Universitat de Girona
Facultat de Medicina

Prehospital use of blood transfusion to manage haemorragic shock

Final degree project

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I would like to dedicate my work to all animals and human beings involved in scientific research. Our current progress would not be the same without them.

I am especially grateful with all personnel working in the emergency department of HUJT for providing me the opportunity to immerse in their activity and participate.

Special thanks to my tutors, Àngels Gispert and Rafel Ramos, for guiding me through this new project and providing me essential information.

I do not forget those people who helped me through my harsh moments during the career. I will be eternally grateful.

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1. Abstract

Introduction

Polytrauma is one of the main causes of death and disability among young healthy people, causing a significant loss of life quality and potential years of life.
The main cause of early preventable death in these patients is exanguination due to blood loss.

Currently, the use of crystalloids is the only way to initiate fluid resuscitation during prehospital medical attention, delaying the use of transfusion until arrival to the emergency department.
This situation may delay the use of a potentially life-saving therapeutic measure in the critically injured patient.

Justification

Current measures of prehospital fluid resuscitation may be insufficient and even worse patient's situation iatrogenically when used in excessive amount.

Multiple military forces have tested the use of prehospital transfusion in the critically injured patient, showing promising results.
Current evidence regarding civilian use of this measure is scarce, increasing the need of testing this potentially life-saving measure in a civilian environment.

Objectives

To evaluate if the use of prehospital blood transfusion in severe polytrauma patients suffering haemorraghic shock is related to reduced mortality and reduced use of in-hospital blood products compared to patients in similar condition before implementation of the protocol.

Methodology

This study will be a multicenter quasi-experimental study that will be carried out by 17 medical centers along Catalonia.
The sample will be composed by two groups of severe polytrauma patients suffering haemorraghic shock: one group will be formed by patients registered in TraumCat before implementation of the protocol (control group) and the other group will be formed by patients attended by these medical centers after implementation of the protocol.

Finally, mortality rate and in-hospital use of blood products will be compared between the two groups.

Keywords

Prehospital transfusion, Severe polytrauma

Haemorraghic shock, Mortality.

2. Abbreviations

pRBC: Packed red blood cells

FFP: Frozen fresh plasma

MT: Massive transfusion

DCR: Damage control resuscitation

TIC: Trauma induced coagulopathy

ATLS: Advanced Trauma Life Support

ISS: Injury Severity Score

GCS: Glasgow Coma Scale

NISS: New Injury Severity Score

AIS: Abbreviated Injury Score

HUJT: Hospital Universitari Doctor Josep Trueta

SEM: Sistema d'Emergències Mèdiques

3. Introduction

3.1 Polytrauma patient

Traumatic injury is one of the leading causes of mortality and disability among young population, causing a significant loss of quality of life and years of life.(1–4)

In order to classify the severity of the traumatic patient, we may use several scores or scales(1):

- **Abbreviated Injury Scale (AIS)**: It takes into account the characteristics of the injury and sets an score depending on the severity, which is considered to be related to mortality.
  It's usually used as an intermediate score to calculate other scores.
  Its values are shown in Table 1.

- **Injury Severity Score (ISS)**: It's an anatomical severity score that takes into account the highest 3 AIS scores in each 6 different body regions. After that, the ISS is calculated summing the squares of these 3 scores, obtaining a result between 0-75. (5)
  An example of its calculation is shown is Table 2.

  The presence of an AIS score of 6, automatically assigns an ISS score of 75.
  One disadvantage of this score is that it may not take into account multiple severe lessions within the same body region, making it understimate severity.
  It's considered a moderately good predictor of mortality

- **New Injury Severity Score (NISS)**: It's an anatomical severity score created to overcome the ISS disadvantage of severity understimation in cases of multiple severe lessions in the same body region.

  It's calculated summing the squares of the 3 highest AIS scores independently of its region.

An ISS/NISS score ≥16 indicates the patient presents a polytrauma. It's considered severe if the ISS/NISS is equal to 25 or higher.(1,2)

The main value of these scores is that they are related to anatomical severity, which is linked to higher mortality when the score is higher than 16 or especially if it's higher than 25.(2,5)

Abbreviated Injury Scale (AIS)	
Score	***Lession***
1	Minor
2	Moderate
3	Serious
4	Severe
5	Critical
6	Unsurvivable

Table 1: Abbreviated Injury Score. Adapted from (1)

Injury Severity Score calculation		
Body Region	***AIS value***	***Total value***
Head and Neck	0	
Face	2	4
Thorax	1	
Abdomen	4	16
Extremities	3	9
External	0	
		29

Table 2: An example of ISS calculation. Adapted from (1,5)

In case of NISS calculation, if we had a patient suffering similar injuries as the patient described in **Table 2**, but presenting another injury in the abdomen considered to reach an AIS score of 4, the score would be calculated in the following way:

$$NISS = 4^2 + 4^2 + 3^2 = 41$$

If the ISS was used, severity would have been understimated as it only takes into account the injury related to the highest AIS value in a particular region, not evaluating multiple injuries affecting the same region that would have a similar severity.

Evaluation and treatment of severely injured patients is usually time-critical, since it may compromise their prognosis. (6,7)
One of the main causes of early death,within the first 3-6 hours, in trauma patients is exanguination due to massive haemorraghe, which may be potentially treatable if the patient is treated earlier. (3,4,8,9)

In order to reduce morbimortality related to traumatic injuries, some health centers among different countries have established protocols such as "*Codi Politrauma"*, aiming to provide a quick and efficient attention to the polytraumatised patient, hence improving outcomes such as mortality and prognosis.

3.1.1 Codi Politrauma(6)

"Codi Politrauma" is a protocol developed by Catsalut in order to improve the attention and management of the polytrauma patient in Catalonia.

This protocol involves different levels of priority depending on the characteristics of the trauma patient:

- ***Priority 0***: Patient meets criteria of haemodynamic instability or decreased level of consciousness.
- ***Priority 1***: Patient presents a severe traumatic injury but it's stable haemodynamically and presents a Glasgow Coma Scale (GCS) score equal or higher than 13.
- ***Priority 2***: Patient has been exposed to a high energy trauma mechanism but doesn't meet criteria for other levels of priority.
- ***Priority 3***: Patient meets special criteria that may aggravate the consequences of trauma and doesn't meet criteria for other levels of priority.

Further information about priority criteria is provided in Annex 1.

Once activation criteria are met, the protocol is activated by **prehospital** emergency services, the SEM, calling to the emergency department and providing information about the patient, like its level of priority, injuries, haemodynamic stability and level of consciousness.

Depending on priority level, **inhospital** protocol is activated at a different moment:

- ***Priority 0***: Five minutes before arrival of the patient.
- ***Priority 1***: After initial evaluation by emergency department staff.
- ***Priority 2/3***: Activated if emergency department staff consider it's necessary.

All personnel required to attend the patient will be warned when inhospital protocol is activated in case the priority level is 0/1.
If priority level is 2/3, emergency department staff will warn selectively the required personnel.

3.1.2 Epidemiology of trauma in Girona

Hospital Universitari Josep Trueta (HUJT) is the reference trauma center in the province of Girona.
Due to the availability of its services and characteristics of its facilities, it's considered a trauma center class **CAT-2b** (Annex 2).

After the implementation of *"Codi Politrauma"* in Catalonia in 2011(10), **TraumCat** was developed in order to register all information regarding to the attention of the patient suffering trauma.(2)
It is mandatory to register the following types of situations:

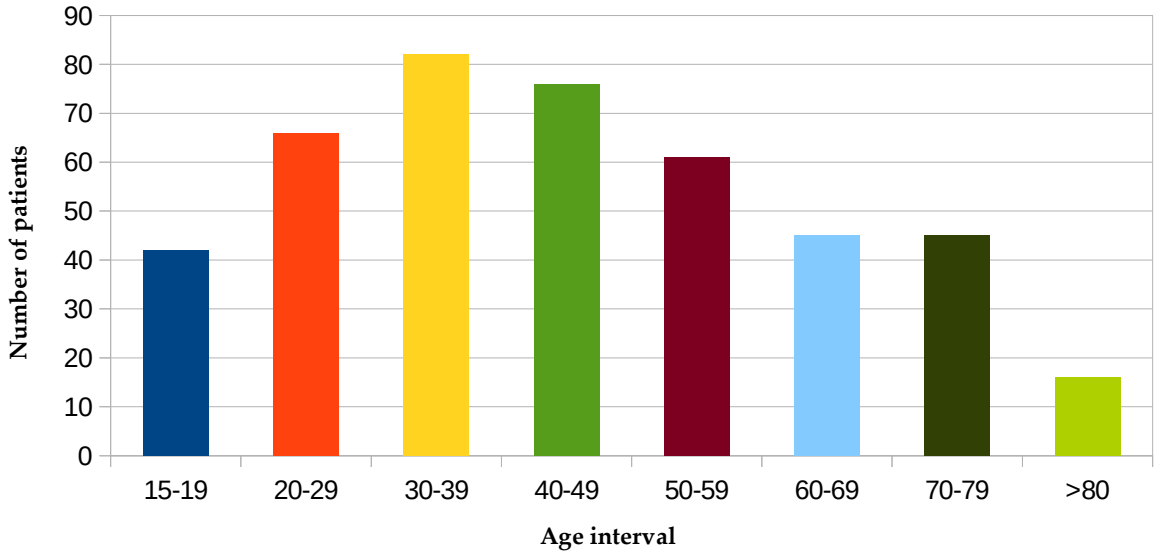
- Patients meeting criteria for activation of priority 0/1.
- Patients admitted to an Intensive Care Unit or Intermediate Care Unit due to trauma.
- Patients who die after being admitted to the hospital due to trauma.

Patients who meet criteria for priority 2 or 3 are registered at will by the medical team.

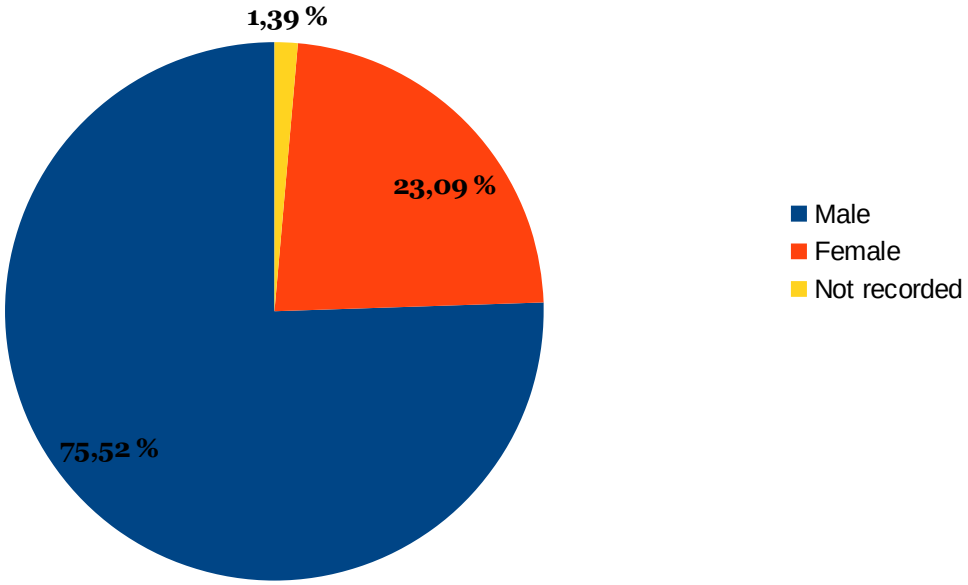
According to TraumCat, the emergency department of HUJT attended 433 patients older than 14 years old suffering polytrauma over a period of 5 years between 2012 and 2017. On average, 80-90 patients per year were attended by this trauma center.

Analysis of this information regarding age, sex and polytrauma priority distribution shows the following results:

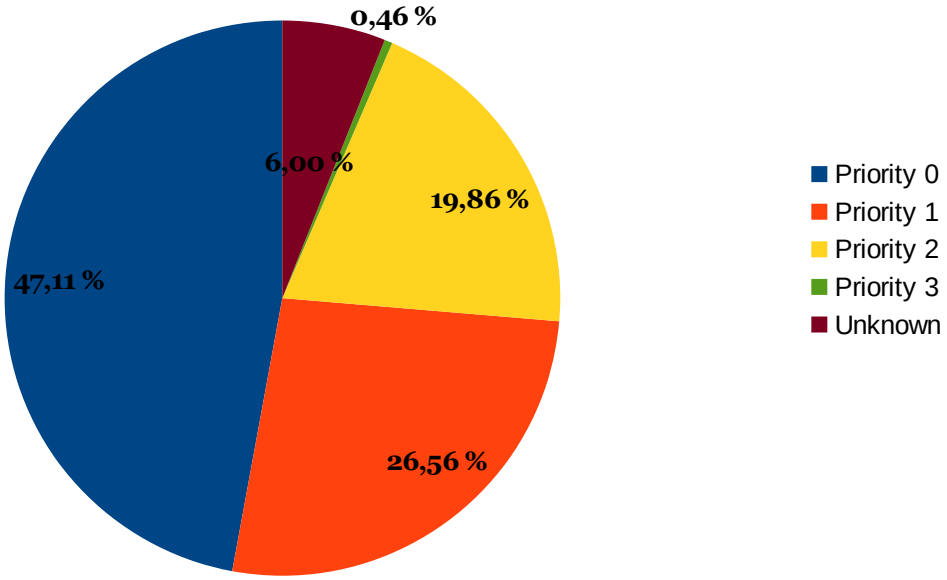
Distribution of polytrauma by age



Distribution of polytrauma by genre



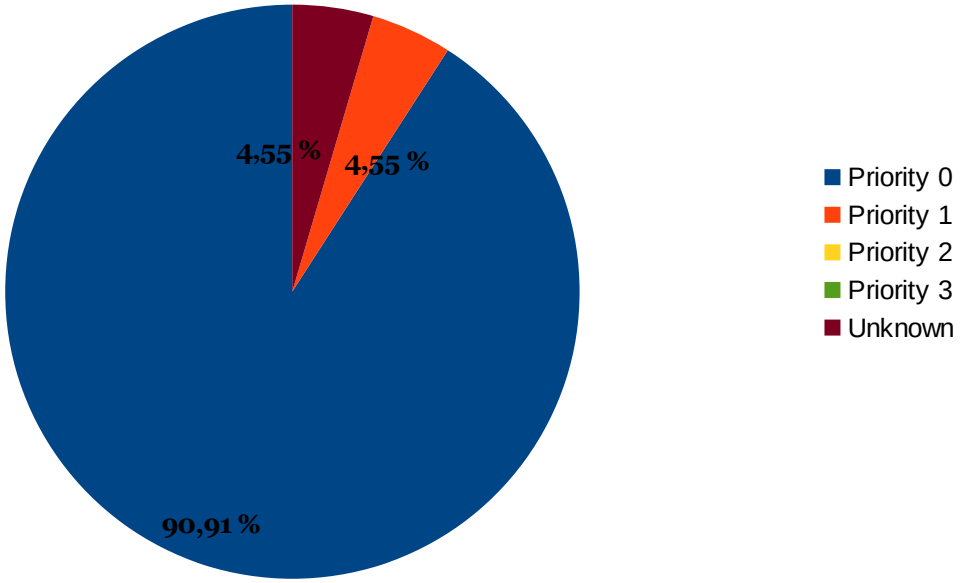
Distribution of polytrauma depending on priority



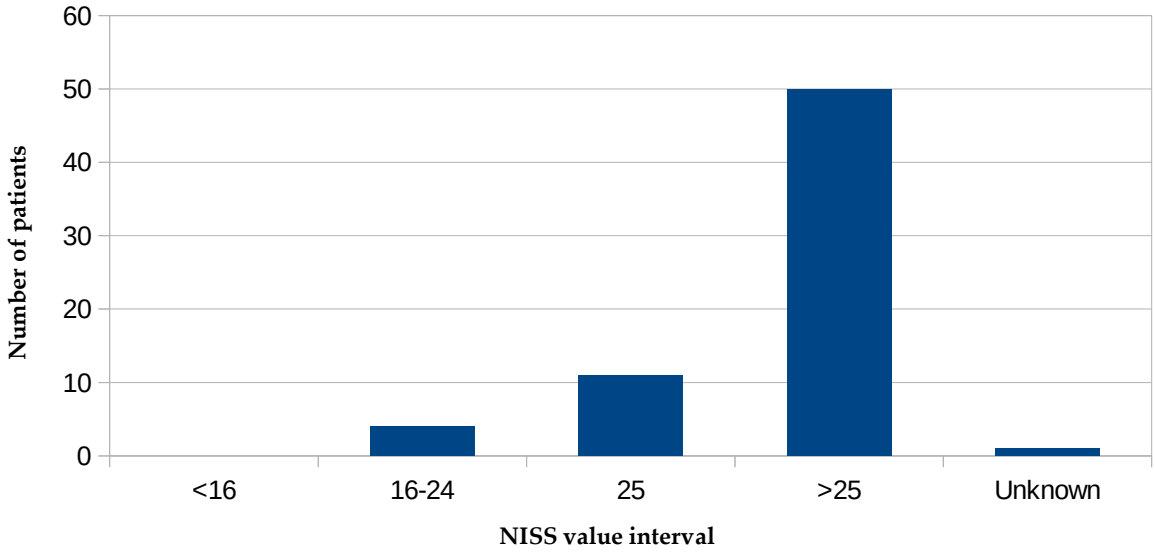
This data shows that the typical profile of the patient suffering polytrauma is a young male, usually younger than 40 years old.

66 patients died, producing an estimate mortality of 15,24 %.

Level of priority among patients who died

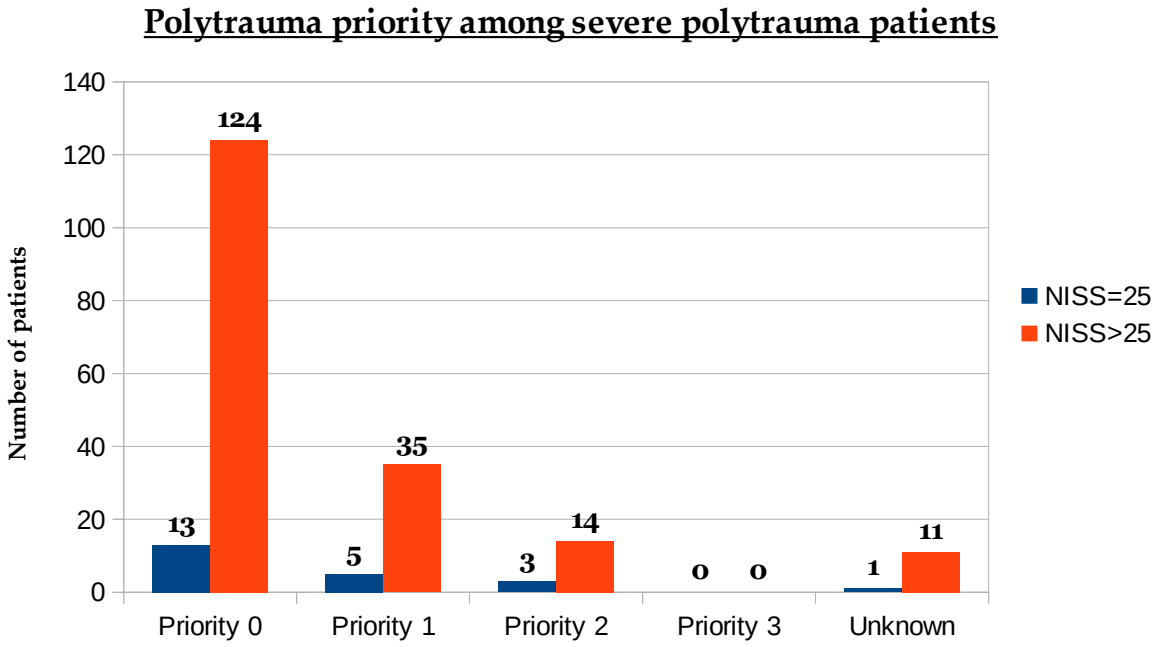


NISS value among patients who died



Most of patients who died met criteria for activation of priority 0 or had a NISS value higher than 25.
Mortality seems to increase directly proportional to the NISS value, showing a dramatic increase when the NISS value is higher than 25.

Patients achieving a value of NISS equal or higher to 25 are considered to suffer severe polytrauma.



Most of the patients meeting criteria for priority 0 or 1 had a NISS value equal or higher of 25.
It can be extrapolated that there is correlation between NISS value and priority of activation.

During the 5 years period of register, 92 patients required the administration of blood products during their admission to the emergency department. We may extrapolate that these patients were suffering haemorraghic shock.

Most of these patients, 76,09 %, were haemodynamically unstable upon admission. It's likely that the rest of patients became unstable during medical attention.

28 of these patients died, causing a mortality rate of 30,43 % among patients suffering haemorraghic shock.
Thus, mortality rate among patients with haemorraghic shock was twice the mortality rate presented in general polytrauma patients.

3.1.3 Initial evaluation of the traumatic patient (6,11)

Initial evaluation is critical for the polytrauma patient, being useful to detect and solve time-critical events.

It's mainly performed following the ABCDE assesment, based on Advanced Trauma Life Support (ATLS) protocols, which is useful to quickly diagnose and treat the conditions that may compromise patient's life.

It's important to reasses each parameter before switching to the next one.
This assesment takes into account the following parameters in a step-wise manner:

- **A**irway
  It's important to keep the airway permeable.
  Performing jaw-thrust or chin-lift maneuver is recommended to improve the permeability of the airway.

  Fractures involving neck, maxilla, jaw or injuries afecting directly the airway may require placement of a definitive airway .
  Low level of consciousness (GCS <8) or presence of foreign bodies are other important causes.

  Noisy breathing or tracheal deviation on exploration are suggestive of airway obstruction.

  The most common way to establish a definitive airway is through orotracheal intubation.

  Immobilization of cervical spine using a device is also mandatory until neck injury is ruled out through complementary tests.
  This is performed in order to prevent worsening any possible cervical spine injury.

- **B**reathing
  Parameters that should be evaluated include $SatO_2$, respiratory rate, use of accessory respiratory muscles, symmetry of respiratory movements and presence of cyanosis.
  All patients should receive oxygen therapy.

  Through palpation, we should look for tracheal deviation, fractures and subcutaneous emphysema.
  Penetrating injuries in chest wall may also impair breathing function.

  It's important to evaluate the presence of hypophonesis during auscultation, which may be suggestive of low gas flow through the airway.

  It's important to quickly evaluate and rule out or treat the following thoracic injuries, as they may significantly worse the patient's condition in short term:

  - Tension pneumothorax
  - Open pneumothorax
  - Flail chest
  - Massive hemothorax

- **C**irculation
  It's the main feature used to evaluate if the patient is suffering shock, especially hypovolemic shock due to blood loss in case tension pneumothorax is ruled out.

It's evaluated through the following parameters:

- *Level of consciousness*
  Hypovolemia may impair brain perfusion, leading to decreased level of consciousness.
- *Skin colour*
  Pale skin may be a sign of significant hypovolemia.
- *Pulse*
  It should be checked in central arteries, such as femoral or carotid arteries.
  It has to be assesed bilaterally, evaluating its rate, regularity and amplitude.

  Presence of rapid and thready pulse is suggestive of hypovolemia.
  Absence of central arterial pulses is generally related to critical hypovolemia if other causes have been ruled out.

Treating any source of bleeding is a priority in order to prevent hypovolemia.
The main source of bleeding in the traumatic patient are:

- *External*
- *Pelvis*
- *Long bones*, such as femur
- *Thorax*
- *Abdomen and retroperitoneum*

External hemorrhage is usually detected upon inspection, while internal bleeding assesment requires imaging test in general.
Initial management to stop the hemorrhage involves compression, manually or through devices such as pelvic binders.

Blood loss may compromise cellular and tissue perfusion due to hypovolemia, leading to shock.
In order to treat this situation, it's important to initiate the administration of intravenous fluids to restore volemia. If it's indicated, early administration of blood products should be performed.

- **D**isability
  It's performed evaluating pupils size, their reaction to light, and calculating the GCS score.

  It's important to take into account that some drugs and medical conditions such as hypoglycemia may alter neurologic functions.

- **E**xposure
  Since it's necessary to undress the patient to perform a proper evaluation, it's important to assess whether the patient presents hypothermia or not.

In order to prevent or treat hypothermia, the patient should be covered with warm blankets after initial evaluation.
Other measures include using warm intravenous fluids and increasing room temperature.

The need of use of a nasogastric or orogastric tube to perform gastric decompression, or the insertion of a bladder catheter to monitor urine output will be evaluated during this step.

Bladder catheterization is mandatory for management of polytrauma patients classified as priority 0-1.

Initial assesment should be repeated periodically in order to detect any change in patient's condition.

3.2 Shock(12)

Shock is defined as a state of cellular and tissue hypoxia due to reduced oxygen delivery, increased oxygen consumption or inadequate oxygen utilization.
It's commonly the result of circulatory failure.(13)

Depending on base deficit, which reflects the amount of base needed to reach a normal value of blood pH, we may differenciate the following degrees of shock:

	Class I	Class II	Class III	Class IV
Shock	Absent	Mild	Moderate	Severe
Base deficit	≤2 mmol/L	2-6 mmol/L	6-10 mmol/L	≥10 mmol/L
Need to transfuse	Observation	Consider	Transfusion	Massive transfusion

Table 3: Shock degree based on base deficit. Adapted from (6)

It's very important to recognize it and treat its cause early, since it may cause death of the trauma patient in short term.

3.2.1. Physiopathology of shock

In order to understand shock physiopathology, it's necessary to know cardiac physiology.
Cardiac output is defined as the volume of blood pumped by the heart each minute, being calculated through multiplication of heart rate and stroke volume.

Stroke volume is the amount of blood pumped by heart during each contraction, and depends on the following parameters:

- *Preload*
  It's the volume of venous blood returning to heart, which is determined by venous capacitance, volume status and gradient of pressure between venous systemic pressure and right atrium.
  Around 70 % of total blood volume is located in the venous circuit.

- *Myocardial contractility*
  It's the pumping system.
  Preload influences this parameter due to the fact that it determines muscle fiber length after ventricular filling at the end of diastole.

  Muscle fiber length is related to its contractile properties based on the Starling's law.

- *Afterload*
  It's the systemic vascular resistance, which generates an opposite force to forward blood flow.

3.2.2 Haemorrhagic shock

Haemorrhagic shock, a type of hypovolemic shock, is the main cause of shock after severe trauma.
It's also one of the main causes of early death among trauma patients.(3,4,14)

Haemorrhage is defined as the acute loss of circulating blood volume.
Blood volume in an adult male weighting 70 kg is estimated to be around 5 L.

Acute blood loss is compensated initially through sympathetic nervous system activation, which increases heart rate, diastolic blood pressure, venous return and causes vasoconstriction of cutaneous circulation.
Therefore, early signs of shock may be suspected if tachycardia and cool skin is present.

As blood loss persists, compensating mechanisms fail, causing systolic blood pressure to decrease.
It's important to take into account that injuries related to trauma are linked to edema in the affected soft tissues, contributing to intravascular volume depletion.

Other signs of established shock include lactic acidosis due to an increase in anaerobic metabolism among tissues, and a significant decrease in urinary output due to kidney hypoperfusion.

Levels of hemoglobin or hematocrit are not reliable when evaluating acute blood loss, since it may show minimal decrease compared to the degree of blood loss.
Very low levels of hematocrit are suggestive of pre-existing anemia or massive blood loss.

However, lactate and base deficit are useful parameters to monitor the evolution of a patient suffering shock.

Depending on the amount of blood lost, we are able to classify haemorrhage in the following categories, based on an adult male weighting 70 kg:

Estimated blood loss based on clinical presentation				
	Class I	**Class II**	**Class III**	**Class IV**
Blood loss (ml)	Up to 750	750-1500	1500-2000	>2000
Blood loss (%)	Up to 15 %	15%-30%	30%-40%	>40 %
Pulse rate (bpm)	<100	100-120	120-140	>140
Systolic blood pressure (mmHg)	Normal	Normal	Decreased	Decreased
Pulse pressure (mmHg)	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate	14-20	20-30	30-40	>35
Urine output (ml/hr)	>30	20-30	5-15	Minimum
Mental status	Slightly anxious	Mildly anxious	Confused	Lethargic
Initial fluid replacement	Crystalloid	Crystalloid	Crystalloid and blood	Crystalloid and blood

Table 4: Estimated blood loss based on clinical presentation. Adapted from (12)

3.2.3 Initial management of haemorrhagic shock

Diagnosis and treatment should be performed almost simultaneously.
It's time-critical to stop the bleeding and replace lost volume.

Initial management through physical exploration requires a quick ABCDE assesment and identification of life-threatening injuries.

It's important to obtain at least two peripheral venous lines using large-caliber catheters in order to infuse large amounts of fluid quickly.

Unless there was any sign of traumatic injury to the urethra, bladder catheterization should be performed to evaluate urine output.

3.2.3.1 Initial fluid therapy

Initial fluid resuscitation usually requires the use of 1-2 L of crystalloids, like saline, in order to evaluate the response of the patient to intravascular expansion.
These fluids should always be administered warmed, reducing the risk of iatrogenic hypothermia.

The ideal goals for systolic blood pressure (SBP) and mean arterial pressure (MAP) depend on patient's injuries and mechanism of injury:

-***Blunt trauma***: If there are features suggestive of traumatic brain injury or spinal cord injury, it's important to keep MAP around 85 mm Hg in order to prevent brain and spinal cord hypoperfusion.

-***Penetrating trauma***: SBP should be kept around 90 mm Hg with a MAP of 65 mm Hg.

However, high volumes of fluid infused in a short time may increase blood pressure too fast, increasing the risk of bleeding if the haemorrhage is not definitively controlled. Excessive fluid administration can also worse the lethal triad of shock: *coagulopathy, hypothermia and acidosis*. (3,8,12,15–18)

This situation led to the creation of the concept "*hypotensive resuscitation"*, which is part of the damage control resuscitation (DCR) strategies(8,12,18,19), and focuses on a balance between haemodynamic stabilization and risk of worsening bleeding iatrogenically.
One way to achieve this goal is reducing crystalloid use and introducing blood products earlier(3,8,11,12,18).

Current evidence recommends the use of crystalloids only until blood products become available or SBP goals are reached.(18)

Response to initial fluid resuscitation is monitored through blood pressure, heart rate, pulse pressure, urine output and level of consciousness.
Depending on the changes upon fluid administration, we may classify the response as:

Response to initial fluid resuscitation			
	Rapid response	**Transient response**	**No response**
Vital signs	Return to normal	Transient improvement, worsening later	No improvement
Estimated blood loss	Minimal (10 %-20 %)	Moderate and active (20%-40 %)	Severe (>40%)
Need for more crystalloid	Low	Low-Moderate	Moderate as a bridge to transfusion
Need for blood	Low	Moderate-High	Immediate
Blood preparation	Type and crossmatch	Type-specific	Emergency blood release
Need for operative intervention	Possibly	Likely	Highly likely
Early presence of surgeon	Yes	Yes	Yes

Table 5: Response to initial fluid resuscitation. Adapted from (12)

3.2.3.2 Blood replacement

Early use of blood transfusion is based on patient's response to initial fluid resuscitation.
Transfusion is indicated when patients show transient or no response.

The use of blood products requires specific tests to check compatibility between donor's and recipient's blood.
Depending on how urgent is the need of blood transfusion, the blood bank will perform the following blood preparations:

- ***Crossmatched blood***
  It requires around 1 hour to be completed.
  Blood bank will check ABO, Rh and will perform further compatibility tests crossing samples of donor's blood and recipient's serum.

  It's used when the patient is stable or has shown a rapid response to initial fluid resuscitation.

- ***Type specific blood***
  It requires approximately 10 minutes to be completed.
  Blood bank will only check ABO and Rh compatibility.

  It's used if the patient has shown transient response.
  Crossmatching will be performed later.

- ***0 negative blood***
  In case of immediate risk of exanguination, 0 negative blood will be provide to the patient as it's considered compatible with all blood groups.

A small set of patients suffering haemorraghic shock may require massive transfusion.
Massive transfusion (MT) is usually defined as the use of >10 units of pRBC within first 24 hours. (4,15,20–22)
Current evidence recommends the use of 1:1:1 ratio compared to 1:1:2 ratio when transfusing multiple blood products (pRBC:FFP:Platelets).(3,6,8,15,18)
This ratio seems to show no problems regarding safety, and evidence has shown that it may improve the success to achieve hemostasis when using surgical or interventional radiology techniques.(3)

The need for MT may be assesed using the Assesment of Blood Consumption (ABC) score(18), which relies on 4 parameters that account 1 point each one:

- Penetrating mechanism of injury
- Positive FAST ultrasound examination.
- SBP ≤ 90 mm Hg
- Heart rate ≥ 120 beats per minute

The patient is considered to require MT if achieves a score of 2 or more.

The use of MT may lead to hypocalcemia and hypomagnesemia due to the use of citrate as an anticoagulant and preservative in blood products.
Thus, levels of ionized calcium should be monitored in patients receiving MT, administering calcium supplements if necessary.(12,21)

Hypocalcemia may also impair coagulation profile, thus contributing to TIC.

3.2.3.1 Management of coagulopathy

Trauma and severe haemorraghe cause consumption and loss of both coagulation factors and platelets, leading to coagulopathy if uncontrolled.
Coagulopathy may be present in up to 30 % of patients affected by severe trauma. (12,16,20)

Presence or risk of coagulopathy may be assesed through platelets count, fibrinogen levels and coagulation profile (Prothrombin time and partial thromboplastin time).

Multiple mechanisms have been suggested, as shown in Figure 1:

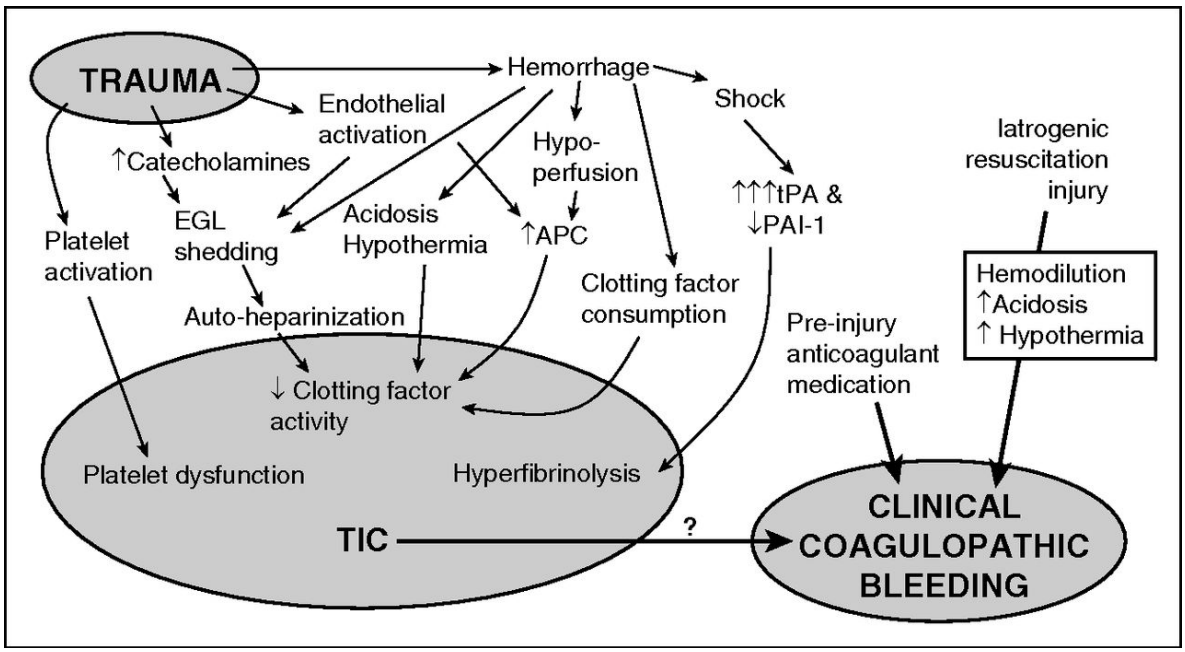


Figure 1: Mechanisms involved in TIC pathogenesis.(14)

Such mechanisms can be summed up as:

- **Decreased levels of platelets and presence of platelet dysfunction**
- **Loss of coagulation factors through consumption and bleeding**
- **Hyperfibrinolysis**

Hyperfibrinolysis can be managed through early administration, within first 3 hours, of tranexamic acid, an antifibrinolytic drug.
It has been shown to reduce mortality among patients suffering massive bleeding. (16,20–22)

The role of platelet dysfunction in TIC as well as the use of platelet concentrates is controversial due to poor evidence about its benefit.(16)

Low levels of fibrinogen (<100 mg/dL) are a strong predictor of mortality among trauma patients.(20,22)
Fibrinogen concentrates may be useful if administered early in order to prevent reaching critical low levels of this clotting factor. (22)

The use of FFP can be useful to expand intravascular volume and provide coagulation factors, minimizing the risk of suffering iatrogenic worsening of TIC and improving the coagulation profile. (3)

3.3 Current evidence about prehospital use of blood products to treat haemorraghic shock

The use of blood products during prehospital attention of trauma patient is a relatively young concept.
Most of evidence regarding early use of blood products comes from the military experience.(7,9,14)

One major issue that difficults the adoption of such practice is the relative short shelf life of some blood products and the conditions needed for their preservation.(22,23)
For example, the most commonly used blood products require the following conditions:

- ***pRBC***: Up to 35 days since donation when stored at 2-6 ºC
- ***FFP***: 3 years when frozen at -25ºC. Up to 24 hours when thawed and stored at 4ºC.
- ***Pooled platelets***: Up to 5 days when stored at 22ºC and constanly agitated.

It's important to consider that blood products approaching their expiration date may show different characteristics, increasing the risk of adverse effects and providing lower benefit.(21)
One way to manage this potential concern is rotating the products back to the hospital when expiration date is approaching, also reducing wastage of blood products.(19)

The use of **freeze dried plasma** might overcome the strict conditions of preservation and especially short shelf life of FFP when used in prehospital medical attention.(22)

Another major issue would be the safety of administering large amounts of blood products, which may cause potentially severe adverse effects.
However, current evidence doesn't show a higher incidence of adverse effects when blood products were used during prehospital attention. (14)

Most of studies reporting current experience about civilian prehospital use of blood products in trauma patients used helicopters carrying 2-3 units of 0 negative pRBC and 2 units of AB FFP.(8,19,22)
One study chose to carry 2 units of pRBC.(9)

One systematic review concluded there were no benefits regarding prehospital transfusion in trauma patients. No prospective studies were found.
However, it took into account studies involved in both military and civilian environments, lowering potential extrapolation of the results to the civilian environment.(14)

Brown JB et al found that transfusion of pRBC during prehospital attention improved 24 H survival, decreased incidence of shock at admission and lowered the requirement of 24 h pRBC.(9)

Henriksen HH et al found that prehospital plasma transfusion improved coagulation profile, haemodynamic instability and shock upon hospital arrival.(8)

Holcomb JB et al found that prehospital transfusion was related to better acid-base balance at hospital arrival and improved mortality within first 6 hours in those patients who were immediately admitted for critical treatment. (19)

So, current evidence is heterogeneous regarding its benefits.
Results are promising and new studies should be performed in larger prospective cohorts in order to achieve higher levels of evidence.

4. Justification

Polytrauma is one of the main causes of death and morbidity among young population, causing a potential loss of quality of life and years of life.(2–4,16)

Exanguination within the first hours after traumatic event is the main cause of early and preventable death in polytrauma patients. (3,4,9,16,19,21,22)
The fact that exanguination can be prevented, emphatizes the need of finding measures to improve the initial management of severe bleeding in polytrauma patients.

Current measures to stabilize the haemodinamically unstable traumatic patient require the use of high amounts of crystalloids, potentially worsening coagulopathy iatrogenically and difficulting early control of the hemorrhage. (12,16,21)

One alternative therapeutic measure for these patients would be the prehospital use of blood products, as a part of DCR measures.(3,9,15,19,22)
Achieving early control of haemorraghe may reduce the incidence of this early cause of death in polytrauma patients.

Current data about the need of blood products after admission is scarce and controversial. (8,9,14,19)
Improved hemostasis and haemodynamic stability upon arrival may reduce the need of such products.

Preliminary results in military population are promising, empowering the need to test the potential benefits of this strategy in the civilian environment.(9,19,22)
Very few studies have tested this strategy in civilian environment, and current evidence obtained by them is confusing. (8,9,12,15)

This situation empathizes the need to test the results of using such therapeutic approach in a large prospective study among civilian population.

5. Hypothesis

Main hypothesis

Prehospital use of blood transfusion reduces mortality among severe polytrauma patients suffering haemorraghic shock compared to standard management using crystalloids before implementation of the protocol.

Secondary hypothesis

Prehospital use of blood transfusion reduces in-hospital requirements of pRBC during first 24 hours in severe polytrauma patients suffering haemorraghic shock compared to standard management using crystalloids before implementation of the protocol.

6. Objectives

Main objective

This study aims to evaluate if the use of blood transfusion during prehospital management of the severe polytrauma patient suffering haemorraghic shock is related to reduced mortality when compared to standard management using crystalloids before the implemention of the protocol.

Secondary objective

The secondary aim of this study is to evaluate if the use of blood transfusion during prehospital management of the severe polytrauma patient suffering haemorraghic shock is related to reduced use of in-hospital pRBC during first 24 hours when compared to standard management using crystalloids before the implementation of the protocol.

7. Material and methods

7.1 Study design

This study is designed as a quasi-experimental study.

7.2 Study setting

This study is designed to be multicenter.
It will be set among 17 medical centers that currently report data to TraumCat(2).

Medical centers that will be included in the study are specified in Annex 3.
Hospital Sant Joan de Déu will be excluded from the study as it is not an adult trauma medical center.

7.3 Study population

The study population will be all patients suffering polytrauma admitted to the Emergency Department of any of the medical centers, that fulfill the following requirements:

7.3.1 Inclusion criteria

1. Criteria for activation of priority 0 or 1 of *"Codi Politrauma"*.
2. Transient or no response to initial fluid resuscitation.
3. Age ≥ 15 years old.

7.3.2 Exclusion criteria

1. Criteria for activation of priority 2 or 3 of *"Codi Politrauma"*.
2. Rapid response to initial fluid resuscitation.
3. Age < 15 years old.
4. Isolated lession.
5. Burns along ≥ 20 % of total body surface.
6. Patients transferred from another medical center.
7. Patients denying informed consent.

7.4 Sample

7.4.1 Sample selection

The sample will be composed by 2 groups:

- **First group** ***(Control group)***: Composed by patients meeting all inclusion criteria and none of the exclusion criteria 1-6 before the implementation of the protocol.
  This group will require the following inclusion criteria to extrapolate that they were suffering haemorraghic shock:
  - Administration of at least 1 unit of pRBC after admission to the emergency department registered in TraumCat.

  As these patients will not require intervention, informed consent is not a requirement.

- **Second group** ***(Protocol group)***: Composed by patients meeting all inclusion criteria and none of the exclusion criteria after implementation of the protocol.

The **control group** will be selected among patients registered in TraumCat before the implementation of the protocol.

The **protocol group** will be formed using a non probabilistic consecutive sampling method among patients attended in the emergency department of the selected medical centers after the implementation of the protocol.

7.4.2 Sample size

The free online application GRANMO has been used to calculate the sample size.(24)

Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, 292 patients are necessary in first group and 292 patients are necessary in second group (584 patients in total) to recognize as statistically significant a proportion difference expected to be of 0.3 in group 1 (average mortality among severe polytrauma patients suffering haemorraghic shock) and 0.2 in group 2.
It has been anticipated a drop-out rate of 0%.

According to TraumCat's 2014 report, 536 potentially eligible patients were attented during 2014 in 17 hospitals of Catalonia.(2)
Thus, it is estimated that at least 18 months will be necessary to reach the number of patients needed to complete the study.

In case the number of patients recruited reached the needed number of patients, recruitment will be stopped until further analysis determines if there is benefit to the patient when using this therapeutic measure.

7.5 Variables and methods of measurement

Data regarding variables in **control group** will be collected retrospectively through TraumCat register.

Data from patients forming the **protocol group** will be collected prospectively using information regarding prehospital and emergency department medical assistance, and filling an especifically designed data collection sheet (Annex 4).

7.5.1 Main variables

- **Prehospital administration of pRBC**: It is a discrete quantitative variable. Patients belonging to **control group** couldn't be transfused during prehospital attention, since the protocol wasn't established. This group presents a value equal to 0 in this variable.

  Patients attended after implementation of the protocol may require different number of units of pRBC to be administered during prehospital assistance.

  It will be expressed as mean and standard deviation.

- **Mortality**: It is a nominal dichotomous variable (Yes/No).
  It requires diagnosis of death after inclusion of the patient in the study. We will not take into account brain death.

  It will be expressed as percentage.

- **24 hours in-hospital administration of pRBC**: It is a discrete quantitative variable.

  It will be expressed as mean and standard deviation.

7.5.2 Covariates

We will take into account the following covariates, as they may act as confounding factors:

- **Age**: It is a discrete quantitative variable.
  It will be calculated through the date of event minus the date of birth obtained from the patient's ID card or other valid document.

  It will be measured in years, calculating its mean and standard deviation.

- **Gender**: It is a nominal qualitative variable (Male/Female/Unknown).
  It will be collected from the patient's ID or other valid document during admission.

  It will be expressed as a percentage.

- **Priority**: It is a nominal dichotomous qualitative variable (Priority 0/Priority 1). Patient will be classified based on first priority criteria of *"Codi Politrauma"* that it meets.

  It will be expressed as a percentage.

- **Medical center category**: It is a nominal qualitative variable.
  It will be classified depending on the medical center attending the patient.

  It will be expressed as a percentage.

- **Systolic blood pressure**: It is a continuous quantitative variable.
  It will be taken into account the first value obtained after patient's admission to the emergency department.

  It will be expressed as a mean and standard deviation.

- **Base deficit**: It is a continuous quantitative variable.
  It will be measured from an arterial sample obtained upon arrival of the patient to the emergency department.

  It will be expressed as a mean and standard deviation.

- **NISS**: It is an ordinal qualitative variable.
  It will be analyzed dividing the patients in the following groups: <16, 16-24, >24.

  It will be expressed as a percentage.

- **Mechanism of injury**: It is a dichotomous nominal qualitative variable (Blunt trauma/Penetrating trauma).
  It will be considered as Blunt trauma, patients admitted due to:
  - Road accident.
  - Push.
  - Trauma caused by blunt objects such as fists, stones, hammer, etc.

  We will consider as Penetrating trauma, patients admitted due to:
  - Injury caused by a firearm.
  - Stabbing caused by a sharp object.

  In case that the patient presents multiple injuries caused by both mechanisms, it will be considered the mechanism causing the injury achieving the highest AIS value.

  It will be expressed as a percentage.

Variable	Type	Categories or values	Measure instrument
Prehospital administration of pRBC	Discrete quantitative	Number of units administered	SEM report of treatment
Mortality	Nominal dichotomous qualitative	Yes/No	Alive or dead at discharge
24 hours in-hospital administration of pRBC	Discrete quantitative	Number of units administered	24 hours medical assistance report after admission
Age	Discrete quantitative	Number of years	Date of event minus date of birth obtained from ID card or other valid document
Gender	Nominal qualitative	Male/Female/Unknown	ID card or other valid document
Priority	Nominal dichotomous qualitative	Priority 0/Priority 1	SEM report after initial evaluation
Medical center category	Nominal qualitative	CAT-2a/CAT-2b/ CAT-3/CAT-3e	Category of medical center attending the patient
Systolic blood pressure	Continuous quantitative	mm of Hg	Automatic oscillometer
Base deficit	Continuous quantitative	mmol/L	Arterial blood gasometry
NISS	Ordinal qualitative	Stratified as: • <16 • 16-24 • >24	Physical examination and radiological findings
Mechanism of injury	Nominal dichotomous qualitative	Blunt trauma /Penetrating trauma	Scene evaluation by SEM, anamnesis and physical exploration

Table 6: Variables of the study

7.6 Method of data collection

Data collection of the patients belonging to **control group** will be performed retrospectively through Catsalut's database TraumCat.
In order to reduce confusion due to epidemiological differences regarding polytrauma population across time, included patients will be selected backwardly since the date of beginning of the study until the needed number of pacients is reached.

Data collection of the patients belonging to **protocol group** will be performed prospectively by a multidisciplinary team during a maximum period of time of 18 months.
Data collection sheets will be distributed among personnel belonging to SEM ambulances and helicopters providing service to the medical centers participating in the study.

When a potential patient is found, SEM team will inform the patient about the study and ask for consent (Annex 5). In case the patient is unconscious, suitable for the study, and the intervention is considered to be beneficial, patient will be included automatically in the study, as it doesn't violate patient's autonomy according to current law.(25)

SEM personnel will collect the following data:

- Date of birth
- Date of event
- Genre
- Priority
- Mechanism of injury
- Prehospital administration of pRBC

Upon arrival to the emergency department, SEM team will provide the data collection sheet to the emergency physician.
This physician will collect the following data:

- Systolic blood pressure
- Base deficit

After 24 hours, in case all diagnostic tests had been performed, the physician will calculate NISS and collect data regarding 24 hours in-hospital administration of pRBC.

The physician will follow patient's evolution up to discharge in order to evaluate mortality.

If the patient was unconscious during SEM's inclusion in the study but recovered conciousness during first 24 hours after admission, patient will be asked to if he or she still desires to be part of the study, respecting patient's autonomy.
In case that the patient is still unconscious, first-degree relative will be asked for consent.

All data regarding patient's attention will be registered in TraumCat, as it's mandatory to register data related to patients meeting criteria for priority 0 and 1.

8. Statistical analysis

8.1 Univariant analysis

A descriptive analysis of the variables will be performed.

Qualitative variables results will be expressed as frequencies and percentages for each category.

Quantitive variables results will be expressed as mean and standard deviation (in case of variables with normal distribution) or as median and quartiles (in case of variables without normal distribution)

8.2 Bivariate analysis

For the analysis between the main dependent variable mortality and the independent variable prehospital administration of pRBC, a chi-square (x^2) test will be performed.

The analysis between the main dependent variable 24 hours in-hospital administration of pRBC and the independent variable prehospital administration of pRBC will be performed using a chi-square (x^2) test.

8.3 Multivariate analysis

The analysis of the mortality rate between patients before and after implementation of the protocol based on the number of pRBC administered in the prehospital environment will be performed using a Multiple Logistic Regression model.

The analysis of the 24 hours in-hospital administration of pRBC between patients before and after implementation of the protocol will be performed using a Multiple Logistic Regression model.

Analysis will be adjusted for covariates.
Differences between groups will be considered statistically significant in case p-value <0.05.

9. Ethical considerations

This study will be performed following the ethical principles for medical research established by the World Medical Association (WMA) in Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects (June, 1964).
Last revision was in 2013.(26)

This study involves the use of biological tissues for clinical research. However, it is confusing to know wether this intervention is considered invasive or not.
According to current legislation(27,28), the following procedures must be performed before starting the study:

- Presentation of the study to the Clinical Research Ethics Comitee (CEIC, *"Comitè Ètic d'Investigació Clínica"*) of every medical center participating in the study in order to get its approval and decide if this intervention is considered invasive or not.

In case that the intervention is considered invasive, we will perform the following procedures:

- Obtaining authorization from the autonomous community.
- Contracting of an insurance.

All personal and clinical data obtained from the patient will be codified prior registration to TraumCat in order to anonymize the information, obeying *"Ley Orgánica 15/1999, de 13 de Diciembre, de Protección de Datos de Carácter Personal"*.

Informed consent will be asked by SEM team during initial attention if the patient meets the required criteria. In case that the patient was unconscious, it will be automatically included in the study as the intervention is considered potentially beneficial.

After arrival to the hospital, if the patient regained conciousness, he/she will be asked about his/her desire to be included in the study.
In case that the patient still was unconscious, informed consent will be asked to a first-degree relative.

The use of new therapeutic measures in critically injured patients may raise ethical issues about prognosis regarding quality of life among survivors.(29)

10. Study limitations

This study is designed as a quasi-experimental study. It can prove that there is association between variables, but it is weaker for demonstrating there is true causality between the intervention and outcomes.
The optimal design to overcome this issue would be the use of a randomized clinical trial design. However, it is ethically unaceptable, as lack of intervention may lead to death as a consecuence.

The use of retrospective data to analyze the control group may raise confusion, since it is uncertain wether the death cause was exanguination or any other cause, such as brain herniation or unidentified tension pneumothorax.
Another potential source of confusion would be the difference in polytrauma epidemiology across the time.
In order to overcome these limitations, data will be analyzed backwardly since the day of implementation of the protocol, and an additional inclusion criteria was established for the control group.

There is a risk of data loss in the protocol group due to the fact that data information sheets must be transferred by SEM to the emergency department physician during patient admission. This could lead to unnecesary prolongation of the study.
It will be considered an important issue during training courses, attempting to avoid this issue.

Multiple confounding factors may influence association between dependent and independent variables.
We will try to avoid confusion through a multivariate analysis.

A technical limitation of the study is related to the absence of availability of freeze dried plasma in our environment, which is an important component of prehospital transfusion and may also have beneficial effects.
Future studies about prehospital transfusion should be conducted once it is available to increase evidence related to its use.

11. Work plan

The research team will develop the tasks of coordination, interpretation and presentation of the results. The sequence of the activities will be developed in the following order:

- **Stage 0**: **Study design** {*December 2017 - January 2018*}

  → Bibliographic research and protocol elaboration.

  → Investigator 1.

- **Stage 1**: **Ethical evaluation of the protocol** {*February 2018 – March 2018*}

  → Presentation and evaluation of the protocol by the Clinical Research Ethics Committee of every medical center involved in the study.

  → Contracting an insurance and requesting of authorization by the autonomous community in case that the intervention is considered as invasive.

- **Stage 2**: **First meeting of research team, multiple meeting with the multidisciplinary teams, instruction and purchase of needed materials** {*April 2018 – May 2018*}

  → First meeting of research team to organize tasks and discuss how to teach to fill the data information sheet.

  → Meetings with multidisciplinary teams and instruction about how to fill the data information sheet and sequence of data transference.

  → Purchase of needed materials for conservation of blood products in medical helicopters and fast response vehicles.

  → A project manager will be hired in order to organize and coordinate the tasks between the medical centers.

  → Investigators 1, 2 and 3.

- **Stage 3**: **Patient recruitment and filling of data information sheets** {*May 2018 – October 2019*}

  → Date limit to reach the desired number of patients in the second group is October 2019. In case it is reached before, Stage 4 will be started.

  → Data from the recruited patients will be registered in TraumCat, as it is mandatory.

  → SEM personnel and physicians of the emergency departments belonging to the involved medical centers.

  The project manager will coordinate the tasks and contact the medical centers periodically.

- **<u>Stage 4</u>: Data compilation {*November 2019*}**

  → Data from each group will be compiled and refined in order to prepare it for statistical analysis.

  → Investigator 1.

- **<u>Stage 5</u>: Statistical analysis {*December 2019}***

  → A qualified statistician will process data using the proper software.

  → Qualified statistician.

- **<u>Stage 6</u>: Interpretation of the results {*January 2020 – February 2020*}**

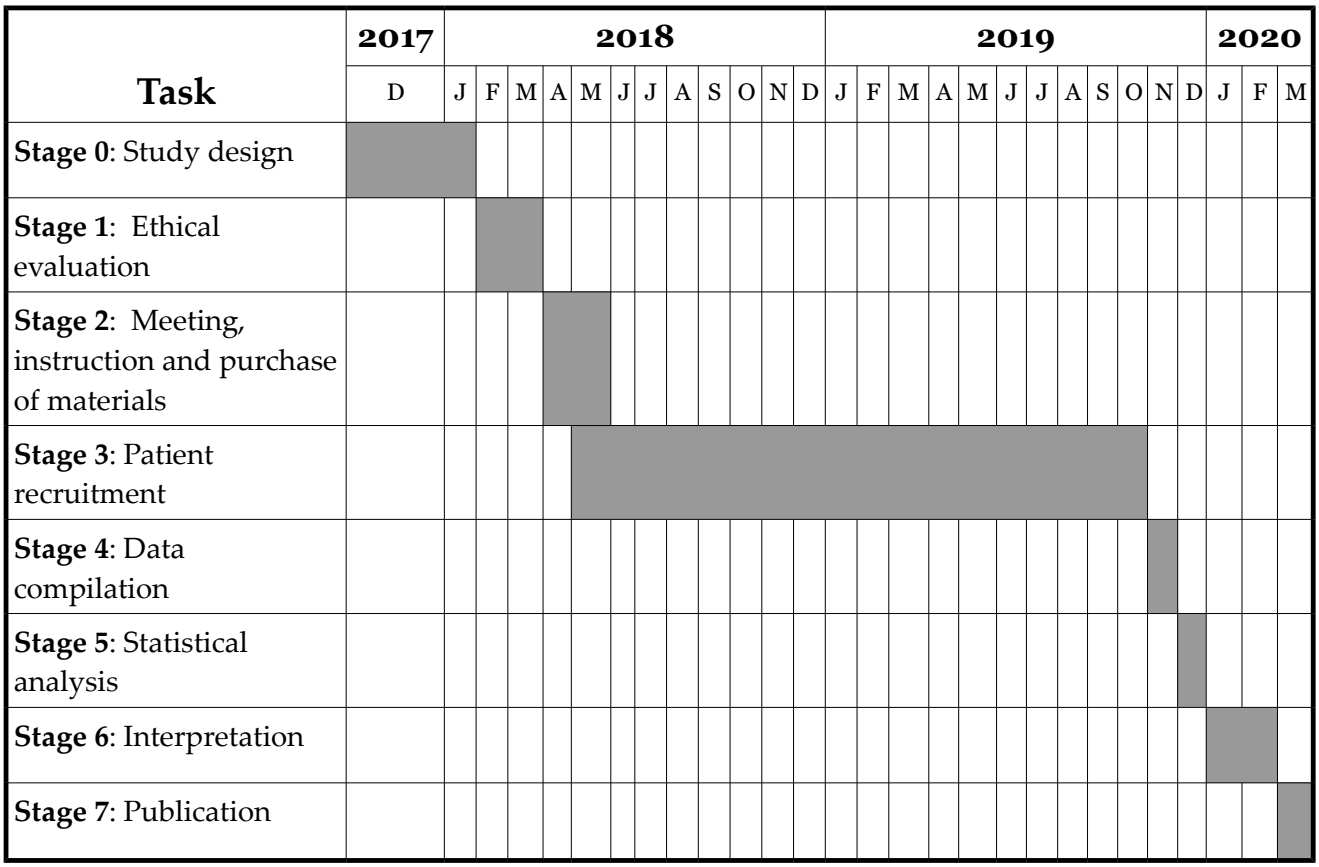
  → The research team will keep in contact and meet in order to analyze, interpret and discuss the results.

  → Investigators 1, 2 and 3.

- **<u>Stage 7</u>: Publication of the results {*March 2020*}**

  → Results will be presented in national conferences. We will also try to publish the study in an emergency journal.

  → Investigators 1, 2 and 3.



12. Budget

Estimated budget needed to complete all the stages of the study is detailed in the following table:

Item	Cost (€)
Personnel expenses	0 €
Goods and services • ***Project manager*** ◦ 25 €/h x 4 hours/day x 1 day/week x 19 months	7600 €
• ***Qualified statistician*** ◦ 20 €/h x 8 hours/day x 2 days/week x 2 weeks	640 €
• ***Insurance*** ◦ 20 € per patient in **protocol** group (292 patients)	5840 €
• ***Material needed for prehospital blood conservation*** ◦ **1 refrigerating box/helicopter x 4 helicopters** ▪ 300 €/unit	1200 €
◦ **1 portable refrigerator/fast response vehicle x 16 fast response vehicles** ▪ 170 €/unit	2720 €
National conferences attendance	900 €
Publication expenses	1000 €
TOTAL:	19900 €

Investigators 1, 2 and 3 will not receive any financial compensation for their partipation in the study.

13. Clinical and healthcare impact

Trauma is one of the main causes of death and morbidity among young people.
It is unacceptable the premature death and reduced quality of life in people who is expected to live a much longer life.

Loss of human lives in young population also worsens an important issue of the modern societies: Population aging.

The main cause of early preventable death among people suffering severe trauma is massive haemorrhage.
Thus, it is extremely important to develop measures to improve the management of this event in order to reduce trauma mortality.

Results of preliminary studies in military trauma population are promising, empowering the need to test the benefits in civilian trauma population.

Our study also aims to test wether the use of prehospital transfusion or not is related to a reduced need of in-hospital transfusion.
As blood products are scarce, it is important to test any measure that may potentially reduce the use of them.

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Annexes

Annex 1: Priority criteria in Codi PPT

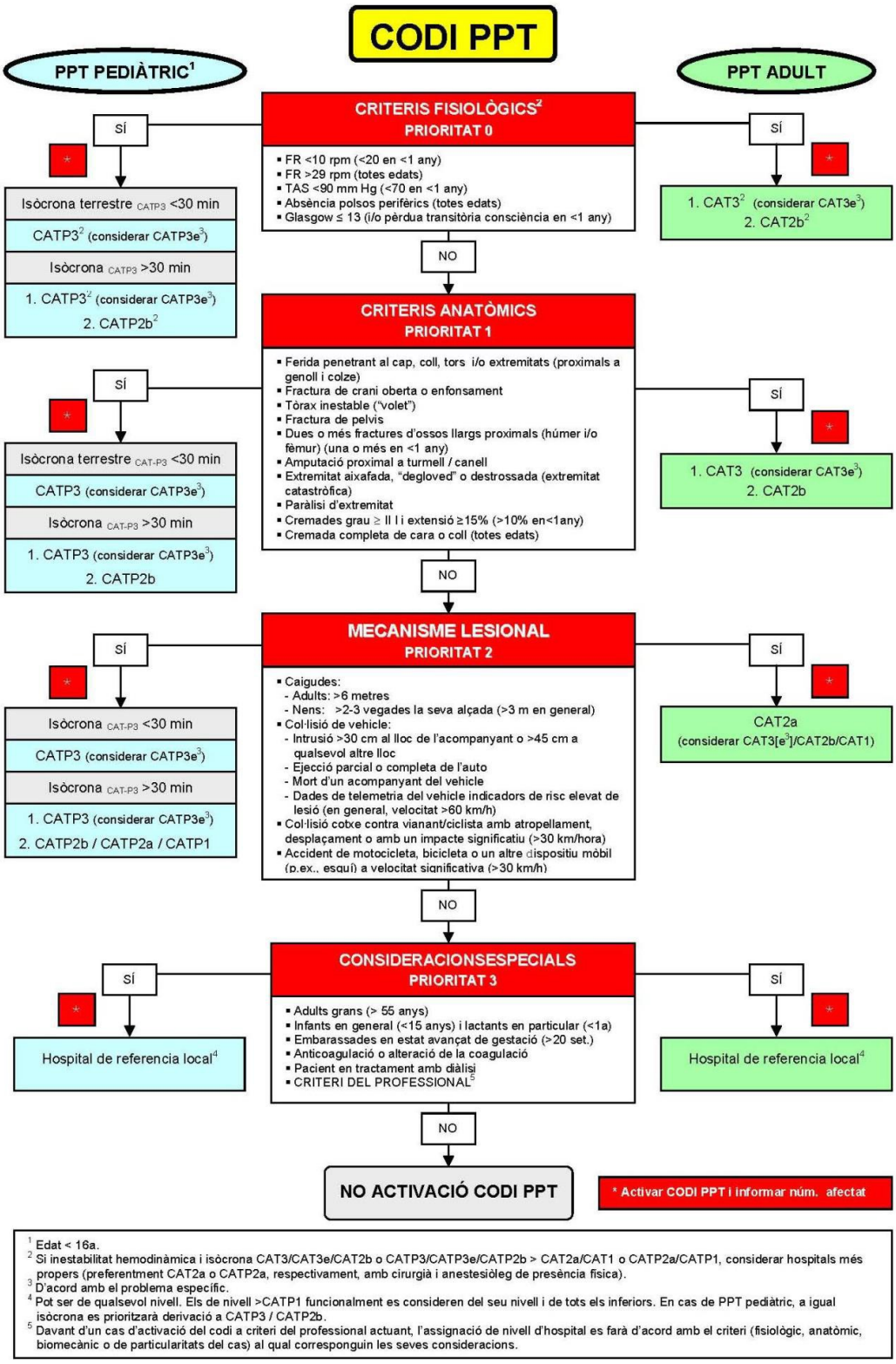

Figure from: Prat S, Espinosa L, Muñoz L, Arias J, Martinez O, Espallargues M. Registre de traumatismes greus de Catalunya (TraumCat). Informe global de resultats 2014[Internet]. Barcelona: Agència de Qualitat i Avaluació Sanitàries de Catalunya. Departament de Salut. Generalitat de Catalunya; 2017

Annex 2: Requirements for trauma assistance levels CAT-2/3

Persona pacient adulta	
Centre d'Atenció al Trauma nivell 3 (CAT-3)	
Hospital	Hospital amb activitat terciària
Funció	Atenció urgent, estabilització, ingrés i atenció especialitzada. Eventualment, derivació a unitat especialitzada CAT3e o derivació de retorn al CAT de nivell inferior corresponent.
Serveis*	Cirurgia general 24 h COT 24 h Radiologia convencional i intervencionista, i TC 24 h Unitat de crítics Cirurgia del raquis Neurocirurgia 24 h Cirurgia toràcica 24 h Cirurgia vascular 24 h Cirurgia maxil·lofacial 24 h
Requeriments	Experiència en el tractament de pacients amb ISS>15 (nombre de pacients desitjable ≥100/any). Equip assistencial organitzat per donar atenció al trauma greu durant 24 h. Quiròfan d'urgències disponibles 24 h. Existència d'un programa d'atenció al trauma greu, amb un coordinador, i que inclogui formació de residents, la formació continuada i la recerca en l'àmbit del trauma greu.
* L'existència en els hospitals d'aquest nivell de serveis altament especialitzats com l'atenció a cremats, atenció a lesionats medul·lars (24 h), reimplantació de membres (24 h) o d'altres, determinen la seva catalogació com a **centre d'atenció al trauma especialitzat (CAT 3e).**	

***Figure from**:* CatSalut. Instrucció 04/2011. Ordenació i configuració del model organitzatiu i dispositius per a l'atenció inicial a la persona pacient traumàtica greu. 2011

Centre d'Atenció al Trauma nivell 2 (CAT-2)	
Hospital	Hospital referent territorial
Funció	Atenció urgent, estabilització, ingrés i, si escau, derivació a un centre d'atenció al trauma de nivell superior.
Serveis	Cirurgia general 24 h COT 24 h Radiologia convencional amb TC 24 h **Nivell 2a** : Unitat de crítics **Nivell 2b**: Unitat de crítics Neurocirurgia 24 h
Requeriments	Equip assistencial organitzat per donar atenció al trauma greu durant 24 h Quiròfan d'urgències disponibles 24 h Els centres CAT 2b: - han de tenir experiència en el tractament de pacients amb ISS>15 (nombre de pacients desitjable ≥100/any); - han de tenir programa de formació de residents i recerca científica en l'àmbit del trauma greu.

***Figure from**:* CatSalut. Instrucció 04/2011. Ordenació i configuració del model organitzatiu i dispositius per a l'atenció inicial a la persona pacient traumàtica greu. 2011

Annex 3: Medical centers participating in the study(10)

Name of the medical center	Category
Hospital Althaia de Manresa	**CAT-2a**
Hospital U. Germans Trias i Pujol	**CAT-3**
Hospital Clínic de Barcelona	**CAT-3e**
Hospital General de Granollers	**CAT-2a**
Hospital Mútua de Terrasa	**CAT-3e**
Hospital U. Arnau de Vilanova de Lleida	**CAT-2b**
Hospital U. Joan XXIII de Tarragona	**CAT-2b**
Hospital U. Vall d'Hebron	**CAT-3e**
Hospital U. De Bellvitge	**CAT-3**
Hospital Verge de la Cinta de Tortosa	**CAT-2a**
Fundació Hospital Residència Sant Camil	**CAT-2a**
Hospital de Mataró	**CAT-2a**
Hospital de Sabadell	**CAT-3e**
Hospital de la Santa Creu i Sant Pau	**CAT-3**
Hospital del Mar	**CAT-2b**
Hospital U. Doctor Josep Trueta	**CAT-2b**
Hospital General de Vic	**CAT-2a**

Annex 4: Data collection sheet (generic)

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Hoja de recogida de datos **TRAUMA GRAVE ADULTO** (Prioridad 0/1 Codi Politrauma)	**Proyecto** Prehospital use of blood transfusion to manage haemorraghic shock

Instrucciones:

Para la inclusión del paciente por parte del SEM en el proyecto, es **imprescindible** que el paciente cumpla **todos** los criterios de ***inclusión*** y **ninguno** de los criterios de ***exclusión***.

Criterios de inclusión	
Politrauma prioridad 0 o 1	☐
Respuesta ausente o transitoria a fluidoterapia inicial	☐
Edad ≥ 15 años	☐

Criterios de exclusión	
Politrauma prioridad 2 o 3	☐
Respuesta rápida a fluidoterapia inicial	☐
Edad < 15 años	☐
Lesión aislada	☐
Quemaduras en superficie corporal total ≥ 20 %	☐
Paciente transferido desde otro centro	☐
Rechazo de consentimiento	☐

A rellenar por SEM

Datos básicos del paciente		
Nombre y apellidos		
Fecha de nacimiento	/ /	Género: Hombre ☐ Mujer ☐
Fecha de incidente	/ /	
Edad		

Atención prehospitalaria		
Prioridad de activación		
Mecanismo lesional	**Contuso** ☐ -Accidente de tráfico -Atropello -Lesión por objeto contundente	**Penetrante** ☐ -Arma de fuego -Arma blanca
Número de concentrados de hematíes administrado		

A rellenar por Médico de Urgencias

Atención hospitalaria	
Presión arterial sistólica al ingreso	
Déficit de base	
Número de concentrados de hematíes administrados en 24 horas tras ingreso	
Éxitus: Sí ☐ No ☐	

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Annex 5: Study information for the patient and informed consent

Annex 5.1: Study information for the patient

Hoja informativa para pacientes

Investigadores principales: Juan José Paterna Gómez, M. Àngels Gispert Ametller

Codigo de proyecto: .....

1. **Generalidades del proyecto**: El proyecto es llevado a cabo por 17 hospitales de Cataluña en colaboración con el SEM, con una duración aproximada de 28 meses. Como participante, debe autorizar la transfusión de productos sanguíneos durante el tratamiento prehospitalario y la recogida de datos personales y clínicos de interés.

2. **Objetivos y finalidad del estudio**: La finalidad del estudio es valorar si el uso de transfusión prehospitalaria en el paciente que sufre un traumatismo grave asociado con hemorragia grave, reduce la mortalidad y/o la necesidad de transfusión de eritrocitos en 24 horas tras el ingreso.

3. **Participación**: Su participación es totalmente voluntaria. El participante es libre de abandonar el estudio si así lo desea, antes o después de la transfusión, sin necesidad de justificarse y con garantía de que ello no afectará su asistencia sanitaria.
   La participación en el estudio no conlleva compensación económica.

4. **Confidencialidad y protección de datos**: En cumplimiento de la *Ley Orgánica de Protección de Datos de Carácter Personal*, se han adoptado medidas para garantizar la confidencialidad.
   Sus datos serán tratados de forma anónima y exclusivamente con fines de investigación.

5. **Tarea del participante del estudio**: El participante autorizará la transfusión de productos sanguíneos durante el tratamiento prehospitalario, así como la recogida de datos personales y clínicos para su uso con fines de investigación.

6. **Resultados y beneficios de la investigación**: El participante puede solicitar ser informado de los resultados de la investigación.
   Los resultados derivados de la investigación serán empleados para mejorar la atención prehospitalaria de los pacientes que sufren un traumatismo grave asociado con hemorragia grave.

Muchas gracias por su participación.

Annex 5.2: Informed consent

Consentimiento informado

Yo, ... declaro que:

- He leído y comprendo la hoja informativa sobre el estudio que se me ha entregado.
- He podido hacer las preguntas necesarias respecto al estudio.
- He sido informado/a de las implicaciones y objetivos del estudio.
- Entiendo que mi participación es voluntaria y no remunerada.
- Entiendo que se respetará la confidencialidad de mis datos.
- Entiendo que puedo revocar el consentimiento sin necesidad de justificación y sin que conlleve modificación de mi asistencia sanitaria.

Deseo recibir información por vía telefónica o correo electrónico sobre los futuros resultados del estudio:

Sí ☐ No ☐

Correo electrónico: .....

Teléfono de contacto: .....

Por todo ello, otorgo mi consentimiento para que se me pueda administrar productos sanguíneos durante mi tratamiento prehospitalario y que posteriormente puedan ser analizados los datos obtenidos de mi proceso asistencial.

Firma del paciente

Fecha: / /

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