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# Intraoperative transfusion practices in Europe

J. Meier<sup>1,\*</sup>, D. Filipescu<sup>2</sup>, S. Kozek-Langenecker<sup>3</sup>, J. Llau Pitarch<sup>4</sup>, S. Mallett<sup>5</sup>, P. Martus<sup>6</sup> and I. Matot<sup>7</sup> and the ETPOS collaborators

<sup>1</sup>Clinic of Anesthesiology and Intensive Care Medicine, Faculty of Medicine of the Kepler University Linz, Linz, Austria, <sup>2</sup>Emergency Institute of Cardiovascular Disease, University Bucharest, Bucharest, Romania, <sup>3</sup>Department of Anesthesiology and Intensive Care Medicine, EKH Evangelic Hospital Vienna, Vienna, Austria, <sup>4</sup>Department of Anesthesiology and Intensive Care Medicine, Hospital Clínico Universitario de Valencia, Valencia, Spain, <sup>5</sup>Department of Anesthesiology, Royal Free Hospital Hampstead NHS Trust, London, UK, <sup>6</sup>Clinical Epidemiology, Eberhard Karls University Tübingen, Tübingen, Germany, and <sup>7</sup>Department of Anesthesiology & Intensive Care Medicine & Pain, Tel Aviv Medical Centre, Tel Aviv, Israel

\*Corresponding author. E-mail: jens.meier@gmail.com

#### 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<sup>-1</sup> and increased to 9.8 (1.8) g dl<sup>-1</sup> 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<sup>-1</sup>), 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.<sup>1–3</sup> This is consistent with the current 'patient blood management' (PBM) paradigm, a

multidisciplinary, multimodal approach to best transfusion practice.<sup>4–6</sup> 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.<sup>6–8</sup> 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.<sup>9–11</sup> Little is known about the intraoperative transfusion triggers used and the transfusion strategy applied in clinical practice across Europe.<sup>12</sup> 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 prestudy 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, cryopreciptate, 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 Open-Clinica open source software, version 3.2. (Copyright<sup>®</sup> 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 prestudy 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.

liberal: 12%

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	15,000 (7050, 25,000)
(estimation)	13 000 (7030-23 000)
no. of board certified anaesthetists	26 (13–47)
no. of anaesthetists in training	17 (7–30)
Hospital specialties	, <i>,</i>
Orthopaedics	88%
Visceral surgery	89%
Urology	86%
Gynaecology	90%
Vascular Surgery	79%
Trauma	80%
Far Nose Throat	84%
Thoracic Surgery	62%
Cordina Surgery	03/0 E19/
Neuroeurgery	51%
Neurosurgery	07 %
Hepato – biliary surgery	83%
Dental surgery	64%
Plastics	/4%
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	
<ul> <li>conventional monitoring</li> </ul>	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	
nrotocols	57%
protocols based on packages	21%
- based on ratios	∠⊥/0 079/
- based on radios	2170
- based on conventional coagulation	50%
tests	010/
- based on POC testing	31%
- based on experience	3/%
Transfusion regimen	
- tor pRBCs	liberal: 30%
	restrictive: 63%
- for FFPs	liberal: 31%
	restrictive: 63%
	Continued

# Table 1 Continued - for coagulation factors

- for platelets	restrictive: 82% liberal: 13% restrictive: 80%
Transfusion practice	
<ul> <li>leukocyte reduced pRBCs used</li> </ul>	54%
- non-leukocyte reduced pRBCs used	46%
- cryoprecitates 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 <sup><math>-1</math></sup> )	5674	10.6 (2.4)
INR (%)	4500	1.2 (0.5)
aPTT (sec)	4004	33 (17)
Platelets (n microl <sup>-1</sup> )	5180	265 (132)
Fibrinogen (mg dl <sup>-1</sup> )	1838	400 (177)
Just before transfusion		
Hb (g dl <sup><math>-1</math></sup> )	3977	8.1 (1.7)
INR (%)	630	1.4 (0.9)
aPTT (s)	570	43 (38)
Platelets (n microl <sup>-1</sup> )	844	209 (127)
Fibrinogen (mg dl <sup>-1</sup> )	481	297 (174)
End of surgery		
Hb (g dl <sup><math>-1</math></sup> )	4352	9.8 (1.8)
INR (%)	1985	1.4 (4.7)
aPTT (s)	1944	38 (27)
Platelets (n microl <sup>-1</sup> )	2639	202 (119)
Fibrinogen (mg dl <sup>-1</sup> )	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<sup>-1</sup>, female<12 g dl<sup>-1</sup>) preoperatively with baseline (pre-surgery) Hb concentration of 10.6 (2.4) g dl<sup>-1</sup>. Before transfusion of the first pRBC, measured Hb concentration was 8.1 (1.7) g dl<sup>-1</sup> and increased to 9.8 (1.8) g dl<sup>-1</sup> 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;  $Sv_{O_2}$ , mixed venous oxygen saturation,  $ScvO_2$ , 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 <sub>2</sub> or Sv <sub>O2</sub>	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 Hbbased 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  $ScvO_2$  (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.

	Restrictive (n=3738)	Liberal (n=2065)	P value
Haemoglobin value (g dl <sup>-1</sup> )			
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

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

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.<sup>9–11 13</sup> 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.<sup>14</sup> There is growing evidence that a restrictive transfusion strategy can be used in most clinical settings, with published guide-lines focusing on PBM of the surgical patient.<sup>24</sup>

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<sup>-1</sup>. A Hb trigger of 7–9 g dl<sup>-1</sup> has been recommended during active bleeding by ESA guidelines.<sup>15</sup> Thus, the old commonly used Hb threshold of 10 g dl<sup>-1</sup> 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<sup>-1</sup>), 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<sup>-1</sup>, 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.<sup>16</sup> Furthermore, it has been demonstrated, that even mild or moderate preoperative anaemia is associated with significant morbidity and mortality.<sup>17</sup> Therefore, PBM guidelines state that preoperative optimization of Hb is recommended to avoid unnecessary transfusions.<sup>1 2 4 6 18 19</sup> 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.<sup>20</sup> 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,<sup>21</sup> 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.<sup>15</sup> 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 efficacy<sup>22</sup> 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<sup>-1</sup>), and correction of anaemia before surgery deserves further study. Although the transfusion trigger (Hb 8.1 g dl<sup>-1</sup>) is probably appropriate intraoperatively, post-transfusion Hb values were uniformly high (Hb 9.8 g dl<sup>-1</sup>) 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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Handling editor: P. S. Myles

# Complete list of collaborators to be cited in Pubmed in alphabetical order

All members of the collaborators were involved in patient recruitment and data collection

Accurso	Giuseppe	Policlinico "P Giaccone" (University of Palermo)	Italy
Ahrens	Norbert	University Hospital Regensburg	Germany
Akan	Mert	Dokuz Eylul University Medicine Faculty	Turkey
Åkeröy	Kristin	Sahlgrenska University Hospital	Sweden
Aksov	Omur	Istanbul University, Istanbul Medical Faculty	Turkey
Alanoğlu	Zekeriyye	Ankara University Faculty of Medicine	Turkey
Alfredo	Merten	Hospital Santa Creu I Sant Pau	Spain
Alkis	Neslihan	Ankara University Faculty of Medicine	Turkev
Almeida	Valentina	Hospital da Universidade de Coimbra	Portugal
Alousi	Mohammed	Roval Free Hospital Hampstead Nhs Trust	United Kingdom
Alves	Claudia	Hospital da Universidade de Coimbra	Portugal
Amaral	Ioana	Hospital do Espirito Santo - Évora, E.P.E.	Portugal
Ambrosi	Xavier	University Hospital Nantes-Hopital G et R Laënnec	France
Ana	Izavierdo	Hospital Clínico Universitario de Valencia	Spain
Anastase	Denisa	Orthopedics Hospital FOISOR	Romania
Andersson	Mona	Centralsiukhuset Kristianstad	Sweden
Andreou	Antonis	General air force hospital	Greece
Anthopoulos	Georgios	General air force hospital	Greece
Ananaviciute	Daiva	Kaunas Medical University Hospital Hospital of Lithuanian University	Lithuania
ripuliuviciate	Duiva	of Health Sciences	Intritutina
Arbelaez	Aleiandro	Hospital Vall d Hebron	Snain
Arcade	Anne-Laure	University Hospital of Poitiers	France
Arion-Balescu	Carmen	Prof D Gerota Hospital	Romania
Ariin	Oguzhan	Selcuk university faculty of medicine	Turkey
Azenha	Marta	Hospital da Universidade de Coimbra	Portugal
Bacalbasa	Nicolae	St. Andrei Emergency County Hospital Calati	Romania
Baeten	Wannes	Stedelijk Ziekenbuis Aalst	Relgium
Balandin	Alina	University Hospital Regenshurg	Germany
Barquero López	Marta	Corporación Sanitaria Parc Taulí	Spain
Bargan	Victoria	University Emergency County Hospital Targu Mures	Bomania
Bascuas	Begona	Hospital Universitario Lucus Augusti	Spain
Basora	Misericordia	Hospital Clinic Barcelona	Spain
Baumann	Holger	Academic Medical Centre, University of Amsterdam	Netherlands
Bayer	Andreas	University Hospital Munich	Cermany
Boll	Andrea	Newcastle Upon Type Hospitals NHS Trust The Freeman Hospital High	United Kingdom
ben	Anurea	Heaton	onited Kingdom
Belmonte Cuenca	Julio	Hospital Son Llatzer	Spain
Bengisun	Zuleyha Kazak	Ufuk University Hospital	Turkey
Bento	Carlos	Hospital da Universidade de Coimbra	Portugal
Beran	Maud	ZOL Genk- St Jan Hospital Genk	Belgium
Bermudez Lopez	Maria	Hospital Universitario Lucus Augusti	Spain
Bernardino	Ana	Hospital da Universidade de Coimbra	Portugal
Berthelsen	Kasper Gymoese	University Hospital of North Norway, Tromsø	Norway
Bigat	Zekiye	Akdeniz University Hospital	Turkey
Bilshiene	Diana	Kaunas Medical University Hospital, Hospital of Lithuanian University of Health Sciences	Lithuania
Bilska	Marcela	University Hospital Hradec Kralove	Czech Republic
Bisbe Vives	Elvira	Hospital Mar-Esperanca, Parc de Salut Mar	Spain
Biscioni	Tamara	Azienda USL n.5 di Pisa Ospedale F Lotti	Italy
Biörn	Hevse	Ghent University Hospital	Belgium
Blom	Tommi	Karolinska University Hospital Huddinge	Sweden
Bogdan Prodan	Alexandru	Emergency Institute of Cardiovascular Diseases Inst "Prof C C	Romania
	. inchairtaí a	Iliescu"	
Bogdanovic Dvorscak	Matea	University hospital "Merkur"	Croatia
BOISSON	Matthieu	University Hospital of Poltiers	France

Bolten	Jens	St George's Hospital	United Kingdom
Bona	Francesco	Institute for Cancer Research and treatment	Italy
Borg	Francis	Mater Dei Hospital	Malta
Boros	Cristian	Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu"	Romania
Borys	Michał	Medical University of Lublin	Poland
Boveroux	Pierre	Centre hospitalier Universitaire de Liège	Belgium
Boztug Uz	Neval	Akdeniz University Hospital	Turkey
Brettner	Florian	University Hospital Munich	Germany
Brisard	Laurent	University Hospital Nantes-Hopital G et R Laënnec	France
Britta	De Waal	Maastricht University Medical Center	Netherlands
Browne	Gail	Craigavon Area Hospital	United Kingdom
Budow	Kristin	University Hospital of Wuerzburg	Germany
Buerkle	Hartmut	University Hospital Freiburg	Germany
Buggy	Donal	Mater Misericordiae University Hospital	Ireland
Cain	Alistair	Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton	United Kingdom
Calancea	Esenia	Fundeni Clinical institute - Intensive Care Unit	Romania
Calarasu	Florenta	St. Andrei Emergency County Hospital Galati	Romania
Calder	Verity	Newcastle Upon Type Hospitals NHS Trust The Freeman Hospital High	United Kingdom
Guider	verity	Heaton	omica imgaom
Camci	Ali Emre	Istanbul University, Istanbul Medical Faculty	Turkey
Campiglia	Laura	Ospedale Misericordia e Dolce - Usl4 Prato	Italy
Campos	Beatriz	Hospital da Universidade de Coimbra	Portugal
Camps	Angela	Hospital Vall d Hebron	Spain
Carlos	Delgado	Hospital Clínico Universitario de Valencia	Spain
Carreira	Claudia	Hospital da Universidade de Coimbra	Portugal
Carrilho	Alexandre	Centro Hospitalar De Lisboa Central- EPE Lisboa	Portugal
Carvalho	Peter	Royal Surrey County Hospital NHS Foundation Trust	United Kingdom
Cassinello	Concepcion	Hospital Miguel Servet	Spain
Cattan	Anat	Tel Aviv Medical Center	Israel
Cenni	Leonardo	Ospedale Misericordia e Dolce - Usl4 Prato	Italv
Cerny	Vladimir	University Hospital Hradec Kralove	Czech Republic
Cevda Meco	Basak	Ankara University Faculty of Medicine	Turkev
Chesov	Ion	National Scientific an Practical Center of Emergency Medicine	Moldova
Chishti	Ahmed	Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton	United Kingdom
Chupin	Anne-Marie	University Hospital Nantes-Hopital G et R Laënnec	France
Cikova	Andrea	University Hospital Bratislava Ružinov	Slovakia
Cindea	Iulia	Constanta County Emergency Hospital	Romania
Cintula	Daniel	St. Elizabeth s Cancer Institute and Medical faculty of Comenius University Bratislava	Slovakia
Ciobanasu	Roxana	Fundeni Clinical institute	Romania
Clements	Deborah	Royal Surrey County Hospital NHS Foundation Trust	United Kingdom
Cobiletchi	Serghei	National Scientific an Practical Center of Emergency Medicine	Moldova
Coburn	Mark	University Hospital Aachen	Germany
Coghlan	Liz	Mater Misericordiae University Hospital	Ireland
Collver	Thomas	Harrogate District Hospital	United Kingdom
Copotoiu	Sanda Maria	University Emergency County Hospital Targu Mures	Romania
Copotoiu	Ruxandra	University Emergency County Hospital Targu Mures	Romania
Corneci	Dan	Elias University Emergency Hospital	Romania
Cortegiani	Andrea	Policlinico "P Giaccone" (University of Palermo)	Italv
Coskunfirat	O.Korav	Akdeniz University Hospital	Turkev
Costea	Dan	Constanta County Emergency Hospital	Romania
Czuczwar	Mirosław	Medical University of Lublin	Poland
Davies	Katy	Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High	United Kingdom
De Baerdemaekor	Luc	Chent University Hospital	Belgium
Do Hort	Stefan	Chent University Hospital	Belgium
Dehemardi	Felicino	Institute for Concer Research and treatment	Italy
Decagny	Sulvie	Injuersity Hognital Nantes-Honital C et R Lannon	France
Deger Cochunfirat	Nesil	Akdeniz University Hospital	Turkey
Diana	Toma	Flige University Emergency Hospital	Romania
	i Jilla	mus onversity milergency nospital	Nomania

Diana	Gómez Martinez	Hospital Santa Creu I Sant Pau	Spain
Dias	Sandra	Centro Hospitalar De Lisboa Central- EPE Lisboa	Portugal
Dickinson	Matthew	Royal Surrey County Hospital NHS Foundation Trust	United Kingdom
Dobisova	Anna	University Hospital Bratislava Ružinov	Slovakia
Dragan	Anca	Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu"	Romania
Droc	Gabriela	Fundeni Clinical institute	Romania
Duarte	Sonia	Hospital da Universidade de Coimbra	Portugal
Dunk	Nigel	Kettering General Hospital NHS Foundation Trust	United Kingdom
Ekelund	Kim	Rigshospitalet - Copenhagen University Hospital	Denmark
Ekmekçi	Perihan	Ufuk University Hospital	Turkey
Elena	Ciobanu	Clinical Emergency Hospital of Bucharest	Romania
Ellimah	Tracev	Queens Hospital	United Kingdom
Espie	Laura	Craigavon Area Hospital	United Kingdom
Everett	Lynn	Hospital James Paget University Hospital NHS Foundation Trust	United Kingdom
Ferguson	Andrew	Craigavon Area Hospital	United Kingdom
Fernandes	Melissa	Hospital da Universidade de Coimbra	Portugal
Fernández	T A	Hospital Santa Creu I Sant Pau	Snain
Fornor	Marian	University Medical Conter Johannes Cutenberg Mainz	Cormony
Forreiro	Danial	Uconital de Econital Contes Évera E DE	Dortugol
Ferrie	Daniel	Rospital do Espirito Sailto - Evola, E.F.E.	Fortugal United Vinadem
Ferrie	Rosemary	Rettering General Hospital NHS Foundation Trust	
Filipescu	Daniela	Iliescu"	Romania
Flassikova	Zora	University Hospital Bratislava Ružinov	Slovakia
Fleischer	Andreas	University Hoespital Bonn	Germany
Font	Α.	Hospital Santa Creu I Sant Pau	Spain
Galkova	Katarina	Faculty hospital, Nitra, Slovak republic	Slovakia
Garcia	Irene	Hospital Vall d Hebron	Spain
Garner	Matt	Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton	United Kingdom
Gasenkampf	Andrey	Krasnoyarsk State Medical University	Russia
Gelmanas	Arunas	Kaunas Medical University Hospital, Hospital of Lithuanian University of Health Sciences	Lithuania
Gherghina	Viorel	Constanta County Emergency Hospital	Romania
Gilsanz	Fernando	Hospital Universitario La Paz	Spain
Giokas	George	Aretaieion University Hospital	Greece
Goehel	Illrich	University Hospital Freiburg	Germany
Comes	Piedade	Hospital da Universidade de Coimbra	Portugal
Concelves Aquier	losé Manuel	Centro Hospitalar do Porto	Portugal
Gonçalves Agular	Voronico	Legnital de Meiveoire (Complexe Legnitalarie Universarie de Viga)	Spoin
Gottachallr	Andrá	Diskoniskronkonhous Friederikenstift	Spann
Gouroud	Anule Joan Diorro	University Heapital Nantoa Henital C et B Leännes	Germany
Goulauu	Jean-riene	Ornodolo Minorizordio o Dolog. Hold Proto	Italice
Granngin	Liella	Clinical Emergency Llocatical of Bushavest	Demonio
Gillitescu	Andriv	University Medicine Centre Linkligne	Clouonia
Grynyuk	Alerer	University Medicine Centre Ljubijana	Duccio
Giytsall	Riexey		Russia
Guascii	Emma	Hospital Universital "Meduur"	Spain
Gustin	Denis	Control h conitali en Universitation de Lière	
Hans	Gregory	Centre nospitaller Universitalre de Liege	Beigium
Harazim	Hana		Czech Republic
Hervig	lore .	Haukeland University Hospital	Norway
Hidalgo	Francisco	University of Navarra	Spain
Higham	Charley	Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton	United Kingdom
Hirschauer	Nicola	Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton	United Kingdom
Hoeft	Andreas	University Hoespital Bonn	Germany
Innerhofer	Petra	Medical University Hospital Innsbruck	Austria
Innerhofer-	Nicole	Medical University Hospital Innsbruck	Austria
Pompernigg			
Jacobs	Stefan	Stedelijk Ziekenhuis Aalst	Belgium
Jakobs	Nicolas	Diakoniekrankenhaus Friederikenstift	Germany
Jamaer	Luc	Jessa Ziekenhuis Hasselt	Belgium

James Jawad Iesus Ihanii Jipa Lavina Iokinen Iovanovic Jubera Kahn Karjagin Kasnik Katsanoulas Kelle Kelleher Kessler Kirigin Kiskira Kivik Klimi Klučka Koers Kontrimaviciut Koopman-van Gemert Korfiotis Kosinová Koursoumi Kozek Langenecker Kranke Kresic Krobot Kropman Kulikov Kvolik Kvrgic Kyttari Lagarto Lance Laufenberg Lauwick Lecoa Leech lidzborski Liliana Linda Llau Pitarch Lopes Lopez Lopez Alvarez Lorenzi Lorre Lucian Lupis Lupu Macas Macedo Maggi Mallett Mallor Manoleli

Manolescu

Juri

Olga

Iozef

Lena

Egle

Rita

Ana

Luis

Irene

Ana

Rely

Royal Free Hospital Hampstead Nhs Trust United Kingdom Sarah Monir Centralsjukhuset Kristianstad Sweden Ioana Hospital da Universidade de Coimbra Portugal Shaman Royal Marsden Hospital United Kingdom Nicoleta Fundeni Clinical institute Romania Iohanna University Hospital of Wuerzburg Germany Gordana Clinical Centre of Voivodina Serbia Maria Pilar Hospital Miguel Servet Spain David UCL Belgium Tartu University Hospital Estonia Darja Slovenia General Hospital Slovenj Gradec Konstantinos Ippokrateio Hippokrateion General Hospital of Thessaloniki Greece Hened University Clinical Center Sarajevo Bosnia and Herzegovina Mortimer Mater Misericordiae University Hospital Ireland Florian University Hospital Bonn Germany Borana University Hospital "Sveti Duh" Croatia Molaoi Hospital Greece North Estonian Center Estonia Peeter Pelagia "Alexandra" General Hospital of Athens Greece Faculty Hospital Brno Czech Republic Academic Medical Centre, University of Amsterdam Netherlands Vilnius University Hospital - Santariskiu Clinics Lithuania A.W.M.M. Albert schweitzer Hospital Netherlands Ippokrateio Hippokrateion General Hospital of Thessaloniki Demetrios Greece Martina Faculty Hospital Brno Czech Republic Eygenia Attikon University Hospital Greece Sibylle EKH Evangelic Hospital Vienna Austria Peter University Hospital of Wuerzburg Germany University Clinical Hospital Osijek Marina Croatia Renatas Generala Hospital Varazdin Croatia Lucienne Maastricht University Medical Center Netherlands Alexander Burdenko Neurosurgery Institute Russia Slavica University Clinical Hospital Osijek Croatia Ivana Clinical Centre of Voivodina Serbia Aikaterini Attikon University Hospital Greece Filipa Centro Hospitalar do Porto Portugal Marcus D. Maastricht University Medical Center Netherlands University Medical Center Johannes Gutenberg Mainz Germany Severine Centre hospitalier Universitaire de Liège Belgium Jean-Pierre Centre hospitalier Universitaire de Liège Belgium Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High United Kingdom Leech Heaton Groupe Hospitalier Cochin Lionel France Hospital Clínico Universitario de Valencia Henao Spain Filipe Hospital Garcia de orta Portugal Juan Vicente Hospital Clínico Universitario de Valencia Spain Hospital da Universidade de Coimbra Portugal University of Navarra Spain Alexo Hospital do Meixoeiro (Complexo Hospitalario Universario de Vigo) Spain Azienda USL n.5 di Pisa Ospedale F. Lotti Italy Gilbert CHD Vendée France Horhota Spital orasenesc Bolintin Vale Romania University hospital "Merkur" Croatia Tamara St. Andrei Emergency County Hospital Galati Mary Nicoleta Romania Andrius Lithuanian University of Health Sciences, Kaunas Clinics Lithuania Hospital da Universidade de Coimbra Portugal Genaro Hospital Universitario La Paz Spain Susan Royal Free Hospital Hampstead Nhs Trust United Kingdom Thomas Hospital San Jorge Spain Alexandra Clinical Emergency Hospital of Bucharest Romania Elias University Emergency Hospital Romania

Manrique	Susana	Hospital Vall d Hebron	Spain
Maquoi	Isabelle	Centre hospitalier Universitaire de Liège	Belgium
Marios-Konstantinos	Tasoulis	Aretaieion University Hospital	Greece
Markovic Bozic	Jasmina	University Medicine Centre Ljubljana	Slovenia
Markus W.	Hollmann	Academic Medical Centre, University of Amsterdam	Netherlands
Marques	Margarida	Hospital da Universidade de Coimbra	Portugal
Martinez	Raul	Hospital Universitario La Paz	Spain
Martinez	Ever	Hospital Universitario La Paz	Spain
Martínez	Esther	Hospital Universitari Germans Trias I Puiol	Spain
Martinho	Helder	Hospital da Universidade de Coimbra	Portugal
Martins	Diogo	Centro Hospitalar de Lisboa Ocidental. E.P.E. Hospital de S. Francisco	Portugal
	. 0 .	Xavier	
Martires	Emilia	Hospital da Universidade de Coimbra	Portugal
Martus	Peter	Universitätsklinikum Tubingen	Germany
Matias	Francisco	Hospital da Universidade de Coimbra	Portugal
Matot	Idit	Tel Aviv Medical Center	Israel
Mauff	Susanne	University Medical Center Johannes Gutenberg Mainz	Germany
Meale	Paula	Roval Free Hospital Hampstead Nhs Trust	United Kingdom
Meier	Jens	Kepler University Clinic Linz	Austria
Merz	Hannah	Universitätsklinikum Tubingen	Germany
Mevbohm	Patrick	University Hospital Frankfurt	Germany
Militello	Maria Grazia	Azienda USL n.5 di Pisa Ospedale F. Lotti	Italy
Mincu	Natalia	Prof. D.Gerota Hospital	Romania
Miranda	Maria Lina	Instituto Português Oncologia	Portugal
Mirea	Liliana	Clinical Emergency Hospital of Bucharest	Romania
Moghildea	Victoria	National Scientific an Practical Center of Emergency Medicine	Moldova
Moise	Alida	Prof. D.Gerota Hospital	Romania
Molano Diaz	Pablo	Hospital General De Mostoles	Spain
Moltó	Luís	Hospital Mar-Esperanca, Parc de Salut Mar	Spain
Monedero	Pablo	University of Navarra	Spain
Moral	Victoria	Hospital Santa Creu I Sant Pau	Spain
Moreira	Zélia	Centro Hospitalar do Porto	Portugal
Moret	Enrique	Hospital Universitari Germans Trias I Pujol	Spain
Mulders	Freva	Jessa Ziekenhuis Hasselt	Belgium
Munteanu	Anna Maria	Orthopedics Hospital FOISOR	Romania
Nadia Diana	Kinast	Hospital Santa Creu I Sant Pau	Spain
Nair	Ashok	Royal Surrey County Hospital NHS Foundation Trust	United Kingdom
Neskovic	Vojislava	Military Medical Academy	Serbia
Ninane	Vincent	Centre hospitalier Universitaire de Liège	Belgium
Nitu	Denisa	Elias University Emergency Hospital	Romania
Oberhofer	Dagmar	University Hospital "Sveti Duh"	Croatia
Odeberg-Wernerman	Suzanne	Karolinska University Hospital Huddinge	Sweden
Oganjan	Juri	North Estonian Center	Estonia
Omur	Dilek	Dokuz Eylul University Medicine Faculty	Turkey
Orallo Moran	Marian Angeles	Hospital do Meixoeiro (Complexo Hospitalario Universario de Vigo)	Spain
Ozkardesler	Sevda	Dokuz Eylul University Medicine Faculty	Turkey
Pacasová	Rita	Faculty Hospital Brno	Czech Republic
Paklar	Nataša	University hospital "Merkur"	Croatia
Pandazi	Ageliki	Attikon University Hospital	Greece
Papaspyros	Fotios	Ippokrateio Hippokrateion General Hospital of Thessaloniki	Greece
Paraskeuopoulos	Tilemachos	Molaoi Hospital	Greece
Parente	Suzana	Centro Hospitalar de Lisboa Ocidental, E.P.E. Hospital de S. Francisco	Portugal
		Xavier	
Paunescu	Marilena Alina	Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu"	Romania
Pavičić Šarić	Jadranka	University hospital "Merkur"	Croatia
Pereira	Filina	Centro Hospitalar do Porto	Portugal
Pereira	Flizabete	Hospital da Universidade de Coimbra	Portugal
Pereira	Luciane	Hospital da Universidade de Coimbra	Portugal
Perry	Chris	Newcastle Unon Type Hospitals NHS Trust The Freeman Hospital High	Inited Kingdom
. City	GIIIID	Heaton	
Petri	Attila	Colchester Hospital University Foundation Trust	United Kingdom
Petrovic	Uros	Military Medical Academy	Serbia

Continued

Pica	Silvia	Hospital Garcia de ort
Pinheiro	Filipe	Hospital da Universid
Pinto	José	Centro Hospitalar De
Pinto	Fernando	Hospital da Universid
Piwowarczyk	Paweł	Medical University of
Platteau	Sofie	Stedelijk Ziekenhuis A
Poeira	Rita	Centro Hospitalar De
Popescu	Ravzan	Constanta County Em
Popica	Georgian	Elias University Emer
Poredos	Peter	University Medicine C
Prasser	Christopher	University Hospital Re
Preckel	Benedikt	Academic Medical Cer
Prospiech	Audrey	UCL
Pujol	Roger	Hospital Clinic Barcel
Raimundo	Ana	Hospital da Universid
Raineri	Santi Maurizio	Policlinico "P Giaccon
Rakic	Dragana	Clinical Centre of Voiv
Ramadan	Mohammed	Queens Hospital
Ramazanoğlu	Atilla	Akdeniz University He
Rantis	Athanasios	General air force hosp
Raquel	Ferrandis	Hospital Clínico Unive
Rätsep	Indrek	North Estonian Cente
Real	Catia	Hospital da Universid
Reikvam	Tore	Haukeland University
Reis	Ligia	Hospital do Espirito S
Rigal	Jean-	University Hospital N
5	Christophe	у I
Rohner	Anne	University Hospital Bo
Rokk	Alar	Tartu University Hosp
Roman Fernandez	Adriana	Hospital do Meixoeiro
Rosenberger	Peter	Universitätsklinikum
Rossaint	Rolf	University Hospital A
Rozec	Bertrand	University Hospital N
Rudolph	Till	Sahlgrenska Universit
Saeed	Yousif	Centralsjukhuset Kris
Safonov	Sergej	Centralsjukhuset Kris
Saka	Esra	Istanbul University, Is
Samama	Charles Marc	Groupe Hospitalier Co
Sánchez López	Óscar	Hospital General De M
Sanchez Perez	David	Hospital General De M
Sanchez Sanchez	Yvan Enrique	Hospital do Meixoeiro
Sandeep	Varma	Mid Yorkshire Hospita
Sandu	Madalina Nina	St. Andrei Emergency
Sanlı	Suat	Akdeniz University H
Saraiva	Alexandra	Hospital da Universid
Scarlatescu	Ecaterina	Fundeni Clinical insti
Schiraldi	Renato	Hospital Universitaric
Schittek	Gregor	Carl – Thiem Klinikun
Schnitter	Bettina	University Hospital Fr
Schuster	Michael	University Medical Ce
Seco	Carlos	Hospital da Universid
Selvi	Onur	Maltepe University
Senard	Marc	Centre hospitalier Un
Serra	Sofia	Instituto Português O
Serrano	Helena	Hospital Vall d Hebror
Shmigelsky	Alexander	Burdenko Neurosurge
Silva	Luisa	Hospital da Universid
Simeson	Karen	Mid Yorkshire Hospit
Singh	Rita	Newcastle Upon Type
- o		Heaton
Sipylaite	Jurate	Vilnius University Ho
Skitek	Kornel	Carl – Thiem Klinikun
Skok	Ira	University Hospital "S
		,

ital Garcia de orta	Portugal
vital da Universidade de Coimbra	Portugal
ro Hospitalar De Lisboa Central- EPE Lisboa	Portugal
vital da Universidade de Coimbra	Portugal
cal University of Lublin	Poland
eliik Ziekenhuis Aalst	Belgium
ro Hospitalar De Lisboa Central- EPE Lisboa	Portugal
tanta County Emergency Hospital	Romania
University Emergency Hospital	Romania
ersity Medicine Centre Liubliana	Slovenia
ersity Hospital Regenshurg	Germany
emic Medical Centre University of Amsterdam	Netherlands
chile medical centre, oniversity of milisteraam	Relgium
ital Clinic Barcelona	Snain
ital da Universidade de Coimbra	Portugal
linico "P Giaccone" (University of Palermo)	Italy
cal Centre of Voivodina	Serbia
ans Hospital	United Kingdom
niz Ilniversity Hospital	Turkov
aral air force hospital	Greece
nal al Torce Hospital	Snain
h Fetonian Center	Fetonia
sital da Universidade de Coimbra	Portugal
zaland University Hospital	Norway
vital do Fenirito Santo - Évora E PE	Portugal
ersity Hospital Nantes-Honital C et R Lagannes	France
eisity nospital valles-nopital 6 et k Laennee	Tance
ersity Hospital Bonn	Germany
ı University Hospital	Estonia
vital do Meixoeiro (Complexo Hospitalario Universario de Vigo)	Spain
ersitätsklinikum Tubingen	Germany
ersity Hospital Aachen	Germany
ersity Hospital Nantes-Hopital G et R Laënnec	France
grenska University Hospital	Sweden
ralsjukhuset Kristianstad	Sweden
ralsjukhuset Kristianstad	Sweden
bul University, Istanbul Medical Faculty	Turkey
pe Hospitalier Cochin	France
vital General De Mostoles	Spain
vital General De Mostoles	Spain
vital do Meixoeiro (Complexo Hospitalario Universario de Vigo)	Spain
Yorkshire Hospitals NHS Trust; Pinderfields Hospital	United Kingdom
ndrei Emergency County Hospital Galati	Romania
eniz University Hospital	Turkey
vital da Universidade de Coimbra	Portugal
leni Clinical institute - Intensive Care Unit	Romania
vital Universitario La Paz	Spain
– Thiem Klinikum Cottbus	Germany
ersity Hospital Freiburg	Germany
ersity Medical Center Johannes Gutenberg Mainz	Germany
vital da Universidade de Coimbra	Portugal
epe University	Turkey
re hospitalier Universitaire de Liège	Belgium
tuto Português Oncologia	Portugal
vital Vall d Hebron	Spain
enko Neurosurgery Institute	Russia
ital da Universidade de Coimbra	Portugal
Yorkshire Hospitals NHS Trust; Pinderfields Hospital	United Kingdom
castle Upon Tyne Hospitals NHS Trust The Freeman Hospital High	United Kingdom
leaton	0
us University Hospital - Santariskiu Clinics	Lithuania
– Thiem Klinikum Cottbus	Germany
ersity Hospital "Sveti Duh"	Croatia

Smékalová Smirnova Sofia Soler Pedrola: Söndergaard	Olga Nadezda Machado Maria Sören	Faculty Hospital Brno North Estonian Center Hospital Clínico Universitario de Valencia Hospital Son Llatzer Sablgrenska University Hospital	Czech Republic Estonia Spain Spain Sweden
Sõrmus	Alar	Tartu University Hospital	Estonia
Sørvoll	Ingvild	University Hospital of North Norway, Tromsø	Norway
oprom	Hausberg		Norway
Soumelidis	Christos	Ippokratejo Hippokratejon General Hospital of Thessaloniki	Greece
Spindler Yesel	Alenka	University Medicine Centre Liubliana	Slovenia
Stefan	Mihai	Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C.	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
Trovan	Galina	Zaporizhzhia State Medical University	Ukraine
Unic-Stojanovic	Dragana	Cardiovascular Institute Dedinie Belgrade	Serbia
Unterrainer	Axel	Christian-Doppler-Klinik	Austria
Uraniek	Jasna	General Hospital Sloveni Gradec	Slovenia
Valsamidis	Dimitrios	"Alexandra" General Hospital of Athens	Greece
van Dasselaar	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 Universario 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	Ikic	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
Vujanovič	Vojislav	University Hospital Banja Luka	Bosnia and
Vukovic	Rade	Military Medical Academy	Herzegovina Serbia

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
Yılmaz	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