



European Society of
Regional Anaesthesia
& Pain Therapy
ESRA ITALIA

ESRA *Cè*

XXIX

CONGRESSO NAZIONALE

ESRA Italian Chapter
CESENA, Cesena fiere

Presidente del congresso
Vanni Agnoletti
Domenico Pietro Santonastaso
Andrea Tognù

7-9
Novembre
2024



 **MZ**
EVENTS



ALGORITMO NELLA GESTIONE DELL'EMORRAGIA POST PARTUM
**Terapia di supporto, ripristino della volemia
e impiego degli emoderivati.**

Maria Grazia FRIGO

UOSID Anestesia e Rianimazione Ostetrica ,
Ospedale Isola Tiberina, Gemelli Isola, Roma



Quali obiettivi?



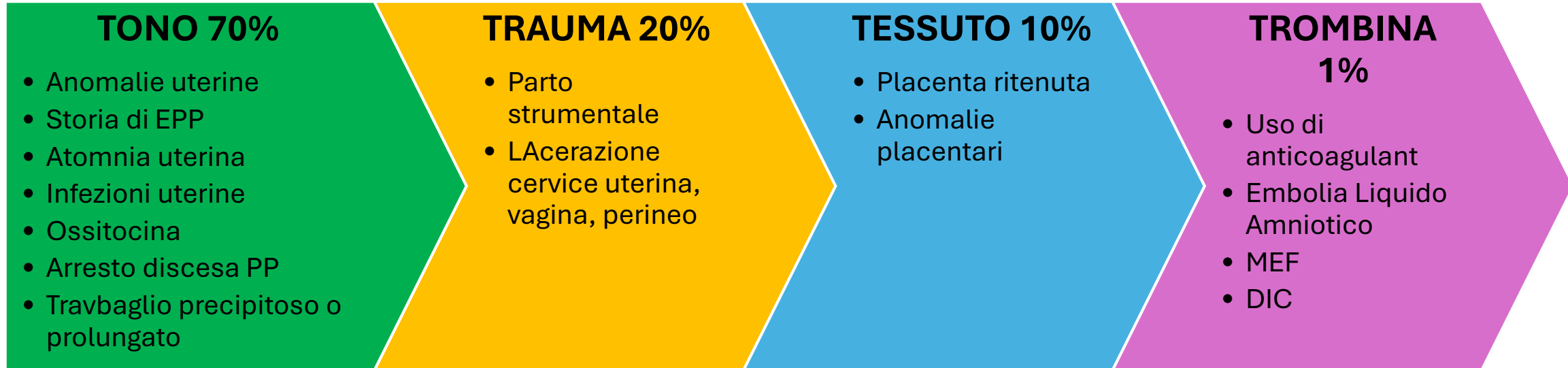
Quale algoritmo?

- 1 Riconoscere la causa eziologica
- 2 Mantenere la contrattilità uterina con mezzi fisici e/o farmacologici
- 3 Ripristinare e mantenere la volemia (e quindi la capacità di trasporto dell'O₂)
- 4 Prevenire/Trattare la coagulopatia emorragica eventualmente instauratesi e trasferire in SO

**RIVALUTAZIONE
CONTINUA**



QUANTO TEMPO ABBIAMO?
Si stima, che se non adeguatamente trattata, la morte si verifichi in media in **2h nell'EPP primaria**



Cause sconosciute:

- Rottura/Inversione Uterina
- Emorragia non evidente (emoperitoneo)
- Cause non genitali: rotture epatiche e/o spleniche

RACCOMANDAZIONI

In presenza di EPP si raccomanda come trattamento farmacologico di prima linea:

– ossitocina 5 UI in bolo endovenoso lento (non meno di 1-2 minuti; non meno di 5 minuti in donne con rischio cardiovascolare)

oppure

– ergometrina (2 fiale 0,2 mg per via intramuscolare)

oppure

– combinazione di ossitocina 5 UI per via endovenosa (non meno di 1-2 minuti; non meno di 5 minuti in donne con rischio cardiovascolare) ed ergometrina (2 fiale 0,2 mg intramuscolare) da associare a una terapia di mantenimento con ossitocina per infusione (10 UI in soluzione isotonica per 2 ore).

raccomandazione forte, prove di qualità molto bassa

In presenza di EPP, si raccomanda di associare al trattamento farmacologico il massaggio del fondo dell'utero fino alla sua contrazione o alla riduzione del sanguinamento avvertendo la donna che la manovra può essere dolorosa.

raccomandazione forte, prove di qualità bassa

Si raccomanda di valutare come trattamento farmacologico di seconda linea, in presenza di EPP non responsiva al trattamento di prima linea:

– ergometrina (2 fiale 0,2 mg intramuscolare)

e/o

– sulprostone (1 fiala 0,50 mg per via endovenosa in 250 cc; da 0,1 a 0,4 mg/h fino a un max di 1,5 mg nelle 24 ore).

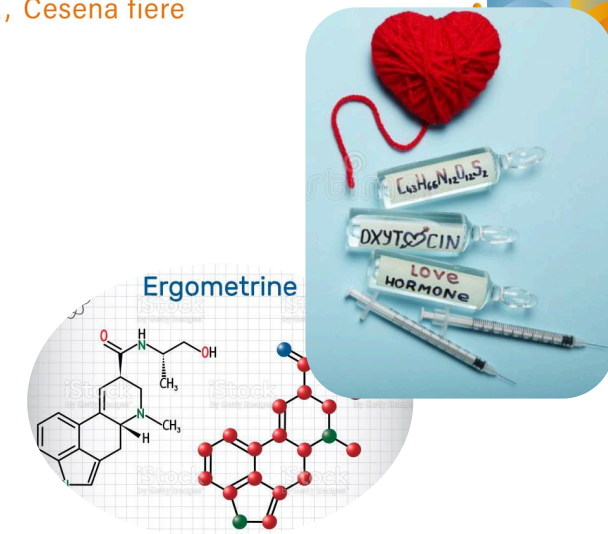
raccomandazione debole, prove di qualità molto bassa

In assenza di prove che permettano di raccomandare un intervento farmacologico di seconda linea come più efficace rispetto agli altri si raccomanda di scegliere il trattamento in base alle condizioni cliniche della paziente, all'expertise del professionista, alla disponibilità dei farmaci e alle loro controindicazioni.

raccomandazione di buona pratica clinica basata sull'esperienza del panel

7-9 Novembre 2024

CESENA, Cesena fiere



Terapia Uterotonica



Emorragia post partum:
come prevenirla,
come curarla

Remember!

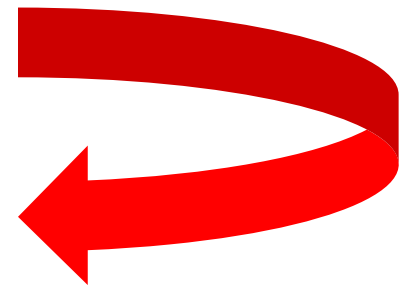
PLETHORA GRAVIDARUM: ipervolemia protettiva

ESRA Italia e di Apple
CONGRESSO
XXIX NAZIONALE
CESENA, Cesena fiere

- La gittata cardiaca aumenta dal 30 al 50% a partire dalla 6^o settimana
- Il volume totale di sangue aumenta proporzionalmente alla gittata cardiaca, ma l'aumento del volume plasmatico è maggiore rispetto alla massa dei globuli rossi

- Volume plasmatico aumenta del 48% pari a 1250 ml
- Massa eritrocitaria aumenta del 18% pari a 250 ml
- Ematocrito dal 40% si riduce al 33%
- L' emoglobina si riduce per diluizione (da 13.3 a circa 12.1 g/dl)

Riduzione della viscosità ematica che migliora la perfusione placentare favorendo gli scambi materno fetali di gas e sostanze nutritive





La donna gravida è diversamente fisiologica

ESRA Italian Chapter
CONGRESSO
XXIX NAZIONALE

CESENA, Cesena fiere

"Seeing is not believing - it is only seeing."

George MacDonald,
The Princess and the Goblin



QUANTIFICARE E' MEGLIO CHE STIMARE

Non tutte le emorragie sono visibili

La stima visiva sottostima di circa il 30-50%

La quantificazione delle perdite di sangue (QBL) è un modo significativo più preciso di EBL

QBL riduce il rischio di sottostima e di ritardo nel trattamento

La simulazione può migliorare l'abilità visiva di EBL ma tale abilità si deteriora entro 9 mesi

COME MISURARE IL QBL

- Misurare la perdita di liquidi e sangue utilizzando sacca graduata e/o pesare le garze imbevute di sangue e coaguli
- Misurare la perdita prima e dopo il secondamento

1 grammo = 1 millilitro di sangue

A Systematic Review of the Relationship between Blood Loss and Clinical Signs

Rodolfo Carvalho Pacagnella^{1*}, João Paulo Souza², Jill Durocher³, Pablo Perel⁴, Jennifer Blum³, Beverly Winikoff³, Ahmet Metin Gülmezoglu²

- **Introduction:** This systematic review examines the relationship between blood loss and clinical signs and explores its use to trigger clinical interventions in the management of obstetric haemorrhage.
- **Conclusion:** This systematic review found a substantial variability in the relationship between blood loss and clinical signs, making it very difficult to establish specific cut-off points for clinical signs that could be **used as triggers of clinical interventions. However, the shock index was found to be an accurate indicator of compensatory changes** in the cardiovascular system due to blood loss.

Indice di Shock

FC/PAS

0,5 – 0,7

0,7 – 0,9

Indice di Shock

Ostetrico

se > 1 indicatore di gravità
clinica e di necessità
di trasfondere





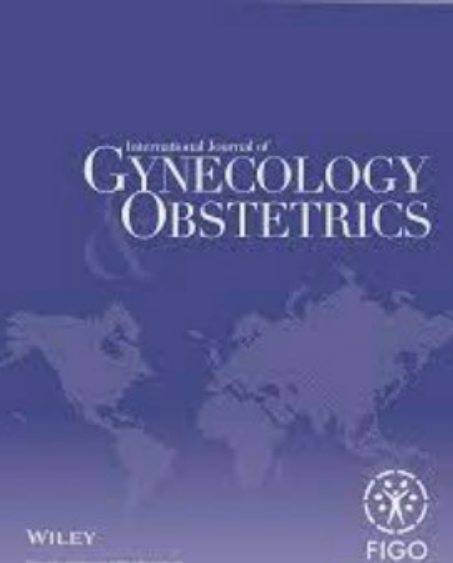
European Society of
Regional Anaesthesia
& Pain Therapy

ESRA ITALIA

SHOCK INDEX

& clinica

	CLASSE 1 Compensato	CLASSE 2 Lieve	CLASSE 3 Moderato	CLASSE 4 Grave
PERDITA EMATICA %	10-15%	15-25%	25-35%	35-45%
PRESSIONE SISTOLICA	normale	Lieve riduzione 80-100mmHg	Importante riduzione 70-80mmHg	Notevole riduzione 50-70mmHg
FREQUENZA CARDIACA	< 100 bpm	>100 bpm	>120 bpm	>140 bpm
FREQUENZA RESPIRATORI A	14-20 atti/min	20-30 atti/min	30-40 atti/min	>40 atti/min
SEGNI/ SINTOMI	Palpitazioni, tremori, tachicardia	Debolezza, sudorazione, tachicardia	Agitazione, pallore, oliguria	Collasso, fame d'aria, anuria
SHOCK INDEX	>0.6	> 0.6 <1.0	>1 <1.4	>1.4
Management	Osservazione / integrazione	Integrazione e uterotonici	Management attivo urgente	Management attivo critico



5 | SHOCK INDEX EVIDENCE IN POSTPARTUM HEMORRHAGE EVALUATION AND MANAGEMENT

Shock refers to a reduction in tissue perfusion, which is insufficient to meet the metabolic requirements of tissues and organs. Insufficient blood flow may be clinically identified as the development of one or more of the following: lactic acidosis, altered mental status, oliguria, and tachycardia. Vital signs monitoring is key to hemodynamic assessment and prompt intervention.¹ In healthy pregnant and postpartum women, cardiologic physiologic compensatory mechanisms prevent changes in vital signs until a large volume of blood has been lost (usually >1000 ml). Hence, changes in clinical and vital signs that result from hemorrhage appear late in the process and may not lead to early identification of PPH. This in turn makes it difficult to establish cutoff points to trigger clinical interventions. Moreover, because traditional vital signs change late and are less reliable as triggers for clinical actions, other indicators could help to characterize maternal hypovolemia caused by bleeding.² Although the use of conventional individual vital signs (pulse and systolic blood pressure) may lack accuracy in the assessment of hypotension, both may transform routine clinical parameters into a more accurate indicator of hypovolemia. The ratio of heart rate to systolic blood pressure, the shock index (SI), aids early identification of hypovolemia, the result of obstetric cause. It has been proposed as a reliable indicator of adverse maternal outcomes,⁶ and its values have been set to indicate clinical management.⁷ However, the association between shock parameters and advanced treatment modalities in severe PPH has yet to be reported.

5.1 | Assessment of circulating blood volume in postpartum hemorrhage

The essential cornerstone of management of PPH involves prompt diagnosis and rapid replacement of lost blood volume, as well as the oxygen-carrying capacity of blood, accompanied by immediate medical and surgical measures to address the underlying cause(s), and hence prevent more loss. To assess the patient's condition, SI has been introduced as a simple and clinically effective vital sign.

The SI has been shown to have an inverse linear relationship with left ventricular stroke work in acute circulatory failure. Therefore, a concurrent reduction of left ventricular stroke work (induced by hemorrhage, trauma, or sepsis) was associated with an elevation of the SI and a deterioration in left ventricular mechanical performance. Poor left ventricular function or persistent abnormal elevation of the SI after aggressive therapy and hemodynamic stabilization was associated with increased mortality in critically ill, traumatized patients.⁸ In obstetric and nonobstetric circumstances, the absence of a significant drop in blood pressure in patients with

PPH may mask the actual hypovolemic status due to physiological compensatory mechanisms. The SI was the only promising marker that indicated the severity of blood loss.^{2,5} The SI, together with other parameters, may aid clinicians in assessing the severity of blood loss and the degree of hypovolemia. The rule of 30, are used to determine the severity of blood loss, and thus the SI increases with the degree of blood loss, and thus the SI increases with the degree of blood loss. It has been shown that an SI ≥ 0.9 is associated with increased mortality and an SI > 1 increases the likelihood of blood transfusion.^{11,12} To date, standard obstetric SI has been defined as 0.7–0.9 compared with 0.5–0.7 for the nonpregnant population, taking into account the hemodynamic changes of pregnancy may delay the recognition of hypovolemia.⁵ If intravascular volume depletion is suspected, a rapid clinical assessment is required because the patient's clinical condition can deteriorate, leading to the development of hemorrhagic shock rapidly. Proper medical record-taking skills may highlight symptoms associated with shock such as pain and overt blood loss, as well as general malaise, anxiety, and dyspnea. Notably, in settings where few PPH treatment options exist, and in cases of home deliveries, diagnosis and treatment or referral must occur even earlier than in hospital settings to improve outcomes. For that reason, SI may be a valuable threshold in LMICs, where mortality is highest and is often related to delays in complication recognition, transportation, and level of care at the facility.² A threshold of SI ≥ 0.9 should be tested to alert community healthcare providers of the need for urgent transfer.¹³

BOX 2 FIGO recommends use of the shock index in the diagnosis and management of PPH.

FIGO considers that the shock index can be a marker of the severity of PPH and can alert teams to hemodynamic instability when its value is greater than 0.9.

REFERENCES

- Schorn MN. Measurement of blood loss: review of the literature. *J Midwifery Womens Health*. 2010;55:20–27.
- Borovac-Pinheiro A, Pacagnella RC, Cecatti JG, et al Postpartum hemorrhage: new insights for definition and diagnosis. *Am J Obstet Gynecol*. 2018;219:162–168.
- Arulkumaran S, Karoshi M, Keith LG, Lalonde AB, B-Lynch C. *A comprehensive textbook of postpartum hemorrhage: an essential clinical reference for effective management*. Sapiens Publishing; 2012.
- Rady MY, Nightingale P, Little RA, Edwards JD. Shock index: a re-evaluation in acute circulatory failure. *Resuscitation*. 1992;23:227–234.
- Pacagnella RC, Souza JP, Durocher J, et al A systematic review of the relationship between blood loss and clinical signs. *PLoS One*. 2013;8:e57594.

FIGO recommendations on the management of postpartum hemorrhage 2022



Se.....

PAS scende di 30mmHg

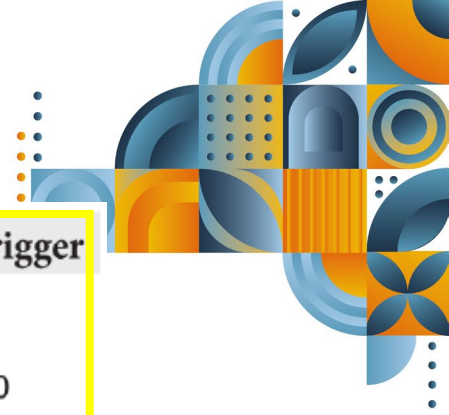
Aumento Fc > 30bpm

Aumento FR > 30 atti/minuto

Output urinario <30ml/h

L'Hb e Hct diminuiscono del 30%

....è probabile che la donna abbia perso il 30% del volume di sangue circolante, configurandosi un quadro di **SHOCK da MODERATO a GRAVE**



	Ora													
Atti respiratori/min.	≥ 25													
	20-24													
	11-19													
	≤ 10													
SpO2	96-100%													
	≤ 95%													
Temperatura °C	≥ 38													
	37,5-37,9													
	36-37,4													
	35,1-35,9													
Frequenza cardiaca bpm	≤ 35													
	≥ 120													
	100-119													
	60-99													
Pressione sistolica mmHg	50-59													
	< 50													
	≥ 160													
	140-159													
Pressione diastolica mmHg	100-139													
	91-99													
	≤ 90													
	≥ 100													
Diuresi	90-99													
	50-89													
	41-49													
	≤ 40													
Livello di coscienza	> 30 cc/h													
	≤ 30 cc/h													
	Vigile													
	Voce													
Dolore	Dolore													
	Non responsiva													
	0													
Dolore	1													
	2													
	0													
Totale parametri rossi														
Totale parametri gialli														

	Red trigger	Yellow trigger
Temperature; °C	< 35 or > 38	35-36
Systolic BP; mmHg	< 90 or > 160	150-160 or 90-100
Diastolic BP; mmHg	> 100	90-100
Heart rate; beats.min ⁻¹	< 40 or > 120	100-120 or 40-50
Respiratory rate; breaths.min ⁻¹	< 10 or > 30	21-30
Oxygen saturation; %	< 95	-
Pain score	-	2-3
Neurological response	Unresponsive, pain	Voice

1	■	Ripetere controllo parametri tra i 30 e i 60 minuti
2	■	Chiamare medico per valutazione. Ripetere parametri a 30 minuti
1	■	
>2	■	Chiamare medico per valutazione immediata. Ripetere parametri dopo 15 minuti
>1	■	

Singh S, McGlennan A, et al. A validation study of the CEMACH recommended modified early obstetric warning system (MEOWS). Anaesthesia 2012

Table 1. Changes in coagulation and fibrinolysis parameters at term gestation (6–10).

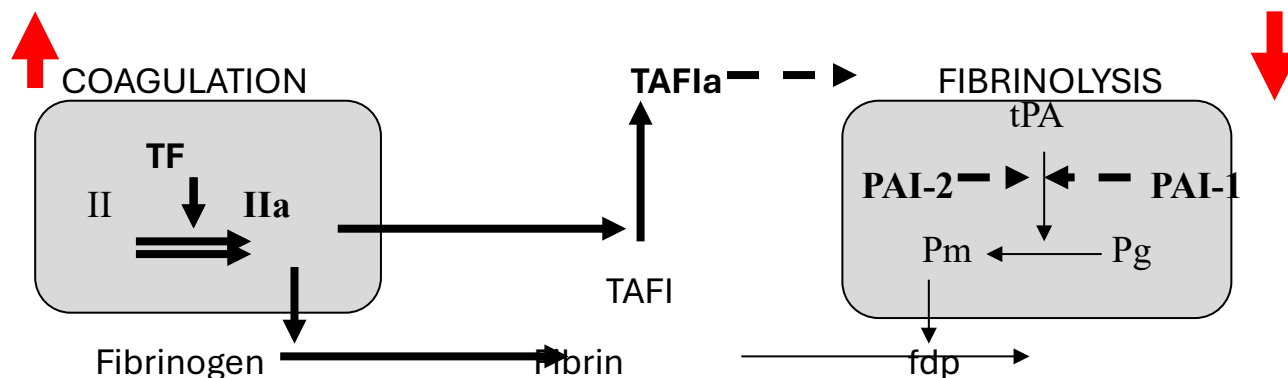
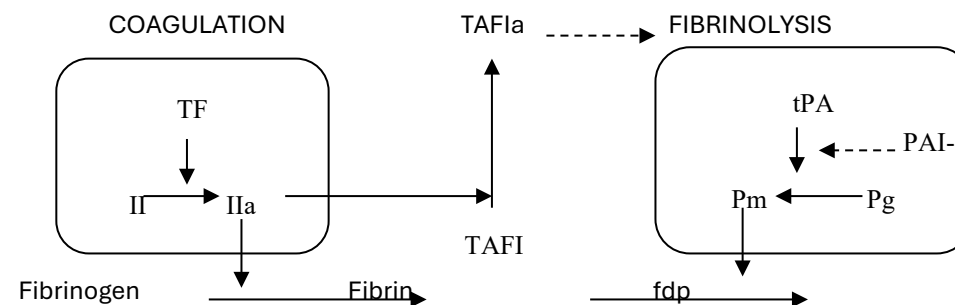
Blood coagulation factors	
Factor I (fibrinogen)	Increased
Factor II (prothrombin)	No change or increased
Factor V (proaccelerin)	No change or increased
Factor VII (proconvertin)	No change or increased
Factor VIII (antihemophilic factor)	Increased
Factor IX (Christmas factor)	No change or increased
Factor X (Stuart-Power factor)	Increased
Factor XI (thromboplastin antecedent)	No change or decreased
Factor XII (Hageman factor)	No change or increased
Factor XIII (fibrin stabilizing factor)	Increased
Von Willebrand factor	Increased
Tissue factor	No change or increased
Other coagulation parameters	
Platelet count	No change or decreased
Prothrombin time	Shortened
Activated partial thromboplastin time	Shortened
Fibrin degradation products	Increased
Blood coagulation inhibitors	
Antithrombin III	No change or decreased
Protein C	No change or increased or decreased
Protein S	Decreased
Thrombomodulin	Increased
Tissue factor pathway inhibitor	Increased
Fibrinolysis	
Plasminogen	Increased
Tissue-type plasminogen activator	No change or increased
Plasminogen activator inhibitor-1 (produced in endothelial cells)	Increased
Plasminogen activator inhibitor-2 (produced in placenta)	Increased

CONGRESSO
NAZIONALE

7-9 Novembre 2024

CESENA, Cesena fiere

NORMAL ENDOTHELIUM



PLACENTAL TROPHOBLAST

Profilo coagulativo.....

Cosa cambia in gravidanza??

NON ATTENDERE I RISULTATI DEL LABORATORIO PER INIZIARE IL TRATTAMENTO

*.....rivalutare i parametri
ogni 30-60 minuti*



EGA: pH, Hb, Lattati
ESAMI DI LABORATO
ROTEM/TEG
CENTRO TRASFUSI

TRIADDE FATALE:
ACIDOSI
IPOTERMIA
COAGULOPATIA

zione, Gruppo
nazio leucodeplete

START



OPEN

REVIEW ARTICLE

Haemostatic support in postpartum haemorrhage

A review of the literature and expert opinion

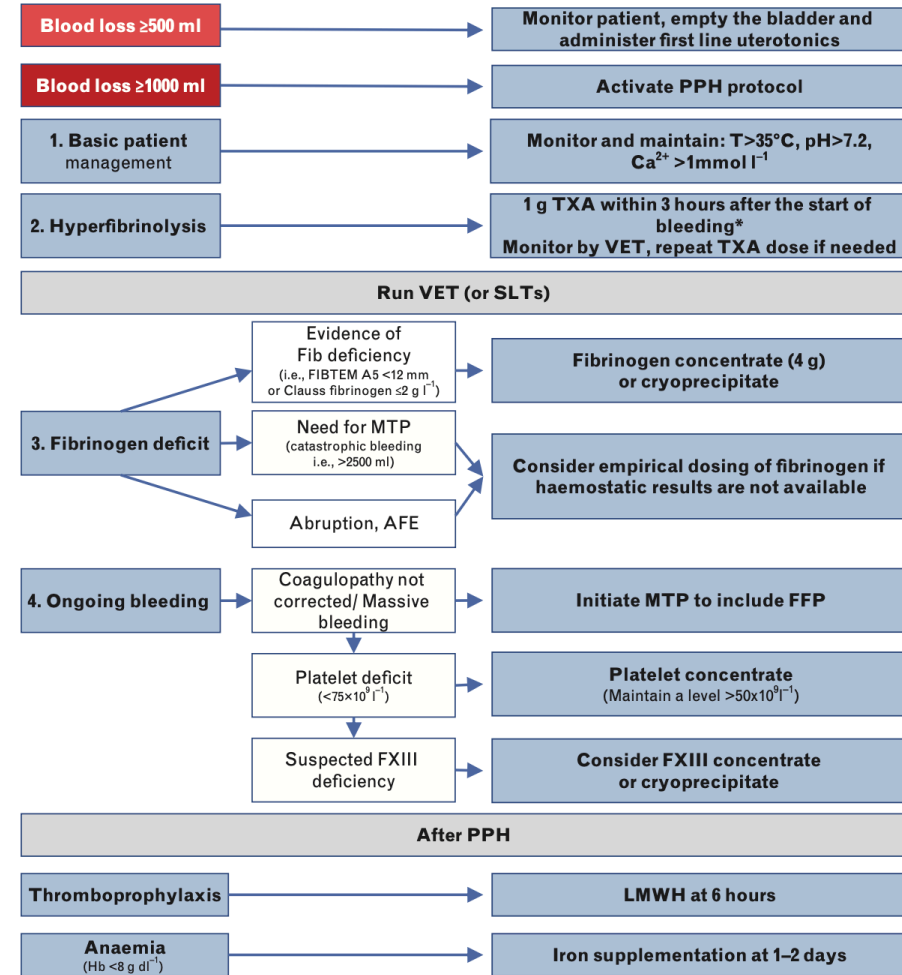
Stefan Hofer, Jan Blaha, Peter W. Collins, Anne-Sophie Ducloy-Bouthors, Emilia Guasch, Francesco Labate, Filipa Lança, Lill Trine Nyfløt, Kostja Steiner and Marc Van de Velde

Treatment of coagulopathy should be considered early and simultaneously with the other strategies...

Iniziazione di haemostatic treatment is guided by the volume of blood loss.

Blood loss equal or greater than 500 ml should trigger infusion of TXA and close monitoring of the patient, including initial SLTs (Clauss fibrinogen), VET (ROTEM/TEG).

Fig. 4 Suggested haemostatic treatment algorithm in PPH.



*Caution is needed in patients receiving more than 2 g day⁻¹ due to potential renal and epileptogenic effects of TXA. AFE, amniotic fluid embolus; F, factor; FFP, fresh frozen plasma; FIBTEM, fibrinogen thromboelastometry; Fib, fibrinogen; Hb, haemoglobin; LMWH, low-molecular-weight heparin; MTP, massive transfusion protocol; PPH, postpartum haemorrhage; SLTs, standard laboratory tests; TXA, tranexamic acid; VET, viscoelastic testing.

Randomized Trial of Early Detection and Treatment of Postpartum Hemorrhage

I. Gallos, A. Devall, J. Martin, L. Middleton, L. Beeson, H. Galadanci, F. Alwy Al-beity, Z. Qureshi, G.J. H N. Moran, S. Fawcus, L. Sheikh, G. Gwako, A. Osoti, A. Aswat, K.-M. Mammoliti, K.N. Sindhu, M. Poc I. Horne, R. Timms, I. Yunas, J. Okore, M. Singata-Madliki, E. Arends, A.A. Wakili, A. Mwampashi, S. Na S. Muhammad, P. Latthe, C. Evans, S. Akter, G. Forbes, D. Lissauer, S. Meher, A. Weeks, A. Shenn: A. Ammerdorffer, E. Williams, T. Roberts, M. Widmer, O.T. Oladapo, F. Lorencatto, M.A. Bohren, S. h F. Althabe, M. Gülmezoglu, J.M. Smith, K. Hemming, and A. Coomarasamy

E-MOTIVE

Trial randomizzato

210.132 donne, parto vaginale

Diagnosi precoce

+

Interventi combinati



EPP > 1000ml

Laparotomia

Morte materna

E M O T I V E

Early Detection and Trigger Criteria

Calibrated drape for the the collection of blood, with trigger lines at 300 ml and 500 ml for the first hr after birth

Observations (blood loss, blood flow, uterine tone) every 15 min documented on the blood-loss monitoring chart

Blood pressure and pulse monitored once in the first hr post partum and documented on the blood-loss monitoring chart

Trigger Criteria

Clinical judgment
Blood loss \geq 500 ml
Blood loss \geq 300 ml plus one abnormal observation

Massage of Uterus

Massage until uterus has contracted or for 1 min

Oxytocic Drugs

10 IU IV oxytocin injected or diluted in 200–500 ml crystalloid administered over 10-min period, plus a maintenance dose of 20 IU IV oxytocin diluted in 1000 ml saline administered over 4-hr period (with misoprostol 800 μ g if used)

Tranexamic Acid

1 g IV tranexamic acid injected or diluted in 200 ml crystalloid administered over 10-min period

IV Fluids

IV fluids in addition to the infusion should be given if clinically indicated for resuscitation and will require a second intravenous access

Examination and Escalation

Ensure bladder is empty, evacuate clots, check for tears with an internal examination and placenta for completeness
Escalate if bleeding does not stop after first response or clinician is unable to identify or manage cause of bleeding

Implementation Strategies

Audit newsletters: Sharing with all staff monthly rates of detection and bundle use, along with rates of PPH, severe PPH, blood transfusion, laparotomy, and death from PPH and giving feedback at monthly departmental meetings

Champions: Midwife and doctor to oversee change, troubleshoot, give feedback on audit newsletters, connect with other champions by means of chats, meetings, and websites for sharing knowledge and lessons learned

Trolley or carry case: Restocking of all medicines and devices used for treatment of PPH after every use and completion of a stocking checklist at the start of every shift

Training: Onsite, simulation-based, and peer-assisted training, lasting from 90 min to an entire workday, facilitated by the use of provider guides, flipcharts, and job aids displayed in labor wards

*Reintegrare il volume circolante con infusione di cristalloidi...
....in attesa di emazie,
per sostenere la volemia e mantenere la perfusione tissutale*

- **Boli da 500ml**
- **Soluzioni bilanciate per ridurre il rischio di ac iperCloremica**
- **Dopo ogni bolo rivalutare lo stato clinico del pz**

TARGET PRESSORIO

MAP 50-60 mmHg

PAS 80-90 mmHg

**Fino al controllo dell'emorragia
(Raccomandazione 1C)**

N.B. L'utilizzo di elevati volumi di cristalloidi può determinare una coagulopatia diluizionale

11.2.2 | Intravenous fluids

Among the initial strategies for reanimation, the administration of crystalloids in small boluses of 500 ml is recommended.¹⁰ Scientific

balanced crystalloid solution at first

the worsening of kidney function with chlorine-rich fluids (saline solution).⁷ This is particularly important for LMICs, where saline-based solutions are in abundance. After the administration of each bolus, physicians must assess the clinical status of patients, looking for an improvement in signs and symptoms of shock resulting from blood loss.¹⁰

11.2.1 | Hypotensive resuscitation

The concept of hypotensive resuscitation is because administering small crystalloid volumes reduces the risk of dilutional coagulopathy

RESEARCH

Open Access



The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition

Rolf Rossaint¹, Bertil Bouillon², Vladimír Cerný^{3,4,5,6}, Timothy J. Coats⁷, Jacques Duranteau⁸, Enrique Fernández-Mondéjar⁹, Daniela Filipescu¹⁰, Beverley J. Hunt¹¹, Radko Komadina¹², Giuseppe Nardi¹³, Edmund A. M. Neugebauer¹⁴, Yves Ozier¹⁵, Louis Riddez¹⁶, Arthur Schultz¹⁷, Jean-Louis Vincent¹⁸ and Donat R. Spahn^{19*}



...**early and aggressive fluid administration to restore blood volume**. This approach may, however, **increase the hydrostatic pressure on the wound, cause dislodgement of blood clots, a dilution of coagulation factors and undesirable cooling of the patient.**



The concept of low volume fluid resuscitation, so-called “**PERMISSIVE HYPOTENSION**”, avoids the adverse effects of early aggressive resuscitation while maintaining a level of tissue perfusion that, although lower than normal, is adequate for short periods...

La decisione di iniziare la trasfusione è CLINICA

1

Trasfondere **Emazie** leucodeplete omogruppo o Zero Rh neg

La trasfusione di 1U di GR aumenta l'Hb di 1gr/dL e l'Hct del 2-3%

2

Trigger trasfusionale delle **piastrine** è di 75×10^9 .

Se una donna RhD negativa riceve Piastrine RhD positive è necessaria una profilassi anti-D

3

Plasma Fresco Concentrato (PFC), quando persiste l'emorragia anche dopo la somministrazione di 4 U di GR. Dose di 15-20ml/kg.

4

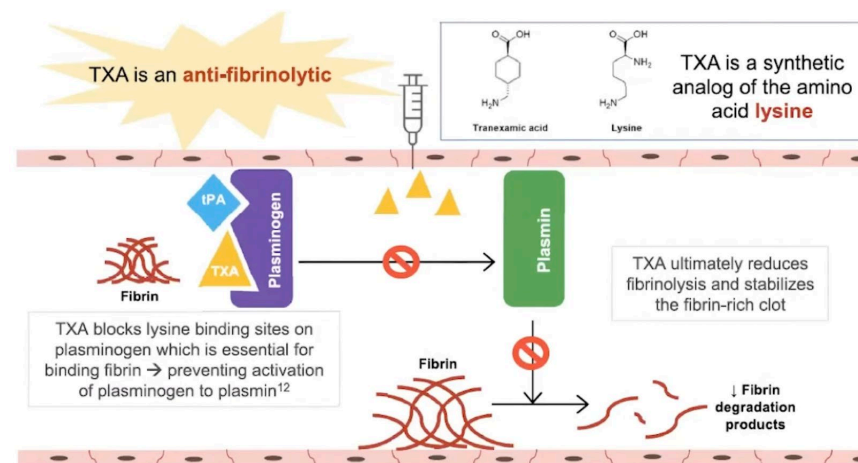
Non è raccomandata una profilassi anti-D se una donna RhD negativa riceve plasma fresco congelato RhD positivi

5

Aumentato rischio di sviluppare sovraccarico circolatorio (**TACO**) o un danno polmonare acuto correlato alla terapia trasfusionale (**TRALI**)

ACIDO TRANEXAMICO

Tranexamic acid evidence and controversies: An illustrated review



Relke N et al. Res Pract Thromb Haemost. 2021;5:e12546.

Raccomandazione WHO e ISS suggeriscono

somministrazione precoce antifibrinolitico, entro 3h dal parto,

di **1 gr in 10'**, in donne con EPP dopo parto vaginale o TC,

in aggiunta al trattamento standard con uterotonici,

ripetibile dopo 30' o entro 24h dalla prima dose,

in caso ripresa sanguinamento di emorragia

WHO recommendation
on tranexamic acid
for the treatment of
postpartum haemorrhage



...l'acido tranexamico
riduce la mortalità dovuta a
sanguinamento nelle
donne con PPH primaria,
indipendentemente dalla
modalità del parto e senza
aumentare i rischi di eventi
tromboembolici



Cochrane
Library

Cochrane Database of Systematic Reviews

Antifibrinolytic drugs for treating primary postpartum haemorrhage (Review)

Shakur H, Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Mousa HA

Tranexamic acid versus oxytocin prophylaxis in reducing post-partum blood loss, in low-risk pregnant women: TRANOXY STUDY, a phase III randomized clinical trial

Antonio Ragusa,^a Fernando Ficarola,^{b,c,*} Amerigo Ferrari,^d Nicoletta Spirito,^e Mario Ardovino,^f Domenico Giraldi,^f Elisario Stuzziero,^f Denise Rinaldo,^g Roberto Procaccianti,^h Giovanni Larciprete,ⁱ Caterina De Luca,ⁱ Sara D'Avino,ⁱ Giulia Principi,^j Roberto Angioli,^b and Alessandro Svelatoⁱ

Background To assess the equivalence of tranexamic acid (TRAN) versus synthetic oxytocin (OXY) in reducing post-partum blood loss, in full-term patients (37–42 weeks), at low risk of post-partum hemorrhage, with vaginal childbirth.

Methods Phase III, randomized (1:1), open-label, longitudinal, multi-center, prospective clinical trial (Prot. n 63209, [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02775773) Identifier: NCT02775773). From January 7, 2020, to June 30, 2023, a total of 256 women were enrolled at two general urban community hospitals in Italy, serving a multi-ethnic patient population with National Health Insurance. The primary outcome was to explore a potential equivalence between the two treatments (OXY and TRAN) in preventing total blood loss. Therefore, we randomized 231 women into two groups: Group A (OXY), 127 women who were administered 10UI intramuscularly within 5 min from childbirth; Group B (TRAN), 104 women to whom 1-g slow intravenous infusion was administered within 5 min from childbirth.

Findings At the time of delivery, mean blood loss for OXY group versus TRAN group was 269.12 mL versus 263.88 mL, respectively, with equivalence between the two groups. Similarly, there was equivalence in total blood loss between the OXY and the TRAN group (397.66 mL versus 405.64 mL, respectively). No statistical differences between Hb levels at admission and discharge in the two groups were reported. No difference was found in terms of additional uterotonic and surgical therapies between the two groups of patients. Neither group showed thrombotic complications at check-up performed after 7 days or after a questionnaire regarding adverse effects, subjected after 40 days.

Interpretation The study shows the equivalence of tranexamic acid versus synthetic oxytocin in post-partum blood loss prophylaxis in term patients at low risk of PPH with vaginal childbirth. The safety profiles of OXY and TRAN were similar.

FIBRINOGENO

La sua concentrazione aumenta in gravidanza, 4-6gr/L nel III trimestre

Biomarker accurato di progressione dell'EPP da moderata a grave, E' il 1° fattore della coagulazione a ridursi in corso di EPP

A causa del suo fisiologico aumento in gravidanza, una concentrazione <2gr/L riflette un livello di consumo significativo, e concentrazioni inferiori sono predittive di aggravamento

Livelli <2g/L : TARGET per il rimpiazzo

	FIBRINOGENO CONCENTRATO	CRIOPRECIPITATO
Efficacia	Buona	Buona
Tempo di preparazione	Breve	Lungo (scongelamento)
Costo	Elevato	Basso
Rischio infettivo	Basso (pastorizzazione)	Moderato (NO pastorizzazione)
Rischio Reazioni Trasmusione	Basso (anafilassi)	Elevato (reazioni allergiche)
Fattori coagulazione	I (1gr)	I (200-300mg) VIII (80-120U) XIII (40-60U) vWF (80U)
Gruppo sanguigno ABO	Non necessario	ABO noto
Conservazione	Temperatura ambiente	Congelato (max 1 anno)

Calcio

OBSTETRIC ANAESTHESIA

Association between ionised calcium and severity of postpartum haemorrhage: a retrospective cohort study

Danny Epstein^{1,*}, Neta Solomon^{2,3}, Alexander Korytny^{4,5}, Erez Marcusohn⁶, Yaacov Freund⁵, Ron Avrahami⁷, Ami Neuberger^{1,5,8}, Aeyal Raz^{5,9} and Asaf Miller¹⁰

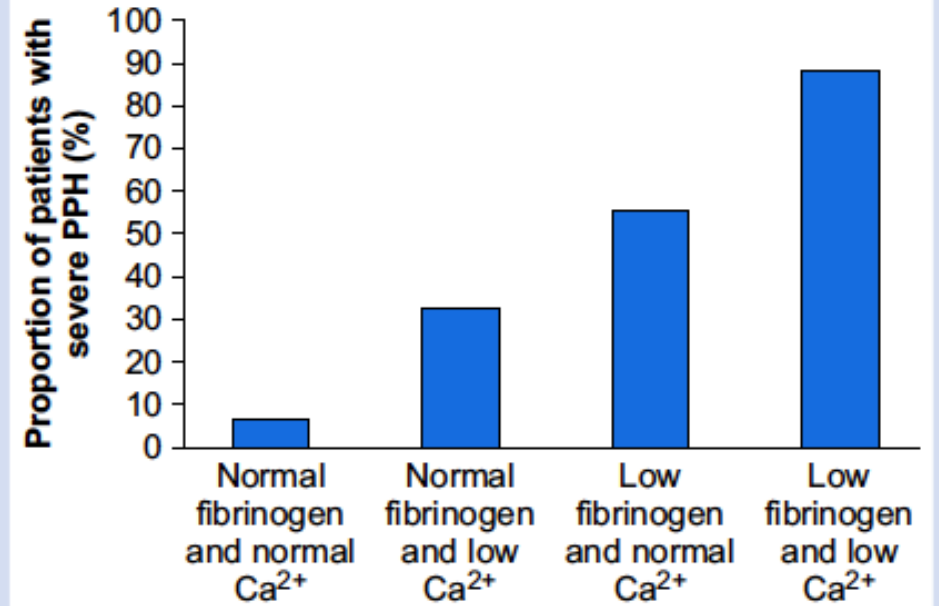


Fig 2. The relationships between fibrinogen, ionised calcium, and clinical outcome. Low fibrinogen was defined as fibrinogen $<200 \text{ mg dl}^{-1}$ and low Ca^{2+} was defined as $\text{Ca}^{2+} <1.16 \text{ mmol L}^{-1}$. Ca^{2+} , ionised calcium; PPH, postpartum haemorrhage.

rFVIIa

...aggiornamento scheda tecnica, Maggio 2022

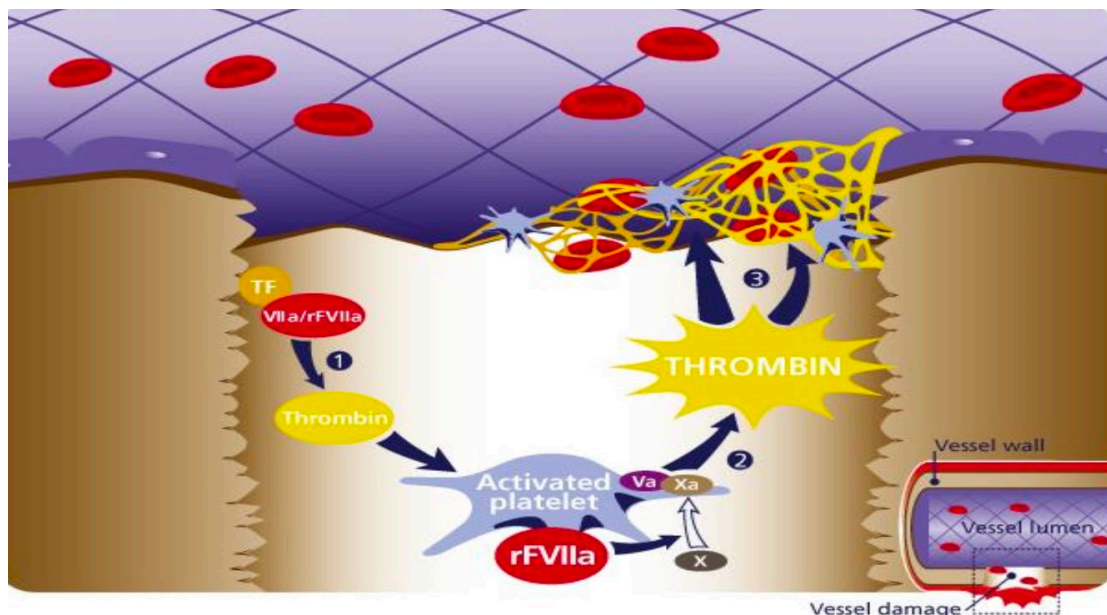
« il rFVIIa è indicato per il trattamento dell'emorragia post partum severa,

quando i gli Uterotonici non sono sufficienti a raggiungere l'emostasi.

La dose raccomandata è 60-90 µg/Kg in bolo endovenoso

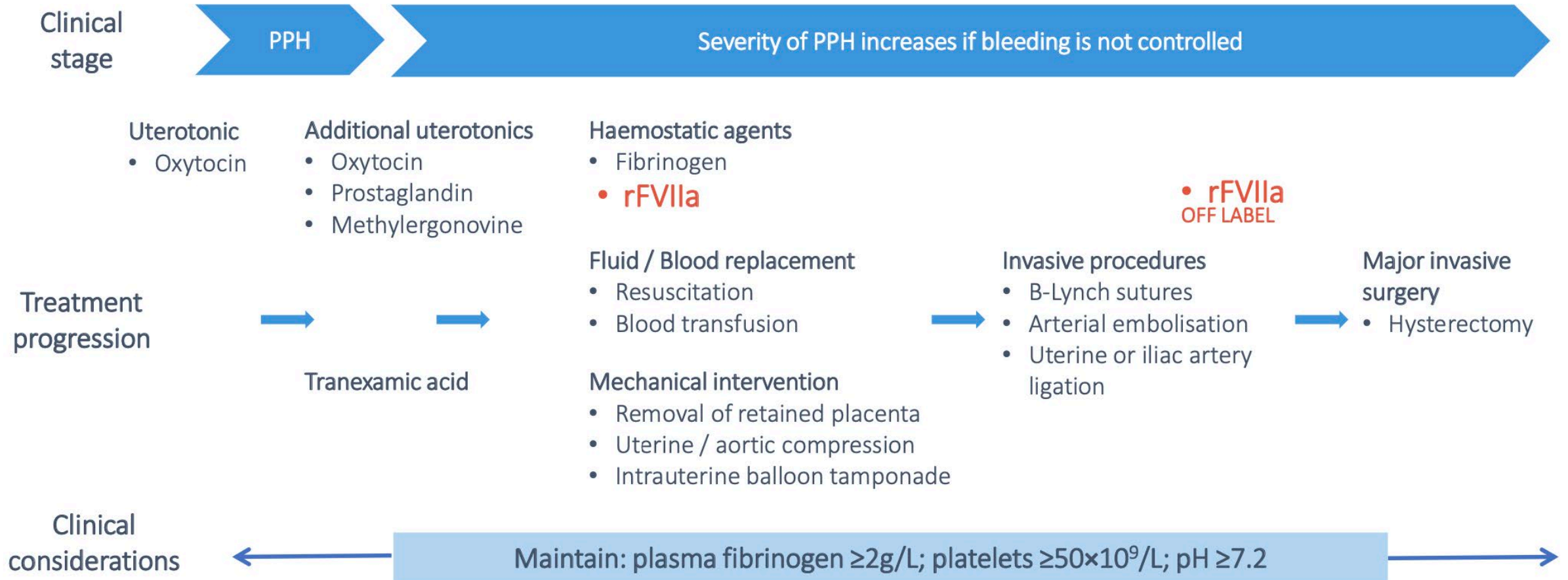
Il picco di attività anticoagulante è di 10 minuti

Se risposta insufficiente seconda dose 30 minuti



- Nel sito della lesione laddove viene esposto il TF
- Il legame con il TF genera piccole quantità di trombina (1)
- Dosi farmacologiche di rFVIIa attivano direttamente FX sulla superficie delle PLT attivate
- Burst di trombina (2)
- Formazione di tappo emostatico di fibrina stabile e resistente (3)

rFVIIa nella gestione della sPPH dopo la nuova indicazione



ORIGINAL ARTICLE

Recombinant human FVIIa for reducing the need for invasive second-line therapies in severe refractory postpartum hemorrhage: a multicenter, randomized, open controlled trial

G. LAVIGNE-LISSALDE,*† A. G. AYA,‡ F. J. MERCIER,§ S. ROGER-CHRISTOPH,¶ C. CHAULEUR,** E. MORAU,†† A. S. DUCLOY-BOUTHORS,‡‡ A. MIGNON,§§ M. RAUCOULES,¶¶ A. BONGAIN,*** F. BOEHLEN,††† P. DE MOERLOOSE,††† S. BOUVET,‡‡‡ P. FABBRO-PERAY‡‡‡ and J.-C. GRIS*†

*RCT Franco-Svizzero
Aprile 2007 - Novembre 2010*

Eventi di TromboEmbolismo Venoso(VTE) e Arterioso(ATE)

rFVIIa treated:

VTEs: in 1.2% of patients
ATEs: in 0.2% of patients

NOT rFVIIa treated:

VTEs: in 1.4% of patients
ATEs: in 0.2% of patients

- E' uno studio randomizzato, open label, condotto in 8 centri tra Francia e Svizzera
- Lo studio aveva lo scopo di valutare l'efficacia e la sicurezza di una dose singola di FVIIa in donne con sPPH in corso dopo fallimento con Sulprostone
- Sono state randomizzate 84 pazienti con sPPH: 42 a utilizzare rFVIIa dopo fallimento con Sulprostone e 42 a essere gestite con lo «standard of care» del centro di appartenenza

« L'uso di rFVIIa in aggiunta all'attuale standard care può migliorare i risultati senza aumentare ulteriormente i rischi associati a sPPH»

COMPLESSI PROTROMBINICI

Prothrombin Complex Concentrate: Anticoagulation Reversal and Beyond

O. Grottke and H. Schöchl



...the *European trauma guidelines* recommend that **PCC be administered in bleeding trauma** patients with normal Fibrinogen levels, based on evidence of delayed coagulation initiation from viscoelastic monitoring

Prothrombin complex concentrate

Prothrombin complex concentrates (PCCs) contain a concentrate of coagulation factors II, VII, IX, X and proteins S and C (and some heparin), and are recommended for urgent reversal of the effect of vitamin K antagonists¹¹⁹⁻¹²¹. Successful use of PCC was described in a case report of massive PPH¹²². In an ongoing trial,

PCC and fibrinogen are being compared to plasma in PPH (trial identifier: NCT01910675). **At the moment, there is no evidence to support the use of PCCs in the management of PPH,** and their use should be limited to clinical trials in order to gather evidence on their efficacy and, in particular, on their safety.

FIGO recommendations on the management of postpartum hemorrhage 2022

DCR
***Damage
Control
Resuscitation***



Il **DCR** si fonda su:

- **Minimizzare le perdite**
- **Prevenire la triade: acidosi, coagulopatia, ipotermia**
- **Massimizzare l'ossigenazione tissutale**

- ✓ Protocollo trasfusione massiva
- ✓ Uso limitato di cristalloidi
- ✓ Controllo del sanguinamento associando anche:
 - DCS: Damage Control Surgery
 - DCIR: Damage Control Interventional Radiology
- ✓ Stabilizzazione in ICU per:
 - Disturbi della coagulazione
 - Anomalie metaboliche
 - Emodinamica
 - Terapie di supporto

«STASIS»

Algoritmo di management nella PPH refrattaria

“STASIS” Algorithm	Management Steps
S: Shift	Shift to operating room (with bimanual compression anti-shock garment in place if transfer is required)
T: Tissue, trauma, tamponade	Exclude the presence of retained tissue or lacerations; proceed with tamponade (balloon)
A: Apply compression	Apply compression sutures
S: Systematic devascularization	Ligate uterine (O’Leary), ovarian, hypogastric, quadruple
I: Interventional radiology	Uterine artery embolization
S: Subtotal/total hysterectomy	Proceed with hysterectomy

GUIDELINES

Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care

Second update 2022

- L'emorecupero in ambito ostetrico è utilizzato, **GRADO C**
a condizione che vengano prese precauzioni contro l'isoimmunizzazione
- L'utilizzo dell'emorecupero perioperatorio durante il Parto Cesareo ad alto rischio di PPH può ridurre la trasfusione omologa

GRADO 2B

EMORECUPERO

Usi:

- **Disturbi placentari**
- **Fattori di rischio per PPH**
- **Disturbi ematologici con necessità di trasfusioni**

Misure precauzionali:

- **Fonte di aspirazione separata per il liquido amniotico**
- **Iniziare la procedura di emorecupero dopo l'espulsione della placenta**
- **Uso di filtri per la deplezione dei leucociti**

L'uso di filtri a deplezione leucocitaria fa sì che il livello di cellule squamose fetali sono presenti in livelli paragonabili a quelli del sangue materno dopo l'espulsione della placenta e che il TF derivato dal liquido amniotico che può causare coagulazione intravascolare può essere rimosso con successo

Quale strategia???



PA
AGGRE S S I V E