherlands |
| van Poorten | J.F. | Reinier De Graaf Gasthuis Delft | Netherlands |
| Vanderlaenen | Margot | ZOL Genk- St Jan Hospital Genk | Belgium |
| Varela Garcia | Olalla | Hospital do Meixoeiro (Complexo Hospitalario Universitario de Vigo) | Spain |
| Velasco | Ana | Hospital Universitario Lucus Augusti | Spain |
| Veljovic | Milic | Military Medical Academy | Serbia |
| Vera Bella | Jorge | Hospital San Jorge | Spain |
| Vercauteren | Marcel | UZA | Belgium |
| Verdouw | Bas | Reinier De Graaf Gasthuis Delft | Netherlands |
| Verenkin | Vladimir | Tel Aviv Medical Center | Israel |
| Veselovsky | Tomas | St. Elizabeth s Cancer Institute and Medical faculty of Comenius University Bratislava, | Slovakia |
| Vieira | Helena | Hospital da Universidade de Coimbra | Portugal |
| Villar | Tania | Hospital Mar-Esperança. Parc de Salut Mar | Spain |
| Visnja | Ikcic | University Clinical Hospital Osijek | Croatia |
| Voje | Minca | University Medicine Centre Ljubljana | Slovenia |
| von Dossow- Hanfstingl | Vera | University Hospital Munich | Germany |
| Von Langen | Daniel | Medical University Hospital Innsbruck | Austria |
| Vorotyntsev | Sergiy | Zaporizhzhia State Medical University | Ukraine |
| Vujanović | Vojislav | University Hospital Banja Luka | Bosnia and Herzegovina |
| Vukovic | Rade | Military Medical Academy | Serbia |

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| Watt | Philip | Kettering General Hospital NHS Foundation Trust | United Kingdom |
| Werner | Eva | University Hospital Regensburg | Germany |
| Wernerman | Jan | Karolinska University Hospital Huddinge | Sweden |
| Wittmann | Maria | University Hospital Bonn | Germany |
| Wright | Margaret | Hospital James Paget University Hospital NHS Foundation Trust | United Kingdom |
| Wunder | Christian | University Hospital of Wuerzburg | Germany |
| Wyffels | Piet | Ghent University Hospital | Belgium |
| Yakymenko | Yevgen | Zaporizhzhia State Medical University | Ukraine |
| Yıldırım | Çiğdem | Ankara University Faculty of Medicine | Turkey |
| Yilmaz | Hakan | Ufuk University Hospital | Turkey |
| Zacharowski | Kai | University Hospital Frankfurt | Germany |
| Záhorec | Roman | St. Elizabeth s Cancer Institute and Medical faculty of Comenius University Bratislava | Slovakia |
| Zarif | Maged | Hospital da Universidade de Coimbra | Portugal |
| Zielinska - Skitek | Ewa | Carl – Thiem Klinikum Cottbus | Germany |
| Zsisku | Lajos | Colchester Hospital University Foundation Trust | United Kingdom |