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

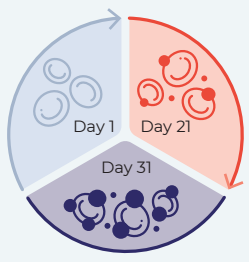
The new definition of PBM includes, for the first time, the concepts of patient safety and empowerment[1]

"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

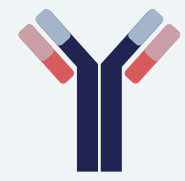


Storage lesions

Infections

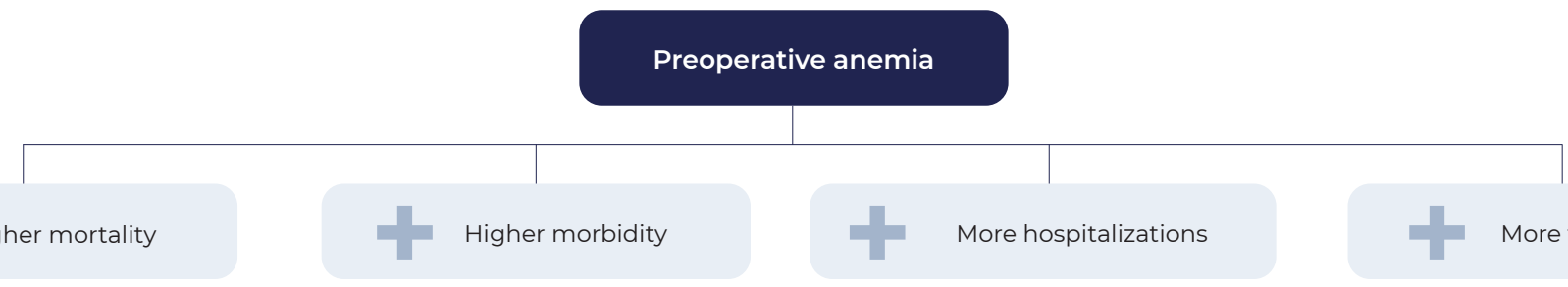
Cost increase

Limited resources



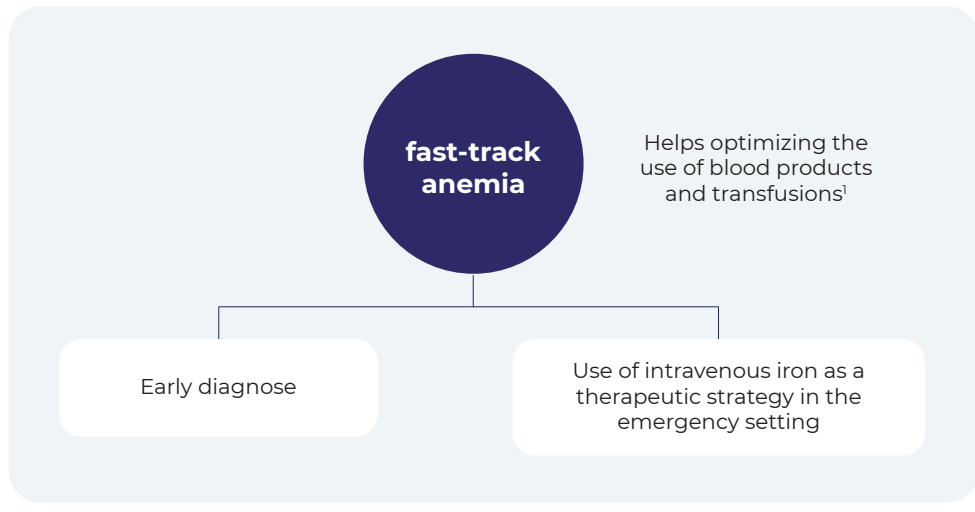
Transfusion errors, TRIM, CARS, SIRS, TRALI, TACO, GVHT

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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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

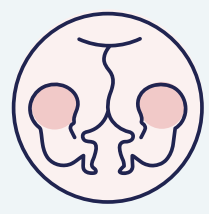
- Masking due to the physiological changes of pregnancy
- Ability to compensate at the start
- Contamination by amniotic fluid

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]

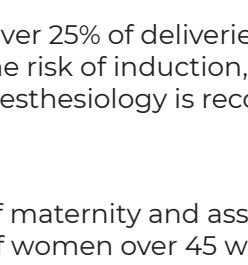
- Present in over 25% of deliveries
- Increases the risk of induction, C-section, postpartum complications, and mortality
- A visit to Anesthesiology is recommended before delivery

Older age[10]

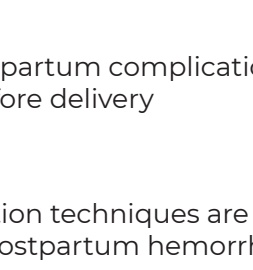
- The delay of maternity and assisted reproduction techniques are pushing up the age of pregnant women
- Nearly 5% of women over 45 will suffer from postpartum hemorrhage

Abnormally invasive placenta (acreta, increta, percreta)

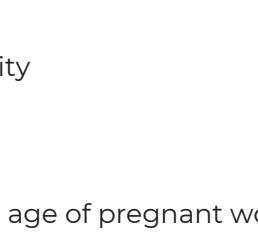
- Risk factors:
  - Previous C-section
  - Older age
  - Smoking
- Factors that may increase morbidity, even in cases of minor hemorrhage:
  - Heart condition
  - Pulmonary hypertension
  - Refusal to receive transfusions
  - Anemia
- Abnormally invasive placenta entails a risk of **massive bleeding, 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

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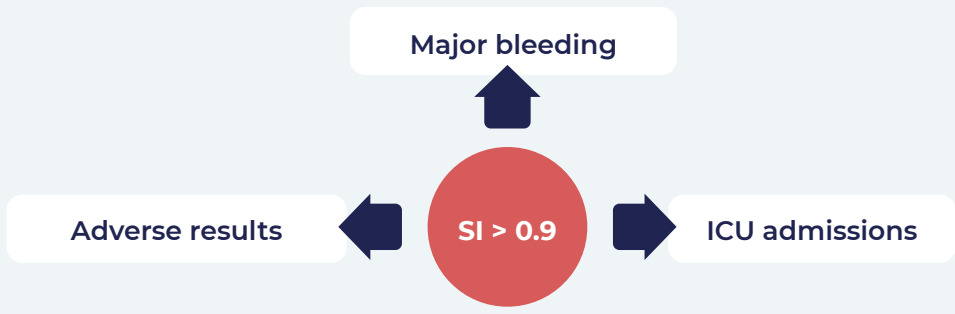
2 ON-SITE ASSESSMENT

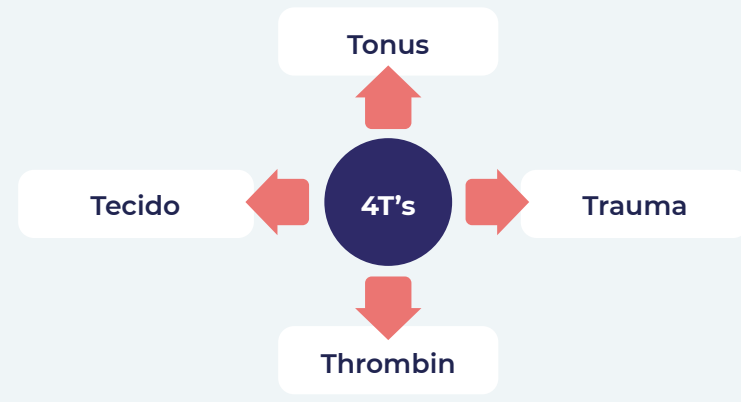
- The **shock index**, combining physiological variables of heart rate and systolic blood pressure, has been suggested as a predictor of cardiovascular changes secondary to bleeding and to worse results in women with postpartum hemorrhage[14,15].
- An **ultrasound at the point of care** can also be useful 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

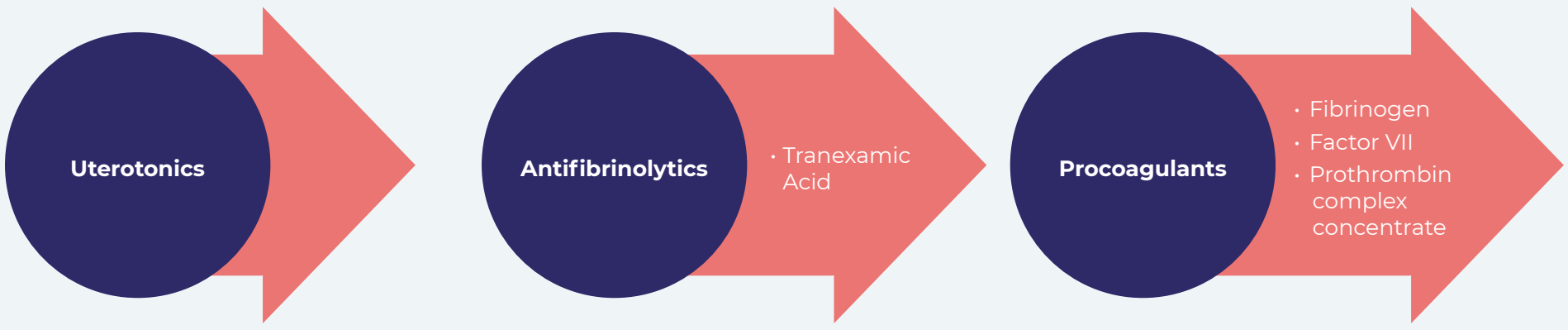
4T Rule



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].

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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.

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

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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.

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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.

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.

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