Universitat de Girona
Facultat de Medicina

Hospital Universitari de Girona
Doctor Josep Trueta

FINAL DEGREE PROJECT

HOSPITAL USE OF VISCOELASTIC TESTING FOR GUIDED MANAGEMENT OF MASSIVE HAEMORRHAGE

A UNICENTER QUASI-EXPERIMENTAL STUDY

Author: Oihana Urretabizkaia Berasategi

Clinical tutor: Dra. Ramió Lluch

Methodological tutor: Dr. Gallardo Giralt

.

November 2023

To Cristina Ramió Lluch, for teaching me the meaning of professionalism and true dedication to each patient.

To the entire emergency department of the Hospital Universitari Dr. Josep Trueta for their valuable contribution to my training.

To David Gallardo Giralt and Rafel Ramos Blanes, for their collaboration in the project.

To my family and friends, especially Marta, Maider and Bea, for your constant support over the years despite the distance.

To Clara, Dani, Bea and Mar.

To anyone who takes the time to read this work.

Thank you very much

“… en la tardanza dicen que suele estar el peligro”

Miguel de Cervantes Saavedra

El ingenioso hidalgo Don Quijote de la Mancha

Capítulo XXIX

TABLE OF CONTENTS

INDEX OF FIGURES

INDEX OF TABLES

1. ABSTRACT

Background: Massive haemorrhage is a condition in which bleeding occurs at a volume and rate that overwhelms the body's physiological compensatory mechanisms. It is a lethal circumstance leading to numerous preventable deaths. Viscoelastic tests have been incorporated into the management of patients with massive haemorrhage, due to their improvements over conventional coagulation tests. However, the effectiveness of reducing mortality rates remains uncertain due to contradicting research findings.

Objectives: The main objective of this study is to evaluate whether the use of viscoelastic testing during hospital management of patients with massive hemorrhage is associated with reduced mortality at 24 hours compared to standard management using conventional testing.

Desing and setting: This study is designed as a unicenter quasi-experimental study. The study will compare two methods for treating massive haemorrhage: one guided by viscoelastic testing and the other guided by conventional coagulation testing.

Participants and methods: We will select 290 participants to carry out the study. To be included they must have a massive haemorrhage, be over 18 years of age, must not receive anticoagulants or antiplatelet medications or have a known coagulopathy. An intervention group of 145 patients enrrolled using a consecutive samplig during 12 months will be set up to treat massive haemorrhage guided by viscoelastic testing. The control group of 145 patients enrolled retrospectively from hospital databases, will consist of patients with massive haemorrhage who have received treatment guided by conventional coagulation testing.

KEYWORDS: Massive haemorrhage, massive transfusion, haemorraghic shock, viscoelastic testing, rotational thromboelastography, thromboelastography, conventional coagulation testing.

2. ABREVIATIONS

The following are the abbreviations discussed throughout the document:

ACS: American College of Surgeons

aPTT: Activated partial thromboplastin time

ATLS: Advanced Trauma Life Support

A10: amplitude 10

A5: amplitude 5

CCTs: Conventional coagulation tests

CEIC: Comitè Ètic d´Investigació Clínica

CFT: Clot formation time

CI: Co-investigator

CLI: Clot lysis index

CT: Clotting time

DM: Data manager

EUSEM: European Emergency Medicine Congress

FAST: Focused abdominal sonography for trauma

FFP: Fresh frozen plasma

GI: Gastrointestinal

HC: Hospital coordinator

HCO3: Bicarbonate

HEMOMAS: Documento multidisciplinar de consenso sobre el manejo de la hemorragia masiva

HUJT: Hospital Universitari Dr. Josep Trueta

CI: Informed consent

INR: International normalised ratio

K: K value

Ly 30: Lysis at 30 minutes as ratio of maximum amplitude

MA: Maximum amplitude

MCF: Maximum clot firmness

MI: Main investigator

mmHg: Milimetres of mercury

MT: Massive transfusion

PaCO2: Partial pressure of arterial carbon dioxide

PaO2: Partial pressure of oxygen

PCC: Prothrombim complex concentrates

pRBCs: Packed red blood cells

PT: Prothrombin time

ROTEM: Rotational thromboelastography

SAP: Systems Applications and Products in Data Processing registry

SC: Study coordinator

SEMES: Spanish Society of Emergency Medicine

TASH: Trauma- Associated Severe Hemorrhage

TAX: Tranexamic acid

TEG: Thromboelastography

VET: Viscoelastic testing

WMA: World Medical Association

3. INTRODUCTION

3.1. MASSIVE HAEMORRHAGE

3.1.1. Definition

A massive hemorrhage is known as a blood loss of sufficient volume and velocity to overwhelm the body's physiological compensatory mechanisms. This can lead to tissue hypoperfusion and circulatory failure resulting in hypovolemic shock.(1)

When establishing the parameters for considering a haemorrhage as massive, we are faced with a large degree of variability and heterogeneity. This makes the interpretation and identification difficult in daily clinical practice. (2)

We will mainly use the definition of the massive transfusion document developed by the members of the Transfusion Commission of the Hospital Universitari Dr Josep Trueta, as it includes several variations of the term based on the amount of blood loss, the speed of the bleeding and the number of transfusions.

A bleed can be defined as massive when:

- Loss of one blood volume (70ml/kg) in 24 hours.
- Loss of 1-1.5 volemia in 24 hours.
- Loss of 50% of blood volume in 3 hours.
- Loss of blood volume at a rate of 150mL/min.
- Loss of the volemia in 24 hours. This is equivalent to a transfusion of at least 10 red cell concentrates.
- Major hemorrhage requiring transfusion of 4 red cell concentrates in one hour.
- Blood loss greater than 150mL/min for more than 10 minutes.
- Loss of 1.5mL/kg/min for more than 20 minutes.
- Major life-threatening hemorrhage resulting in massive transfusion.

Given these various definitions, we must accept that it all situations is not possible to correctly quantify blood loss. (1)

3.1.2. Aetiology

There are several causes that can lead to this condition, the most frequent being: (1–3)

1. Traumatic hemorrhages
2. Haemorrhages caused by surgical complications
3. Haemorrhages caused by obstetrical complications
4. Gastrointestinal hemorrhages
5. Retroperitoneal hemorrhages
6. Pulmonary hemorrhages
7. Haemorrhages caused by ruptured aneurysms

3.1.2.1. Traumatic haemorrhages

Hemorrhage in acute trauma can be divided into bleeding from external injuries, intracranial bleeding, bleeding from the thoracic cavity, bleeding from the abdominal cavity, bleeding from the retroperitoneum and bleeding from fractures of long bones. These haemorrhages can be massive, although they mainly develop in the context of the polytrauma patient. (4)

Polytrauma is used to refer to severely injured patients who usually have two or more severe injuries in at least two areas of the body. Each year millions of patients require medical care because of trauma, and a significant proportion of these patients suffer life-changing or life-limiting injuries. (5)

In severe trauma patients with massive bleeding during or after surgery, failure of physiological homeostasis, including haemostatic disorders, is the leading cause of death (6).These patients also present with severe metabolic abnormalities, often characterised by the “triad of death” consisting of hypothermia, acidosis and coagulopathy. (7)

We define coagulopathy as any disorder of haemostasis that manifests as a haemorrhagic and/or thrombotic event.(8)

This concept of “triad of death” or “lethal triad” emerged as a description of terminal events associated with a high risk of death in the context of traumatic haemorrhage. Over time, this concept has been extended to non-traumatic haemorrhage scenarios. In

recent years, with the expansion of knowledge, this concept has evolved into “pentad of death”, consisting of hypothermia, acidosis, hypoxaemia, hyperglycaemia and hypocalcaemia. (9,10)

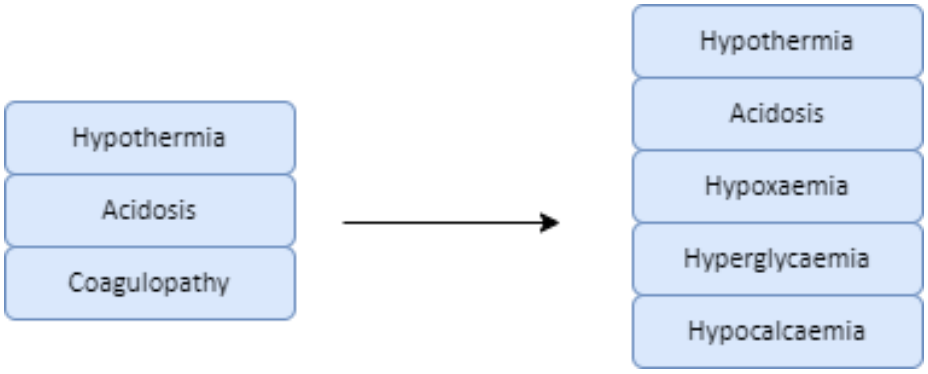

Figure 1. *Representation of the concepts of the “triad of death “and “pentad of death”.*

3.1.2.2. Haemorrhages caused by surgical complications

Bleeding is a complication that can occur with any type of surgery. The risk of unexpected major haemorrhage increases with the length and complexity of the procedure. It is therefore a major challenge for surgeons and anaesthetists (11). Massive bleeding mainly occurs in cardiovascular, hepatobiliary and transplant surgeries. (1)

This bleeding situation can occur in both emergency and elective surgery. For perspective, 2/3 of bleeding deaths occurred during emergency surgery in patients with underlying bleeding and 1/3 during elective surgery.(12)

Almost all reviews of intraoperative and early postoperative bleeding indicate that 75% to 90% of all bleeding is technical in origin.(13)

The majority of this bleeding, an average of 75% to 90%, is caused by the local surgical or vascular disruption and 10% to 25% is caused by an acquired or congenital coagulopathy(14). Surgical problems associated with human factors include: inappropriate judgement (27%), underdeveloped skills of the surgeon (26%), delay in recognising the presence of bleeding during endoscopic procedures (3%) and incorrect handling of surgical devices (3%). (12)

3.1.2.3. Haemorrhages caused by obstetrical complications

According to its temporality, maternal haemorrhage can be classified as antepartum, intrapartum and postpartum. They refer to bleeding from the maternal genital tract before, during or after childbirth, in that order. Postpartum haemorrhage can be classified as early haemorrhage, if it occurs within 24 hours of delivery, or late haemorrhage, if it occurs after 24 hours of delivery and before 6 weeks. Postpartum haemorrhage, depending on its aetiology, can be primary or secondary. Generally, the most severe conditions are due to primary postpartum haemorrhage, and up to 90% of cases it is a consequence of uterine atony. (15,16)

Aetiology of Postpartum Haemorrhage	
Primary haemorrhage	Secondary Haemorrhage
○ Uterine atony ○ Retained placenta (especially placenta accreta) ○ Defects in coagulation ○ Uterine inversion	○ Subinvolution of placental site ○ Retained products of conception ○ Infection ○ Inherited coagulation defects

Table 1. *Aetiology of postpartum haemorrhage (17)*

During pregnancy, red blood cell mass increases by about 25% and plasma volume increases by about 40%. This is because the body is physiologically preparing for childbirth, trying to anticipate the blood loss that will occur naturally.(18)

If this bleeding exceeds a certain amount, it is considered pathological. There are different definitions of obstetric haemorrhage (Annex 1), but in general it is considered massive if there is a loss of > 2,500 ml of blood and is associated with the need for admission to intensive care and/or hysterectomy. (19)

3.1.2.4. Gastrointestinal haemorrhages

Gastrointestinal (GI) haemorrhages can be classified in different ways according to their origin, clinical manifestation and evolution time.

Depending on the anatomical location of the bleeding, we distinguish between upper and lower GI bleeding. The ligament of Treitz, also known as the suspensory ligament of

the duodenum, is the anatomical landmark that separates upper from lower bleeding. The associated clinical presentation is strongly related to the anatomical location of the source of bleeding:

- Hematemesis: Vomiting blood or blood mixed with stomach contents
- Rectorrhagia: Expulsion of undigested red blood through rectum.
- Hematochezia: Expulsion of undigested red blood mixed with faeces from the rectum.
- Melena: Expulsion of partially or fully digested blood through the rectum. The appearance of the faeces is dark and tarry. It typically has a strong characteristic odour caused by the activity of digestive enzymes and intestinal bacteria on haemoglobin.

Upper GI bleeding may present as haematemesis and/or melena. In contrast, lower GI bleeding will manifest as melena, haematochezia or rectorrhagia.

In terms of timing, we can define it as acute if it is bleeding with an acute onset and is observable, and chronic if it is persistent and minimal blood loss, often presenting as occult blood in faeces. (20–23)

In terms of aetiology, 90% are due to peptic ulcer disease, erosive gastritis, oesophageal varices or Mallory-Weiss syndrome. The most frequent causes are summarised in the following table:

Aetiology of GI haemorrhage		
Upper GI haemorrhage	Lower GI haemorrhage	
○ Peptic ulcer disease ○ Acute gastric mucosal lesions, as gastritis ○ Oesophageal varices ○ Mallory-Weiss tears ○ Upper GI tumors ○ Dieulafoy lesion	< 60 years of age	> 60 years of age
	○ Diverticulosis ○ Polyps ○ Tumors	○ Angiodysplasia ○ Diverticulosis ○ Ischemic colitis

Table 2. *Aetiology of GI haemorrhage based on (20–23)*

3.1.2.5. Retroperitoneal hemorrhages

Retroperitoneal haemorrhage is a situation in which there is blood behind the posterior reflection of the abdominal peritoneum. Organs in this space include the oesophagus, aorta, inferior vena cava, kidneys, ureters, adrenal glands, rectum, parts of the duodenum, parts of the pancreas and parts of the colon.

We can classify it according to its origin as traumatic or non-traumatic, the latter can be subdivided into non-spontaneous or spontaneous:

Classification of retroperitoneal hematoma		
Traumatic	Non- traumatic	
	Non-spontaneous	Spontaneuos

Table 3. *Classification of retroperitoneal hematoma based on* (24,25)

In traumatic retroperitoneal hematoma, the mechanism of injury may be blunt or penetrating. The majority of retroperitoneal haematomas seen in practice are due to blunt trauma. (24,25)

As we have described the non-traumatic retroperitoneal hematoma is classified as non-spontaneous, caused by iatrogenic injury during aortic and femoral cannulation or direct injury during abdominal or pelvic exploration, and spontaneous, includes any extravasation of blood into the retroperitoneal space in the absence of external trauma, prior endourological or endovascular manipulation. (26–28)

Aetiology of spontaneous retroperitoneal haemorrhage	
Local causes	Systemic causes
○ Abdominal aortic aneurysm rupture ○ Renal origin: Angiomyolipoma, adenocarcinoma, renal artery aneurys, infections, nefritis… ○ Adrenal origin: Pheocromocytoma, adenoma, sepsis, prolonged corticosteroid and ACTH treatments, idiopathic adrenal apoplexy… ○ Retroperitoneal organs: Pancreas, retroperitoneal tumors, retroperitoneal vessels	○ Coagulation disorders: ○ Anticoagulant or antiplatelet therapy ○ Blood dyscrasias ○ Haemodialysis ○ Vasculitis

Table 4. Aetiology of spontaneous retroperitoneal haemorrhage based on (29)

3.1.2.6. Pulmonary hemorrhages

Airway hemorrhage can be divided into proximal airway hemorrhage and distal airway hemorrhage. The former originates in the proximal airways, such as the trachea, main bronchi and proximal lobar bronchi. The second originates from the distal airways.

The most common cause of proximal airway bleeding is malignant airway tumours. The aetiology of distal bleeding is more heterogeneous, as virtually all lung pathologies can cause some form of bleeding. These are summarised in the table below. (30)

Aetiology of airway bleeding	
Proximal airway bleeding	Distal airway bleeding
○ Malignant: Squamous cell cancer, adenoid cystic carcinoma, carcinoid and mucoepidermoid cancer ○ Benign: Iatrogenic, trachea-innominate fistula, broncholithiasis, inflammatory lesions of the airway…	○ Vasculites and coagulopathy ○ Cardiovascular disease: Mitral stenosis, arteriovenous malformation, pulmonary embolism ○ Pulmonary parenchymal diseases ○ Infections: Bronchiectasis, aspergillosis… ○ Malignancy: primary lung cancer and metastases ○ Iatrogenic

Tabla 5. *Aetiology of airway bleeding based on (30)*

The usual source of massive pulmonary haemorrhage is bronchial, accounting for up to 90% of massive haemoptysis. This type of haemoptysis can lead to asphyxia and airway obstruction, shock and exsanguination. (31,32)

3.1.2.7. Haemorrhages caused by ruptured aneurysms

An aneurysm is an abnormal widening of the walls of an artery. Although most aneurysms develop in the aorta, they can occur in arteries in many different parts of the body. Depending on their location, they can be abdominal aortic aneurysms, thoracic aortic aneurysms, cerebral aneurysms or peripheral aneurysms if they occur in areas such as the neck, legs or groin. When an aneurysm ruptures, bleeding occurs, and depending on its characteristics it may or may not generate massive haemorrhage.(33,34)

3.1.3. Epidemiology

As explained above, massive haemorrhage is a concept that is defined in different ways. As a result, it is difficult to determine the true incidence and is thought to be an under-recognised entity, both in terms of diagnosis and importance.(2)

3.1.3.1. Traumatical haemorrhages

Severe trauma is the leading cause of death in patients under 45 years of age and the third leading cause of death in all age ranges. Injuries, both unintentional and due to violence, are the cause of death for about 5 million people every year. This represents about 9% of all deaths.(35–37)

In the trauma patient, massive haemorrhage is responsible for 50% of deaths in the first 24 hours and 80% of deaths in the operating theatre. It is a major preventable cause of death in these patients. (38,39)

3.1.3.2. Haemorrhages caused by surgical complications

Bleeding is the leading cause of death in the operating theatre worldwide (40). In a retrospective analysis of 25,000 patients, it was observed that 32-68% may suffer from uncontrolled surgical bleeding despite current haemostat use (41). Intraoperative haemorrhage has even been associated with 33% of cases of cardiac arrest (42).

Although the overall mortality rate for both elective and emergency surgery is low 0.1%, although some surgeries as vascular surgery, have a baseline mortality of 5-8%. Major, unexpected and unmanageable bleeds in surgery increase mortality rates from 1% to 20%, which is costly and consumes significant clinical and human resources. (11,14)

Major surgery for liver disease, such as partial hepatectomy and orthotopic liver transplantation, is associated with significant blood loss. Mortality can increase to 30-40% if damage of major organ, such as liver rupture, occurs. Cardiac surgery is also often associated with major bleeding. (11,43)

3.1.3.3. Haemorrhages caused by obstetrical complications

Massive haemorrhage has a presentation rate of 6 in 10,000 births and a mortality rate within these of 1 in 12,000. In the UK, a developed country, it is the third leading cause of direct maternal mortality. (19,44)

3.1.3.4. Gastrointestinal haemorrhages

Gastrointestinal bleeding accounts for a significant number of hospital emergencies, accounting for 1 to 2% of all medical-surgical admissions (21).

Upper gastrointestinal haemorrhage is one of the leading causes of hospital admissions worldwide, with an overall average incidence of 34.45 per 100,000 population in Spain. The incidence of bleeding in the lower gastrointestinal tract is about 1/3 of the incidence of bleeding in the upper gastrointestinal tract (45).

Although the mortality rate for all patients ranges from 3% to 14%, the mortality rate for massive haemorrhage is much higher. However, it is difficult to obtain a concrete figure because, as mentioned above, there is no consensus on the definition of massive haemorrhage. (46,47)

3.1.3.5. Retroperitoneal hemorrhages

In general, the incidence of retroperitoneal haemorrhage in abdominal emergencies is between 3.5% and 5% (48). Spontaneous retroperitoneal haemorrhage has a low published incidence of less than 0.6%. However, it has a relatively high all-cause mortality of up to 22% in published case series (49).

3.1.3.6. Pulmonary hemorrhages

In severe pulmonary haemorrhage, mortality rates of 50-100% have been observed (50). The usual source of massive pulmonary haemorrhage is the bronchial vasculature, which is responsible for up to 90% of massive haemoptysis (31).

While haemoptysis is a common clinical finding, accounting for 6.8% of outpatient pulmonary clinic visits, 11% of hospital admissions to a pulmonary unit and 38% of patients referred to a thoracic surgery unit, massive haemoptysis is relatively rare. Some studies estimate that 4.8-14% of patients presenting with haemoptysis will have massive haemoptysis. (32,51)

The bleeding rate correlates with the risk of death from haemoptysis. In an early study, patients with a bleeding rate of more than 600 ml in 4 hours (h) were reported to have a mortality rate of more than 70% (50).

3.1.3.7. Haemorrhages caused by ruptured aneurysms

It is a common condition that affects about 2% of people over the age of 65. In Spain, around 1,000 people die each year from a ruptured aneurysm. About 80% of these occur in the abdominal aorta. (52)

3.2. BLOOD LOSS PATHOPHYSIOLOGY

During acute haemorrhage, systolic, diastolic and pulse pressures fall, while cardiac stroke volume decreases and pulse rate increases. This situation triggers the activation of feedback mechanisms that tend to maintain blood pressure.

- To preserve blood flow to the brain, heart and kidneys, there will be a progressive **vasoconstriction** of the cutaneous, muscular and visceral circulation.
- To maintain the cardiac ouput there will be an **increase in the heart rate**. The clinical manifestation of this will usually be tachycardia, and it will be important to assess this as it is the earliest measurable circulatory sign of shock.
- To increase diastolic blood pressure and reduce pulse pressure, there is an **increase in peripheral vascular resistance** through the release of endogenous catemolamines.
- To maintain venous return the compensatory mechanism of **blood volume contraction in the venous system** will occur in earlier stages of blood loos situation.

When the haemorrhage becomes more severe and blood pressure falls below 60 millimetres of mercury (mmHg), hypoperfusion of peripheral carotid body chemoreceptors occurs. These receptors detect hypoxia and activate peripheral chemoreceptor reflexes in response. This leads to an increase in peripheral sympathetic nervous system activity and generating increased stimulation of respiration. As a consequence, there will be an increase in respiratory rate.

If blood pressure falls below 40 mmHg, activation of the sympathetic nervous system will intensify, causing extreme vasoconstriction in response to cerebral ischaemia.

At the cellular level there is an inability to maintain aerobic metabolism so anaerobic metabolism is activated to compensate, generating lactic acid and causing metabolic acidosis.

The acidity of the medium and the slowing of the circulation cause an increase in blood viscosity, which promotes intravascular coagulation with consumption of clotting factors and release of lytic enzymes leading to autolysis. The result is a thin, delayed formation of the fibrin clot, which is more rapidly broken down by fibrinolysis.

It is important to note that haemoglobin or haematocrit levels are not reliable in assessing acute blood loss, as they may show a minimal decrease compared to the degree of blood loss. (53–55)

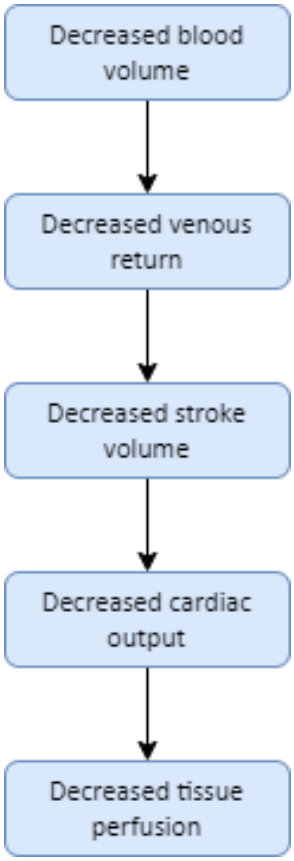

Figure 2. *Representation of the pathophysiology of blood loss based on (56)*

3.3. SHOCK

3.3.1. Definition

The American College of Surgeon (ACS) defines it as an abnormality of the circulatory system that results to inadequate organ perfusion and tissue oxygenation. (53)

Shock syndrome is a clinical and haemodynamic situation in which there is an imbalance between oxygen supply and demand, anaerobic metabolism, lactic acidosis, cellular and organ dysfunction and metabolic abnormalities. If the hypoperfusion is prolonged, the end result will be death. (57–59)

We can classify the types of shock into 4 main groups: hypovolemic, cardiogenic, obstructive and distributive. In hypovolemic, cardiogenic and obstructive shock, hypoperfusion is due to low cardiac output. In distributive shock, cardiac output is usually normal or high. In the latter, hypoperfusion and hypotension are the result of poor blood flow distribution and low systemic vascular resistance. (58)

3.3.2. Hypovolemic and haemorrhagic shock

It is important to distinguish between hypovolemic shock and haemorrhagic shock. In hypovolemic shock, tissues do not receive enough oxygen due to loss of blood or body fluids other than blood. Bleeding can be caused, among other things, by the aetiologies of massive haemorrhage described above. Causes of non-blood fluid loss include diarrhea, vomiting, reduced intake, third-degree burns and diabetic ketoacidosis.(60–62)

In conclusion, haemorrhagic shock is a subtype of hypovolemic shock caused by blood loss, as in the case of massive haemorrhage. We can classify it according to the base deficit. It refers to the amount of base needed to reach a normal blood pH value. (63)

	Class I	Class II	Class III	Class IV
Shock	Absent	Mild	Moderate	Severe
Base deficit at admission, mmol/L	≤ 2 mmol/L	> 2.0 to 6.0	> 6.0 to 10.0	> 10.0
Need for blood products	Watch	Consider	Act	Massive transfusion

Table 6. *Deficit based classification of hypovolemic shock based on (54)*

Physiologic classification

Hemorrhage is classified into four categories according to the estimated blood loss based on early clinical presentation and pathophysiology.

For an adult a normal blood volume would be approximately 7% of body weight. In a 70kg adult male it would correspond to a blood volume of 5L. It is important to emphasize that in obese patients we will make this calculation on their ideal weight to avoid overestimation.

- Class I: Is equivalent to the clinical situation of a person who has donated a unit of blood.
- Class II: Is an uncomplicated hemorrhage.
- Class III: Is a complicated hemorrhagic state.
- Class IV: a preterminal situation that can lead to death within minutes. (53)

To assess the extent of hemorrhage, the Advanced Trauma Life Support (ATLS) scale is classically used because of its speed of application, accessibility and lack of laboratory requirements. (64)

	CLASS I	CLASS II	CLASS III	CLASS IV
Blood loss (%)	< 15%	15% - 30%	31%- 40%	> 40%
Blood loss (ml)	< 750	750 – 1500	1500 – 2000	> 2000
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 7. *Clinical ATLS classification of haemorrhagic shock, taking as a reference an adult male of 70 kilos, based on (53).*

3.4. DIAGNOSTIC/CLINIC PATHWAYS OF MASSIVE HAEMORRHAGE

3.4.1. Evaluation of the patient

We have a number of scales to help us identify patients at risk of developing massive bleeding and requiring a massive transfusion (MT). Although they are indicative, early diagnosis and action is key in these situations.(65)

In polytrauma patients we will use the Trauma- Associated Severe Hemorrhage (TASH) score and in non-trauma patients we suggest using the "resuscitation intensity".

The TASH score has been shown to correctly classify 88.8% of patients who will require a MT. Seven variables are used in its calculation: Systolic blood pressure, haemoglobin, focused abdominal sonography for trauma (FAST), presence of long bone or pelvic fracture, heart rate, base excess and sex. The variables are weighted and the scores are added together.(53,64)

Variable	Result	Score
Gender	Male	1
	Female	0
Hemoglobin	< 7 g/dl	8
	< 9 g/dl	6
	< 10 g/dl	4
	< 11 g/dl	3
	< 12 d/dl	2
	≥ 12 g/dl	0
Base excess	< -10 mmol/L	4
	< -6 mmol/L	3
	< -3 mmol/L	1
	≥ -2 mmol/L	0
Systolic blood pressure	< 100 mmHg	4
	< 120 mmHg	1
	≥ 120 mmHg	0
Heart rate	> 120	2
	≤ 120	0
Positive FAST	Yes	3
	No	0
Unstable pelvis fracture	Yes	6
	No	0
Open or dislocated femur fracture	Yes	3
	No	0

Table 8. *TASH score classification based on (53)*

For early identification of patients who will benefit from activation of the massive transfusion protocol in non-trauma patients, it is suggested that "resuscitation intensity" be used, defined as transfusion of at least 4 units of packed red blood cells in 1 hour.(64)

3.4.2. Assess for clinical sings

In situations of massive haemorrhage, it is recommended that the initial assessment be based on clinical history and anamnesis, if possible.(2)

Dynamic monitoring of tissue perfusion status and degree of hypovolemic shock will include blood pressure, heart rate, respiratory rate, oxygen saturation and electrocardiography in addition to clinical signs and symptoms. Temperature and diuresis will also be monitored.

Maintaining normothermia reduces bleeding and transfusion requirements and should be a priority in patients with massive haemorrhage patients, as hypothermia (core temperature below 35◦C) is associated with acidosis, hypotension and coagulopathy. (64,66–68)

3.4.3. Laboratory measurements

One of the most useful laboratoy data for assessing a patient's condition in the presence of massive haemorrhage is the early and serial determination of basic haematological parameters such as haemoglobin, lactate, base excess and conventional coagulation tests (prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, platelet count and international normalised ratio (INR). These tests are useful to detect the presence of coagulopathy as early as possible, especially in the presence of hypothermia and acidosis. (2)

Serum lactate and base deficit values are not strictly related to the severity of injury, but they provide information on the degree of hypoperfusion and tissue hypoxia. (69)

Until a few years ago, conventional coagulation tests (CCTs) were the only laboratory tool available for the assessment of coagulation status and the only tests recommended by clinical guidelines for the development of blood product transfusion protocols.

But it is true that these tests have certain inherent limitations:

- **Turnaround time**: These tests are performed in a central laboratory, so it is difficult for the turnaround time to be less than 45 minutes. Speed of action is paramount in patients with massive haemorrhage.
- **Coagulation study:**
  - The different processes of coagulation are studied independently and not integrated.
  - Lack of information on clot stability and firmness.

The emergence of viscoelastic testing (VET) is a significant advancement because it resolves issues connected to traditional coagulation tests by providing faster response times and enabling a comprehensive, dynamic, and real-time assessment that considers all cellular elements involved in the coagulation procedure (coagulation factors, fibrinogen, platelets, and the fibrinolytic system).

CCTs	VET
Slower turnaround (usually > 1 hour)	Rapid turnaround (usually < 30 minutes)
Less expensive reagent and labor costs	More expensive reagent and labor costs
Performed on plasma	Performed on whole blood
Specimen must be centrifuged	No centrifuging needed
Best suited as anticoagulant screening test in stable, nonbleeding patients	Associated with less product usage and better outcomes in acutely bleeding patients
Unable to detect hyperfibrinolysis	Can detect hyperfibrinolysis
Multiple devices required to measure clotting factors, PLTs, and fibrinogen	One device evaluates clotting factors, PLTs, and fibrinogen
Highly artificial measurement of hemostasis	More closely resembles in vivo hemostasis
Unable to assess total clot strength, just clot initiation	Measures total clot strength

Table 9. *Differences between conventional coagulation study tests and viscoelastic tests based on (70).*

This enables us to improve the global monitoring of haemostasis, provide homeostatic therapy that is tailored to individual deficiencies, enhance the management of transfusions, and optimise the utilisation of blood products.

Viscoelastic testing

While Dr. Hellmut Harter initially described these tests in 1948 during the Second World War, it was only in the mid-1980s that the application of these procedures gained widespread use for managing massive bleeding in cardiac surgery and liver transplantation.

Thromboelastography (TEG) and rotational thromboelastometry (ROTEM) measure the kinetics of clot formation and dissolution. This information is obtained by applying a continuous rotational force to a fully citrated blood sample and the clotting activator reagent corresponding to the parameter of interest, which are placed in a cuvette.

In the **TEG**, a pin suspended from a torsion wire is inserted into the cuvette. The cuvette begins to oscillate continuously. The sample will increase in viscosity as it coagulates and fibrin and platelet interactions will form between the cuvette and the pin. As a result of this binding, the pin will perform the same oscillatory motion as the cuvette, and this motion will be transmitted to the torsion wire and detected by a mechanical transducer. When fibrinolysis occurs and the clot dissolves, the same process is recorded in reverse.

In the **ROTEM**, on the other hand, the mechanism is the opposite. The cuvette remains static, with the pin suspended in the cuvette oscillating continuously. As the clot forms, the resistance to rotation is greater and the rotation slows down. Conversely, when fibrinolysis occurs, the resistance exerted on the pin will decrease and the initial oscillation values will return.

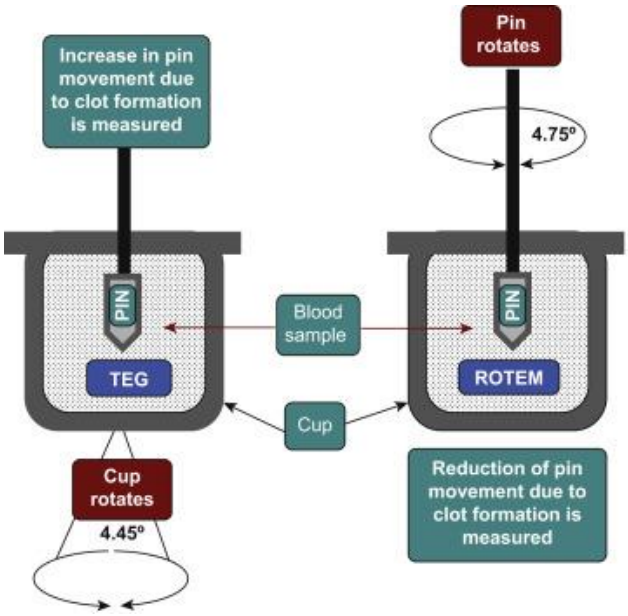

Figure 3. *Representation of the mechanism of TEVs based on (71)*

The outcomes are recorded graphically by a computer system, allowing clear differentiation between a typical graph (Annex 2) and an altered graph (Annex 3). (8,70–72)

Although the tests have their own characteristics (Annex 4), we can obtain equivalent results in both tests. These equivalences are represented in the following table:

	Test	Parameter	Events	Abnormality: Cause
Clotting initiation	ROTEM	**CT** (clotting time) in s	Time till initiations of fibrin clot formation	↑ parameter: ↓ factors Prolonged by deficiencies of coagulation factors and by consumption of anticoagulants ↓ parameter: hypercoagulability
	TEG	**R** (reaction time)in min		
Clot Kinetics	ROTEM	**CFT** (clot formation time)	Time from 2mm to 20 mm clot length on assay representing thrombin-platetet interaction	↑ parameter: ↓ fibrinogen Prolonged in deficiency of clotting factors or by consumption of antiplatet agents. ↓ parameter: increased platet function
	TEG	**K** (K value)		
	ROTEM	**α** (angle in degrees)	Angle of propagation from 2mm to 20mm clot formation, rate at which fibrin crosslinking occurs	↓ parameter: ↓ fibrinogen ↑ parameter: ↑ platelet aggregation and ↑fibrinogen
	TEG	**α** (angle in degrees)		
Clot strength	ROTEM	**MCF** (maximum clot firmness)	Maximum strength of clot	↓ parameter: ↓ platelet count and/ or function
	TEG	**MA** (maximum amplitude)		
Clot stability	ROTEM	**CLI** (clot lysis index)	Percentage of loss of amplitude at fixed time after maximum amplitude	↑ parameter: ↑clot breakdown
	TEG	**Ly 30** (Lysis at 30 minutes as ratio of MA)		

Table 10. *Parameters of TEG and ROTEM.* (73–75)

To predict maximal clot firmness early, two parameters reporting clot amplitude at 5 minutes (A5) and 10 minutes (A10) must be considered. These parameters are highly correlated with MCF, enabling faster decision-making. (8)

These tests allow to study coagulation and fibrinolysis from different perspectives using different assays that can be performed simultaneously. For this purpose, different coagulation activator reagents and additional reagents will be used. This will be represented in two summary tables on the following page, with the main parameters and their normal value:

ROTEM				
Test	Content	Action and relevance	Reference ranges	
INTEM	Ellagic acid and phospholipids	Activates the intrinsic pathway	CT (s)	100-240
		CT corresponds to aPTT	CFT (s)	30-110
			α (°)	70-83
			MCF (mm)	50-72
			A10 (mm)	44-66
			ML 60 min(%)	< 15
HEPTEM	Ellagic acid, phospholipids and herapinasa I	Activates the intrinsic pathway	Same reference ranges as INTEM	
		Heparinasa I degrades heparin		
		A comparison of HEPTEM and INTEM indicates how much coagulation is affected by heparin.		
EXTEM	Tissue factor and phospholipids	Activates the extrinsic pathway	CT (s)	38-79
		CT corresponds to PT		
		Curve represents clot formation, stability and fibrinolysis resulting from extrinsic pathway.	CFT(s)	34-159
			α (°)	63-83
			MCF (mm)	50-72
			A10 (mm)	43-65
			ML 60 min (%)	< 15
APTEM	Tissue factor, phospholipids and aprotinin	Aprotinin inhibits plasmin and therefore fibrinolysis	Same reference ranges as EXTEM	
		Comparing EXTEM and APTEM can rule in or out hyperfibrinolysis		
FIBTEM	Tissue factor, phospholipids and cytochalasin D	Cytochalasin D inhibits platelets	MCF (mm)	9-25
		Allows qualitative assessment of fibrinogen levels.	A10 (mm)	7-23

Table 11. *Tests carried out by ROTEM and their characteristics based on* (76,77)

TEG				
Test	Content	Action and relevance	Reference ranges	
Native TEG	None	Theoretically most sensitive to subtle coagulopathic changes and hyperfibrinolysis. Clot analysis of native blood.	MA (mm)	9-29
Conventional or Kaolin TEG	Kaolin	Test of intrinsic pathway	R (s)	180-480
			K (s)	60-180
			α°	55-78
			MA (mm)	51-69
			Lysis %	< 15
Rapid TEG	Kaolin and tissue factor	Test of both intrinsic and extrinsic pathways	CT (s)	86-118
			CFT(s)	34-138
			α (°)	68-82
			MA (mm)	54-72
			Lysis (%)	< 15
Functional fibrinogen (FF) TEG	Kaolin and GPIIb/IIIa inhibitor	Inhibits platelets to isolate contribution of fibrinogen. In comparison with Kaolin TEG.	MA (mm)	11-24
Kaolin TEG with heparinase	Kaolin and heparinase	Inhibits heparin; presence of heparin (endogenous or exogenous) is suggested when this channel shows improved clotting compared to other channels. In comparison with Kaolin TEG.	R (s)	258-378

Table 12. *Tests carried out by TEG and their characteristics based on* (78–81)

We will determine the treatment based on the altered values. In general, we will administer fresh frozen plasma (FFP), prothrombin complex concentrates (PCC), cryoprecipitate, platelets, or tranexamic acid (TAX) through transfusion.

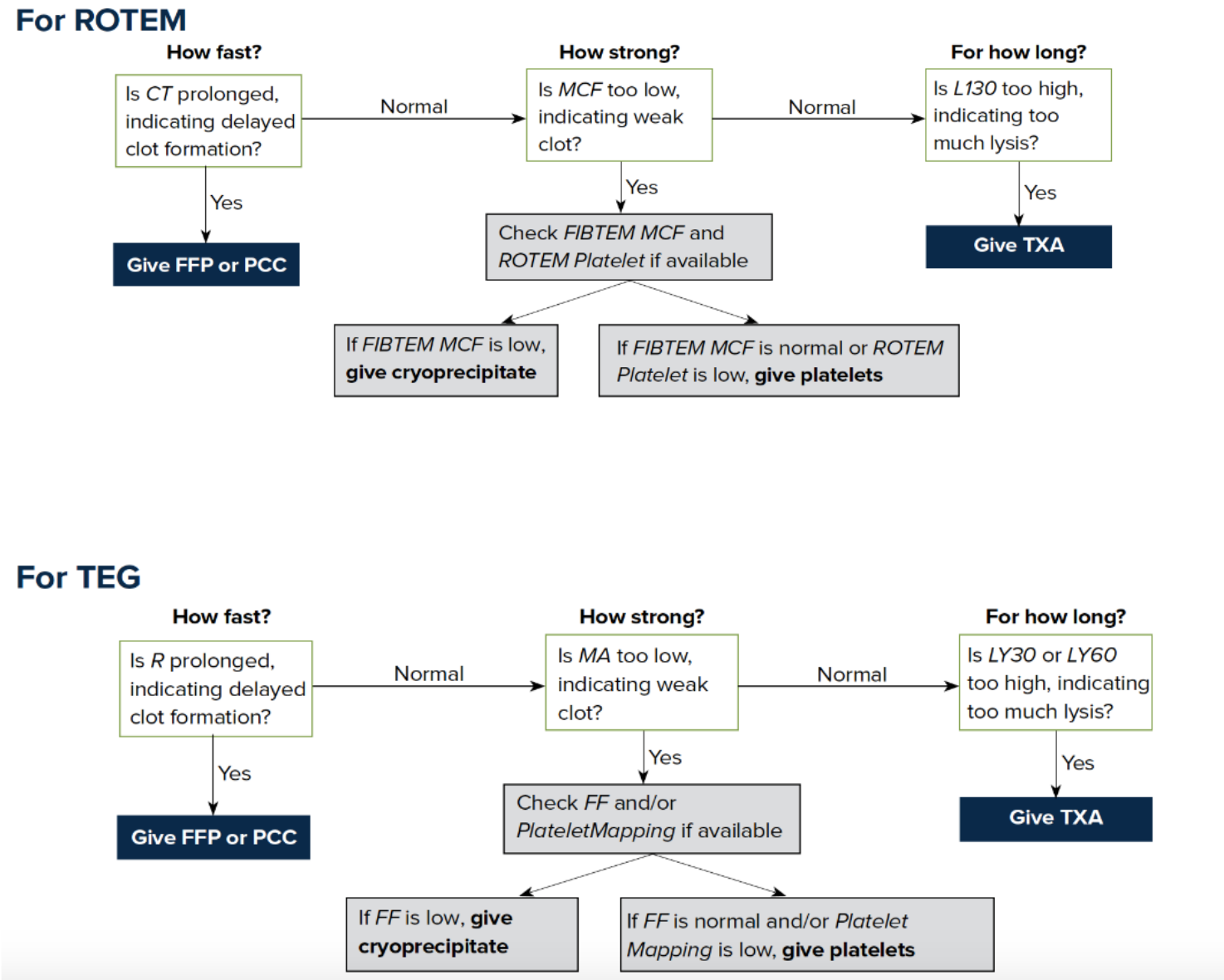

Figure 4. *Summary of TEG- and ROTEM-guided transfusion taken from* (82).

3.5. MASSIVE BLOOD TRANSFUSION

3.5.1. Definition

According to the "Documento multidisciplinar de consenso sobre el manejo de la hemorragia masiva" (HEMOMAS document) massive transfusion can be defined as the transfusion of half a blood volume in 4 h, or more than one blood volume in 24 h (adult blood volume is approximately 70 ml/kg).

However, the most widely accepted definition, on which we will be based, is the administration of at least 10 units of red cell concentrates within 24 hours of starting treatment.

The problem is that the definitions are based on a 24-hour period, so they are not useful in the active management of bleeding. (2,83)

Therapeutic goals for massive transfusion are: (1)

- Haematocrit > 24% or haemoglobin 7-9 g/dl.
- Body temperature > 35ºC
- INR < 1,5 or Quick 50%.
- Fibrinogen > 150mg/dL
- pH > 7,20
- Platelets > 50,000

3.5.2. Epidemiology

It is difficult to establish the incidence of massive haemorrhage because, as mentioned above, it has been defined in many different ways (2). We will then look at a concept linked to massive haemorrhage, which is massive transfusions.

A 2016 review found that in two first-world countries, Denmark and Sweden, 97,000 massive transfusions were performed in consecutive two-day periods over a 25-year period, or about 2.5 per 1,000 people per year. (84)

In the province of Girona, according to official data from the Spanish National Institute of Statistics, the population in 2022 was estimated at 793,478 people.(85)

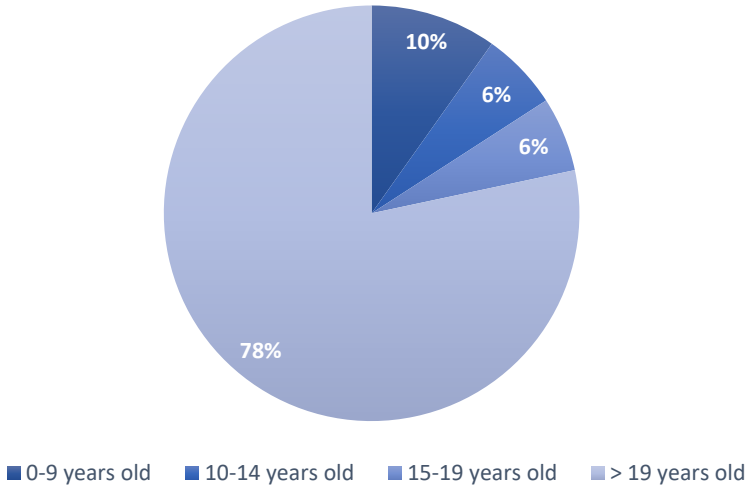

Figure 5. *Population of the province of Girona represented by age groups based on* (85).

3.5.3. Principles of management of massive blood loss

It is based on managing the loss of intravascular volume and the blood components loss. Fluid infusion should be guided by blood loss, bleeding rate and the haemodynamic status of the patient.

Regarding the management of intravascular volume loss, it is important to remember that excessive resuscitation leading to high arterial and venous pressures can be detrimental as it may dislodge haemostatic clots and cause further bleeding.

The management of blood component loss adheres to the massive transfusion protocol. For milder to moderate haemorrhages, crystalloid or colloid infusions may suffice to compensate for blood loss. On the contrary, plasma substitutes may have direct impacts on the coagulation system, especially when administered in quantities greater than 1.5 litres.(83,86)

Relevant considerations:

- In trauma, acute coagulopathy of trauma shock is caused by a combination of tissue injury and shock and can occur in the absence of significant fluid administration, coagulation factor depletion or hypothermia. (87)
- In postpartum haemorrhage, acquired fibrinogen deficiency may be the major coagulopathy associated with obstetric bleeding, compounded by dilutional coagulopathy and hyperfibrinolysis.(88)

3.5.4. Massive transfusion protocol

These are protocols in which the clinician responsible activates the protocol after the use of at least 6 packed red blood cells (pRBCs), this value may vary. It is based on the administration of a predefined ratio of red cells, fresh frozen or cryoprecipitated plasma and platelet units in each pack. Current evidence generally supports a ratio of 1:1:1, which is used in most massive transfusion protocols. The blood bank ensures rapid and timely delivery of all blood components together to facilitate resuscitation once the patient is on the protocol.

These protocols can also incorporate the use of other strategies in different cases such as activated factor VII, antifribinolytic agents and cell salvage. (83,89,90)

3.5.5. Crossmatched, type-Specific and type O Blood

A blood transfusion is used to restore the oxygen-carrying capacity of the intravascular volume.Certain considerations must be taken into account when carrying out a transfusion (53):

- Fully cross-matched pRBCs are the optimal choice. However, the downside is that it takes roughly 60 minutes to carry out the entire cross-matching process.
- If crossmatched pRBCs cannot be obtained, type O pRBCs will be administered.
- For females of childbearing age, it is recommended to administer Rh-negative pRBCs.
- AB plasma is administered when non-crossed plasma is required.

3.5.6. Limitations and complications

Limitations

There is no consensus on the optimal point at which to initiate the protocol, and in the case of initiating the protocol for a non-massive haemorrhage there may be a waste of blood products. There is also discrepancy between the optimal ratio of RBCs and fresh frozen plasma.

Complications

Complications can be acute or delayed:

Acute	Delayed
○ Acute haemolityc transfusión reactions ○ Rebrile nonhaemolityc transfusión reactions ○ Transfusion-related acute lung injury ○ Transfusion-asociated circulatory overlead ○ Allergic reactions ○ Hypocalcaemia, hypokalaemia, hiperkalaemia ○ Acidosis ○ Hypothermia ○ Dilutional coagulopathy ○ Dilutional thromnocytopenia	○ Delayed haemolytic transfusion reactions ○ Transfusion-related immunomodulation ○ Transfusion-transmitted disease ○ Posttransfusion graft-vs-host disease ○ Posttransfusion purpura

Table 13. *Complications associated with massive blood transfusion, based on* (91).

4. JUSTIFICATION

Massive haemorrhage is a very relevant entity worldwide. However, when it comes to understanding its epidemiology and true incidence, we face difficulties due to the fact that there is no consensus on its definition.

It can be caused by any condition that produces bleeding of a volume and rate that overwhelms the body's physiological compensatory mechanisms. The main aetiological entities are traumatic haemorrhage, surgical complications, obstetric complications, gastrointestinal haemorrhage, retroperitoneal haemorrhage, pulmonary haemorrhage and ruptured aneurysm. (1,2)

We can put into context that major trauma is the leading cause of death in patients under 45 and the third leading cause of death in all age groups. Injuries, both unintentional and due to violence, are the cause of death for approximately 5 million people each year. Massive bleeding in trauma patients accounts for 50% of deaths in the first 24 hours and 80% of deaths in the operating theatre. It is one of the leading preventable causes of death in these patients. (35–39)

However, the other aetiologies and their preventable deaths associated with massive haemorrhage cannot be ignored. For this reason, it will be of great value to look at them together in our study, as they all start from the same basis of a life-threatening situation in which rapid action must be taken.

Death has significant impact on our society. On one hand, it relates to the potential loss of years of life for the patient, while on the other hand, it affects their environment. This situation has a major psychological impact on the patient's family and social environment.

In the particular case of the sudden or violent death of a loved one, various theorists have argued for years that there are often specific symptoms of crisis in the grieving process (O'Connor, 1990). Such indications include both severe and prolonged symptoms of depression (Bowlby, 2002), sensations of culpability (Fonnegra, 1996), the onset of alcoholism, instances of panic, assertive conduct, and even suicidal tendencies (Grollman, 1989). (92)

The death of a patient also affects the healthcare professionals who have attended to them. This can generate various feelings, including helplessness and guilt, which may be repressed, become unconscious and manifest through somatic or psychological symptoms.(93)

The emergence of viscoelastic testing represents a notable advance because it solves the problems associated with conventional coagulation testing by providing faster turnaround times and a comprehensive, dynamic, real-time assessment that takes into account all cellular elements involved in the coagulation process. This facilitates the enhancement of global monitoring of haemostasis, homeostatic therapy tailored to individual deficiencies, improved transfusion management and optimised use of blood products. (8,70–72)

In the literature search we found differences between the various studies. Based on research conducted in trauma patients with haemorrhage, we found disparate results. For example, one study reported an improvement in mortality at 24 hours, while another found no improvement in mortality at 28 days. (94,95)

Based on the objective improvements of these tests, we suggest investigating whether there is a decrease in mortality for patients experiencing massive haemorrhage, regardless of its origin. This is because it would be very useful to be able to use a common protocol. In addition, the evolution of the same patient at different times can be assessed to study whether the distribution of mortality changes with the use of guided transfusions.

5. HYPOTHESIS

Main hypothesis:

Patients with massive hemorrhage undergoing viscoelastic testing guided management have a reduction in mortality in the first 24 hours compared to patients managed with conventional coagulation tests.

Secondary hypothesis:

Patients with massive hemorrhage undergoing viscoelastic testing guided management have a reduction a reduction in mortality at 48 hours, 7 days and 30 days, compared to patients managed with conventional coagulation tests.

6. OBJECTIVES

Main objective:

This study aims to evaluate whether the use of viscoelastic testing during hospital management of patients with massive hemorrhage is associated with reduced mortality at 24 hours compared to standard management using conventional testing.

Secondary objectives:

The secondary aim of this study is to evaluate whether the use of viscoelastic testing during hospital management of patients with the massive hemorrhage is associated with reduced mortality at 48 hours, 7 days and 30 days compared to standard management using conventional test.

7. SUBJECTS AND METHODS

7.1. STUDY DESING

This project is designed as an unicenter **quasi-experimental study** to make a superiority comparison of mortality between two strategies for the management of massive hemorrhage using viscoelastic testing.

7.2. STUDY SETTING

This study will be **unicenter** and it will be conducted in Hospital Universitari Dr. Josep Trueta (HUJT). It should be noted that this proposal is subject to the agreement of the hospital to take part in the project.

7.3. STUDY POPULATION

The study aims to include all patients who experience a massive haemorrhage requiring transfusion, including those who are admitted to the Emergency Department and those who are already in hospital for other reasons. To be eligible, patients need to meet the predetermined inclusion and exclusion criteria.

7.3.1. Inclusion criteria

- Age ≥ 18 years old.
- Massive hemorrhage

7.3.2. Exclusion criteria

- Age < 18 years old.
- Patients on anticoagulant therapy
- Patients with antiplatelet therapy
- Patients with diagnosed coagulopathy
- Patients who die before the application of TEV-guided management

7.3.3. Withdrawl criteria

- All patients who refuse or revoke informed consent.

7.4. SAMPLING

7.4.1. Sample size

Accepting an alpha risk of 0.05 and a beta risk of 0.8 in a two-sided test, **145** subjects are necessary in the first group (preintervention) and **145** in the second (postintervention) to recognize as statistically significant a proportion difference, expected to be of 0.5 in group 1 and 0.33 in group 2. It has been anticipated a drop-out rate of 10%.

The calculations were conducted utilizing the online application GRANMO, with the assistance of Dr. Rafel Ramos.

7.4.2. Sample selection and recruitment time

Knowing that **145** patients are needed in each group, the estimated time of recruitment will be **12 months**. If the required number of samples is obtained prior to the scheduled date, the study duration will be modified.

Considering that calculating the incidence of massive haemorrhage is very complex because it is defined in very different ways, the recruitment time was estimated using the expected number of massive transfusions. Based on incidence data of massive transfusions provided by the haematologist of the Blood and Tissue Bank of the HUJT, as explained in the introduction, and the estimated population of the province of Girona aged over 18 years.

In this investigation, a non-probabilistic sequential recruitment technique will be employed due to the inability to forecast a patient's susceptibility to severe hemorrhaging. The occurrence of a massive bleeding episode is an acute event, influenced by a variety of factors.

We will have two study groups:

- **Protocol group (First group):** It includes patients who meet the inclusion and exclusion criteria and who will be treated according to the new intervention described in this study.
- **Control group (Second group):** Includes patients already registered in the Systems Applications and Products in Data Processing registry (SAP) of the HUJT prior to the adoption of the protocol. Patients diagnosed with massive haemorrhage and

underwent CCT-guided transfusion, who fulfill the inclusion and exclusion criteria described will be selected. Informed consent is not necessary of the patients in this group since we will not perform any intervention on them. We will collect data from patients closer to the start of the intervention, avoiding the months when the system was overwhelmed by the global pandemic due to COVID. Mainly data collected between March 2020 and March 2021 will be avoided.

7.5. VARIABLES AND MEASUREMENTS

7.5.1. Independent variable

Protocol group:

The intervention of the study will be the use of viscoelastic testing:

- **Rotational thrombolastometry** intervention: It is a **qualitative nominal dichotomous categorical** variable (Yes/No).
- **Thromboelastography** intervention: It is **a qualitative nominal dichotomous categorical** variable expressed as (Yes/No).

	Variable	Description	Categories	Measure instrument
Independent variable: VET intervention	ROTEM intervention	Qualitative nominal dichotomous categorical	Yes/No	Clinical history
	TEG intervention	Qualitative nominal dichotomous categorical	Yes/No	Clinical history

Table 14. *Independent variable of the protocol group.*

Control group:

Use of conventional coagulation test: PT, aPTT, fibrinogen and platelets. It is a **qualitative nominal dichotomous categorical variable** (Yes/No).

	Variable	Description	Categories	Measure instrument
Independent variable: CCT intervention	CCT intervention	Qualitative nominal dichotomous categorical	Yes/ No	Clinical history

Table 15. *Independent variable of the control group.*

7.5.2. Dependent variable

The dependent variable is mortality. It is **qualitative nominal dichotomous categorical** variable (Yes/No), which we are going to express as a percentage.

The main dependent variable will be 24-hour mortality. As secondary dependent variables, we will study mortality at 48 hours, 7-day and 30-day.

We will include deaths that occur after the patient is enrolled in the trial. Brain death will not be taken into account.

	Variable	Description	Categories	Measure instrument
Dependent variable: Mortality	24-hour mortality	Qualitative nominal dichotomous categorical	Yes/No	Clinical history
	48-hour mortality 7-day mortality 30-day mortality			Clinical history or by telephone call

Table 16. *Dependent variable.*

7.5.3. Covariables

These variables are included in the analysis of results to improve the external and internal validity of the study by reducing their confounding effects.

- **Age**: It is a **quantitative discrete** variable which we will express in number of years.
- **Sex:** It is a **qualitative nominal dichotomous** variable, expressed in male or female.
- **Aetiology of massive haemorrhage**: it is a **qualitative nominal polytomous** variable. It is important to remember that massive haemorrhage can have different aetiologies, and it is imperative to specify them while analysing the outcomes:
  - Traumatic hemorrhages
  - Haemorrhages caused by surgical complications
  - Haemorrhages caused by obstetrical complications
  - Gastrointestinal hemorrhages
  - Retroperitoneal hemorrhages
  - Pulmonary hemorrhages
  - Haemorrhages caused by ruptured aneurysms.

- **Number of transfusions:** It is a **quantitative discrete** variable measured with numbers. It informs us of the number of transfusions that have been performed on the patient and we can relate this to the efficacy of the diagnostic technique used.

- **"Triad of death":** It is a **qualitative ordinal polytomous** variable, we will indicate how many components of the triad the patient has (1 , 2 or 3). It is a medical condition in which the patient presents with acidosis, hypothermia and coagulopathy has been extensively studied in trauma patients and has been associated with higher mortality. The components of this triad are interrelated, with the presence of any one of them being a risk factor for the onset and worsening of the other elements, which together confer a high risk of mortality on the patient. It will be studied based on the following parameters:

Concept	Values
Acidosis	pH ≤ 7,2 (base deficit ≥7 or lactic acid ≤2.4)
Hypothermia	Core body temperature ≤35ºC
Coagulopathy	INR ≥ 1.5

Table 17: Parameters of the *"Triad of death".*

- **"Pentad of death":** It is a **qualitative ordinal polytomous** variable, we will indicate how many components of the pentad the patient has (1, 2, 3, 4 or 5).

  Is a relatively new adaptation of the concept of the deadly triad. It was developed to provide a better explanation of the sequenced occurrences of alterations to adjust the initial treatment. This model identifies hypoxemia as the initial point that triggers hypocalcemia, hyperglycemia, acidosis, and hypothermia. The components of the pentad, like those of the triad, are interrelated, with the presence of any one of them being a risk factor for the appearance and worsening of the other elements. It has been associated to higher mortality rates. It will be studied based on the following parameters:

Concept	Values
Hypoxemia	Pa02 < 80 mmHg
Acidosis	pH < 7,35 (base deficit ≥7 or lactic acid ≤2.4 mmol/L)
Hypothermia	Core body temperature ≤35ºC
Hyperglicemia	> 250-300 mg/dl
Hypocalcemia	< 1,2 mmol/L (ionic calcium)

Table 18. *Parameters of "Pentad of death".*

- **ATLS scale**: It is a **qualitative ordinal polytomous** variable, we will indicate the grade of haemorrhage based on the ATLS scale (class I, class II, class III or class IV). Based on the volume of blood lost in a haemorrhage, the haemorrhage is classified according to the clinical consequences observed. This classification system is useful for stratifying early signs and pathophysiological signs related to the volume of blood loss. (2)

- **TASH score scale:** It is a **qualitative ordinal polytomous** variable, is a scale with a maximum score of 29. Aims to predict the need for massive transfusion for trauma patients. A 50% probability of need for massive transfusion was predicted by a score of 16, and a score of greater than 27 was 100% predictive of the need for massive transfusion (2,53). For this reason, we will classify it in three groups: ≤ 15, 16-26 and ≥ 27.

- **Resuscitation intensity**: It is a **qualitative ordinal dichotomous.** Is a scale for predicting the need for massive transfusion for trauma patients. It is defined as transfusion of at least 4 units of packed red blood cells in 1 hour. We will classify in two groups, depending on how many units have been transfused: < than 4 units or ≥ 4 units.

Covariables	Description	Categories	Measure instrument
Age	Quantitative discrete	Number of years	Date of event minus date of birth obtained from ID card or other valid document
Number of transfusions		Number of transfusions	Clinical history
Aethiology of massive haemorraghe	Qualitative nominal polytomous	-Traumatic -Surgical complications -Obstetrical complications -Gastrointestinal hemorrhages -Retroperitoneal hemorrhages -Pulmonary hemorrhages -Ruptured aneurysms	Clinical history
Sex	Qualitative nominal dichotomous	Male or female	ID card or other valid document
"Triad of death"	Qualitative ordinal polytomous	Stratified as: 1,2 or 3 1: one altered parameter 2: two altered parameters 3: presence of the triad	Arterial blood gasometry
"Pentad of death"		Stratifies as: 1, 2, 3, 4 or 5 1: one altered parameter 2: two altered parameters 3: three altered parameters 4: four altered parameters 5: presence of the pentad	Arterial blood gasometry
Advanced Trauma Life Support scale		Stratified as: class I, II, III or IV	Physical examination, automatic oscillometer and diuresis
Trauma-Associated Severe Haemorrhage		Stratifies as: ○ ≤ 15 ○ 16-26 ○ ≥ 27	Physical examination, blood sample study, automatic oscillometer and ultrasound
Resucitation intensity	Qualitative ordinal dichotomous	< than 4 units in 1 hour or ≥ than 4 units in 1 hour	Clinical history

Table 19. *Covariables.*

7.6. STUDY INTERVENTION

7.6.1. Intervention

The protocol will be initiated when our patient arrives at the emergency department if the onset of the condition has been extrahospitalary or in the area of the hospital where he/she is if the massive haemorrhage situation occurs intrahospitalary.

To initiate the hospitalary protocol, a prompt response team shall proceed to the patient's location. This group comprises a team leader that is going to be an emergency doctor, an intensivist, an anaesthetist, an trauma surgeon, a radiologist, an emergency nurse, and an orderly.

It is important to clarify that massive haemorrhage is an emergency scenario. Depending on the circumstances, it may not always be possible to obtain the patient's informed consent to participate in the study prior to the procedure. However, as viscoelastic testing is a safe procedure with no risk to the patient, it may be sought after the patient's condition has stabilised. If a first-degree relative or legal representative is present, they can consent or refuse on behalf of the patient. If the patient declines to provide consent, their data will not be included in the study.

If the patient is incapable of giving consent to be transfused, prior to transfusion we must check whether he/she has an advance directives document stating that he/she does not want to be transfused. In the absence of evidence that the patient does not wish to be transfused, the most appropriate action will be taken to preserve the patient's life.

Once we are with the patient, a healthcare professional will be responsible for obtaining all consents and, if necessary, reviewing the advance directives document, while the rest of the team begins the intervention.

The team will begin to monitor the blood pressure, heart rate, respiratory rate, oxygen saturation, temperature, diuresis and an electrocardiogram will also be done. They will also begin to stabilise the patient.

As a matter of urgency, the following steps will be taken:

1. Extraction of blood samples for haemogram, serum lactate, coagulation studies (PT, aPTT, fibrinogen, INR and platelet count) and arterial blood gases (Partial pressure of

oxygen (PaO2), partial pressure of arterial carbon dioxide (PaCO2), pH (base excess), bicarbonate (HCO3), serum glucose and ions). It should be carried out prior to the administration of any serum therapy, to avoid false concentration results. If the extrahospitalary health care team has administered serotherapy, the same procedure will be followed, but this will be taken into account when interpreting the results.

2. Collection of blood samples for transfusion testing and assurance of correct patient identification to ensure transfusion safety.
3. We will take a blood sample in order to manage the patient according to the viscoelastic tests. If the patient has a central line or peripheral line, the nursing staff can take blood samples from these.

As we have explained, from the **ROTEM** we will seek to obtain certain data: clotting time, clot formation time, α angle, maximum clot firmness, clot amplitude at 5 minutes, clot amplitude at 10 minutes and the clot lysis index.

In the **TEG** test we will obtain certain data: reaction time, K value, α angle, maximum amplitude and lysis tyme. These parameters are equivalent to those mentioned in the ROTEM study. The standard recommended processing time is 15 minutes, although we will process it as quickly as possible due to the urgency of the situation.

The blood sample obtained is studied in conjunction with various activating reagents to obtain coagulation and fibrinolysis parameters from different approaches that can activate via the intrinsic or extrinsic pathway.

We will have to consider that in the hospital we have a ROTEM in the emergency laboratory and a TEG in the operating theatre. The decision to use one or the other will be based on proximity, as we will be dealing with a life-threatening situation.

Once the results of the VTE tests are obtained, the analyst physician performing the laboratory tests will contact the blood bank, so that an individualised VTE-guided transfusion can be performed. If transfusion is possible, the name, sex, age and medical record number, the service and detailed location of the patient and the name of the responsible physician will be provided. In the case of the HUJT the call will be made to the personal pager number or direct extension of the blood bank.

For subsequent monitoring, we will take blood samples for a coagulation study and arterial blood gas analysis, in order to assess whether values are normalising after the individualised transfusion. This will be done at 6 hours, 24 hours and 48 hours.

7.6.2. Follow up

We will need to know whether the patient has survived or died at different points in time by contacting the area where the patient is admitted or by looking at the medical records. If the patient has been discharged, we can look them up in the medical history. If there is a suspicion that the information has not been updated or we do not have access to it, for example if the patient is not local and the follow-up is not on our system, then a phone call will be made.

We will follow up 24 hours, 48 hours, 7 day and 30 day after the intervention.

7.6.3. Flow diagram of the intervention group

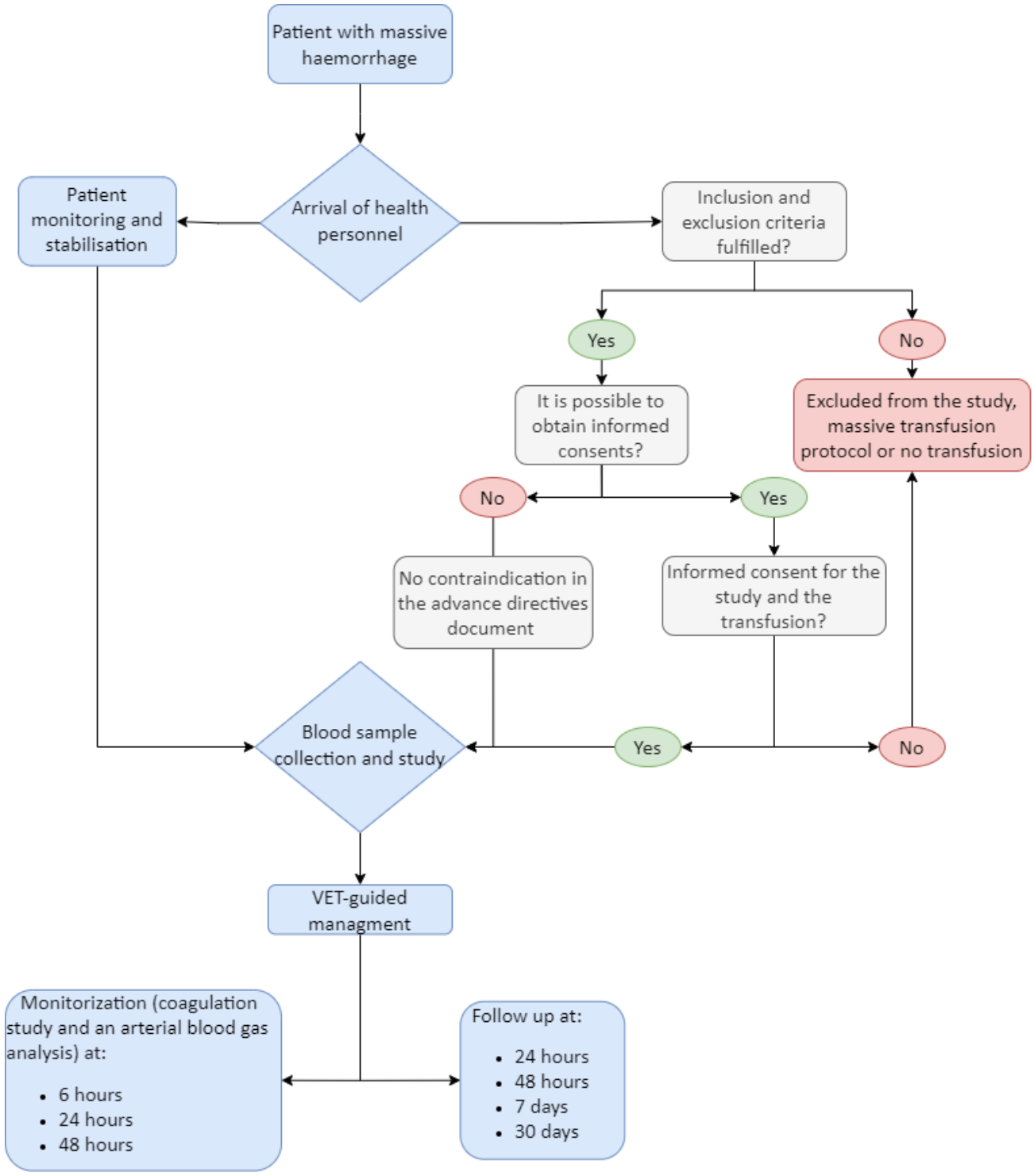

Figure 6. *Flow diagram of the intervention group.*

7.6.4. Data collection

Data collection for the protocol group will be prospective over 13 months, 12 months of intervention plus an additional month to study 30-days mortality. Data will be collected using the REDcap software, which will be prepared by a computer scientist. The data will be entered by the co-investigator coordinator, who will be trained by the computer scientist in the use of the platform to avoid errors.

The control group, retrospective, data will be collected from the SAP computer record. The data will then be entered into the REDcap software by the co-investigator coordinator.

7.6.5. Safety

Thromboelatography and rotational thromboelastometry are safe interventions that involve no risk to the patient. We note that their use is recommended in various clinical practice guidelines. We will use them to obtain additional and rapid information about the patient, in order to provide more specific and individualised treatment.

To avoid any potential risk or harm to patients, the team will be trained and educated so that everyone is assured of the same care.

8. STATISTICAL ANALYSIS

The statistical analysis of the obtained data will be performed by an analyst with expertise in the respective field. The interpretation of the data will be done in a blinded way to avoid any influence on the conclusion. We will employ the Statistical Package for Social Sciences (SPSS) program, version 29 (29.0.10) for the analysis. A confidence interval of 95% will be set for all analyses, and a p-value of 0.05 will be considered statistically significant.

8.1. UNIVARIANT ANALYSIS

A descriptive analysis of the variables will be carried out. We will perform and identical analysis in both groups.

Qualitative variables will be described using **means of proportions**. This applies to the independent variable (laboratory test intervention) and the dependent variable (mortality).

Quantitative variables will be presented using **medians and interquartile range**. This approach is applicable to variables such as age or number of transfusions.

8.2. BIVARIATE ANALYSIS

Bivariate analysis involves analysing two variables to determine the relationships between them.

We will use the **Chi-square or Fisher´s exact test** if the expected number of cases in a cell will be lower than a 5) for the difference of proportions of the qualitative variables (suchs as test viscoelastic intervention and mortality).

To study if there are differences with respect to the quantitative variables (such as age) we will use the **T-Student**.

8.3. MULTIVARIATE ANALYSIS

A **binary logistic regression model** is used for this analysis. The examination will be adjusted for covariates.

9. ETHICAL AND LEGAL CONSIDERATIONS

Ethical principles

The study will be conducted in accordance with the requirements of the World Medical Association (WMA) in the Declaration of Helsinki of Ethical Principles for Medical Research Involving Human Subjects (last revision in the 64th General Assembly, in October 2013).

This quasi-experimental study obeys the Principles of Biomedical Ethics redacted by Tom L. Beachaump and James F.Childress: beneficience, non-maleficience, justice and autonomy.

Beneficience it is respected because in this study we employ a technique, viscoelastic testing, the use of which is recommended by clinical practice guidelines. In addition, based on the previous bibliographic study, we hope to increase patient survival with this practice. **Non-maleficience** is ensured, we will not expose the patient to any greater risk because we will be treating them more specifically in their individual clinical context. **Justice** will be guaranteed, all patients arriving at the hospital who meet the inclusion and exclusion criteria will be invited to participate in the study. To respect **autonomy**, priority will be given to the patient's voluntary and informed decision before the procedure. However, as this is a life-threatening medical situation, it is possible that the decision will be made by the patient's relatives and close associates or, by default, by the patient himself/herself, but after the procedure has been carried out. To guarantee autonomy, we will use informed consent and withdraw of consent as tools.

As indicated in the working plan, the project must be evaluated and approved by the Comitè Ètic d´Investigació Clínica (CEIC) of the HUJT.

Informed consent, withdraw consent and advance directives document

Before entering the study, an information document about the protocol (Annex 5) will be provided in a language that the potential participant can understand. We will ensure the patient comprehends the document without ambiguity, answering his/her possible questions.

If the patient agrees to participate in the study, he/she must accept the informed consent (IC) form (Annex 6). It is important to note that our study will be conducted on patients who are in a medical emergency medical situation where the patient may not be able to accept such a document, so permission will be sought from their relatives and close associates where possible.

If it has not been possible to obtain consent prior to action, the intervention is carried out because it is a safe intervention supported by clinical practice guidelines.

Once the intervention has been completed, it is mandatory to provide the patient or his/her legal representative with information about the procedure performed. If the informed consent form is signed, the patient will be included in the study; if it is not signed, the patient's data will be deleted and he/she will not be included in the study.

In this situation, the principle of beneficence may take precedence over the principle of autonomy in our efforts to save the patient's life.

Participants have the right to refuse to take part in the study at any time during the process by withdrawing their consent to participate. (Annex 7)

During this process of explaining the procedure and obtaining informed consent, we will also provide an information document about blood transfusion and its respective informed consent (Annex 8). If the patient is unable to cooperate, a member of the healthcare team can check if the patient's advance directives state that they do not want to be transfused. If this cannot be checked, the priority is to save the patient's life.

Privacy and confidentiality

All clinical information obtained from patients will be anonymised and assigned to a registration code in REDcap. These data may only be reviewed by the research team for research purposes.

Transparency

Researchers will conduct the trial with the sole purpose of improving the health of patients. All results will be published, whether the data are as expected or not. They will

also declare that they have no conflicts of interest and agree with the ethical basis of the trial.

Adherence to the legal framework

The necessary parameters for conducting research on human subjects, as well as the protection to be afforded to research participants, will be complied with according to the law regulating biomedical research, **"Ley 14/2007, de 3 de julio, de Investigación biomédica"**.(96)

Researchers must respect the patient's right to decide whether to accept or refuse participation in the study in accordance with ***"Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica***".(97)**.** Article 9 of this law provides for the situation of consent by representation.

All data related to the participant will be treated privately and confidentially according to ***Regulation 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data*** (98) and ***"Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales i Garantía de los Derechos Digitales (LOPD- GDD)".***(99)

10.LIMITATIONS AND STRENGTHS

10.1. LIMITATIONS

Selection bias

We will have limitations inherent in a **quasi-experimental study**. This type of study is generally used in situations where it is not possible or unethical to use experimental methodology. They are **non-randomised** research studies. Because the groups are not equivalent and the sampling method is a consecutive non-probabilistic one, selection bias can occur when a sample does not reflect the reality of the population. This may mean that the results obtained are not representative, limiting the ability of the study to establish a causal relationship between an intervention and an outcome. These are reduced by adjusting for the effects of potential confounders, thereby increasing the interval validity of the study.

Confounding factors

Several confounding factors may affect the association between dependent and independent variables. We will try to avoid confounding by using multivariate analysis. A massive bleeding situation is a condition that can have many etiologies. Therefore, our patients are very diverse with different associated complications due to their pathologies or underlying conditions. For this reason, we will take this into account as a covariate when interpreting the results.

Incidence

Massive haemorrhage is a clinical and medical situation that has been interpreted and defined in very heterogeneous ways, so that it is thought to be an underestimated entity, both in terms of diagnosis and importance. This makes it difficult to obtain data on its true incidence in different clinical scenarios. For this purpose, we have strictly defined the situations in which we consider a haemorrhage to be massive and will take into account the incidence of massive transfusions performed. However, in our study we have a retrospective control group, so we will have to consider if there is enough information on the patients in the control group to be able to perform an optimal analysis.

Preanalytic variability

Since the control group will be obtained retrospectively, we will not be able to control for pre-analytical variability. It will be important to take this into account when interpreting test results.

Life-threatening situation

Another limitation of the study is the context in which we are going to intervene. We will be in a context where the patient is in a life-threatening situation, so health workers may forget to include the patient in the study or to record the necessary data, thus reducing the sample. To avoid this, we will have a team trained and informed about the steps to take. It is important to remember that we may need to adjust the timing of the study to ensure that the required number of samples are collected.

Informed consent

In certain clinical contexts, the decision to accept or refuse informed consent cannot be made by the patient. In cases where it is possible to interact with the patient after the procedure, we will ensure that he/she is informed directly. The participant will always be offered the possibility to revoke informed consent and to remove his/her data from the study.

Studio equipment

The study is based on the use of different laboratory machines. We need to be prepared in case the equipment has some kind of internal problem. We will ensure that it passes the necessary periodic inspections and checks.

10.2. STRENGTHS

Viscoelastic testing

The use of viscoelastic tests is a recommendation that can be found in various clinical practice guidelines, due to the speed with which results can be obtained.

Level of evidence

There is a higher level of evidence in a quasi-experimental trial than in an observational trial, which is where most complications reported in literature originate.

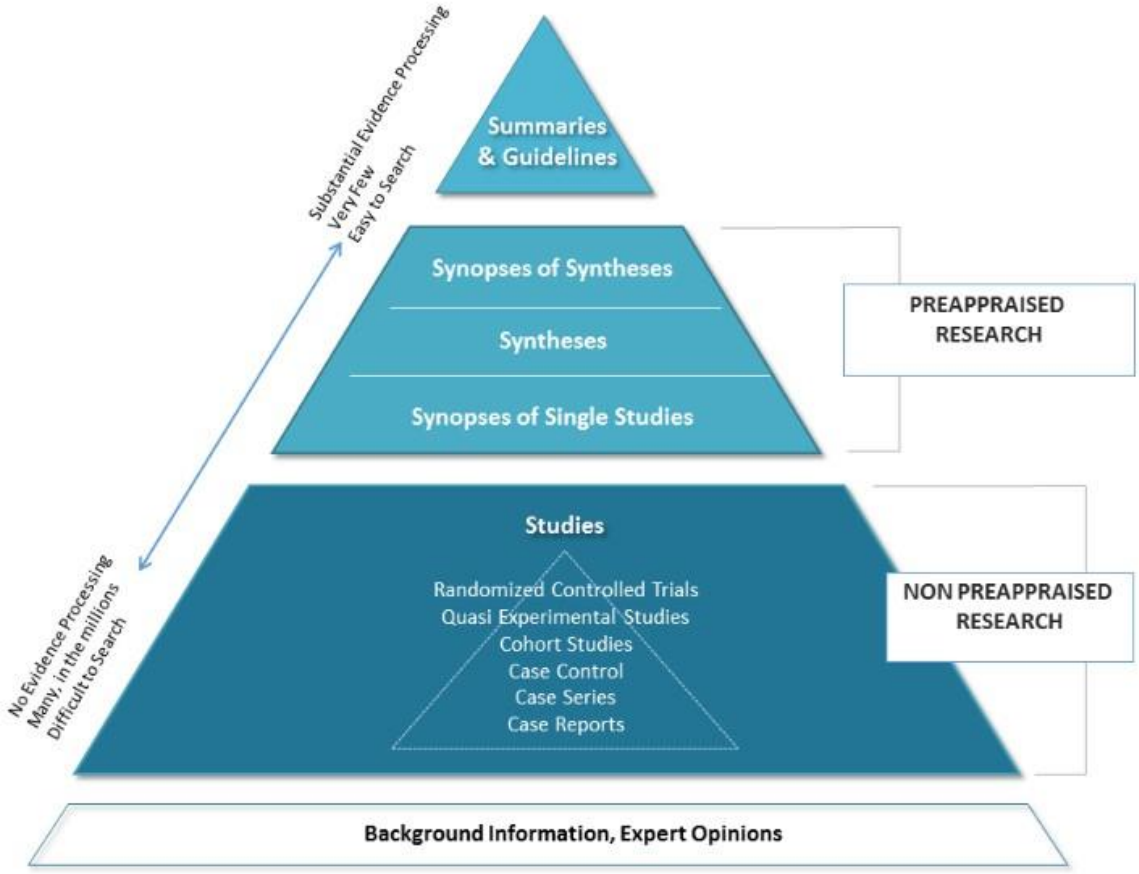

Figure 7. *Pyramid of scientific evidence taken from* (100)

One-centre study

The trial will be conducted in a single centre, so the members of the study team will have the same training and equipment during the process. In multi-centre trials, this could lead to significant differences.

Computer register

An anonymous record will be created for each patient in REDcap as soon as he/she accepts informed consent, thus having close control over the storage of information.

11.WORK PLAN AND CHRONOGRAM

11.1. PARTICIPATING CENTRE

As mentioned above, the study was designed to be conducted in the Hospital Universitari Dr. Josep Trueta.

11.2. RESEARCH TEAM MEMBERS

To carry out the study, we need a multidisciplinary team. This will include:

- **Study coordinator (SC):** This person will oversee the study by coordinating the research team. Is the responsible for assigned tasks and developed activities. He/she will be an emergency medical specialist.
- **Main investigator (MI):** He/she will be responsible for formulating the study, writing the protocol and submitting it for approval, leading recruitment of participants and managing the informed consent process.
- **Co-investigator coordinator/ Hospital coordinator (HC):** He/ she will be in charge of coordinating the co-researchers as well as collecting the data and making sure that the whole procedure is being carried out correctly in his/her hospital.

  They will have to attend meetings with the study coordinator and the main investigator.
- **Co-investigators (CI):** We will need to appoint several co-investigators when we look at the distribution of hospital staff. We must ensure that all shifts are covered, bearing in mind that the emergency department is always kept open. We will assign the following professionals.
  - **Emergency medicine professional**: Is the person in charge of treating the patient with massive haemorrhage and supervising the intervention, is the team leader.
  - **Clinical Analyst**: will be responsible for training the rest of the analysts in the handling and study of the blood sample for use in the ROTEM and TEG apparatus. He/she will be responsible for calling the blood bank when the results of the tested blood are available so that they can prepare the specific products for the guided transfusion.

- **Haematology professional**: will be an haematologist linked to the blood bank, in order to keep a proper record of the transfusion processes carried out.

- **Data manager (DM):** This person will be responsible for managing the data collection during the study. Will be in charge of data processing, quality control and report writing for the interim and final analysis of the data.
- **Independent statistic specialist:** He/ She will be responsible for the statistical analysis of the study.
- **Health care professionals**: This includes healthcare professionals who may be found at the scene of a major haemorrhage and those who will form the rapid response teams, such as radiologists, traumatologists, anaesthetists, intensive care physicians, surgeons, emergency nurses, orderlies, etc. We will have nursing staff with experience in blood sampling, transfusion application and patient support.
- **Other staff:** computer scientist, nursing assistants… and the hospital staff.

11.3. STUDY STAGES

This study will be carried out in 7 stages of work:

STAGE 1: Elaboration of the protocol and study design *(September 2023-November 2023)*

1. **First session** *(September 2023, completed):* The first meeting between the study coordinator and the principal investigator takes place. The development and design of this study is agreed.
2. **Bibliographic research and protocol drafting** *(September 2023- November 2023, completed):* Extensive bibliographical research is carried out to obtain a correct basis for the study. The final protocol is written and reviewed.
3. **Meeting with selected hospital** *(November 2023):* The MI will contact the selected hospital and offer to take part in the study.

STAGE 2: Ethical approval *(December 2023- February 2024)*

4. **Presentation, evaluation and approval by the Clinical Research Ethical Committee (CEIC):** The MI will submit the protocol to the CEIC of the medical centre involved in the study for ethical approval. All suggested modification will be considered and modified accordingly.

STAGE 3: Coordination, formation and database creation *(March 2024)*

5. **First meeting:** The SC and the IM will go to the hospital involved in the study to meet with the co-investigator coordinator to introduce themselves, clear up any doubts and distribute the work.
6. **Formation sessions:** Joint training will be carried out so that the whole team works in coordination. We will contact the authors of the HEMOMAS document to see if they could provide training. It is a multidisciplinary consensus document on the management of massive haemorrhage created at national level, in which recommendations based on scientific evidence are compiled.
7. **Creation of the REDcap database:** The SC and the IM will contract and have a meeting with a computer scientist to explain the project and its characteristics. This will allow him to develop a programme to collect the data according to our study.

STAGE 4: Field research and data collection *(April 2024- May 2025)*

During this phase, the study coordinator, the main investigator, the co-investigator coordinator and the data manager will meet every 3 weeks to discuss together the evolution of the study.

8. **Patient recruitment, intervention and follow up**: It is estimated that it will take 12 months to obtain the required sample. It will be based on the management of massive haemorrhage guided by viscoelastic tests and on studying the associated mortality at different time periods. We will need another month after the last patient is enrolled because one of the secondary objectives is to assess 30-day mortality. If we get the required sample before the expected time, we will move on to the next phase.
9. **Data collection:** As cases come in, the hospital coordinator will record all the data collected from the various variables in the database. The hospital coordinator will also carry out the bibliographic check for the control group.

STAGE 5: Analysis of the data collected *(June 2025)*

10. **Statistical analysis:** A masked statistician will be responsible for analysing all data collected during the study. Descriptive, bivariate and multivariate analysis will be performed. The data manager will supervise this phase and perform quality controls.

STAGE 6: Interpretation of the data collected *(July 2025)*

11. **Results and conclusions:** The SC and MI will meet to interpret the results and draw conclusions.

STAGE 7: Results publication and dissemination *(August 2025 - November 2025)*

12. **Article development and publication** ***(****August 2025 – September 2025)*: The IM will be responsible for writing and revising the article. A translator will also be hired to ensure the correct wording before publication.
13. **Dissemination** *(October 2025 – November 2025)*: The results of the study will be presented at national and international conferences by the main investigator and the study coordinator.

11.4. CHRONOGRAM

TASKS	STAFF	PERIOD																													
		2023				2024												2025													
		S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N			
STAGE 1: Elaboration of the protocol and study design																															
1. First session	SC and MI																														
2. Bibliographic research and protocol drafting	MI																														
3. Meeting with selected hospital																															
STAGE 2: Ethical approval																															
4. Presentation, evaluation and aproval by the CEIC	CEIC																														
STAGE 3: Coordination, formation and database creation																															
5. First meeting	All team																														
6. Formation sessions	All team																														
7. Creation of REDcap database	Computer Scientist																														
STAGE 4: Field research and data collection																															
8. Patient recruitment, intervention and follow up	All team																														
9. Data collection	HC																														
STAGE 5: Analysis of the data collected																															
10. Statistical analysis	DM and statistic																														
STAGE 6: Interpretation of the data collected																															
11. Results and conclusions	SC and MI																														
STAGE 7: Results publication and dissemination																															
12. Article development and publication	MI and translator																														
13. Dissemination	SC and MI																														

Table 20. *Chronogram of the study.*

12.BUDGET

For the purpose of calculating the budget required to carry out the study, we have organized the data into the following sections:

- **Personal expenses:** The personnel who will care for the patients in the trial are the same as those who are part of the emergency medical team. As we will not need any additional staff, this is not included in the budget.
- **Subcontrated services:** We will need to hire staff from outside the healthcare team. We will need a computer scientist to create the profile in REDcap and a data manager and statistical analyst to analyse and ensure an optimal data study process. In addition, to ensure the correct wording of the article prior to publication, we will hire a certified translator.
- **Execution expenses:** Both TEG and ROTEM, as well as the tools needed to obtain the blood sample (needles, gauze, disinfectants, etc.) and reagents, are used in daily clinical practice in the hospital. For this reason, there is no need for any additional material or goods.
- **Insurance contract:** No insurance is required as the study interventions are considered safe, recommended by experts and used in different settings in the hospital.
- **Publication:** The article will be published in a journal article, the cost of which will be included in the budget.
- **Dissemination:** The study will be presented at several national and international congresses. Preference will be given to the annual congress of Spanish Society of Emergency Medicine (SEMES) and European Emergency Medicine Congress (EUSEM). The budget will include transport, daily allowance and accommodation.

Type of cost	Description	Unit cost	Units	Cost
Personal expenses	Healthcare personnel	-	-	0€
Subcontrated services	Training team	-	-	1.500€
	Data manager	35€/h	125h	4.375€
	Statistical analysis	35€/h	125h	4.375€
	Computer scientist	20€/h	10h	200€
	Linguistic correction by certified traductor	300€/ article	1	300€
Execution expenses	ROTEM	-	-	0€
	TEG	-	-	0€
Publication	Article publication (Open access)	1.500€/ publication	1	1.500€
Dissemination Congress inscription	National congress	1.250€	1	1.250€
	International congress	2.500 €	1	2.500€
			TOTAL COST	16.000€

Table 21. *Budget of the study.*

13.CLINICAL AND HEALTH SYSTEM IMPACT AND FEASIBILITY

13.1. IMPACT ON HEALTH SYSTEM

Massive haemorrhage is a condition which, as we have seen, has a very diverse aetiology and can occur in a wide range of patient profiles. It is essential to remember that it is the cause of a large number of preventable deaths.

In this study we have mortality as the dependent variable. We are dealing with a situation that is mostly unpredictable and unexpected and has a high associated mortality.

Death is a situation that has a great impact on society. On the one hand the loss of years of life potentially lost in the patient and on the other hand the effect it has on the patient's environment. The psychological impact on the patient's family and colleagues, as well as on the healthcare professionals who have cared for the patient, must be considered. In this type of life-threatening situation, staff are exposed to a very high level of stress and responsibility, and often we are dealing with patients who do not have co-morbidities but for some reason find themselves in a life-threatening situation.

Viscoelastic tests, on the other hand, are recommended for management because of their rapidity.

We hope to assess the overall difference in mortality in patients with different aetiologies of massive haemorrhage and what the survival outcome is at different time points, not just at a single time point.

It would be important to establish whether there is a relationship between increased survival in the same patient at different time periods and to compare the outcome in CCT-guided patients to see whether massive transfusion could be displaced by guided transfusion.

If this hypothesis is confirmed, we may be able to encourage future studies and implement a guided transfusion protocol in our hospitals as a basic treatment for this type of patient.

13.2. FEASIBILITY

We consider this a feasible study.

This study will be conducted in Hospital Universitari Dr. Josep Trueta. For the protocol group, we need 145 patients to agree to consent, which we calculate will be recruited in 12 months. From a logistical point of view, this is an acceptable period of time. Information on the 145 patients in the control group will be obtained retrospectively from the SAP.

The trial will be conducted mainly in the emergency department of the hospital, with the help of a multidisciplinary team. The hospital already has the necessary medical staff, such as emergency physicians, medical analysts and haematologists.

A joint training course will be held for all health professionals involved in the study and the group that produced the HEMOMAS document (Multidisciplinary consensus document on the management of massive haemorrhage) will be contacted for this purpose.

We can find the recommendation to use viscoelastic tests in several documents such as HEMOMAS. This is due to their rapidity in obtaining results and that we do not expose patients to additional risk compared to conventional coagulation studies.

Data manager and statistician would be employed to ensure proper management, recording and statistical analysis.

14.BIBLIOGRAPHY

1. Ramió C, Murcia C, Grífols JR, Albiol M, Castrillo I, Domingo R, et al. Guia de transfusió massiva. Girona: Hospital Universitari de Girona Doctor Josep Trueta; 2022.

2. Llau JV, Acosta FJ, Escolar G, Fernández-Mondéjar E, Guasch E, Marco P, et al. Documento multidisciplinar de consenso sobre el manejo de la hemorragia masiva (documento HEMOMAS). Med Intensiva [Internet]. 2015 Nov 1 [cited 2023 Oct 26];39(8):483–504. Available from: http://www.medintensiva.org/es-documento-multidisciplinar-consenso-sobre-el-articulo-S0210569115001138

3. García Díaz EM, Dusseck Brutus R, Leal Noval SR. Hemorragia masiva no traumática. In: Manuales Clínicos [Internet]. Sevilla: Hospital Universitario Virgen del Rocío; 2020 [cited 2023 Oct 26]. p. 1–3. Available from: https://manualclinico.hospitaluvrocio.es/urgencias/emergencias-generales/hemorragia-masiva-no-traumatica/

4. Johnson AB, Burns B. Hemorrhage. In: StatPearls [Internet]. Florida: StatPearls Publishing; 2023 [cited 2023 Nov 4]. p. 1–8. Available from: http://www.ncbi.nlm.nih.gov/books/NBK542273/

5. Marsden NJ, Tuma F. Polytraumatized Patient. In: StatPearls [Internet]. Florida: StatPearls Publishing; 2023 [cited 2023 Nov 4]. p. 1–7. Available from: http://www.ncbi.nlm.nih.gov/books/NBK554426/

6. Endo A, Shiraishi A, Otomo Y, Kushimoto S, Saitoh D, Hayakawa M, et al. Development of Novel Criteria of the 'Lethal Triad' as an Indicator of Decision Making in Current Trauma Care: A Retrospective Multicenter Observational Study in Japan. Crit Care Med [Internet]. 2016 [cited 2023 Nov 4];44(9):e797-803. Available from: https://pubmed.ncbi.nlm.nih.gov/27046085/

7. Eddy VA, Morris JA, Cullinane DC. Hypothermia, coagulopathy, and acidosis. Surg Clin North Am [Internet]. 2000 [cited 2023 Nov 4];80(3):845–54. Available from: https://pubmed.ncbi.nlm.nih.gov/10897264/

8. Cueto-Felgueroso Ojeda C, Abelardo Barea Mendoza J, Chico Fernández M. Pruebas viscoelásticas a pie de cama. Buscando la utilidad clínica. Soc Esp Med Lab. 2022 2023;(61):63–80.

9. Quintana-Díaz M, Garay-Fernández M, Ariza-Cadena F. Advancing in the understanding of coagulopathy during hemorrhagic shock: From the triad to the deadly pentad. Colomb J Anesthesiol [Internet]. 2022 [cited 2023 Nov 4];50:1–8. Available from: https://www.revcolanest.com.co/index.php/rca/article/view/1038

10. Gómez LJM, Khan TH. Hypothermia in trauma. Anaesth Pain Intensive Care [Internet]. 2017 [cited 2023 Nov 4];21(2):232–40. Available from: https://www.apicareonline.com/index.php/APIC/article/view/100

11. Marietta M, Facchini L, Pedrazzi P, Busani S, Torelli G. Pathophysiology of bleeding in surgery. Transplant Proc [Internet]. 2006 Apr [cited 2023 Oct 26];38(3):812–4. Available from: https://www.sciencedirect.com/science/article/pii/S0041134506000480?via%3Dihub

12. Peña-Pérez CA. Manejo de la hemorragia intraoperatoria. Rev Mex Anestesiol [Internet]. 2015 [cited 2023 Oct 26];38(2):380–5. Available from: https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=58872

13. Bevan DH. Cardiac bypass haemostasis: putting blood through the mill. Br J Haematol [Internet]. 1999 Feb [cited 2023 Oct 26];104(2):208–19. Available from: https://onlinelibrary.wiley.com/doi/full/10.1046/j.1365-2141.1999.01182.x

14. Shander A. Financial and clinical outcomes associated with surgical bleeding complications. Surgery [Internet]. 2007 Oct [cited 2023 Oct 26];142(4 Suppl):S20-25. Available from: https://www.surgjournal.com/article/S0039-6060(07)00416-3/fulltext

15. Karlsson H, Pérez Sanz C. Hemorragia postparto. Sist Sanit Navar [Internet]. 2009 [cited 2023 Oct 26];32:159–67. Available from: https://scielo.isciii.es/pdf/asisna/v32s1/obstetricia6.pdf

16. AbouZahr C. Global burden of maternal death and disability. Br Med Bull [Internet]. 2003 [cited 2023 Oct 26];67:1–11. Available from: https://pubmed.ncbi.nlm.nih.gov/14711750/

17. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists Number 76, October 2006: postpartum hemorrhage. Obstet Gynecol [Internet]. 2006 Oct [cited 2023 Oct 26];108(4):1039–47. Available from: https://pubmed.ncbi.nlm.nih.gov/17012482/

18. Chesley LC. Plasma and red cell volumes during pregnancy. Am J Obstet Gynecol [Internet]. 1972 Feb 1 [cited 2023 Oct 26];112(3):440–50. Available from: https://pubmed.ncbi.nlm.nih.gov/4551251/

19. Guasch E, Gilsanz F. Hemorragia masiva obstétrica: enfoque terapéutico actual. Med Intensiva [Internet]. 2016 Jun 1 [cited 2023 Oct 26];40(5):298–310. Available from: https://www.medintensiva.org/es-hemorragia-masiva-obstetrica-enfoque-terapeutico-articulo-S021056911630002X

20. Hospital Son Llàtzer. Protocolo hemorragia digestiva [Internet]. Palma de Mallorca: Govern de les Illes Balears; 2009 [cited 2023 Oct 26]. 1–18 p. Available from: https://www.fundacionsigno.com/bazar/1/Protocolo_hemorragia_digestiva.pdf

21. Ostabal Artigas MI. La hemorragia digestiva aguda. Med Integral [Internet]. 2021 Feb [cited 2023 Oct 26];37(4):141–4. Available from: https://www.elsevier.es/es-revista-medicina-integral-63-pdf-10021655

22. DiGregorio AM, Alvey H. Gastrointestinal Bleeding. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Oct 26]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK537291/

23. Hemorragia digestiva. In: Empendium [Internet]. Kraków: Medycyna Praktyczna; 2023 [cited 2023 Oct 26]. Available from: https://empendium.com/manualmibe/compendio/social/chapter/B34.II.4.31.

24. Weil PH. Management of retroperitoneal trauma. Curr Probl Surg [Internet]. 1983 Sep 1 [cited 2023 Oct 26];20(9):539–620. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0011384083800094

25. Mondie C, Maguire NJ, Rentea RM. Retroperitoneal Hematoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Oct 26]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK558928/

26. Baekgaard JS, Eskesen TG, Lee JM, Yeh DD, Kaafarani HMA, Fagenholz PJ, et al. Spontaneous Retroperitoneal and Rectus Sheath Hemorrhage-Management, Risk Factors and Outcomes. World J Surg [Internet]. 2019 Aug [cited 2023 Oct 26];43(8):1890–7. Available from: https://pubmed.ncbi.nlm.nih.gov/30963204/

27. Kwok CS, Kontopantelis E, Kinnaird T, Potts J, Rashid M, Shoaib A, et al. Retroperitoneal Hemorrhage After Percutaneous Coronary Intervention. Circ Cardiovasc Interv [Internet]. 2018 Feb [cited 2023 Oct 26];11(2):1–28. Available from: https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.117.005866

28. Pode D, Caine M. Spontaneous retroperitoneal hemorrhage. J Urol [Internet]. 1992 Feb [cited 2023 Oct 26];147(2):311–8. Available from: https://pubmed.ncbi.nlm.nih.gov/1346277/

29. Gimeno Argente V, Bosquet Sanz M, Ramírez Backhaus M, Trassierra Villa M, Arlandis Guzmán S, Jiménez Cruz JF. Hemorragia retroperitoneal espontánea: nuestra experiencia en los últimos 10 años. In: Medline plus [Internet]. Valencia: Hospital Universitario la Fe; 2007 [cited 2023 Oct 26]. p. 521–7. Available from: https://medlineplus.gov/spanish/aorticaneurysm.html

30. Yendamuri S. Massive Airway Hemorrhage. Thorac Surg Clin [Internet]. 2015 Aug [cited 2023 Oct 26];25(3):255–60. Available from: https://pubmed.ncbi.nlm.nih.gov/26210922/

31. Radchenko C, Alraiyes AH, Shojaee S. A systematic approach to the management of massive hemoptysis. J Thorac Dis [Internet]. 2017 Sep [cited 2023 Oct 26];9(Suppl 10):S1069–86. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5696556/

32. Dweik RA, Stoller JK. Role of bronchoscopy in massive hemoptysis. Clin Chest Med [Internet]. 1999 Mar [cited 2023 Oct 26];20(1):89–105. Available from: https://pubmed.ncbi.nlm.nih.gov/10205720/

33. Aneurisma aórtico. In: Medline plus [Internet]. Bethesda: National Library of Medicine; 2021 [cited 2023 Oct 26]. Available from: https://medlineplus.gov/spanish/aorticaneurysm.html

34. Aneurismas: Síntomas y causas. In: Mayo Clinic [Internet]. Minnesota: Mayo Clinic; 2023 [cited 2023 Oct 26]. Available from: https://www.mayoclinic.org/es/diseases-conditions/aneurysms/symptoms-causes/syc-20354633

35. González ZM, Lorenzo LR. Hemorragia en el enfermo politraumatizado grave. ReMUE [Internet]. 2014 [cited 2023 Oct 26];1:26–30. Available from: http://www.remue.cat/view_document.php?tpd=2&i=2699

36. Weltgesundheitsorganisation, Weltgesundheitsorganisation, editors. The injury chartbook: a graphical overview of the global burden of injuries. Geneva: Dept. of Injuries and Violence Prevention, Noncommunicable Diseases and Mental Health Cluster, World Health Organization; 2002.

37. Injuries and violence. In: WHO [Internet]. Ginebra: World....; 2021 [cited 2023 Oct 26]. Available from: https://www.who.int/news-room/fact-sheets/detail/injuries-and-violence

38. Davenport RA, Guerreiro M, Frith D, Rourke C, Platton S, Cohen M, et al. Activated Protein C Drives the Hyperfibrinolysis of Acute Traumatic Coagulopathy. Anesthesiology [Internet]. 2017 Jan [cited 2023 Oct 26];126(1):115–27. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5257267/

39. Amézaga Menéndez R, Leal-Noval SR. Massive haemorrhage: we can do it better. Rev Esp Anestesiol Reanim Engl Ed [Internet]. 2023 Aug 1 [cited 2023 Oct 26];70(7):371–2. Available from: https://www.sciencedirect.com/science/article/pii/S2341192923001191

40. Irita K. Risk and crisis management in intraoperative hemorrhage: Human factors in hemorrhagic critical events. Korean J Anesthesiol [Internet]. 2011 Mar 30 [cited 2023 Oct 26];60(3):151–60. Available from: https://ekja.org/journal/view.php?doi=10.4097/kjae.2011.60.3.151

41. Corral M, Ferko N, Hollmann S, Broder MS, Chang E. Health and economic outcomes associated with uncontrolled surgical bleeding: a retrospective analysis of the Premier Perspectives Database. Clin Outcomes Res CEOR [Internet]. 2015 [cited 2023 Oct 26];7:409–21. Available from: https://pubmed.ncbi.nlm.nih.gov/26229495/

42. Irita K, Kawashima Y, Morita K, Seo N, Iwao Y, Sanuki M, et al. [Supplemental survey in 2003 concerning life-threatening hemorrhagic events in the operating room]. Masui [Internet]. 2005 Jan [cited 2023 Oct 26];54(1):77–86. Available from: https://pubmed.ncbi.nlm.nih.gov/15717475/#:~:text=Results%3A%20In%20patients%20who%20developed,5%20g%20x%20dl(%2D1).

43. Groenland TH, Porte RJ, Metselaar HJ. Liver transplantation and risk of bleeding. Curr Opin Organ Transplant [Internet]. 2007 Jun [cited 2023 Oct 26];12(3):287–93. Available from: https://pubmed.ncbi.nlm.nih.gov/27711020/

44. Knight M, Bunch K, Tuffnell D, Patel R, Shakespeare J, Kotnis R, et al. Saving Lives, Improving Mothers´ Care [Internet]. Oxford: BCQ; 2021 [cited 2023 Oct 26]. Available from: https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/maternal-report-2021/MBRRACE-UK_Maternal_Report_2021_-_FINAL_-_WEB_VERSION.pdf

45. Álvarez-Ibáñez C, Guerra-García MM. Evolución de la incidencia de la hemorragia digestiva alta en España en relación con el consumo de antiulcerosos. Aten Primaria [Internet]. 2012 Aug [cited 2023 Oct 26];44(8):478–84. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7025277/

46. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol [Internet]. 2008 [cited 2023 Oct 26];22(2):209–24. Available from: https://pubmed.ncbi.nlm.nih.gov/18346679/

47. Rodríguez I, Enrique C. Epidemiología de la Hemorragia Digestiva. Acta Médica Peru [Internet]. 2006 Sep [cited 2023 Oct 26];23(3):152–5. Available from: http://www.scielo.org.pe/scielo.php?script=sci_abstract&pid=S1728-59172006000300005&lng=es&nrm=iso&tlng=es

48. Lozada A, Camargo Á, Rodriguez M. Hematomas Retroperitoneales. Rev Médica [Internet]. 2014 [cited 2023 Oct 26];4(1):34–42. Available from: https://revistamedicaclcountry.com/posts/hematomas-retroperitoneales

49. Lukies M, Gipson J, Tan SY, Clements W. Spontaneous Retroperitoneal Haemorrhage: Efficacy of Conservative Management and Embolisation. Cardiovasc Intervent Radiol [Internet]. 2023 Apr 1 [cited 2023 Oct 26];46(4):488–95. Available from: https://doi.org/10.1007/s00270-023-03359-4

50. Crocco JA, Rooney JJ, Fankushen DS, DiBenedetto RJ, Lyons HA. Massive hemoptysis. Arch Intern Med [Internet]. 1968 Jun [cited 2023 Oct 26];121(6):495–8. Available from: https://pubmed.ncbi.nlm.nih.gov/5652400/

51. Larici AR, Franchi P, Occhipinti M, Contegiacomo A, del Ciello A, Calandriello L, et al. Diagnosis and management of hemoptysis. Diagn Interv Radiol Ank Turk [Internet]. 2014 [cited 2023 Oct 26];20(4):299–309. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4463269/

52. Claves de los aneurismas de aorta abdominal. In: Hospital Universitario Nuestra Señora del Rosario [Internet]. Madrid: Bureau Veritas; 2022 [cited 2023 Nov 4]. Available from: https://www.hospitalrosario.es/noticias/claves-de-los-aneurismas-de-aorta-abdominal/

53. The American College of Surgeons C on T. Chapter 3 Shock. In: ATLS Advanced Trauma Life Support Student Course Manual. 10th ed. Chicago: American College of Surgeons; 2018. p. 42–61.

54. Pope A, French G, Longnecker DE. Pathophysiology of Acute Hemorrhagic Shock. In: Fluid Resuscitation: State of the Science for Treating Combat Casualties and Civilian Injuries [Internet]. Washington: National Academies Press (US); 1999 [cited 2023 Oct 31]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK224592/

55. Mejía-Gómez LJ. Fisiopatología choque hemorrágico. Rev Mex Anestesiol [Internet]. 2014 [cited 2023 Oct 31];37(1):70–6. Available from: https://www.medigraphic.com/pdfs/rma/cma-2014/cmas141v.pdf

56. Hypovolemic Shock. In: BrainKart [Internet]. Chennai: Therital; 2018 [cited 2023 Nov 4]. Available from: https://www.brainkart.com/article/Hypovolemic-Shock_31727/

57. Longmore M, Wilkinson IB, Davidson EH, Foulkes A, Mafi AR. Shock. In: Oxford Handbook of Clinical Medicine. 8th ed. Oxford: Oxford University Press; 2010. p. 804.

58. Kumar A, Parrillo JE. Chapter 22 - Shock: Classification, Pathophysiology, and Approach to Management. In: Parrillo JE, Dellinger RP, editors. Critical Care Medicine (Third Edition) [Internet]. Philadelphia: Mosby; 2008 [cited 2023 Oct 31]. p. 379–422. Available from: https://www.sciencedirect.com/science/article/pii/B9780323048415500248

59. Houston MC. Pathophysiology of shock. Crit Care Nurs Clin North Am [Internet]. 1990 Jun [cited 2023 Oct 26];2(2):143–9. Available from: https://pubmed.ncbi.nlm.nih.gov/2192723/

60. Cannon JW. Hemorrhagic Shock. N Engl J Med [Internet]. 2018 Jan 25 [cited 2023 Oct 31];378(4):370–9. Available from: http://www.nejm.org/doi/10.1056/NEJMra1705649

61. Hooper N, Armstrong TJ. Hemorrhagic Shock. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Oct 31]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK470382/

62. Belgaumi N, Salik A, Siddiqui N ur R, Belgaumi N, Salik A, Siddiqui N ur R. Shock Pathophysiology: Classifications and Management. In: Management of Shock - Recent Advances [Internet]. Pakistan: IntechOpen; 2022 [cited 2023 Oct 31]. p. 1–19. Available from: https://www.intechopen.com/chapters/83503

63. Mutschler M, Nienaber U, Brockamp T, Wafaisade A, Fabian T, Paffrath T, et al. Renaissance of base deficit for the initial assessment of trauma patients: a base deficit-based classification for hypovolemic shock developed on data from 16,305 patients derived from the TraumaRegister DGU®. Crit Care Lond Engl. 2013 Mar 6;17(2):1–9.

64. Llau JV, Aldecoa C, Guasch E, Marco P, Marcos-Neira P, Paniagua P, et al. Documento multidisciplinar de consenso sobre el manejo de la hemorragia masiva. Primera actualización 2023 (documento HEMOMAS-II). Med Intensiva [Internet]. 2023 Aug [cited 2023 Oct 31];47(8):454–67. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0210569123000797

65. Burman S, Cotton BA. Trauma patients at risk for massive transfusion: the role of scoring systems and the impact of early identification on patient outcomes. Expert Rev Hematol [Internet]. 2012 Apr [cited 2023 Oct 31];5(2):211–8. Available from: https://pubmed.ncbi.nlm.nih.gov/22475289/

66. American Society of Anesthesiologists Task Force on Perioperative Blood Management. Practice guidelines for perioperative blood management. Anesthesiology [Internet]. 2015 Feb [cited 2023 Oct 31];122(2):241–75. Available from: https://pubmed.ncbi.nlm.nih.gov/25545654/

67. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CAA, De Robertis E, Filipescu DC, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol [Internet]. 2013 Jun [cited 2023 Oct 31];30(6):270–382. Available from: https://pubmed.ncbi.nlm.nih.gov/36855941/

68. Spahn DR, Bouillon B, Cerny V, Duranteau J, Filipescu D, Hunt BJ, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. Crit Care Lond Engl [Internet]. 2019 Mar 27 [cited 2023 Oct 31];23(1):98. Available from: https://pubmed.ncbi.nlm.nih.gov/30917843/

69. Esquivel AAC, Morales XO, Ibáñez EXT, Cruz FL. Déficit de base como marcador de gravedad y predictor de transfusión temprana en pacientes con hemorragia del tubo digestivo. Medigraphic [Internet]. 2018 [cited 2023 Oct 26];63(1):20–5. Available from: https://www.medigraphic.com/pdfs/abc/bc-2018/bc181d.pdf

70. Cohen T, Haas T, Cushing MM. The strengths and weaknesses of viscoelastic testing compared to traditional coagulation testing. Transfusion (Paris) [Internet]. 2020 Oct [cited 2023 Oct 31];60 Suppl 6:S21–8. Available from: https://pubmed.ncbi.nlm.nih.gov/33089934/

71. Samoš M, Škorňová I, Bolek T, Stančiaková L, Korpallová B, Galajda P, et al. Viscoelastic Hemostatic Assays and Platelet Function Testing in Patients with Atherosclerotic Vascular Diseases. Diagn Basel Switz [Internet]. 2021 Jan 19 [cited 2023 Oct 31];11(1):143. Available from: https://pubmed.ncbi.nlm.nih.gov/33478051/

72. Chacón DM. Sangrado masivo: Uso de tromboelastometría y tomboelastografía rotacional. Rev Médica Costa Rica Centroamérica [Internet]. 2013 [cited 2023 Oct 31];70(608):607–13.

Available from: https://www.medigraphic.com/cgi-bin/new/resumenI.cgi?IDARTICULO=47785

73. Winearls J, Reade M, Miles H, Bulmer A, Campbell D, Görlinger K, et al. Targeted Coagulation Management in Severe Trauma: The Controversies and the Evidence. Anesth Analg [Internet]. 2016 Oct [cited 2023 Nov 2];123(4):910–24. Available from: https://pubmed.ncbi.nlm.nih.gov/27636575/

74. Rishi. Interpreting Thromboelastography (TEG). In: RKMD [Internet]. Texas: RK.MD; 2014 [cited 2023 Nov 2]. Available from: https://rk.md/2014/thromboelastography-teg/

75. Rali AS, Salem AM, Gebre M, Garies TM, Taduru S, Baracey Jr AW. Viscoelastic Haemostatic Assays in Cardiovascular Critical Care. 2021 [cited 2023 Nov 2];7:1–8. Available from: https://www.cfrjournal.com/articles/viscoelastic-haemostatic-assays-cardiovascular-critical-care

76. Calatzis A, Görlinger K, Spannagl M, Vorweg M. ROTEM Analysis Targeted Treatment of Acute Haemostatic Disorders [Internet]. Munich: Tem Innovations GmbH; 2016 [cited 2023 Nov 2]. Available from: https://www.ttuhsc.edu/medicine/odessa/internal/documents/ttim-manual/ROTEM_Analysis.pdf

77. Thomas OD, Gustafsson A, Schött U. Rotational thromboelastometry and multiple electrode platelet aggregometry in four patients with abnormal routine coagulation studies before removal of epidural catheters after major surgery: a case series and research study. J Med Case Reports [Internet]. 2013 Dec 30 [cited 2023 Nov 2];7:1–10. Available from: https://pubmed.ncbi.nlm.nih.gov/24377397/

78. Davis JPE, Northup PG, Caldwell SH, Intagliata NM. Viscoelastic Testing in Liver Disease. Ann Hepatol [Internet]. 2018 Mar 1 [cited 2023 Nov 2];17(2):205–13. Available from: https://pubmed.ncbi.nlm.nih.gov/29469043/

79. Tanaka KA, Bader SO, Görlinger K. Novel approaches in management of perioperative coagulopathy. Curr Opin Anaesthesiol [Internet]. 2014 [cited 2023 Nov 2];27(1):72–80. Available from: https://pubmed.ncbi.nlm.nih.gov/24263685/

80. University of Wisconsin Hospitals and Clinics. Coagulation, Rapid TEG Heparinase without Lysis. In: UW Health [Internet]. Wisconsin: University of Wisconsin; 2023 [cited 2023 Nov 2]. Available from: https://www.uwhealth.org/lab-test-directory/coagulation/name-169630-en.html

81. Benes J, Zatloukal J, Kletecka J. Viscoelastic Methods of Blood Clotting Assessment - A Multidisciplinary Review. Front Med [Internet]. 2015 [cited 2023 Nov 2];2:62. Available from: https://pubmed.ncbi.nlm.nih.gov/26442265/

82. A Simplified Treatment-Based Approach to TEG and ROTEM [Internet]. [cited 2023 Nov 2]. Available from: https://www.emra.org/emresident/article/teg-and-rotem

83. Patil V, Shetmahajan M. Massive transfusion and massive transfusion protocol. Indian J Anaesth [Internet]. 2014 [cited 2023 Nov 5];58(5):590–5. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4260305/

84. Halmin M, Chiesa F, Vasan SK, Wikman A, Norda R, Rostgaard K, et al. Epidemiology of Massive Transfusion: A Binational Study From Sweden and Denmark. Crit Care Med

[Internet]. 2016 [cited 2023 Nov 3];44(3):468–77. Available from: https://pubmed.ncbi.nlm.nih.gov/26901542/

85. Population (Spaniards/foreigners) by provinces, age (five year groups), sex and year. In: INE [Internet]. España: Instituto Nacional de Estadística; 2022 [cited 2023 Nov 5]. Available from: https://www.ine.es/jaxiPx/Datos.htm?path=/t20/e245/p08/l0/&file=03002.px#!tabs-tabla

86. Levi M, Jonge E de. Clinical relevance of the effects of plasma expanders on coagulation. Semin Thromb Hemost [Internet]. 2007 [cited 2023 Nov 3];33(8):810–5. Available from: https://pubmed.ncbi.nlm.nih.gov/18175286/

87. Floccard B, Rugeri L, Faure A, Saint Denis M, Boyle EM, Peguet O, et al. Early coagulopathy in trauma patients: an on-scene and hospital admission study. Injury [Internet]. 2012 [cited 2023 Nov 3];43(1):26–32. Available from: https://pubmed.ncbi.nlm.nih.gov/21112053/

88. Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. Br J Anaesth [Internet]. 2012 [cited 2023 Nov 3];109(6):851–63. Available from: https://pubmed.ncbi.nlm.nih.gov/23075633/

89. Pham HP, Shaz BH. Update on massive transfusion. Br J Anaesth [Internet]. 2013 [cited 2023 Nov 5];111:71–82. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0007091217309327

90. Fernández-Hinojosa E, Murillo-Cabezas F. Alternativas terapéuticas de la hemorragia masiva. 2011 [cited 2023 Nov 3];36(7):1–8. Available from: https://scielo.isciii.es/pdf/medinte/v36n7/revision1.pdf

91. Sihler KC, Napolitano LM. Complications of massive transfusion. Chest [Internet]. 2010 [cited 2023 Nov 3];137(1):209–20. Available from: https://pubmed.ncbi.nlm.nih.gov/20051407/

92. Parada Muñoz LM. Duelo por muerte súbita desde el enfoque apreciativo: una opción de vida desde la pérdida. Diversitas [Internet]. 2007 [cited 2023 Nov 5];3(1):55–66. Available from: http://pepsic.bvsalud.org/scielo.php?script=sci_abstract&pid=S1794-99982007000100005&lng=pt&nrm=iso&tlng=es

93. Gómez Esteban R. El médico frente a la muerte. Rev Asoc Esp Neuropsiquiatría [Internet]. 2012 [cited 2023 Nov 5];32(113):67–82. Available from: https://scielo.isciii.es/scielo.php?script=sci_abstract&pid=S0211-57352012000100006&lng=es&nrm=iso&tlng=es

94. Baksaas-Aasen K, Gall LS, Stensballe J, Juffermans NP, Curry N, Maegele M, et al. Viscoelastic haemostatic assay augmented protocols for major trauma haemorrhage (ITACTIC): a randomized, controlled trial. Intensive Care Med [Internet]. 2021 [cited 2023 Nov 5];47(1):49–59. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7550843/

95. Pigna F, Lippi G, Saronni S, Cervellin G. Trauma-induced coagulopathy. A narrative review of goal-directed hemostatic resuscitation. Emerg Care J [Internet]. 2018 [cited 2023 Nov 4];14:96–101. Available from: https://www.researchgate.net/publication/329588802_Trauma-induced_coagulopathy_A_narrative_review_of_goal-directed_hemostatic_resuscitation

96. Ley 14/2007, de 3 de julio, de Investigación biomédica. BOE. 2007. Num. 159.Pp. 28826-28848 [Internet]. Available from: https://www.boe.es/eli/es/l/2007/07/03/14

97. Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica. BOE. 2002. Num. 274. Pp. 1-14 [Internet]. Available from: https://www.boe.es/buscar/act.php?id=BOE-A-2002-22188

98. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing. Official Journal of the European Union. 2016. Num 119. Pp 1-88. [Internet]. Available from: https://eur-lex.europa.eu/eli/reg/2016/679/oj

99. BOE-A-2018-16673 Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales. BOE. 2018. Num. 294. Pp. 1-68 [Internet]. Available from: https://www.boe.es/buscar/act.php?id=BOE-A-2018-16673

100. Library HS. Subject Guides: Dentistry & Dental Hygiene: Finding the Evidence. In: University of Alberta Library [Internet]. Canada: Sperber Health Sciences Library; 2023 [cited 2023 Nov 5]. Available from: https://guides.library.ualberta.ca/c.php?g=301239&p=2621330

101. Nickson C. Thromboelastogram (TEG). In: LITFL.com [Internet]. Melbourne: Medmastery; 2019 [cited 2023 Nov 2]. Available from: https://litfl.com/thromboelastogram-teg/

15. ANNEXES

15.1. ANNEX 1- Definitions of obstretic haemorrhage.

Clinical guidelines	Definitions
Australian, 2008	Blood loss > 500ml after delivery and 750 ml after caesarean section
Austrian, 2008	Blood loss of 500-1,000 ml and signs of hypovolemic or hypovolaemic or bleeding > 1,000 ml
German 2008	Blood loss > 500 ml after delivery Severe: blood loss > 1,000 ml in 24 h
Royal College of Obstetricians and Gynaecologists from the United Kingdom	Primary: estimated loss > 500-1,000 ml without signs of shock Severe: estimated loss > 1,000 ml or signs of shock
World Health Organization	Loss > 500 ml in 24 h after delivery Severe: loss > 1,000 ml in 24 h

Table: *Adapted from (19).*

15.2. ANNEX 2- Graph of viscoelasting test results.

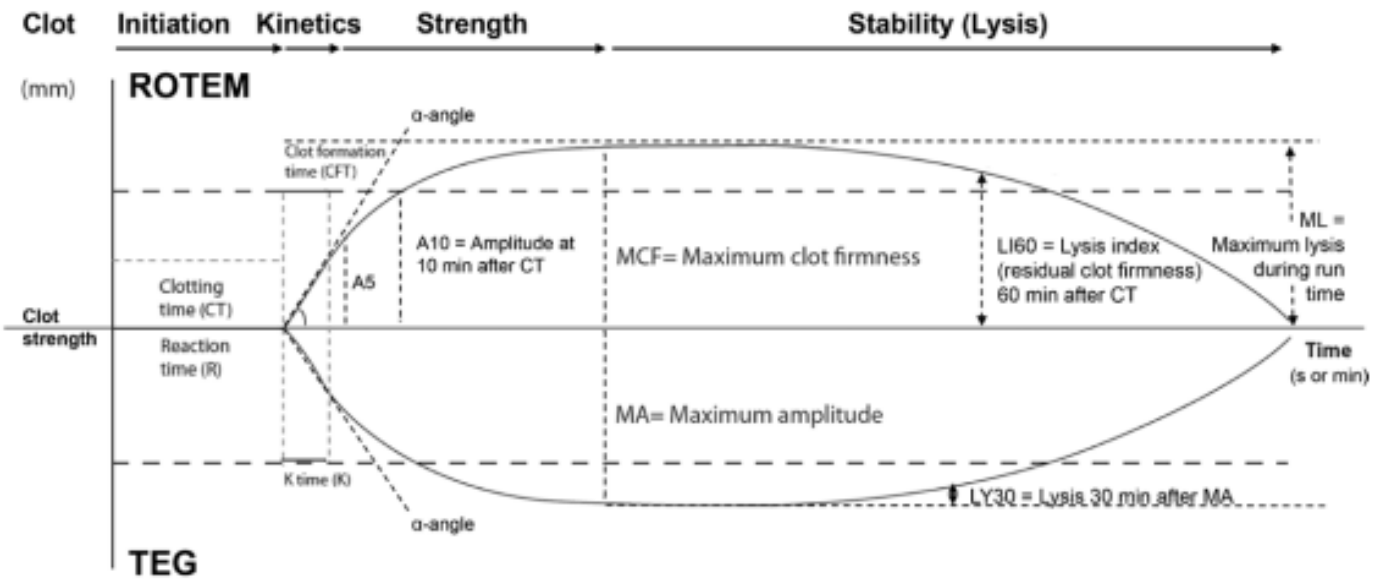

Image. *Taken from (73).*

15.3. ANNEX 3- Representation of normal and altered TEG outputs.

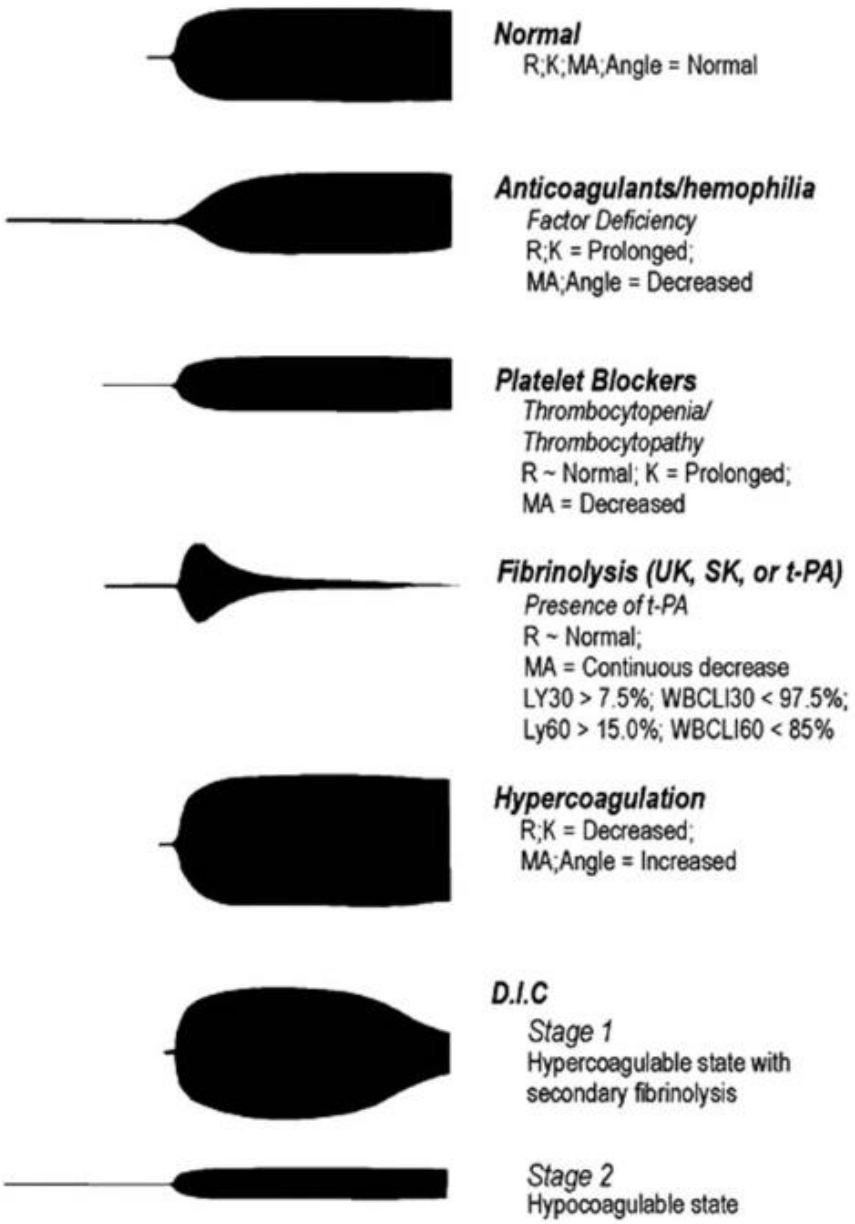

Image: *Taken from* (101).

15.4. ANNEX 4- Characteristics and Performance of TEG and ROTEM

Table. Characteristics and Performance of TEG and ROTEM

Key Characteristics	TEG 5000	ROTEM Delta
Mechanical robustness, susceptibility to artifacts[78–81]	Cup is moving, and clot firmness is detected by a torsion wire. Can be susceptible to agitation and movement artifacts and may limit its mobile use at the bedside. TEG devices are often located in the central laboratory.	Cup is fixed and pin is moving; stabilization of the pin axis by a ball-bearing and contactless optical detection of the pin movement results in low susceptibility to agitation and movement artifacts; this enables bedside testing and mobile use.
Pipetting and reproducibility of results[81,82]	Manual pipetting can result in higher intraoperator and interoperator variability of test results.	Software-assisted automatic pipette is user friendly with low intraoperator and interoperator variability of the results and enables a multiuser environment with bedside testing in the ER, OR, and ICU.
QC[81]	No continuous electronic QC; therefore, QC with control reagents is at least once a day (based on the local regulations in some places even every 8 h) required.	Continuous electronic QC of the pin axis movement; therefore, QC with control reagents is only once a week required; this results in reduced staff workload and QC costs.
Number. of channels for viscoelastic testing[78]	2 channels per device (if TEG platelet mapping is performed, channels are blocked for other viscoelastic testing)	4 channels per device (the ROTEM platelet module provides 2 additional channels for impedance aggregometry)
Viscoelastic assays[83,84]	5 different assays (native TEG, kaolin TEG, heparinase TEG, rapid-TEG, TEG functional fibrinogen); only heparinase-TEG can be used during CPB	7 different assays (NATEM, INTEM, HEPTEM, EXTEM, FIBTEM, APTEM, and ECATEM); tissue factor–activated assays (EXTEM, FIBTEM, and APTEM) contain a heparin inhibitor and can be used during CPB. HEPTEM is utilized to assess heparin effects especially post-CPB.
Preferred activation pathway[85,86]	Intrinsic pathway (kaolin); poor correlation to the effect of oral vitamin K antagonists and PCC.	Extrinsic pathway (tissue factor); reasonable correlation to the effect of oral vitamin K antagonists and PCC but does not replace the use of INR for monitoring of VKA.
Turnaround time[87–89]	Reference rang for r-time in kaolin-TEG: 4–8 min; no early variables of clot firmness available; turnaround time 20–30 min.	Reference range for EXTEM: 40–80 s; early variables of clot firmness (A5 and A10) are validated and predict MCF accurately; turnaround time: 10–15 min.
Definition of lysis parameters[90,91]	LY30/LY60 is defined as the reduction of clot firmness 30/60 minutes after MA in percentage of MA.	LI30/LI60 is defined as residual clot firmness 30/60 minutes after CT in percentage of MCF.
Diagnostic performance[29,92–94]	Limited discrimination between fibrinogen deficiency and thrombocytopenia; most often used to predict bleeding rather than to guide hemostatic therapy.	Good discrimination between fibrinogen deficiency and thrombocytopenia; enables guided therapy with allogeneic blood products and coagulation factor concentrates.
Platelet function analysis[26,95–97]	TEG PM; viscoelastic channels are blocked during TEG PM; test principle is based on the use of reptilase + FXIIIa + AA or ADP; long turnaround time, high costs, and high variability of the results.	ROTEM platelet module provides 2 additional channels for whole blood impedance aggregometry; platelet activation with AA (ARATEM), ADP (ADPTEM), or thrombin receptor-activating peptide (TRAPTEM); short turnaround time (10 min), good reproducibility of the results, and good correlation to clinical outcomes.
Fully automated system[98]	TEG 6S (CORA system); cartridge-based system using a new technology based on CORA; interchangeability of TEG 5000 and TEG 6S (CORA) results have to be investigated.	ROTEM sigma; cartridge-based system using the proven pin-and-cup technology but lyophilized beads reagents instead of liquid reagents; ROTEM sigma beads contain a heparin inhibitor as the liquid reagents do; the same algorithms can be used as with the ROTEM delta device.

Abbreviations: A5, amplitude 5 minutes after coagulation time; A10, amplitude 10 minutes after coagulation time; AA, arachidonic acid; ADP, adenosine diphosphate; CORA, coagulation resonance analysis; CPB, cardiopulmonary bypass; CT, coagulation time; ER, emergency room; ICU, intensive care unit; INR, international normalized ratio; LY30/LY60, lysis 30/60; LI30/LI60, lysis index 30/60; MCF, maximum clot firmness; OR, operating room; PCC, prothrombin complex concentrate; PM, platelet mapping; ROTEM, thromboelastometry; TEG, thrombelastography; QC, quality control; VKA, vitamin K antagonists.

Table: *Taken from* (73)

15.5. ANNEX 5- Information sheet for potential participant.

HOJA DE INFORMACIÓN PARA EL POSIBLE PARTICIPANTE

Nombre del estudio: Hospital use of viscoelastic testing for guided management of massive haemorrhage.

Centro de asistencia: Hospital Universitari Dr.Josep Trueta

Investigador/a principal: "Nombre del investigador"

1. Introducción

Mediante este documento buscamos facilitarle la información necesaria para valorar si desea o no participar en nuestro estudio de manera voluntaria y altruista. Este estudio respeta los principios enunciados en la declaración de Helsinki y guías de buena práctica clínica, además de cumplir con la legislación vigente referente al ámbito científico y haber sido aprobado por el comité ético del hospital responsable del estudio, el Hospital Universitario Dr. Josep Trueta.

Le rogamos que lea con detenimiento el siguiente documento y que se ponga en contacto con nosotros si le surge alguna duda.

2. Descripción del estudio

- **Objetivo del estudio:**

La hemorragia masiva es una situación en la que el paciente presenta una gran y rápida pérdida sanguínea que pone en riesgo su vida. Es una condición que puede darse debido a muchas causas y en la mayoría de los casos es impredecible. Por lo que es de vital importancia realizar el manejo más preciso e individualizado sobre cada paciente.

El objetivo de este estudio es valorar si hay una reducción de la mortalidad en diferentes puntos temporales en pacientes que sufren una hemorragia masiva si se realiza una transfusión guiada e individualizada a partir de los resultados obtenidos por los test viscoelásticos (tromboelastometría y tromboelastografía rotacional).

Estas pruebas se aplican sobre una muestra de sangre del paciente, y se emplean para estudiar cambios en las propiedades fisiológicas de la coagulación.

- **Criterios que debe cumplir el paciente para poder participar en el estudio:**

Este estudio se basará en los resultados obtenidos a partir de dos grupos de pacientes. El grupo de estudio será el grupo en el cuál realizaremos una transfusión guiada e individualizada basada en los resultados obtenidos de los test viscoelásticos.

Para poder ser incluido en este grupo de estudio el paciente deberá cumplir los siguientes criterios de inclusión y exclusión del estudio. Estos implican que el usted

tenga una edad igual o superior a 18 años y presente una hemorragia masiva, teniendo en cuenta que no tiene ninguna coagulopatía diagnosticada y no este tomando ningún tipo de tratamiento anticoagulante o antiagregante.

El grupo control, lo obtendremos a partir de bases de datos del Hospital Universitario Dr. Josep Trueta. Serán pacientes que han padecido una hemorragia masiva y se han transfundido con el protocolo de transfusión masiva guiada por pruebas de estudio de coagulación convencionales.

- **Su aportación al estudio:**

Le ofrecemos formar parte del grupo protocolo del estudio, formado por 145 participantes. Esto implicará que estudiaremos su estado de coagulación en el momento en el que padezca una hemorragia masiva para poder realizar una transfusión guiada a partir de los resultados obtenidos.

3. Riesgos y beneficios

- **Riesgos:**

El hecho de participar en este estudio no supone ningún tipo de riesgo añadido. Los test viscoelásticos son procedimientos seguros y no invasivos, debido a que la prueba se realiza sobre una muestra de sangre del paciente y no sobre el mismo. Por lo que con este método buscamos obtener una alternativa individualizada para tratar al paciente.

Informamos de que todos los participantes el equipo que participará en el estudio será formado en conjunto y sobre la misma base.

- **Beneficios:**

Con el empleo de los test viscoelásticos podemos obtener resultados más rápidos y detalladas de su estado de coagulación y así ofrecerle un tratamiento más dirigido e individualizado.

4. Participación voluntaria

Le informamos de que la participación en este estudio es voluntaria, por lo tanto, usted podrá aceptar o rechazar formar parte de él. En caso de que acepte participar, si durante el proceso del estudio cambia de opinión tendrá derecho a dejar el estudio y a que se borren los datos obtenidos sobre su persona. El no aceptar participar o en su defecto abandonar el estudio, no generara ningún perjuicio en su atención sanitaria.

5. Privacidad y confidencialidad

Nos aseguramos de cumplir los principios contemplados en la normativa de protección de datos, tanto a nivel nacional como Europea. Los datos serán anonimizados y manipulados solo por el personal que formará parte del equipo de estudio. Nos basaremos en el cumplimiento del "***Reglamento (UE) 2016/679 del Parlamento***

Europeo y del Consejo, de 27 de abril de 2016, relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación de estos datos" y de la ***"Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales i Garantía de los Derechos Digitales (LOPD- GDD)".***

6. Difusión de los resultados

Los resultados se analizarán al finalizar el estudio y se publicarán independientemente de si los resultados son o no los esperados, debido a que el objetivo es aportar un nuevo conocimiento al ámbito científico. Los datos del paciente se mantendrán en el anonimato en todo momento.

7. Compensación económica

La participación del estudio es voluntaria y no remunerada. Los investigadores que formarán parte del estudio tampoco se verán beneficiados económicamente.

8. Preguntas y apreciaciones

En caso de que deseen resolver alguna duda o realizar una propuesta, estaremos a su entera disposición. Para ponerse en contacto con nosotros puede dirigirse al siguiente correo electrónico: _____.

Le agradecemos de antemano el tiempo implicado en leer este documento.

En_____, a_____ de _____ de _____.

Firma del investigador principal Firma de la persona solicitante o representante

_____ _____

15.6. ANNEX 6- Informed consent document.

CONSENTIMIENTO INFORMADO

Nombre del estudio: Hospital use of viscoelastic testing for guided management of massive haemorrhage.

Centro de asistencia: Hospital Universitari Dr. Josep Trueta

Investigador/a principal: "Nombre del investigador"

Yo, D/Dª _____ con el documento de identificación personal (DNI/NIE) _____ declaro por mí mismo o en su defecto como tutor o representante legal de _____ que:

- He leído y comprendo la hoja informativa sobre el estudio en el que se me ofrece participar.
- He tenido tiempo para reflexionar y realizar las preguntas necesarias respecto al estudio.
- He entendido que mi participación es voluntaria y no remunerada.
- He entendido que se respetará la confidencialidad de mis datos.
- He entendido que puedo revocar el consentimiento informado cuando yo desee sin necesidad de justificación y sin ninguna repercusión mediante el "formulario de revocación del consentimiento informado" ejerciendo mi derecho descrito en la **"Ley 14/2007, de 3 de julio, de Investigación biomédica".**
- He entendido que recibiré una copia firmada de la hoja de información y otra copia firmada de la hoja del consentimiento informado.

Con el presente escrito acepto ser participante del estudio referido.

En _____ , a _____ de _____ de _____.

Firma del investigador principal

Firma del participante o representante

_____

_____

15.7. ANNEX 7- Document for revocation of informed consent.

FORMULARIO PARA LA REVOCACIÓN DEL CONSENTIMIENTO INFORMADO

Nombre del estudio: Hospital use of viscoelastic testing for guided management of massive haemorrhage.

Centro de asistencia: Hospital Universitari Dr. Josep Trueta

Investigador/a principal: "Nombre del investigador"

Yo, D/Dª _____ con el documento de identificación personal (DNI/NIE) _____ declaro por mí mismo, o en su defecto como tutor o representante legal de _____, que mediante el presente escrito revoco de manera oficial el consentimiento para formar parte de este estudio, ejerciendo mi derecho descrito en la **"Ley 14/2007, de 3 de julio, de Investigación biomédica"**, solicitando que se eliminen todos los datos recogidos referentes a mi persona.

En _____ , a _____ de _____ de _____.

Firma del investigador principal

_____

Firma del participante o representante

_____

15.8. ANNEX 8- Documents related to blood or blood products transfusion.

Trueta Hospital de Girona

Institut Català de la Salut

Primer cognom	
Segon cognom	
Nom	
Data de naixement	**Sexe**
NHC	**DNI**
CIP	
Episodi origen	

Consentiment informat

Nom del representant legal en cas d'incapacitat del pacient per consentir, ja sigui per minoria d'edat, incapacitat legal o incompetència, amb la indicació del caràcter en el qual intervé (pare, mare, tutor legal, etc).
Sra./Sr.
amb D.N.I. , en qualitat de .

Nom del procediment

Sol·licitud / Reserva de Transfusió

Descripció del Procediment

El seu metge considera que, per al tractament de la seva malaltia és necessari fer-li una transfusió de sang i/o hemoderivats.
Aquesta sang prové de donants voluntaris que no han rebut cap compensació econòmica a canvi de la seva donació.

Riscos específics

Cada donació de sang s'analitza exhaustivament amb tècniques molt precises per tal de detectar l'hepatitis B i C, sida (VIH) i sífilis. La probabilitat de transfondre sang contaminada per aquests o d'altres agents infecciosos és molt baixa, no obstant això, els períodes d'incubació poden no ser detectables i contagiar-ne la infecció.
També existeix la possibilitat de sensibilització a alguns dels seus components, fet que pot produir reaccions transfusionals que acostumen a ser lleus (febre, picor, etc.) i que, excepcionalment poden ser greus (edema de pulmó, hemòlisi o destrucció dels glòbuls vermells, etc.)

Possibles Alternatives

Actualment no existeixen preparats alternatius que substitueixin els components de la sang, amb l'excepció de l'albúmina, les gammaglobulines i alguns factors de la coagulació (que en cap cas poden evitar la transfusió de glòbuls vermells).

Declaro

Que he estat informat/da de manera comprensible del procediment de la transfusió de sang i/o dels seus derivats i també dels possibles riscos i complicacions, no havent-hi d'altres alternatives terapèutiques que la puguin substituir.
També sé que puc retractar-me i revocar el meu consentiment abans de la transfusió.
Aquest consentiment es formula d'acord amb el que estableix la Llei 16/2010, de 3 de juny, de modificació de la Llei 21/2000, de 29 de desembre, sobre els drets d'informació concernent la salut i l'autonomia del pacient i la documentació clínica, publicada al DOGC núm. 5647 del 10 de juny de 2010.

Servei sol·licitant	**Professional que informa**	**Número d'identificació**

Consentiment informat

Signatura i DNI del/la pacient o responsable **Data** **Signatura del professional**

☐ Accepta

☐ No accepta

Revocació consentiment informat.

Jo, En/Na amb DNI/NIF revoco el consentiment prestat en data i declaro per tant que, després de la informació rebuda, no autoritzo a sotmetre'm al procediment de Sol·licitud / Reserva de Transfusió .