Transfusion AE

Chair: Maria Aurora Espinosa, Manuel Muñoz

Thursday 20th of April 2023

1. OVERTRANSFUSION AN AE?

Thomas Frietsch

Overtransfusion is considered an adverse event

Incidence 27-71%

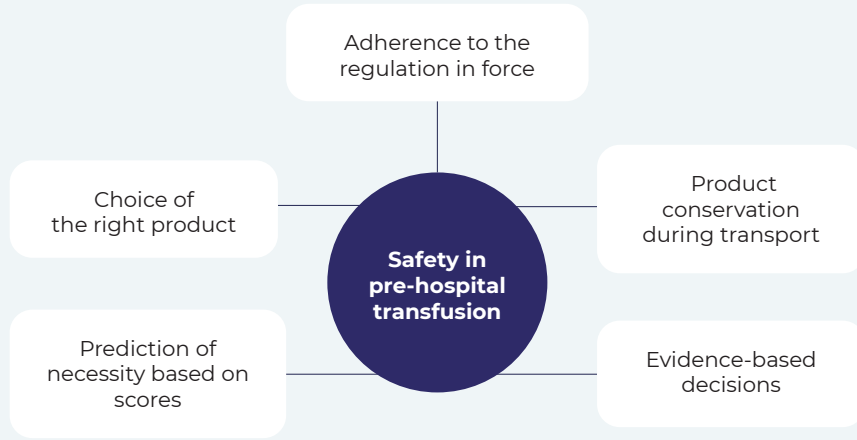
It is necessary to integrate overtransfusion into hemovigilance, to agree on a useful definition, and to work on the factors contributing to its increase

CONSEQUENCES

- Higher mortality in patients with massive transfusion
- Higher mortality in post-surgery patients

TRALI: Transfusion related acute lung injury
TACO: Transfusion associated circulatory overload

Trauma is the main cause for loss of years of life in Western countries, and also the main cause for pre-hospital transfusions, and it can be prevented by managing the hemorrhage



Main causes of transfusion-related death

TACO 3rd more common transfusion-related severe AE

TRALI 6th more common transfusion-related severe AE

Differential diagnose

TRALI (<6 hours)

- TRALI type I: without ARDS risk factors
- TRALI type II: with ARDS risk factors, but no ARDS

TACO (<6-12 hours)

TAD (<6 hours)

TACO/TRALI (<6 hours)

ARDS (worsening over 12 last hours)

Needs

Prevent the onset

Agreeing definitions and criteria

24-hour active hemovigilance with specific detection of TACO and TRALI

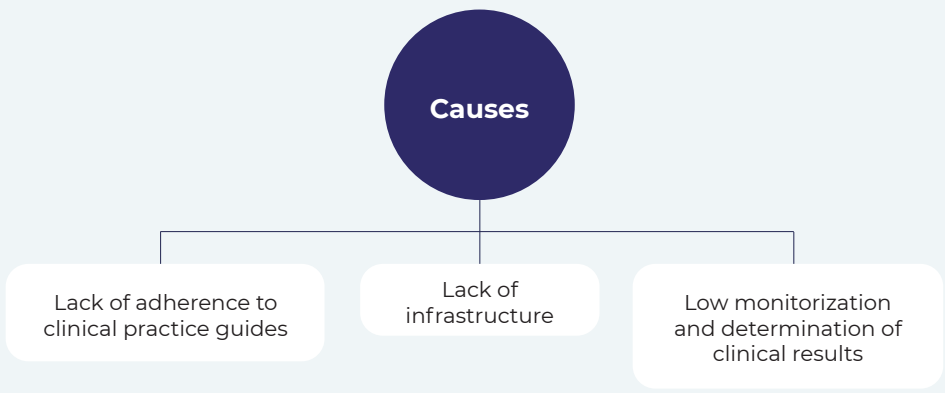
Currently, overtransfusion is underregistered and entails a significant issue, as is the case with undertransfusion[1,2]. Identification and reporting of both events should be integrated as hemovigilance strategies. Overtransfusion rates of 27-71% have been reported, depending on the intervention, the time, and the activation or not of massive transfusion protocols[3-6].

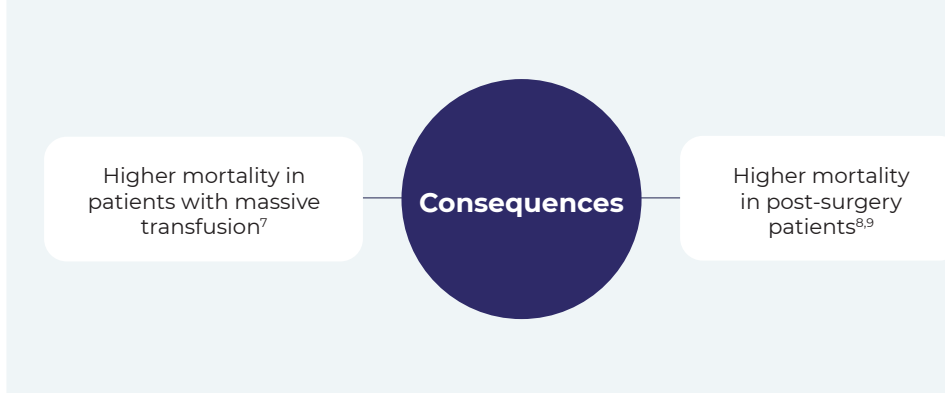
Overtransfusion is considered an adverse event, and lacking a widely agreed definition, it can be defined as follows:

Overdose of
- Blood cell products
- Plasma fluids
- Plasma proteins

in
- Standard situations
- Controlled bleeding
- Controlled volume status, stable intravascular volumen or normovolemia

as
- Treatment or prophylaxis (with no evidence of vital sign improvement)





In order to reduce overtransfusion rates and its consequences, the international working group on overtransfusion wants to include it in hemovigilance strategies, as well as to focus its current work on reaching a consensus around a useful definition for its detection, and the identification of factors contributing to its increase and related consequences.

If you are interested in this field, please register at the following address: **overtransfusion@iakh.deC**

CSL Behring

Expert Comment

Author of the comment: Dra. Sonia María Veiras.

Hospital Clínico Universitario de Santiago de Compostela. Head of Section at the Anesthesia and Resuscitation Department. Province of A Coruña.

Undertransfusion is poorly quantified and registered. The delays in the supply of the requested products, errors, transportation and storage issues, rejection by the patient, supply lower than demand, are factors for undertransfusion (TRANSFUSION, Dec 2021: "incorporating the entity of undertransfusion into hemovigilance monitoring").

Overtransfusion (OT) is also underestimated, and it is a very frequent problem in developed countries.

A search in PubMed of the term overtransfusion yields 130 results, whereas when entering the term TACO (Transfusion Associated Circulatory Overload) or TAD (Transfusion Associated Distress) yields around 25,000 results… Therefore, something is off.

The frequency of OT is unknown.

When reviewing the literature, and OT incidence value of 27% is found in the scenario of multiple trauma patients in Australian reviews (Eur J of Trauma and Emergency Surgery 2022), and up to 71% in North American reviews in scenarios of massive transfusion protocol activation (Trauma Surgery and Acute Care Open 2022). These publications define OT as a transfusion resulting in a hemoglobin value > 11 g/dl. The conclusion of these works is that OT should be followed by Blood Banks and trauma centers and studied as a potential quality measure of the resuscitation of massively transfused patients.

In scheduled surgery scenarios, such as hip replacements, OT rates reach 46.99% on average upon review of the Works published between 2011 and 2023, with a volume of 17273 patients.

As for the influence of OT on the "outcome" of patients, 2.5 odd ratios are found in terms of increased mortality, increased incidence of renal failure, infections, hospital admissions… even though some works do not find such negative influence on the evolution of their patients.

The first pitfall is the lack of definition of the term overtransfusion. There are in fact several definitions:

- High transfusion dose, inappropriate for the needs of the patient (SHOT Report 2011)
- Transfusion for hemoglobin threshold >2g/dl versus pre-transfusion level, in cases of reversible anemia (Warburton KB et al, Future Hospital Journal , 2016)
- Post-transfusion Hb level >10g/dl (levels > 11g/dl will be considered major overtransfusion) (Stokes A et al, Clin Med (Lond) 2015)
- Hb > 12gr/dl on discharge after elective hip replacement (Joshi G et al, Ir J Med Sci 1997)

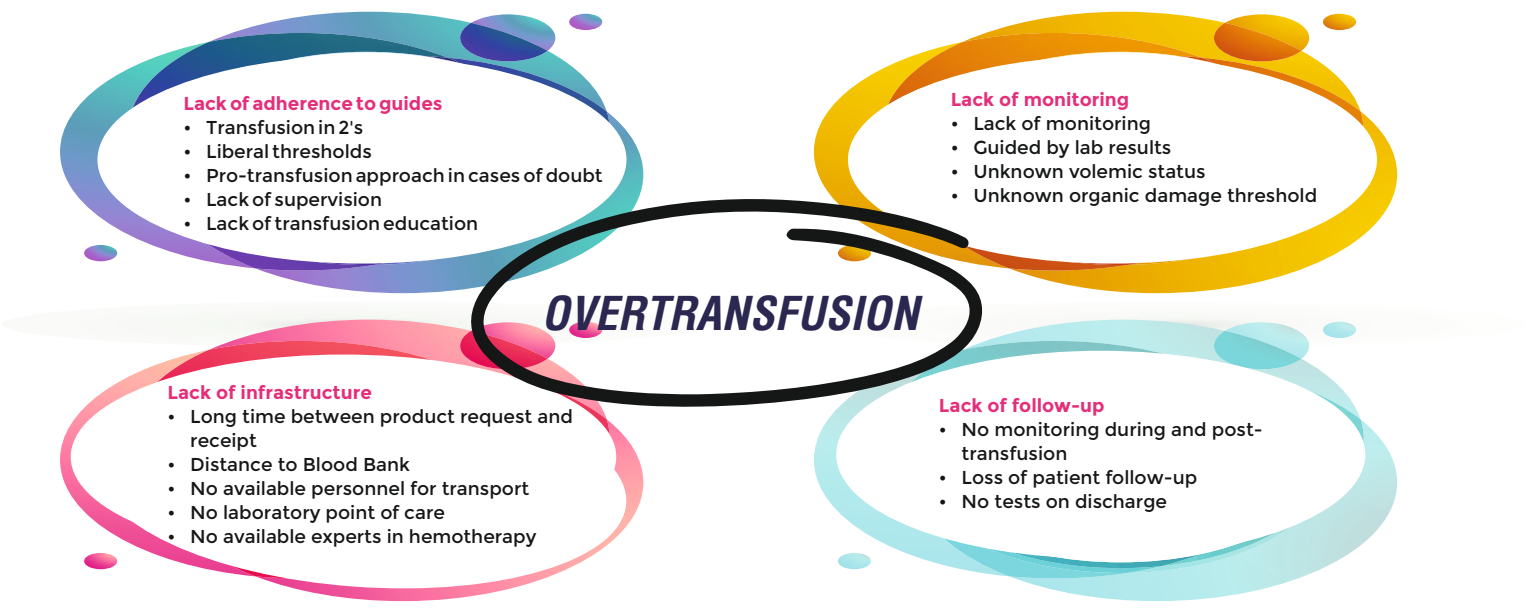
A possible definition of OT (under construction):

Overdose of:
- Blood products (whole blood, red blood cells, platelets)
- Plasma-derived fluids (FPC, albumin)
- Plasma proteins (cryoprecipitates, factor concentrates, CCP)

In:
- Standard situations
- Controlled bleedings
- Normovolemia and stability situations

As:
- Superfluous therapy or prophylaxis (with no evidence of vital sign improvement)

Resulting in adverse events (TACO, TAD, Thrombosis/embolism, alloimmunization, transfusion reaction, HBP, Component errors, tissue ischemia).



The difficulty to administer the product when needed results in overtransfusion.

A NATA working group on overtransfusion is suggested, aimed at defining OT, analyzing contributing factors, reasons for OT, frequency and patient outcome.

OVERTRANSFUSION WORKING GROUP

(contact by e-mail: overtransfusion@iakh.de)

Transfusion AE

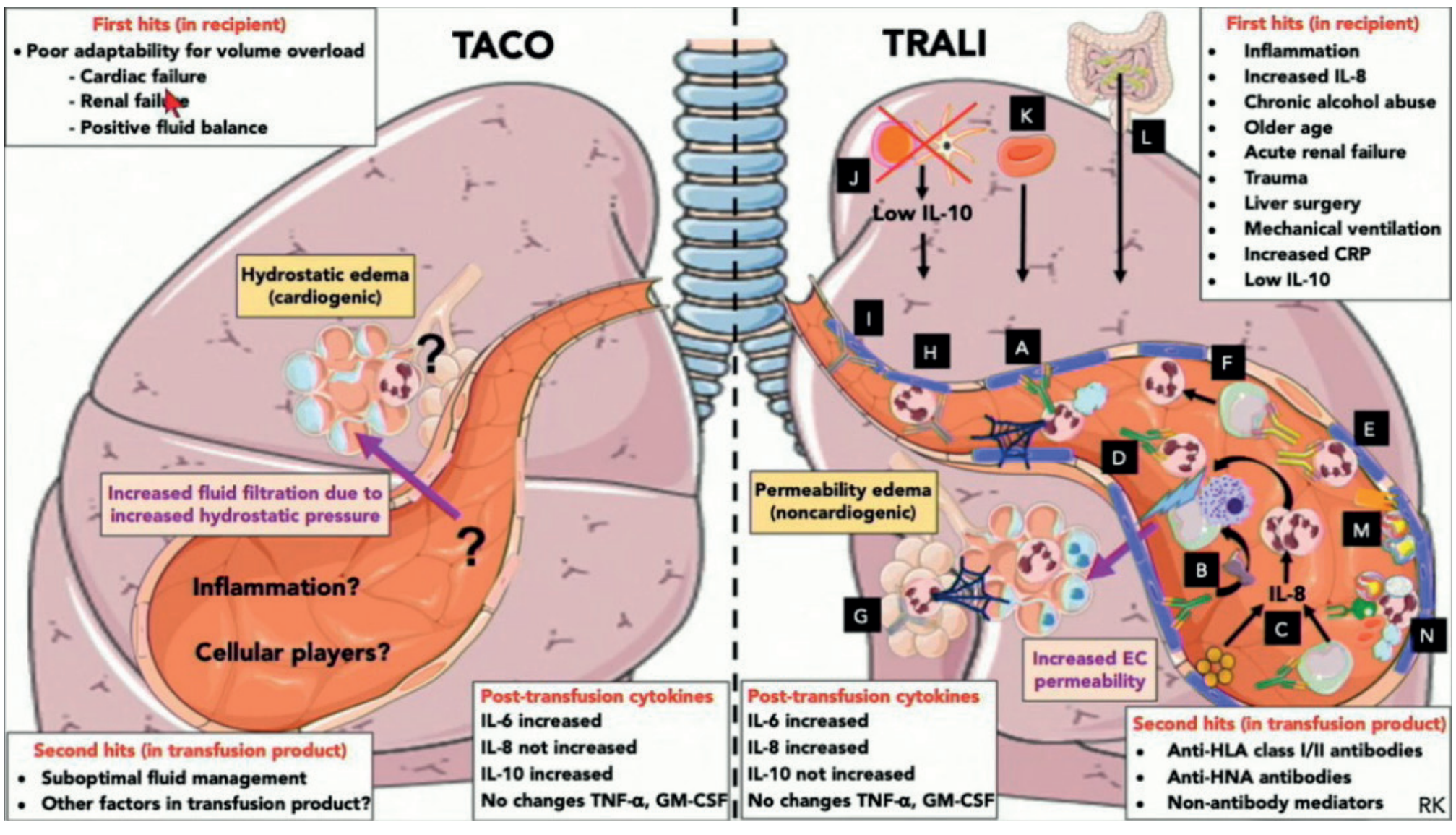
Chair: Maria Aurora Espinosa, Manuel Muñoz

Thursday 20th of April 2023

2. TACO AND TRALI - TWO BREATHTAKING SYNDROMES

José Antonio García Erce

Syndromes causing shortness of breath within 6 hours (approximately) of receiving a transfusion:



TRALI: Transfusion Related Acute Lung Injury

TACO: Transfusion Associated Circulatory Overload

Extracted from Tung et al. Blood Rev, 2022[7]

Presentation

TRALI is presented as an edema with increased permeability (non-cardiogenic), and TACO as a hydrostatic edema (cardiogenic)[8].

Pathophysiology

The pathophysiology of TRALI and TACO is complex and not well defined; the assumption is that is responds to a *2-hit*[7,8] model:

Hit 1: Clinical condition of the patient → **Hit 2:** Transfused product, generally allogeneico

Diagnose

- At the time of the diagnose, it is hard to distinguish between them and from other underlying causes for pulmonary damage[8-10].
- Different definitions and diagnostic criteria for each scientific society.
- 24-hour active hemovigilance programs ➡ crucial in the detection of pulmonary adverse events, less frequent than febrile or allergic ones, but less serious and with a higher impact on mortality.
- Criteria:

TRALI (<6 hours)

- TRALI type I: TRALI type I: without acute respiratory distress syndrome (ARDS) risk factors
- TRALI type II: with ARDS risk factors but no ARDS

TACO (<6-12 hours)

TAD (<6 hours)

TACO/TRALI (<6 hours)

ARDS (worsening in the last 12 hours)

Reach

These are the main causes of transfusion-related death[11].

- TACO was the third most common transfusion-related serious adverse event, and TRALI was the sixth one, according to the old classification[12].
- The lower incidence of TRALI registered can emerge from the implementation of preemptive measures in the selection of blood donors or the new classification put forward by Vlaar in 2019.

Treatment

There are no specific therapies for the treatment of TACO and TRALI and, therefore, the most important thing is to prevent their onset.

CSL Behring

Expert Comment

Author of the comment: Dra. Sonia María Veiras.

Hospital Clínico Universitario de Santiago de Compostela. Head of Section at the Anesthesia and Resuscitation Department. A Coruña Province.

TRALI is the acronym for Transfusion Related Acute Lung Injury. TACO stands for Transfusion Associated Circulatory Overload.

Why do these happen? The most widely accepted theory is that of "double hit," the first hit representing the clinical condition of the patient and the second hit given by the transfusion of the blood product.

In Blood (25 April 2019, Vol 133, Number 17), the pathophysiology of both syndromes is clearly explained.

Vlaar et al (Lancet Vol 382, Sept 14, 2013) explains that the severity of TRALI is related to the antibody titer emerging from the transfusion.

Six potential development paths have been described for TRALI (John Paul Tung et al, Blood reviews), related to monocytes, the endothelium, neutrophyles, the complement... These are complex mechanisms that may explain the theory that receiving blood from female donors leads to a higher risk of respiratory distress.

One of the issues is diagnosing these cases, since there is not a single criterion. Subsequently, a unified definition for TACO was suggested in 2018 (Lancet Haematol 2019) from the International Haemovigilance Network and the American Association of Blood Banks. The fundamental point is for symptoms to be identified within 12 hours from the transfusion.

Vlaar et al (Transfusion vol59, July 2019) suggests a consensus definition for TRALI type I and type II depending on whether patients present risk factors for respiratory distress. Symptoms should be identified within 6 hours from the transfusion. In case the symptoms appear from 6-12 hours after transfusion, we describe it as Transfusion Associated Dyspnea (TAD).

How frequent are these cases? An incidence is reported of 1 TACO case per 13,843 transfusions, which becomes 1 per 33 in perioperative scenarios. Similarly, one TRALI case per 63,940 transfusions, which becomes 1 per 71 in perioperative situations.

According to the WHO, 10% of reported transfusion reactions are TACO, while 3% are TRALI.

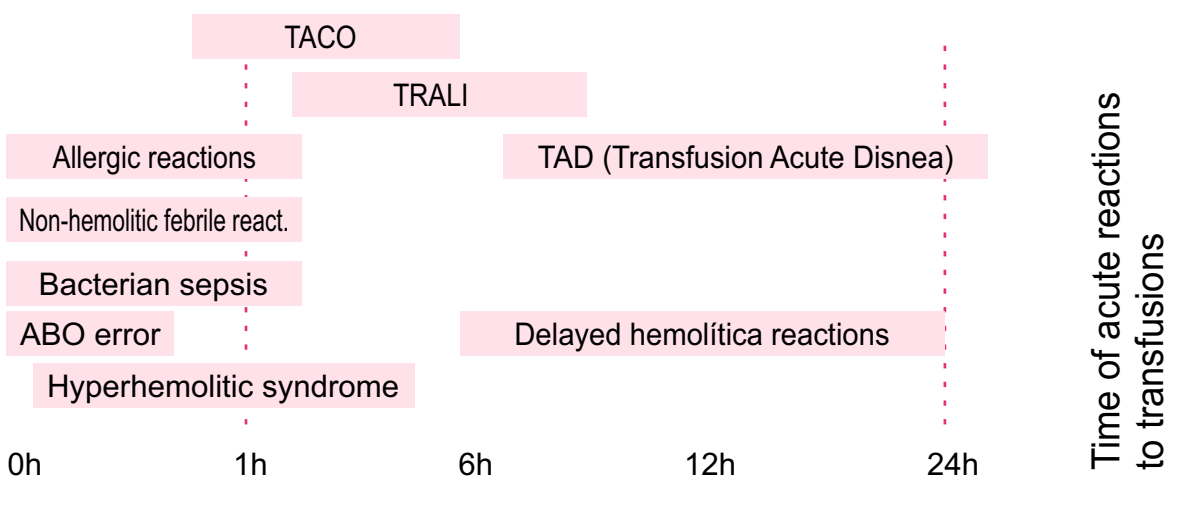
The International Haemovigilance Network Database (ISTARE) reports that TACO and TRALI cases account for 8.3% of all adverse reactions to transfusion, 20.1% of severe adverse events, and 52.2% of transfusion-related deaths.

The SHOT Report (UK) affirms that TACO is the most preventable reaction to transfusion, through practice improvement and monitoring.

In the year 2020, the Swiss series reports 0.15% of TRALI and 88 cases of TACO, 27 of which were life-threatening or even led to death.

In Italy, the 2021 register reports 3.7% of TAD, 0,1% of TRALI, and 1,7% of TACO. The Australian series presents 7.9% of TACO and 0.7% of TRALI.

France reports 10% of TACO, 0.4% of TAD, and 0.3% of TRALI.



At the Puerta de Hierro Hospital, a post-transfusion quarantine surveillance has been established, given that most serious reactions tend to happen several hours later, and frequently the physician in charge is no longer present (HEMACUA program, 24-hour quarantine active hemovigilance). With this post-transfusion surveillance, many more TRALI and TACO events are diagnosed.

Several therapeutic tools have been suggested, including ascorbic acid, although there are no specific treatments.

In conclusion, TACO and TRALI are acute distress syndromes emerging within the first hours after the transfusion, and they the main cause of transfusion-related mortality, with no specific therapy, hard to diagnose and to tell apart, with a complex not fully known pathophysiology. The current hemovigilance records suggest that TACO is the most severe transfusion reaction and that TRALI has a low incidence.

Transfusion AE

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2. SAFETY OF PREHOSPITAL TRANSFUSION

Cristophe Martinaud

Trauma is the main cause for loss of years of life in Western countries, and also the main cause for pre-hospital transfusions. There is a wide variety in terms of pre-hospital transfusion practice in different countries.

In order to **guarantee a safe transfusion in the pre-hospital setting**, it is important to **comply with the following premises:**

1 ADHERENCE TO THE REGULATION IN FORCE

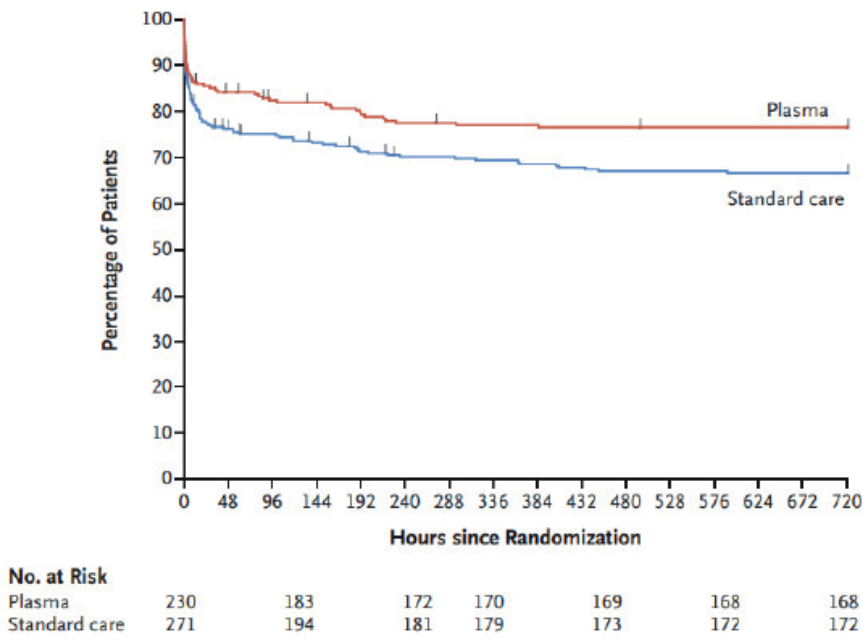
- Immunohematology samples before the transfusion
- Medical prescription
- On-site assessment
- Traceability
- Nurse training
- Patient follow-up

2 NO ALTERING THE PRODUCT DURING TRANSPORT

- Temperature variations
- Mechanical restrictions due to the means of transport
- Time without temperature control
- Systems to optimally preserve blood cells

3 EVIDENCE-BASED DECISIÓN-MAKING

- Two randomized clinical trials have shown benefits from pre-hospital transfusion in more severe patients, and European guides recommend its use.



Sperry et al. N Engl J Med, 2018[13]

	RBC N=223	RBC+P N=391	RCP N=295
	N (%), unless otherwise stated		
Mortality†			
Died on scene	65 (29.1%)	96 (25.2%)	77 (26.5%)
24-h mortality	106 (47.5%)	139 (36.1%)*	117 (40.2%)**
30-day mortality	120 (53.8%)	191 (49.1%)	148 (50.1%)

Sperry et al. N Engl J Med, 2018[13]

4 USING SCORES TO PREDICT THE NEED FOR PRE-HOSPITAL TRANSFUSION

- Making the best choice is a challenge in terms of striking a balance between its sensitivity and specificity.

5 CHOOSING THE RIGHT PRODUCT

- **Lyophilized plasma** ➡ only in the context of activating the massive transfusion protocol or when a time longer than 20 minutes to move to the closest hospital is estimated
- **Red blood cells** ➡ increase of survival and QALYs with red blood cells RhD+ ➡ is a beneficial strategy versus non-transfusion
- **Low-titer type O whole blood** ➡ safe and effective, but further randomized clinical trials are required to prove benefits in terms of survival.

Blood donation is valuable, and we must guarantee safety for donors, even preventing unnecessary expenses.

CSL Behring

Expert Comment

Author of the comment: Dra. Sonia María Veiras.

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Pre-hospital transfusion was first described in military scenarios (during World War 2), and subsequently in civil scenarios (emergency medicine, settings away from hospital care, such as sea cruises, or inter-hospital transport).

In trauma patients, the use of plasma instead of crystalloids outside of the hospital was associated to a 30% decrease in mortality.

Although extra-hospital transfusion practice is widespread in many European countries and beyond, the uneven implementation of this process raises questions.

In the United Kingdom, 91% of air ambulances are equipped for transfusion outside of hospitals. In France, this percentage reaches 72%.

Besides trauma bleeding, gastrointestinal and gyneco-obstetric bleedings are the main causes for pre-hospital transfusion. Up to 50% of pre-hospital transfusions are due to non-trauma causes.

In order to verify the safety of these transfusions, four conditions must be met

1. Adhering to the regulation in force: drawing immunohematology samples before the transfusion, medical prescription, bedside cross-matching, traceability, nurse training, and patient follow-up.
2. Ensuring optimal transport and storage of blood products: extreme temperatures for several hours and transport conditions have not shown significant changes in the morphology of red blood cells or hemolysis. Brunskill et al, (Transfus Med Rev 2012) could not find any negative impact in the quality of red blood cells or in bacterial contamination upon exposure to temperatures of 4+/- 2ºC, from 20 minutes to 42 days. There are various devices (electronic or otherwise) to preserve the right storage temperature
3. Following the current scientific evidence: only two randomized trials, PAMPER for PFC, and Tucker for CH7PFC, have proven the benefit of pre-hospital transfusion. The benefit is almost significant in most severe patients. European guides on trauma bleeding bring to light the lack of evidence of pre-hospital transfusion.
4. Transfusing the right product to the right patient: scores predicting the need for transfusion (TASH, ABC, Larson, PWH...) are essential, but they lack balance in terms of sensitivity and specificity.

Available products in the pre-hospital setting are lyophilized plasma, packed red blood cells, and whole blood for military settings.

Is pre-hospital transfusion safe? In various studies and records, adverse reactions to transfusion are reported in low percentages (0 to 3%) (Moore et al Lancet 2018, Rijnhout et al Injury Int J Care 2019, Angerman et al Prehospital Emergency Care 2022, Rapport Annuel d'Hemovigilance 2021).

Most commonly, type 0 negative blood is available for pre-hospital administration, but it has been reported that the damage from administering Rh positive is lower than not transfusing.

The use of antiA/antiB low-titer type 0 whole blood, with leukodepletion and administered through a platelet-saving filter, has promising results, even though no benefit has been proven in terms of mortality in randomized clinical trials.

The main drawback when using whole blood is the appearance of paroxysmal nocturnal hemoglobinuria.

CSL Behring

Emergency!

Chair: Maria Beatrice Rondinelli, Ravi Rao Baikadi

Thursday 20th of April 2023

1. FAST TRACK ANAEMIA IN THE EMERGENCY DEPARTMENT

Maria Beatrice Rondinelli, Italy

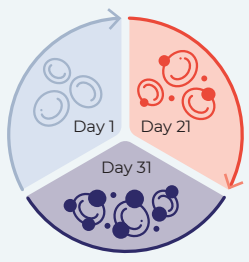
The new definition of PBM includes, for the first time, the concepts of patient safety and empowerment[1]

"PBM is a patient-centered, systematic, evidence-based approach, aimed at improving results through and preservation of the patient's own blood, promoting at the same time safety and patient empowerment"

Transfusions are often an inappropriate therapy, and they may have multiple side effects. In fact, according to the 2018 *Annual Shot Report*, 156 transfusion-related deaths were recorded between 2010 and 2018 in the United Kingdom[2].

BLOOD TRANSFUSION IS OFTEN INAPPROPRIATE THERAPY

Blood transfusion side effects

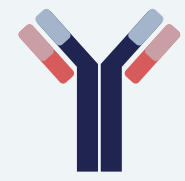


Storage lesions

Infections

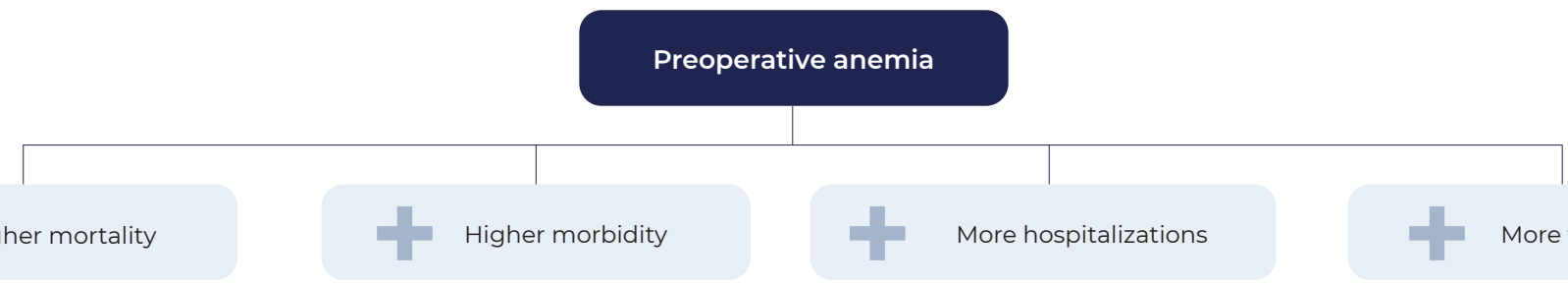
Cost increase

Limited resources



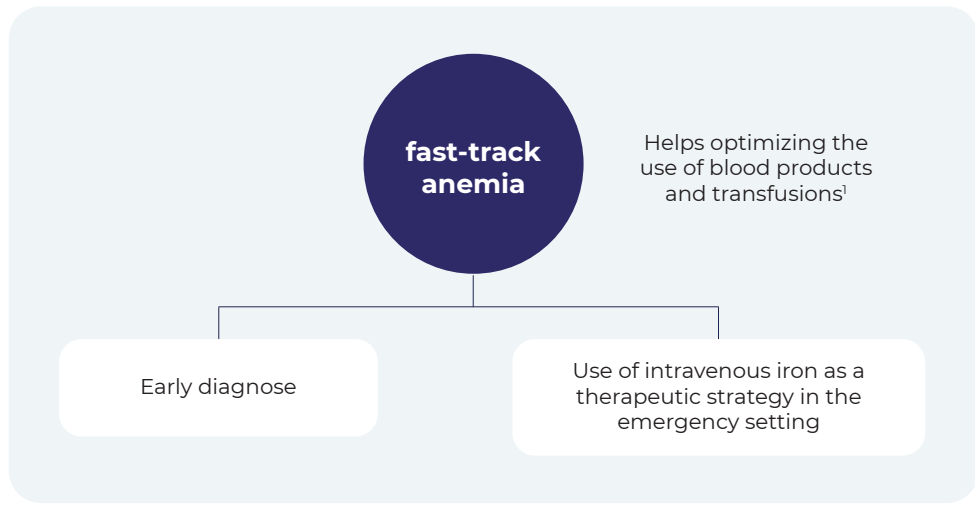
Transfusion errors, TRIM, CARS, SIRS, TRALI, TACO, GVHT

DETECTION OF PREOPERATIVE ANEMIA IN PBM



Iron deficiency in the **Emergency** setting has a diverse etiology, being **gynecological an intestinal conditions** the most **prevalent ones**[4]. Even though these patients had been traditionally treated with transfusions, such transfusions are associated to a non-functional ferritin increase or the interference of inflammatory cytokines.

Management based on a **treatment with intravenous iron** has proven to be **safe, efficient, and cost-effective**, since it improves the use of blood products in emergency services[2-4]. Moreover, it has proven to **progressively improve medullary erythropoiesis** and does not affect inflammatory cytokines, among others.



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Emergency!

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2. MAJOR OBSTETRIC HEMORRHAGE REVISITED: THE ANESTHETIST'S VIEW

Kassiani Theodoraki

Postpartum hemorrhage is the accumulated loss of over 1000 ml of blood, or any volume accompanied by signs or symptoms of hypovolemia within 24 hours of delivery[8].

It is one of the main causes of preventable mortality and morbidity evitable

Early identification of hemorrhages and resource mobilization help prevent the appearance of adverse results[7].

High likelihood of being underestimated at first

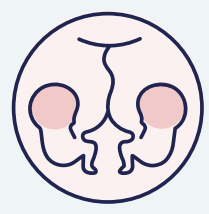
- Masking due to the physiological changes of pregnancy
- Ability to compensate at the start
- Contamination by amniotic fluid

Obvious signs only when the circulating blood volume is very low

Recognizing **postpartum hemorrhage** is a challenge, and so it is important to **stay vigilant, be proactive in diagnosing,** and **proceed as follows:**

1 RISK FACTOR ASSESSMENT:

Previous history of postpartum hemorrhage



Multiple pregnancy

Abnormal placenta or placenta previa

Obesity

Older age

Previous or acquired coagulopathy

Use of anticoagulants

Thrombocytopenia

Obesity[9]

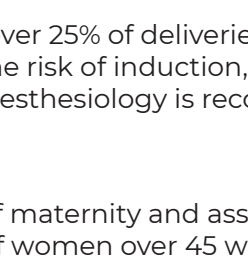
- Present in over 25% of deliveries
- Increases the risk of induction, C-section, postpartum complications, and mortality
- A visit to Anesthesiology is recommended before delivery

Older age[10]

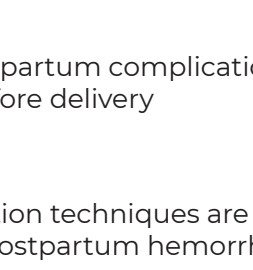
- The delay of maternity and assisted reproduction techniques are pushing up the age of pregnant women
- Nearly 5% of women over 45 will suffer from postpartum hemorrhage

Abnormally invasive placenta (acreta, increta, percreta)

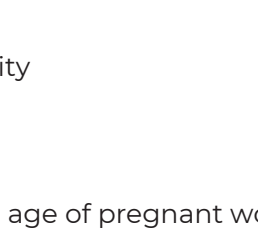
- Risk factors:
  - Previous C-section
  - Older age
  - Smoking
- Factors that may increase morbidity, even in cases of minor hemorrhage:
  - Heart condition
  - Pulmonary hypertension
  - Refusal to receive transfusions
  - Anemia
- Abnormally invasive placenta entails a risk of **massive bleeding, hysterectomy, or need for transfusion** ➡ Referral to a tertiary hospital is recommended, as well as selecting a convenient anesthesia strategy, and a multidisciplinary approach[11].
- There are checklists and protocols applicable in cases of abnormally invasive placenta that promote an early mobilization of blood and blood products, improve the resolution of hemorrhage, and reduce transfusion practice and invasive procedures[12,13].



Normal



Accreta



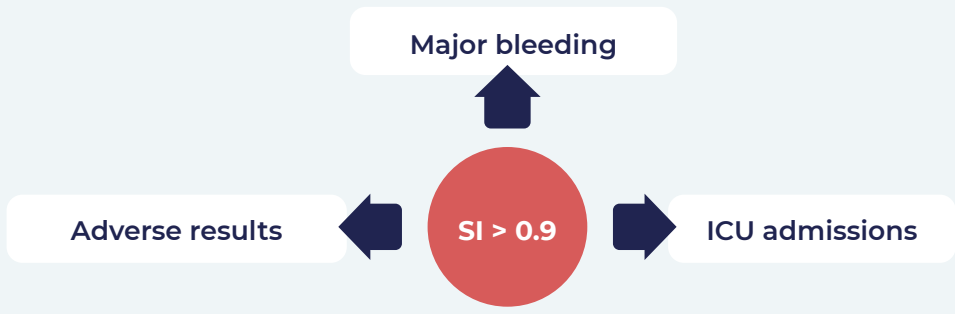
Increta

Percreta

Emergency!

2 ON-SITE ASSESSMENT

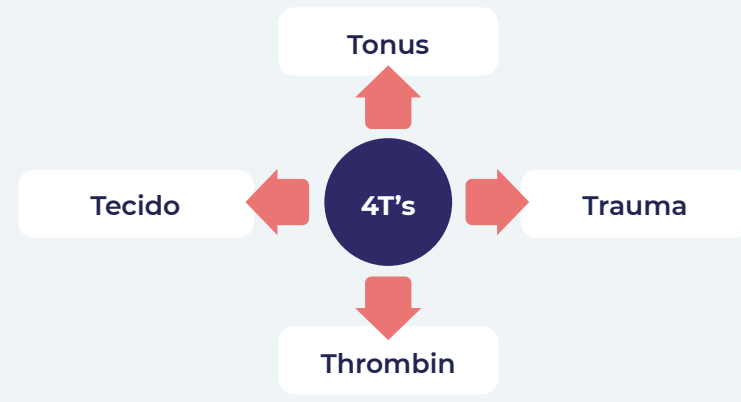
- The **shock index**, combining physiological variables of heart rate and systolic blood pressure, has been suggested as a predictor of cardiovascular changes secondary to bleeding and to worse results in women with postpartum hemorrhage[14,15].
- An **ultrasound at the point of care** can also be useful in the evaluation of hypovolemia, by determining the diameter of the inferior vena cava, even though it takes some time to capture and determine it[16].



3 DETERMINATION OF BLEEDING RISK

Determination at multiple times

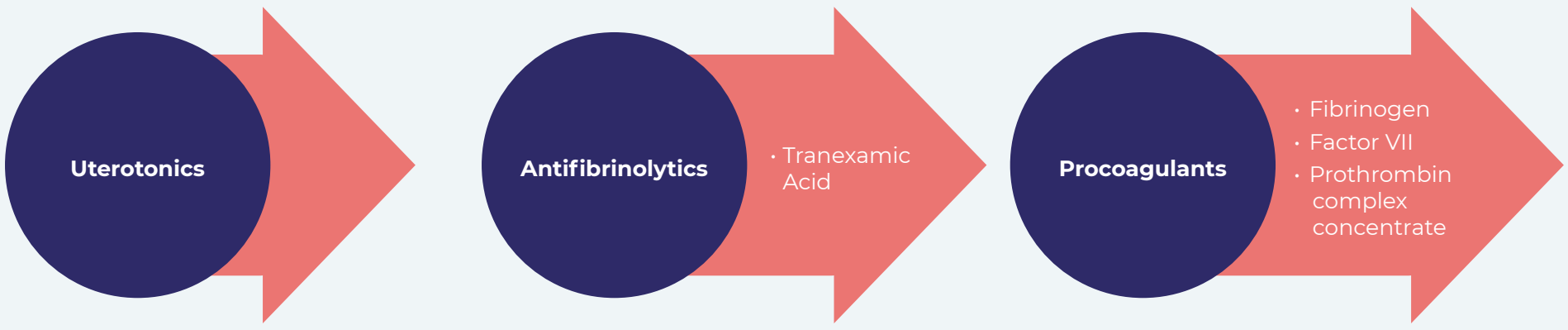
4T Rule



4 TREATMENT

Treatment goals are based on the following aspects:

- Achieving the right uterine tone
- Maintaining cardiovascular stability of the mother



5 CONTROL OF COAGULOPATHY

In order to properly monitor coagulopathy in cases of postpartum hemorrhage, it is recommended to use a test at the point of care, such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM), rather than traditional tests, given the fast availability of results[17].

CSL Behring

Expert Comment

Author of the comment: Dra. Sonia María Veiras.

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Postpartum hemorrhage (PPH) is the main cause of maternal death worldwide.

PPH (ACOG 2014) is defined as accumulated blood losses >1000ml or blood losses concurrent with signs/symptoms of hypovolemia within 24 hours after delivery. Identifying the situation is sometimes hard and underestimated.

The "Shock Index" (SI), which is calculated by dividing the heart rate by the systolic blood pressure, can be a powerful predictor of the real severity of PPH. An SI value>0.9 predicts significant bleeding and hemodynamic impairment.

Measuring the diameter of the inferior vena cava by ultrasound is a useful tool to assess hypovolemia in PPH situations, although after delivery it is difficult to obtain good images.

The treatment goals will be the following:

- Maintaining the uterine tone (by giving uterotonics)
- Maintaining cardiovascular stability—activation of massive transfusion protocols, optimizing hemostasis and deciding whether surgery is necessary.

Identifying which women present a risk of PPH helps us anticipate. This risk can be identified in several stages (before, during, and after delivery). Risk factors include pregnant women over the age of 35, multiple pregnancies, history of PPH in previous pregnancies, abnormal placenta implantation, obesity, maternal thrombocytopenia, anticoagulant therapy, or maternal coagulation disorders, among others.

We must not forget the four-T rule: Tone, Tissue, Trauma, Thrombin.

And we must not forget the four Rs in the management of PPH: Readiness, Recognition, Response, Report and learning.

The anesthetic strategy for C-section in cases of a placenta with an implantation defect can be regional or general, each having benefits and drawbacks that should be considered.

The available pharmacological strategies are:

- Uterotonic drugs as a first-line therapy: oxytocin, ergometrine, prostaglandin F2 alpha analogs, and prostaglandin E1 (misoprostol)
- Tranexamic acid as a fibrinolysis blocker, produced after the detachment of the placenta. Supported by the WOMAN trial, published in Lancet 2017, which established the benefit of TXA administered within 3 hours after delivery in PPH cases. The prophylactic use of TXA is not well established.
- Agents that work on the coagulation cascade: fibrinogen concentrates, recombinant activated factor VII, prothrombin complex concentrate.

Coagulation points of care (TEG, ROTEM) are increasingly used in PPH, given their fast results and the possibility of implementing a goal-oriented therapy, preventing over- and undertransfusion.

Cell Saver is an increasingly used blood salvage device in major obstetric hemorrhage that reduces the risks of allogeneic blood transfusion, although it can entail a potential risk of maternal-fetal alloimmunization and amniotic fluid embolism. Both risks can be mitigated by using filters to leukodeplete salvaged blood. It is not a cheap resource and it is normally not available 24/7. However, it is a good alternative in cases of severe anemia, rare blood types and blood transfusion rejection.

Surgical maneuvers applied to control serious obstetric hemorrhage include: manual extraction of the placenta, uterine packing, balloon intrauterine tamponade, uterine compression sutures, or pelvic vessel ligation. As a last surgical resort, hysterectomy can be used.

Radiological interventionism can seal bleeding vessels, reducing the use of blood products and delaying or preventing hysterectomy, although its availability is often limited and presents potential complications, such as ruptured iliac vessels, infections, formation of pseudoaneurysms, impossibility to control bleeding, and more rarely, uterine necrosis.

Upon controlling PPH, the level of care needed by the mother must be determined, requiring admission to Critical Care in case of prolonged mechanical ventilation due to respiratory failure or TRALI, in multiorgan failure, persistent coagulopathy, hemodynamic instability or urological alterations due to urinary tract obstruction in cases of placenta percreta.

In conclusion, PPH may not be preventable, but the poor results after a severe obstetric hemorrhage are due to:

- Inadequate estimation of blood losses
- Delay in implementing therapy
- Low availability of blood and blood products
- Lack of treatment protocols for these situations
- Lack of communication between the members of the team treating the patient
- Inadequate organization

CSL Behring

Emergency!

Chair: **Maria Beatrice Rondinelli, Ravi Rao Baikadi**

Thursday 20th of April 2023

3. PATIENT BLOOD MANAGEMENT IN MAJOR TRAUMA

Athanasios Chalkias

Mortality in critical patients requiring emergency surgery is around 50%, but the causes are still unknown.

PBM in patients with major trauma → **Little evidencie available** → **Low level of recommendation**

GOALS OF HEMODYNAMIC RESUSCITATION IN PACIENTES WITH TRAUMA AND LOW BLOOD PRESSURE

- Maintenance of organ perfusion and oxygen delivery
- Restoration of intravascular volume
- Correction of coagulopathy

MECHANISMS OF ORGAN DYSFUNCTION TO DECIDE WHETHER PBM IS APPLICABLE[18,19]

Early death	Persistent inflammation-immunosuppressive catabolism syndrome
It occurs within hours or days of the damage, characterized by the presence of profound cardiovascular failure (cardiogenic, hypovolemic, or distributive shock).	It occurs as a consequence of an excessive or dysfunctional immune response after trauma.

PATIENT STATUS ASSESSMENT AND DEFINITION OF TREATMENT GOALS

Vasoconstriction and severe hypotension

- Restoring blood viscosity using blood products
- Imrpoving vasomotor tone

TREATMENT IMPLEMENTATION

Fluid therapy

- Minimizing the use of fluids given the increased associated risk of coagulopathy, hypothermia and worse clinical results.
- Prioritizing the use of balanced crystalloids (Plasma-lyte).

Vasopressors

- When fluid therapy is not enough, the use if vasopressor agents is considered (noradrenaline).

Massive transfusion

PBM can be difficult during initial resuscitation, and it may necessary to include a **massive transfusion protocol** and a part of ***Damage Control Resuscitation*** to prevent or treat hypothermia, acidosis, and hypocalcemia.

- It is difficult to predict the need for massive transfusion. The ABC—Assessment of Blood Consumption—score may prove useful, given its sensitivity and specificity[20].
- Protocols facilitating decision-making[21].

Therapeutic options

Blood products in a 1:1:1 ratio	Minimization of risks (coagulopathy and others)
Whole blood	Higher costs
CaCl2	To correct hypocalcemia
Fibrinogen	To correct hypofibrinogenemia

Viscoelastometry at the point of care

- To control objective-guided hemostatic treatment.
- Even though the current available evidence is not robust, it may prove useful in resuscitation of trauma patients, but particularly after initial stabilization.
- Any test at the point of care should never delay the start of the treatment in cases with potentially-lethal bleeding.

The implementation of PBM protocols may be complicated in more critical patients. In general, when implementing a restrictive transfusion strategy, it is necessary to identify the causes of the coagulopathy, to guide the transfusion need according to blood hemoglobin values and the clinical condition of the patient, and make a clinical assessment after each transfusion.

CSL Behring

Expert Comment

Author of the comment: Dra. Sonia María Veiras.

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Severe trauma is a global health issue, and associated hemorrhage accounts for >2,500,000 deaths every year—it is actually the main cause of mortality in adults under 40.

The question is whether PBM principles can be applied in these scenarios, and for that it is fundamental to understand that two main mechanisms of organ damage are at play in severe trauma:

1. Early deaths within hours or days of the trauma in patients leaving the OR with minimum support and developing a cardiogenic, hypovolemic, or distributive shock in a few hours, with a very little known, difficult to prevent mechanism.
2. Persistent inflammation-immunosuppressive catabolism syndrome, with prolonged multiorgan dysfunction, multiple sepsis episodes. Consequence of an excessive or dysfunctional immune response.

Trauma resuscitation has evolved since 2004, starting during the pre-hospital period, improving care in emergency services and ORs, using hemostatic products and guided by coagulation point of care analyzers. However, mortality figures for critically injured patients requiring surgery are around 50%.

PBM may have a significant role in improving these expectations.

- Control of fluid resuscitation should be part of PBM.
- Fluid resuscitation, including the optimal type and volume, is still an issue that stirs debate. It is unclear what the ideal fluid for resuscitation is, but the benefits of using balanced crystalloids are noted (Ringer's lactate, isotonic saline and Plasmalyte. the latter being possibly the best fit to administer together with blood products).
- Vasopressors in PBM: the pathophysiology of traumatic shock is complex, originally due to hypovolemia; the right balance must be stricken between intravascular volume and y vascular tone. Vasopressors counteract vasodilation in hemorrhage, cranial trauma, medullary injury, multiorgan failure, and vasodilation mediated by anesthetics.

Recent European guides on hemorrhage management and trauma-induced coagulopathy recommend the administration of noradrenaline, on top of fluids, to maintain systolic pressures of 80-90 mmHg or average pressures of 50-60 mmHg. or 85-90 in the case of TBI. Both the dose and the duration should be minimized.

Vasopressin can be a useful tool as a vasopressor, but not enough evidence has been gathered so far (AVERT study).

PBM protocol in trauma patients:

- Stop the bleeding, maintaining volemia, restoring volemia
- It may be difficult during early resuscitation, but recommendations include the use of TXA, fibrinogen, normothermia, minimizing iatrogenic blood losses (e.g. analytical extractions).
- A massive transfusion protocol may be included to determine the dose, frequency, and ratio of blood products, and to predict the need for massive transfusion (scores such as ABC, FAST, TASH)
- Damage control: early hemorrhage control, cell saver, hypothermia prevention and treatment, hypocalcemia, and acidosis.
- Considering the use of whole blood instead of fixed ratios 1:1:1.
- Consider using viscoelastic tests to optimize hemostatic correction.

The goals of resuscitation:

- PBM or transfusion thresholds must be individualized.
- Generally speaking, the goals include. Maintaining average BP of 60-65 mmHg or higher in TBI, HR 60-100 bpm, urinary debit >0.5 ml/kg/h, SpO2>94%, SvO2>70%, Hb 7-9g/dl, PLAQ>50,000, INR<1.5, fibrinogen> 1.5-2 g/l, T. >35°C, pH 7.35-7.45, lactate<2 mmol/ L, EB normalized.
- Upon admission to the ICU, PBM application may be difficult and restrictive transfusion strategies should be implemented. Thresholds should also be defined within which transfusion is or not required (with Hb<7 it seems adequate, with Hb >9 it is generally unnecessary, between 7 and 9, transfusion is not associated with mortality reductions, and it should be based on the need to improve clinical symptoms).
- Routine use of plasma is not recommended in critical patients with coagulopathy, and it generally provides no benefits if INR is lower or equal to 2.
- The established platelet value to perform invasive maneuvers in the ICU with no risk of bleeding is 50,000. If the value is <20,000, platelets should be administered, even in the absence of bleeding.
- Erythropoiesis stimulating agents should not be administered on a routine basis.

CONCLUSIONS:

- There are just a few data and no recommendations regarding the use of PBM in severe trauma, although it can improve the patient's physiology and survival.
- PBM SHOULD be part of the whole resuscitation process, although it can be difficult to apply it to early resuscitation.
- Training for the healthcare personnel is required
- PBM protocols are required in institutions (including massive transfusion and damage control protocols)
- Further research is needed for the successful implementation of PBM programs to improve the evolution of patients.

BIBLIOGRAPHY

1. Shander A, Hardy JF, Ozawa S, Farmer SL, Hofmann A, Frank SM, Kor DJ, Faraoni D, Freedman J (2022) A Global Definition of Patient Blood Management. Anesth Analg 135:476–488

2. Annual SHOT Report 2018. https://www.shotuk.org/wp-content/uploads/myimages/SHOT-Report-2018_Web_Version-1.pdf. Accessed 25 Apr 2023

3. WHO The urgent need to implement patient blood management. Policy brief. https://apps.who.int/iris/bitstream/handle/10665/346655/9789240035744-eng.pdf?sequence=1&isAllowed=y. Accessed 21 Apr 2023

4. Morhaim D, Auerbach M (2016) Iron-deficiency anaemia in the Emergency Room: a new opportunity for the use of intravenous iron. Blood Transfus 14:91–92

5. Gammon RR (2023) Iron, iron everywhere and not a transfusion should be had: Intravenous iron therapy for iron deficiency anemia. Blood Transfus. https://doi.org/10.2450/BLOODTRANSFUS.449

6. Jericó C, Beverina I, Quintana-Diaz M, Salvadori U, Melli C, Rondinelli MB, Recasens V, Brando B, Garcia-Erce JA (2020) Efficacy and safety of high-dose intravenous iron as the first-choice therapy in outpatients with severe iron deficiency anemia. Transfusion 60:1443–1449

7. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, Gülmezoglu AM, Temmerman M, Alkema L (2014) Global causes of maternal death: A WHO systematic analysis. Lancet Glob Heal 2:e323–e333

8. Sharp HT, Johnson J V., Lemieux LA, Currigan SM (2017) Executive Summary of the reVITALize Initiative: Standardizing Gynecologic Data Definitions. Obstet Gynecol 129:603–607

9. Blomberg M (2011) Maternal obesity and risk of postpartum hemorrhage. Obstet Gynecol 118:561–568

10. Sheen JJ, Wright JD, Goffman D, Kern-Goldberger AR, Booker W, Siddiq Z, D'Alton ME, Friedman AM (2018) Maternal age and risk for adverse outcomes. Am J Obstet Gynecol 219:390.e1-390.e15

11. Fitzpatrick KE, Sellers S, Spark P, Kurinczuk JJ, Brocklehurst P, Knight M (2014) The management and outcomes of placenta accreta, increta, and percreta in the UK: a population-based descriptive study. BJOG 121:62–71

12. Shields LE, Wiesner S, Fulton J, Pelletreau B (2015) Comprehensive maternal hemorrhage protocols reduce the use of blood products and improve patient safety. Am J Obstet Gynecol 212:272–280

13. Panigrahi AK, Yeaton-Massey A, Bakhtary S, Andrews J, Lyell DJ, Butwick AJ, Goodnough LT (2017) A Standardized Approach for Transfusion Medicine Support in Patients With Morbidly Adherent Placenta. Anesth Analg 125:603–608

14. Ayadi AME, Nathan HL, Seed PT, Butrick EA, Hezelgrave NL, Shennan AH, Miller S (2016) Vital Sign Prediction of Adverse Maternal Outcomes in Women with Hypovolemic Shock: The Role of Shock Index. PLoS One. https://doi.org/10.1371/JOURNAL.PONE.0148729

15. Nathan HL, El Ayadi A, Hezelgrave NL, Seed P, Butrick E, Miller S, Briley A, Bewley S, Shennan AH (2015) Shock index: an effective predictor of outcome in postpartum haemorrhage? BJOG 122:268–275

16. Sert ZS (2021) Prognostic capacity of inferior vena cava diameter for severe postpartum hemorrhage. Eur J Obstet Gynecol Reprod Biol 267:6–10

17. McNamara H, Kenyon C, Smith R, Mallaiah S, Barclay P (2019) Four years' experience of a ROTEM® -guided algorithm for treatment of coagulopathy in obstetric haemorrhage. Anaesthesia 74:984–991

18. Brohi K, Gruen RL, Holcomb JB (2019) Why are bleeding trauma patients still dying? Intensive Care Med 45:709–711

19. Mira JC, Brakenridge SC, Moldawer LL, Moore FA (2017) Persistent Inflammation, Immunosuppression and Catabolism Syndrome. Crit Care Clin 33:245–258

20. Shih AW, Al Khan S, Wang AYH, Dawe P, Young PY, Greene A, Hudoba M, Vu E (2019) Systematic reviews of scores and predictors to trigger activation of massive transfusion protocols. J Trauma Acute Care Surg 87:717–729

21. National Blood Authority Australia Patient Blood Management Guidelines: Module 1. https://www.blood.gov.au/pubs/pbm/module1/transfusion.html. Accessed 26 Apr 2023

CSL Behring

Expert Comment

1. Cell salvage in cancer surgery. *Dania Fischer, Germany*

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DThere are two reasons that would make using cell saver (CS) blood salvage device in cancer a good idea:

- International guides
- Current evidence

CS is one of the strategies used in the second pillar of PBM.

In the context of cancer, salvaged blood transfusion reduces to zero the immunomodulation caused by allogeneic transfusion.

CS can contribute to mitigate the unbalance between donations and red blood cell demand caused by population aging and the resulting reduction in the number of donations.

What do guides say?

The guide on perioperative bleeding management (European Society of Anaesthesiology and Intensive Care) recommends the use of CS and autotransfusion with leukodepletion filters in liver transplant, including patients with liver cancer (evidence 2C), suggests that CS is not contraindicated in cancer surgery, because blood close to the tumor is not aspirated, and since leukodepletion filters are used (2C), CS can reduce allogeneic transfusion in the gynecological setting, including oncologic surgery (2B).

The recommendations of the Italian Society of Transfusion Medicine and Immunotherapy suggest the use of CS during oncologic surgery, provided that salvaged red blood cells are administered through leukodepletion filters and that they are irradiated (25 Gy) before being reinfused (level-2C evidence). Red blood cell irradiation is a complex procedure, not available in most hospitals.

In 2020, the German Medical Association EXCLUDED the use of CS in oncologic surgery, although this was not the case in guides published before 2014. Among scientific evidence, a meta-analysis (Transfus Med Hemother 2022 May 11;49(3):143-157) covers 34 observational studies, with 8503 subjects, 3161 of which were treated with CS during surgery. Studies compared salvages blood, filtered or not, versus not using CS, and mortality and cancer relapse were reported. The patients in the control group were treated with pre-donated autologous blood, with allogeneic blood, or did not receive any transfusion.

The meta-analysis slightly favors CS in regard to cancer relapse, and there are no differences in terms of mortality.

The big question is, are there tumor cells in the salvaged blood? The work by Zong et al in Anesthesiology 2022, using a complex methodology for chromosome marking of tumor cells, concludes that in the salvaged blood there are between 1 and 21 tumor cells in each 4 ml of blood. It is not known for the time being whether these cells have the ability or not to replicate the tumor. We do not know if it is better to assume the risk of salvaged blood reinfusion versus the immunomodulation induced by the transfusion.

IN CONCLUSION: the benefits of CS during surgery are:

- Lower need of donor blood transfusions
- Higher ability to transport O2 when compared to blood from donors
- Absence of immune adverse effects
- Absence of transfusion restrictions

IN CASES OF MALIGNANCY:

- Low level of evidence, lack of randomized clinical trials
- Data from observational studies suggests that CS, with or without filters, would seem safe.

CSL Behring

Expert Comment

2. TXA in patients at risk of thrombosis. *Patrick Meybohm, Germany*

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Hospital Clínico Universitario de Santiago de Compostela. Head of Section at the Anesthesia and Resuscitation Department. A Coruña Province.

Large randomized clinical trials (CRASH2, WOMAN) have shown the efficacy of tranexamic acid (TXA) in the decrease of bleeding and mortality.

Fibrinolysis is a physiological desirable process that prevents the progression to thrombosis. TXA is included in the second pillar of PBM and, given its efficacy, we may think of a universal use of the drug in all surgical processes.

The question is to analyze whether the widespread use of TXA entails an increase in thromboembolic-ischemic events.

JAMA Surgery published a meta-analysis directed by the presenter, “Association of intravenous TXA with thromboembolic events and mortality”, using all the available evidence.

Inclusion criteria included 216 randomized controlled trials (>125,000 surgical patients), from all medical disciplines, with administration of intravenous TXA versus placebo or no treatment.

A risk difference and risk reduction statistical analysis was performed. All thromboembolic events were measured (TVE, TEP, IAM, ICTUS, Other).

Meta-analysis results favor TXa in terms of overall mortality, with no higher incidence of thromboembolic events of any kind.

Neither in the sub-analysis of patients at high risk of thrombotic events a higher incidence of thromboembolic events or overall mortality were found when using TXA.

One of the limitations of this meta-analysis is the non-performance of a screening ultrasound study in all trials, which means that the detection of thrombotic events might be underestimated. The follow-up of patients in the analyzed studies ranged from 24 hours to several months.

CSL Behring

Expert Comment

3. POC in bleeding patients. *Jakob Stensballe, Denmark*

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The answer to this question can be found in the 2016 Cochrane review, by Wikkelso et al., comparing the management of hemostasis using ROTEM/TEG versus conventional management in adults and children with hemorrhage. The risk of mortality is lower in the group treated according to viscoelastic tests. Furthermore, the use of blood products was significantly reduced.

The coagulation system is complex and it is finely compensated. Until a few years ago, we based our hemostatic therapy in conventional lab tests, but these take time and do not reflect the hemostatic reality, which means that using them as a guide is equals a blind therapy.

Viscoelastic tests (TVE) ROTEM or TEG provide an idea of the speed at which the clot is formed, as well as its strength, using whole blood in a short time.

ROTEM and TEG have different terminologies in their results, but they express the same reality with a very intuitive way of showing which coagulation deficits must be corrected.

In order to guide hemostatic correction, a number of action algorithms have been designed, both with ROTEM and TEG. Algorithms may lead to confusion. We must consider which ones are evidence-based and it would be desirable to agree actions common to all of them.

The Copenhagen model works like that, centralizing all VETs in the Blood Bank, with a remote vision from the OR of the evidence provided by the VET, as well as experts in interpreting VETs available 24/7. This implementation model has worked since 2004.

In spite of the invaluable support provided by VETs in hemostatic correction, there is a new concept which is not yet well known and may explain why different degrees of trauma are correlated to different coagulopathy patterns. This new concept is shock-induced endotheliopathy (SHINE). The recent publication in Frontiers in Physiology (Feb 2023) explains how the progression of endothelial damage and the release of catecholamins are represented in the different coagulopathy patterns of TEG and ROTEM. This correlation also supports the need of using VETs in goal-directed hemostasis.

BIBLIOGRAPHY

1. Rajbhandary S, Andrzejewski C, Fridey J, et al (2022) Incorporating the entity of under-transfusion into hemovigilance monitoring: Documenting cases due to lack of inventory. Transfusion 62:540–545

2. Jadwin DF, Fenderson PG, Friedman MT, et al (2023) Determination of Unnecessary Blood Transfusion by Comprehensive 15-Hospital Record Review. Jt Comm J Qual patient Saf 49:42–52

3. Barmparas G, Huang R, Lee WG, Hashim YM, Pepkowitz SH, Klapper EB, Margulies DR (2022) Overtransfusion of packed red blood cells during massive transfusion activation: a potential quality metric for trauma resuscitation. Trauma Surg acute care open. https://doi.org/10.1136/TSACO-2022-000896

4. Joshi GP, McCarroil M, O'Rourke P, Coffey F (1997) Role of quality assessment in improving red blood cell transfusion practice. Ir J Med Sci 166:16–19

5. Joy PJ, Bennet SJ (2012) The appropriateness of blood transfusion following primary total hip replacement. Ann R Coll Surg Engl. https://doi.org/10.1308/003588412X13171221501384

6. Cowan T, Weaver N, Whitfield A, Bell L, Sebastian A, Hurley S, King KL, Fischer A, Balogh ZJ (2022) The epidemiology of overtransfusion of red cells in trauma resuscitation patients in the context of a mature massive transfusion protocol. Eur J Trauma Emerg Surg 48:2725–2730

7. Tung JP, Chiaretti S, Dean MM, Sultana AJ, Reade MC, Fung YL (2022) Transfusion-related acute lung injury (TRALI): Potential pathways of development, strategies for prevention and treatment, and future research directions. Blood Rev. https://doi.org/10.1016/J.BLRE.2021.100926

8. Semple JW, Rebetz J, Kapur R (2019) Transfusion-associated circulatory overload and transfusion-related acute lung injury. Blood 133:1840–1853

9. Vlaar APJ, Juffermans NP (2013) Transfusion-related acute lung injury: a clinical review. Lancet (London, England) 382:984–994

10. Wiersum-Osselton JC, Whitaker B, Grey S, et al (2019) Revised international surveillance case definition of transfusion-associated circulatory overload: a classification agreement validation study. Lancet Haematol 6:e350–e358

11. Politis C, Wiersum-Osselton J, Richardson C, et al (2022) Adverse reactions following transfusion of blood components, with a focus on some rare reactions: Reports to the International Haemovigilance Network Database (ISTARE) in 2012-2016. Transfus Clin Biol 29:243–249

12. World Health Organization (2022) Global status report on blood safety and availability 2021. https://www.who.int/publications/i/item/9789240051683. Accessed 3 May 2023

13. Sperry JL, Guyette FX, Brown JB, et al (2018) Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock. N Engl J Med 379:315–326

14. Tucker H, Brohi K, Tan J, et al (2023) Association of red blood cells and plasma transfusion versus red blood cell transfusion only with survival for treatment of major traumatic hemorrhage in prehospital setting in England: a multicenter study. Crit Care. https://doi.org/10.1186/S13054-022-04279-4

CSL Behring

Patient Blood Management in Clinical Practice: Time to Get into Action

Sponsored by CSL Behring

Chair: **Elisavet Grouzi**

Thursday 20th of April, 2023

1. THE FIRST STEP IN PATIENT BLOOD MANAGEMENT: CORRECTION OF ANEMIA

Elvira Bisbe

Patient blood management (PBM) is one of the six strategic goals of the WHO to ensure universal access to safe, effective quality blood products[1,2]. This is a patient-centered, multidisciplinary, multimodal, evidence-based concept, aimed at preserving at properly using the patient's own blood as a vital resource. Currently, there is evidence that PBM programs do not only reduce the need for transfusion, complications, and mortality[3].

Unlike the past treatment-centered approach, PBM focuses on the patient and the disease, that is, in anemia, aiming at improving the results.

The last definition available of PBM refers to the multidisciplinary timely application of evidence-based medical and surgical concepts, with the following goals[4]:

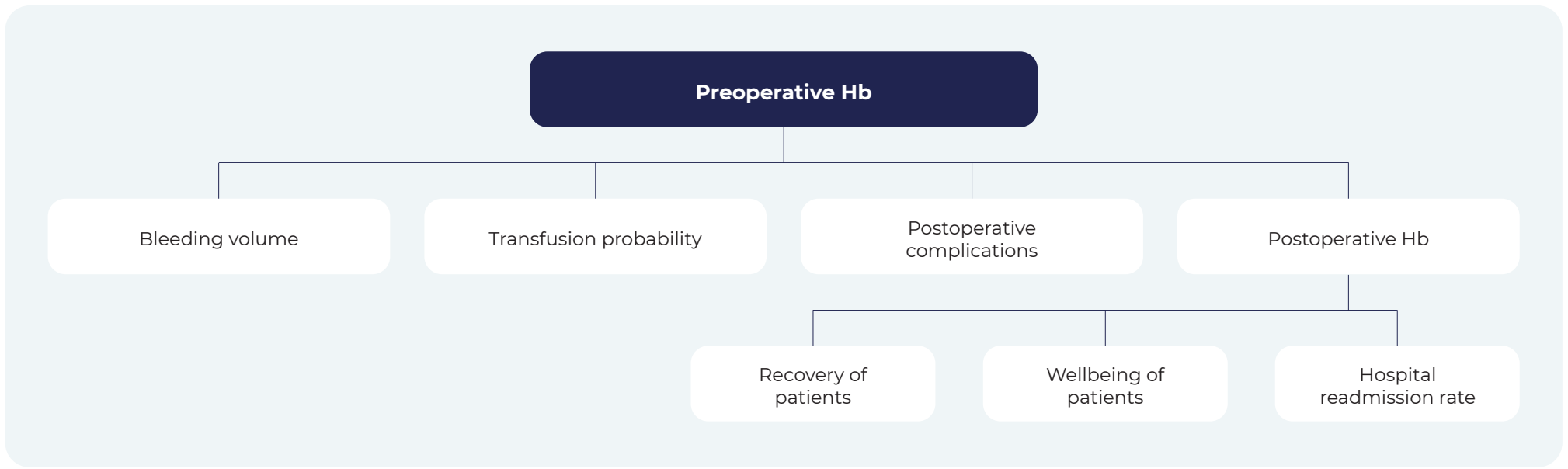
- **Screening, diagnosing, and treating anemia**
- **Minimizing blood loss and managing coagulopathy**
- **Assisting the patient while the right treatment is started**

Therefore, one of three PBM pillars consists of optimizing the red blood cell mass of the patient[5].

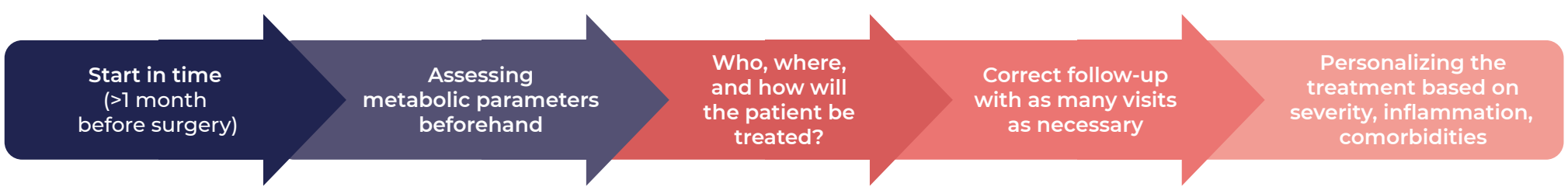
Managing anemia in PBM

The presentation of anemia is an independent risk factor to receive transfusions, with an increased morbidity and mortality[6]. The prevalence of preoperative anemia is high in patient undergoing major surgery1, and it is an independent risk factor of morbidity and mortality[7], even in mild cases[8].

Preoperative hemoglobin levels are related to various results[9-13]:



Anemia correction is the first step of PBM, which can result in an improvement of clinical results, and it involves the following steps:



Many institutions and scientific societies recommend not to perform elective surgeries in case of diagnosed rectifiable anemia.

CSL Behring

Expert Comment

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PBM is not an intervention as such, but it represents the foundations of best clinical practices, focusing on the root of the problem.

PBM is a diamond of healthcare policies, since it improves health, provides better care, cuts down costs, and results in social benefit.

The prevalence of preoperative anemia is very high (20-70%), it is the main risk factor of transfusion, it is an independent risk factor of morbidity and mortality, and its treatment can reduce transfusion and improve postoperative results. Even a mild anemia (Hcto 29-36%) entails a higher morbidity and mortality in surgical procedures other than cardiac surgery.

A meta-analysis by Fowler (BJ Surg 2015), with nearly one million surgical patients, 39% of which suffered anemia, was correlated to a 2.9-fold increase of perioperative mortality, 3.75 times more FRA, 1.93 times more infections, 1.28 times more neurological events in CCA and 5 times more risk of red blood cell transfusion. This is why many scientific societies recommend against performing elective surgeries in patients with diagnosed rectifiable anemia.

Correcting anemia TAKES TIME, as well as a structured approach. Preoperative analysis must be performed on the metabolism of iron, iron and/or erythropoietin should be administered, and patients should be followed to verify the preoperative Hb value.

However, this is not a standard therapy, equal for everyone, but it has to be personalized (PBM seeks a personalized therapeutic approach, based on the cause of the anemia, the surgical procedure, and the characteristics of the patient).

Not treating preoperative anemia means missing a great opportunity, since a great deal of Hb at the time of hospital discharge is associated to faster recoveries, as well as better evolution and outcomes.

Not only surgical patients are important. Prepartum anemia affects 20% of pregnant women, and it is connected to a higher risk of preterm delivery, higher maternal and fetal mortality, and higher rate of infections. NATA recommends correcting prepartum anemia in all pregnant women with an IA evidence-level, as well as an optimal implementation of the first PBM pillar, including optimization of red cell mass before delivery.

KEY MESSAGES:

- Anemia is an independent risk factor for transfusion and the increase of morbidity and mortality.
- Anemia has a high prevalence in major surgery procedures.
- The postoperative Hb level is also associated to postoperative outcomes.
- Prepartum anemia is connected to maternal-fetal adverse events.
- Correcting anemia is the first step of PBM to achieve the main goal of improving the evolution of patients.

CSL Behring

Patient Blood Management in Clinical Practice: Time to Get into Action

Sponsored by CSL Behring

Chair: Maria Aurora Espinosa, Manuel Muñoz

Thursday 20th of April 2023

2. MANAGING COAGULOPATHY IN POSTPARTUM HEMORRHAGE

Fatima Khatoon

The most universal definition of postpartum hemorrhage is the loss of 1000 ml of blood or more14, whereas NATA contemplates the loss of 500 ml in 24 hours, in both cases regardless of the type of delivery[15].

Present in 1-6% of deliveries

Main cause of mortality in developing countries

< 25% of patients present coagulopathy and requere coagulation factors

In obstetrics, prepartum anemia is connected to worse outcomes, both for the mother and the newborn[15,16]. Therefore, it is vital to correct anemia before delivery.

Objective-guided hemostasis consists of determining the deficient coagulation factor and the administration of only such factor.

Objective-guided hemostasis

Goal-directed approach

Decrease in the transfusion rate and associated morbidity

Coagulation objectives according to RCOG and AAGBI:

- Fibrinogen > 2 g/L
- Platelet count > 75k
- PT/aPTT < 1.5

With objective-guided hemostasis, unnecessary transfusions and associated morbidity, among others, can be reduced. Currently, the literature supports objective-guided hemostasis in obstetric patients, since it allows adapting the treatment to the type of coagulopathy. No all women with postpartum hemorrhage present coagulopathy, and in order to make a diagnosis it is essential to understand the etiology of postpartum hemorrhage.

Monitoring of hemostasis

- Traditional tests
  - ↑ time to Obtain resultats
  - Less complete results
  - The objective value of INR is arbitrary
- Thromboelastography (TEG) and rotational thromboelastometry (ROTEM)
  - Provides and overview of hemostasis
  - Reduces transfusions and the use of blood products
  - Improves perisurgical results

Postpartum hemorrhage over 1 500 ml only occurs in 2.7% of deliveries; using ROTEM, it has been estimated that, out of these women, barely 25% present signs of coagulopathy, and almost 50% of them do not require an intervention[17].

Fibrinogen is the first coagulation factor that decreases in patients with postpartum hemorrhage, and often the only one. Its levels are an early severity predictor.

Management of hemostasis in obstetrics must be guided by objectives, and it should identify and correct, at first, the decrease in fibrinogen levels.

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Expert Comment

Author of the comment: Dra. Sonia María Veiras.

Hospital Clínico Universitario de Santiago de Compostela. Head of Section at the Anesthesia and Resuscitation Department. A Coruña Province.

An important premise is that PPH is not exactly the same as post-trauma hemorrhage, and still, some therapy formulas applied to PPH are drawn from multiple trauma patient management guides.

A significant coagulopathy in PPH with bleeding > 1500 ml occurs in 25% of cases.

Hemostasis in PPH depends on the cause of the bleeding. The work by Peter Collins in 2014 shows that hemostasis after bleeding of 1-2 liters stays nearly always unchanged in cases of atony, whereas virtually all amniotic fluid embolisms present a coagulopathy.

Following a single formula would result in overtreatment of some cases and undertreatment of others.

Objective-guided hemostasis can be directed by standard lab tests, but the time between shipping the simple and obtaining the results is too long. These conventional tests do not give us a clear idea of the strength of the clot, and some parameters, such as INR, are not well correlated to the bleeding rate.

Therapy directed by viscoelastic tests (VET) is reliable, provides an overview of the hemostatic capacity of the patient, is adequately correlated with the severity of blood losses, saves transfusions of blood products, improves the evolution of patients, and is cost-effective.

The 2019 NATA consensus for PBM in obstetric hemorrhage is focused on maintaining Hb, correcting hemostasis, and reducing blood losses. NATA's therapeutic strategy recommends starting with tranexamic acid and repeating in case of persistent bleeding, using blood salvage devices, properly monitoring, target fibrinogen above 2 g/liter (or functional fibrinogen above 12 mm in ROTEM or 14 mm in TEG).

Surgical control of bleeding is fundamental and no hemostatic correction will be useful if the source of the bleeding is not surgically corrected.

In summary:

- Standard transfusion ratios lead to unnecessary transfusions and a dilution of fibrinogen levels
- Literature supports the use of objective-guided hemostasis
- Fibrinogen levels during PPH are an early predictor of hemorrhage severity
- Only 25% of women with postpartum bleeding suffer from an associated coagulopathy.
- The etiology of PPH is essential to diagnose the coagulopathy.
- VET-guided therapy is relevant, reliable, cost-effective, and improves perioperative results.

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Patient Blood Management in Clinical Practice: Time to Get into Action

Sponsored by CSL Behring

Chair: **Maria Aurora Espinosa, Manuel Muñoz**

Thursday 20th of April 2023

2. MAKING PATIENT BLOOD MANAGEMENT THE STANDARD OF CARE: WHERE TO BEGIN?

Diana Castro Paupério

The implementation of PBM is an emergency worldwide, but how can it become the standard of care? The steps to implement and institutionalize PBM (PBM-TIPS implemented in Portugal) are summarized below.

1 THE EMERGENCE OF THE NEED

- Identifying the negative impact of pre- and postoperative anemia in patients.
- Receiving advice from experts, both international and national.
- Developing a specific protocol and algorithm.
- Identifying challenges emerging in preoperative, intraoperative, and postoperative periods, when trying to adapt guides to real practice.
- Analysis of PBM implementation results.

2 COMUMNICATION

- Communication of the implementation and the results obtained.

3 CREATION OF THE INFLUENTIAL SUPPORT GROUP

- Creation of regional or national networks of professionals and institutions with an interest on PBM.
- Implementation in pilot centers.
- Program creation: global meetings, tutoring, individualized support to adapt PBM to the needs of each hospital, and cost-benefit analysis.

4 OPPORTUNITY ANALYSIS

- Support from healthcare authorities and scientific societies
- Scaling up PBM to policy level
- Raising awareness on the importance of PBM
- Education of professionals and, whenever possible, working with patient representatives

5 CHALLENGE ANALYSIS

- Patients should be stakeholders
- Lack of awareness or interest
- Lack of robust national policies
- Lack of subsidies
- Interoperability of hospital information systems

CSL Behring

Expert Comment

Author of the comment: Dra. Sonia María Veiras.

Hospital Clínico Universitario de Santiago de Compostela. Head of Section at the Anesthesia and Resuscitation Department. A Coruña Province.

Patient Blood Management is a bespoke solution that follows a set of global rules and should be adapted to each particular context.

Doctor Castro explains the journey followed to reach the implementation and dissemination of PBM programs in her country. She underlines the need for support from political authorities, the creation of a medical network between hospitals of various levels and primary care centers involved in PBM.

She also stresses the importance educating future doctors at universities, as well as training residents.

PBM is not implemented in the infrastructure of our hospitals, and it is not part of our service portfolio—it is a pro bono activity.

In summary, the implementation of PBM is based on education, dissemination, a multidisciplinary approach, and patient empowerment.

BIBLIOGRAPHY

1. WHO The urgent need to implement patient blood management. Policy brief. https://apps.who.int/iris/bitstream/handle/10665/346655/9789240035744-eng.pdf?sequence=1&isAllowed=y. Accessed 21 Apr 2023

2. Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023. https://www.who.int/publications/i/item/9789240000384. Accessed 21 Apr 2023

3. Althoff FC, Neb H, Herrmann E, et al (2019) Multimodal Patient Blood Management Program Based on a Three-pillar Strategy: A Systematic Review and Meta-analysis. Ann Surg 269:794–804

4. Shander A, Hardy JF, Ozawa S, Farmer SL, Hofmann A, Frank SM, Kor DJ, Faraoni D, Freedman J (2022) A Global Definition of Patient Blood Management. Anesth Analg 135:476–488

5. Farmer SL, Towler SC, Leahy MF, Hofmann A (2013) Drivers for change: Western Australia Patient Blood Management Program (WA PBMP), World Health Assembly (WHA) and Advisory Committee on Blood Safety and Availability (ACBSA). Best Pract Res Clin Anaesthesiol 27:43–58

6. Gombotz H, Rehak PH, Shander A, Hofmann A (2007) Blood use in elective surgery: the Austrian benchmark study. Transfusion 47:1468–1480

7. Fowler AJ, Ahmad T, Phull MK, Allard S, Gillies MA, Pearse RM (2015) Meta-analysis of the association between preoperative anaemia and mortality after surgery. Br J Surg 102:1314–1324

8. Musallam KM, Tamim HM, Richards T, et al (2011) Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. Lancet (London, England) 378:1396–1407

9. Abad-Motos A, Ripollés-Melchor J, Jericó C, et al (2023) Identification of the haemoglobin level associated with a lower risk of complications after total hip and knee arthroplasty. Acta Anaesthesiol Scand 67:629–639

10. Basora M, Tió M, Martin N, Lozano L, Salazar F, Sánchez-Etayo G, Raquel B, Pereira A (2014) Should all patients be optimized to the same preoperative hemoglobin level to avoid transfusion in primary knee arthroplasty? Vox Sang 107:148–152

11. Jans Ø, Bandholm T, Kurbegovic S, Solgaard S, Kjærsgaard-Andersen P, Johansson PI, Kehlet H (2016) Postoperative anemia and early functional outcomes after fast-track hip arthroplasty: a prospective cohort study. Transfusion 56:917–925

12. Koch CG, Li L, Sun Z, Hixson ED, Tang A, Chagin K, Kattan M, Phillips SC, Blackstone EH, Henderson JM (2017) Magnitude of Anemia at Discharge Increases 30-Day Hospital Readmissions. J Patient Saf 13:202–206

13. Chaudhry YP, Macmahon A, Rao SS, Mekkawy KL, Toci GR, Oni JK, Sterling RS, Khanuja HS (2022) Predictors and Outcomes of Postoperative Hemoglobin of. J Bone Joint Surg Am 104:166–171

14. Bláha J, Bartošová T (2022) Epidemiology and definition of PPH worldwide. Best Pract Res Clin Anaesthesiol 36:325–339

15. Muñoz M, Stensballe J, Ducloy-Bouthors AS, et al (2019) Patient blood management in obstetrics: prevention and treatment of postpartum haemorrhage. A NATA consensus statement. Blood Transfus 17:112

16. (2008) ACOG Practice Bulletin No. 95: anemia in pregnancy. Obstet Gynecol 112:201–207

17. McNamara H, Kenyon C, Smith R, Mallaiah S, Barclay P (2019) Four years' experience of a ROTEM® -guided algorithm for treatment of coagulopathy in obstetric haemorrhage. Anaesthesia 74:984–991

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Speed up your patient's blood management with autologous platelets and hemostasis management system

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Chair: Donat Spahn

Friday 21st of April 2023

1. PATIENT BLOOD MANAGEMENT: LATEST GUIDELINES

Donat Spahn

The reasons for which Patient Blood Management (PBM) is so important are collected in the WHO document *The urgent need to implement patient blood management*, published in 2019[1]. Currently, there are several clinical practice guides approaching all three pillars of PBM and summarizing the evidence backing its implementation.

The three pillars of PBM are backed by robust evidence and by top-level recommendations from international scientific societies.

2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery[2]

- Se recomienda tratar la anemia antes de la cirugía no cardíaca para reducir la necesidad de la transfusión de hematíes durante la cirugía (Nivel IA).
- In surgery patients with expected blood losses of 500 ml or more, cell salvage is recommended (Level IA)
  - Cell salvage significantly decreases the number of red blood cell transfusions, as well as the hospital stay, among other parameters, and it also improves the clinical outcome[3]. As for the drawbacks, it is not applicable to non-sterile environments and it does not have any coagulation potential. However, retransfusion of both red blood cells and platelets is now possible thanks to the development of new cell salvage devices[4].
- When diagnose systems are available at the point of care, they are recommended as a guide to therapy with blood products (Level IA) → The evidence and recommendation level IA implies that all hospitals should have these systems available.

STS/SCA/AmSECT/SABM Update to the Clinical Practice Guidelines on Patient Blood Management[5]

- Routine use of cell salvage through centrifugation helps preserve blood in surgeries with cardiopulmonary bypass (Level IA).
- In patients undergoing cardiac surgery, a restrictive strategy of red blood cell allogeneic transfusion in the perioperative setting is recommended over a free transfusion strategy (Level IA).

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Speed up your patient's blood management with autologous platelets and hemostasis management system

Sponsored by i-Sep and HemoSonics International

Chair: **Donat Spahn**

Friday 21st of April 2023

2. IMPLEMENTATION OF A NEW VET SYSTEM IN CARDIOTHORACIC SURGERY EXPERIENCE WITH THE QUANTRA

Pierre Tibi

When implementing PBM, every possible effort must be made to avoid a transfusion with allogeneic blood, given the consequences in terms of morbidity and mortality, as well as the associated costs[6-8]. This is why, as recommended by current guides, an assessment at the point of care through viscoelastometry must be integrated in action algorithms[5].

Viscoelastometry tests are an absolutely necessary tool for any hospital practicing cardiac surgery.

Quantra®

Functioning through sonic estimation of elasticity via resonance

Fast results, allowing treatment in real time

- **3-5 minutes:** ability to generate enough thrombin to start coagulation and influence of anticoagulants
- **13-15 minutes:** ability to generate a stable clot and information on platelets and fibrinogen

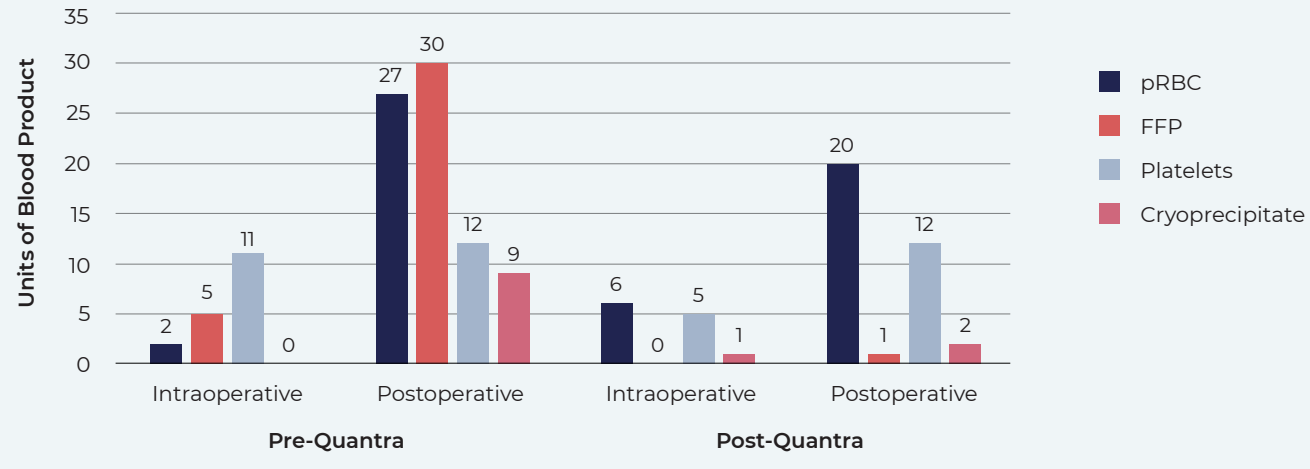
Alternative display of data in curves and trend line

- Treatment with the most appropriate factors
- Saving unnecessary products

In a recent study, a change in the use pattern of blood products has been observed, resulting from the implementation of Quantra® and a specific algorithm, which eventually entails a reduction in the amount of products used and the associated costs[9].

- ✔ Larger reduction of the use of fresh plasma concentrate (probably the most commonly administered product in settings without viscoelastometry, given its price).
- ✔ Sizeable decrease in units of cryoprecipitate, platelets, and red blood cells, yet not significant.
- ✔ Increase in the number of patients who required transfusion of a single blood product, and decrease of those who required one or more.
- ✔ Savings of 41% of the costs (more than 40,000 dollars, overall), resulting from 64 patients.

Blood Products Utilized in the Intra- and Post-Operative Periods



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Friday 21st of April 2023

3. SAMETM BY I-SEP PLATELETS + ERYTHROCYTES: THE NEW INTRA-OPERATIVE CELL SALVAGE GAME CHANGER

Bertrand Rozec

The implementation of a PBM program in the surgery service at the Institut du Thorax in Nantes University Hospital, together with an in-hospital communication & education program on PBM, yielded the following results:

Reduction in the number of patients transfused between 2015 and 2020, mostly with red blood cells and frozen fresh plasma

Reduction of associated costs

accumulated savings exceeding 13 million euros

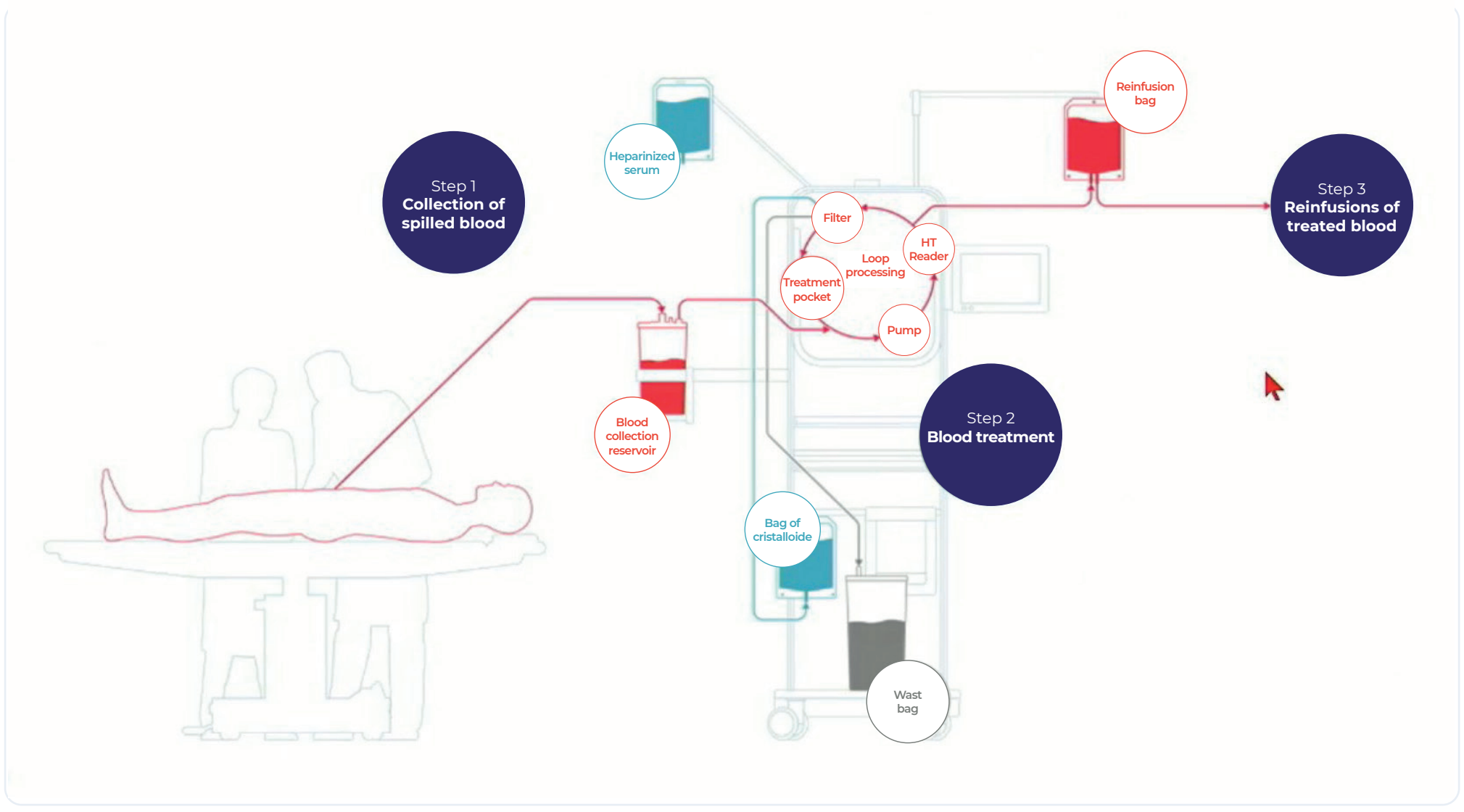
Lower transfusion rate at the cardiac surgery service

Implementation of cell salvage in all ORs, as recommended by current guides[10,11]

The utilization of platelets stayed stable for the period from 2015 to 2021, despite the lower use of red blood cells and frozen fresh plasma

The new cell salvage paradigm covers not only red blood cells, but also platelets.

In France, the i-SEP company developed an autotransfusion device based on the Same™ filtration, which allows salvaging both red blood cells and platelets, with an 88% and 37% performance, respectively[4]. The system causes minimum platelet activation, but a strong response to thrombin stimulation.



A prospective multi-center study will assess its safety and the performance of the device in patients undergoing elective cardiothoracic surgery with risk of hemorrhage, most of them, anemic.

Efficiency in salvaging of red blood cells, platelets, and leukocytes of 86%, 52%, and 90%, respectively

The washout efficiency of heparin, free hemoglobin, proteins, and triglycerides observed is 94 - 99%

No platelet activation has been observed, and so far, 38 cardiac surgeries with cardiopulmonary bypass have been performed

Better results with the Same™ system than with the Xtra™ system by LivaNova, in a series of 4 patients, in terms:

- **Blood volumen lost in 48 hours**
- **Number of transfusions**
- **Days in the ICU**
- **Evaluation parameters of hemostasis via Quantra®**

FUTURE CHALLENGES:

Developing prospective randomized controlled trials to compare cell salvage through centrifugation and through filtration.

Expansion of cell salvage to all kinds of patients undergoing cardiac surgery, and financial evaluation of using these devices.

BIBLIOGRAPHY

1. WHO The urgent need to implement patient blood management. Policy brief. https://apps.who.int/iris/bitstream/handle/10665/346655/9789240035744-eng.pdf?sequence=1&isAllowed=y. Accessed 21 Apr 2023

2. Halvorsen S, Mehilli J, Cassese S, et al (2022) 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgeryDeveloped by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC) Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC). Eur Heart J 43:3826–3924

3. Meybohm P, Choorapoikayil S, Wessels A, Herrmann E, Zacharowski K, Spahn DR (2016) Washed cell salvage in surgical patients: A review and meta-analysis of prospective randomized trials under PRISMA. Medicine (Baltimore). https://doi.org/10.1097/MD.0000000000004490

4. Mansour A, Decouture B, Roussel M, et al (2021) Combined Platelet and Erythrocyte Salvage: Evaluation of a New Filtration-based Autotransfusion Device. Anesthesiology 135:246–257

5. Tibi P, McClure RS, Huang J, et al (2021) STS/SCA/AmSECT/SABM Update to the Clinical Practice Guidelines on Patient Blood Management. J Cardiothorac Vasc Anesth 35:2569–2591

6. Ferraris VA, Davenport DL, Saha SP, Austin PC, Zwischenberger JB (2012) Surgical outcomes and transfusion of minimal amounts of blood in the operating room. Arch Surg 147:49–55

7. Ivascu Girardi N, Cushing MM, Evered LA, Benedetto U, Schwann TA, Kurlansky P, Habib RH, Gaudino MFL (2023) Incidence and Impact of a Single-Unit Red Blood Cell Transfusion: Analysis of The Society of Thoracic Surgeons Database 2010-2019. Ann Thorac Surg. https://doi.org/10.1016/J.ATHORACSUR.2022.11.037

8. Saporito A, La Regina D, Hofmann A, Ruinelli L, Merler A, Mongelli F, Trentino KM, Ferrari P (2022) Perioperative inappropriate red blood cell transfusions significantly increase total costs in elective surgical patients, representing an important economic burden for hospitals. Front Med. https://doi.org/10.3389/FMED.2022.956128

9. Tibi P, Thompson J, Attaran S, Black E (2023) Retrospective study assessing outcomes in cardiac surgery after implementation of Quantra. J Cardiothorac Surg 18:149

10. Mertes PM, Kindo M, Amour J, et al (2022) Guidelines on enhanced recovery after cardiac surgery under cardiopulmonary bypass or off-pump. Anaesthesia, Crit care pain Med. https://doi.org/10.1016/J.ACCPM.2022.101059

11. Kietaibl S, Ahmed A, Afshari A, et al (2023) Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care: Second update 2022. Eur J Anaesthesiol 40:226–304