Gestione del sanguinamento in ambito ostetrico

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EMORRAGIA POST-PARTUM

L'emorragia Post Partum (EPP) è la forma più comune di emorragia ostetrica ed è una delle principali cause di mortalità e grave morbosità materna nel mondo. La EPP primaria complica circa il 5-15% delle gravidanze ed è globalmente responsabile del 25% di tutte le morti materne.

La maggior parte dei decessi avvengono entro le prime 24-48 ore dopo il parto. Secondo i dati dell'ultimo report del Centre for Maternal and Child Enquires sulla mortalità materna, nonostante i miglioramenti registrati negli ultimi 3 anni, il 66% delle morti da PPH, sono riconducibili a substandard care (CMACE 2011).

Gli elementi fondamentali nella gestione dell'EPP sono : comunicazione, rianimazione e monitoraggio, ricerca delle cause e trattamento per arrestare l'emorragia.

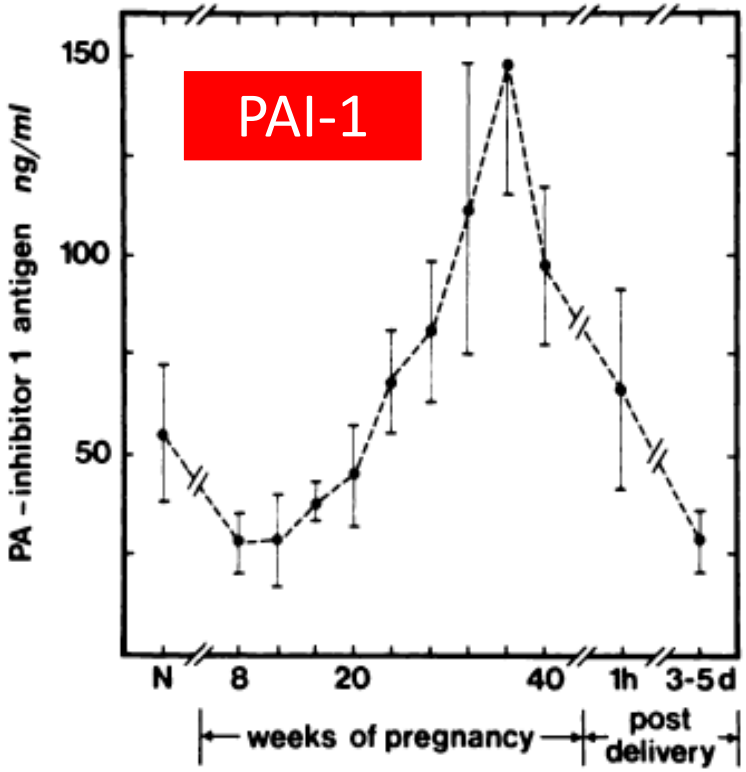
PRESUPPOSTI FISIOPATOLOGICI

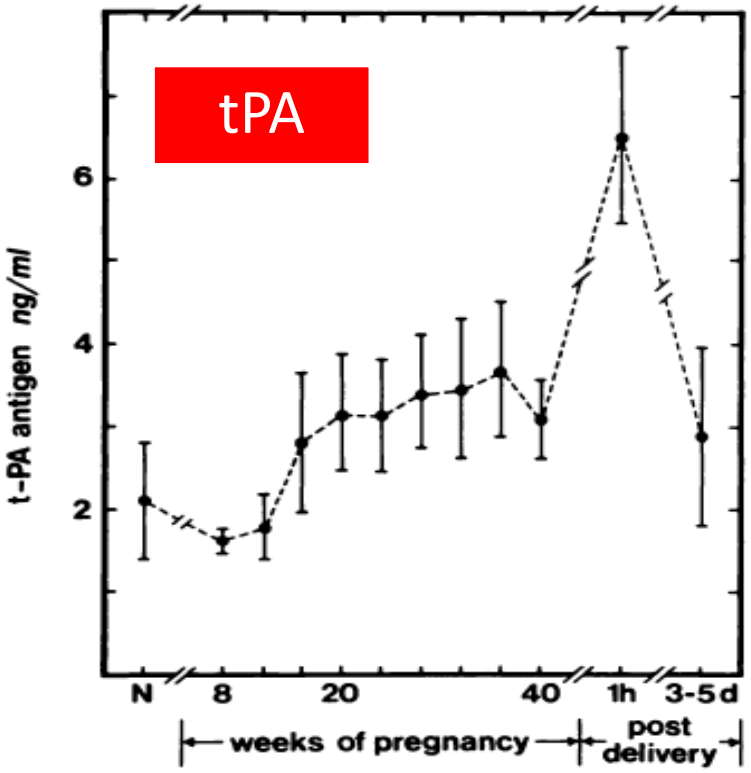
Haemostasis in normal pregnancy	
Factor VIII and Von Willebrand	
Factor V activity	
Factor VII	
Factor XI	
Factor XIII	
FIBRINOGEN	
Antithrombin	
Protein C	
Protein S	
t-PA	
PAI-1, PAI-2	

blood 1987 69: 460-466

Fibrinolysis in pregnancy: a study of plasminogen activator inhibitors

EK Kruithof, C Tran-Thang, A Gudinchet, J Hauert, G Nicoloso, C Genton, H Welti and F Bachmann

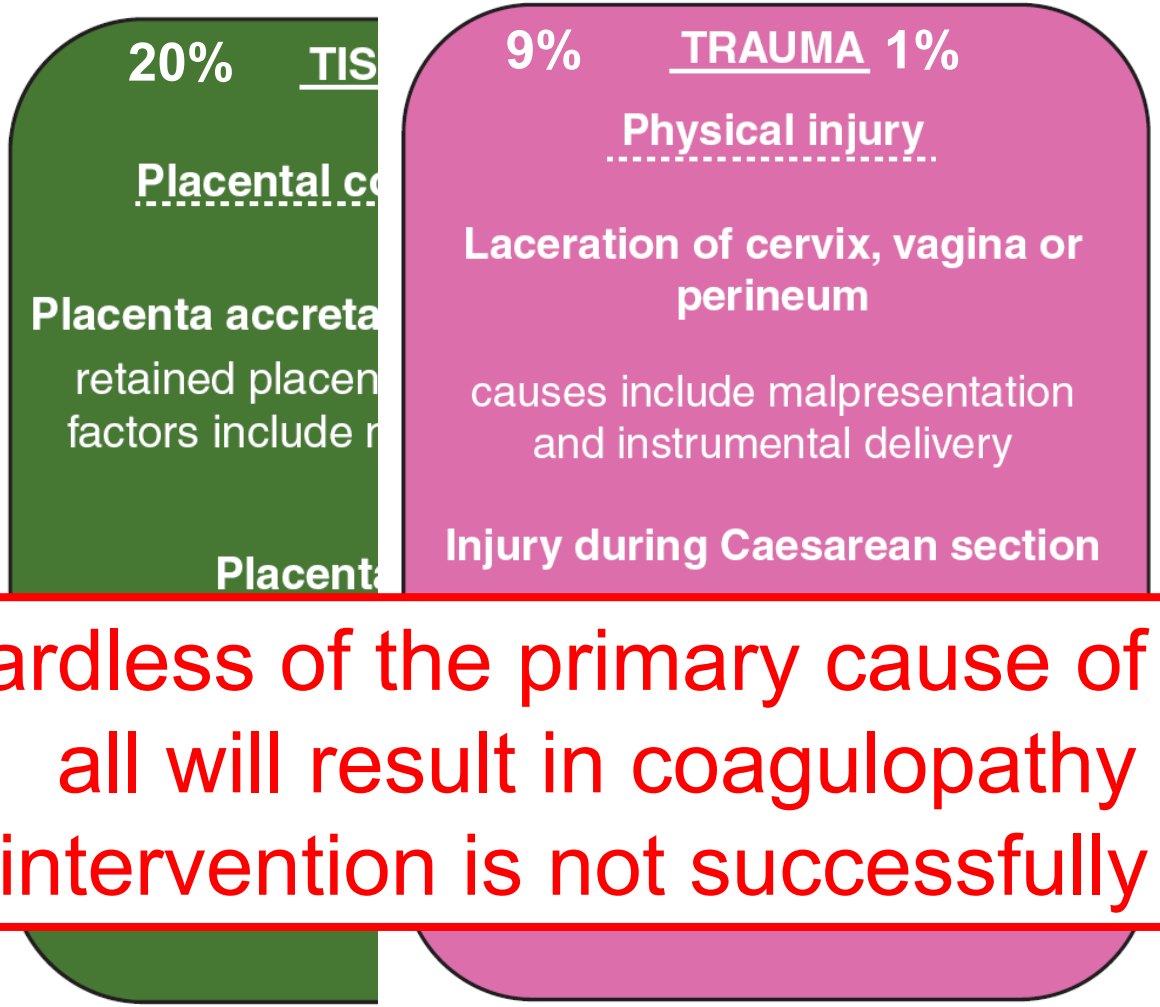




- EPP **minore** in caso di perdita ematica stimata tra 500 e 1.000 ml;
- EPP **maggiore** in caso di perdita ematica stimata >1.000 ml.

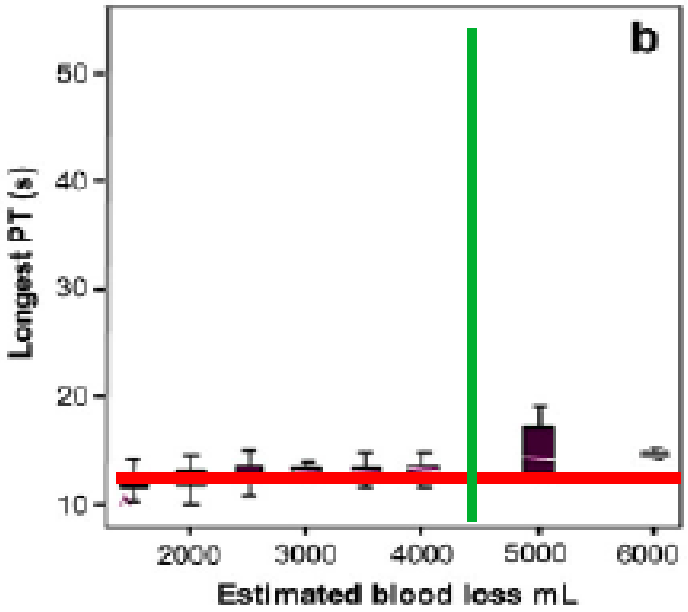
L'EPP maggiore a sua volta è distinta in due condizioni di diversa gravità che comportano un'allerta e una prognosi diversificate:

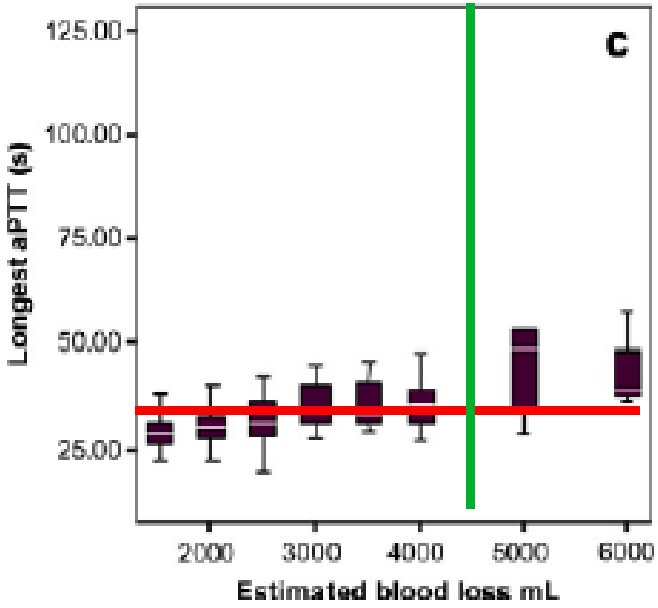
- EPP **maggiore controllata** in caso di perdita ematica controllata, con compromissione delle condizioni materne che richiede un monitoraggio attento;
- EPP **maggiore persistente** in caso di perdita ematica persistente e/o segni di *shock* clinico con una compromissione delle condizioni materne che comporta un pericolo immediato per la vita della donna.



Regardless of the primary cause of PPH,
all will result in coagulopathy
if early intervention is not successfully applied.

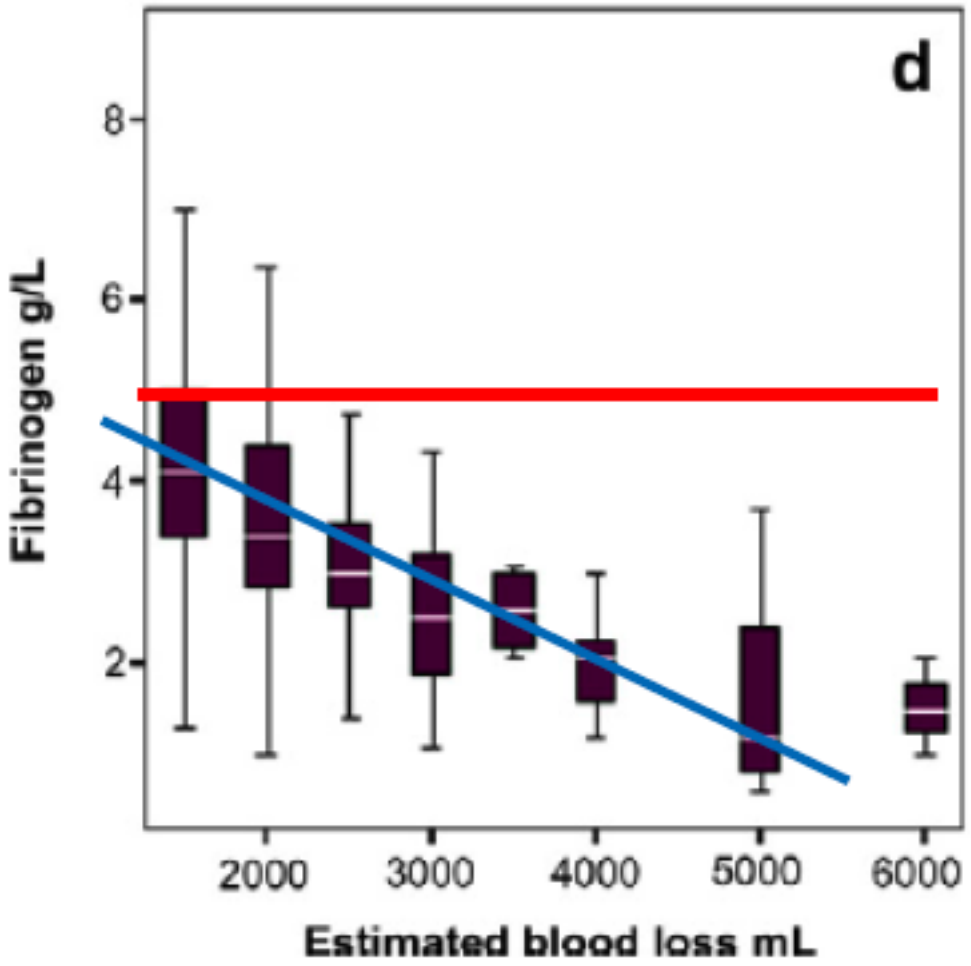
HEAMOSTATIC TESTS WITH INCREASING BLOOD LOSS





PT and aPTT poorly reflect hemostatic impairment in PPH

Standard haemostatic tests following major obstetric haemorrhage



Fibrinogeno miglior marcatore

The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage

B. CHARBIT,*† L. MANDELBROT,‡ E. SAMAIN,§ G. BARON,¶ B. HADDAOUI,‡‡‡ H. KEITA,‡¶
O. SIBONY,** D. MAHIEU-CAPUTO,¶ M. F. HURTAUD-ROUX,** M. G. HUISSE,¶‡‡
M. H. DENNINGER,†‡‡ and D. DE PROST‡†††‡‡ FOR THE PPH STUDY GROUP

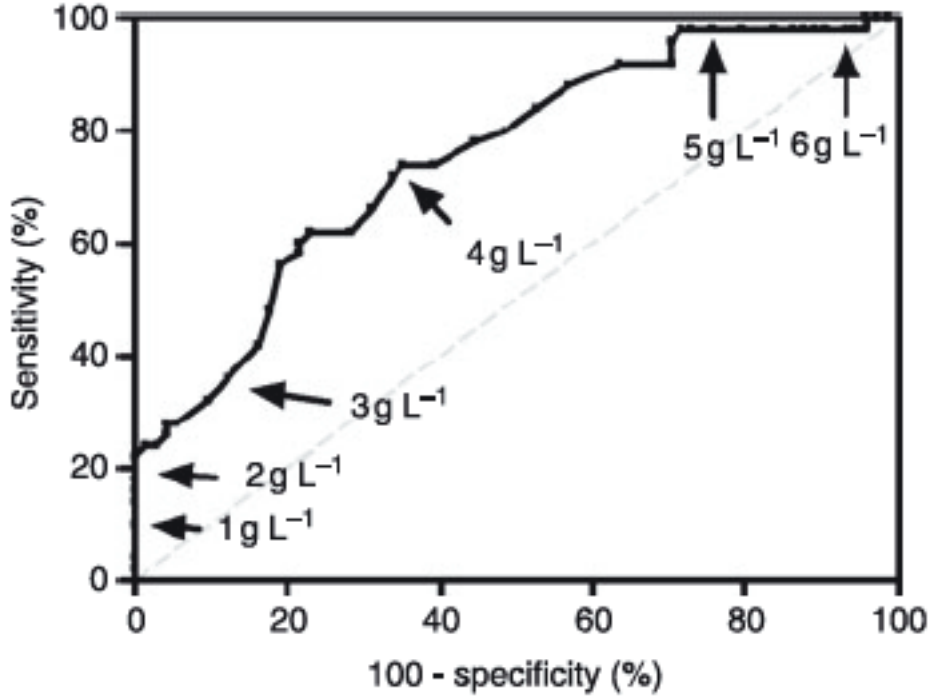


Fig. 3. ROC curve of fibrinogen plasma concentration at H0 for the diagnosis of severe postpartum hemorrhage.

–Fibrinogen **less than 2g/L**
- **100% PPV**

–Fibrinogen **above 4g/L**
- **79% NPV**

Management of coagulopathy associated with postpartum hemorrhage: guidance from the SSC of the ISTH

- We recommend monitoring hemostasis with either PT/aPTT and Clauss fibrinogen or POCTs using thromboelastometry during PPH. If bleeding persists serial measures should be performed.

- If thromboelastometry is used, blood component replacement should be based on a local algorithm and a quality control protocol agreed with hematology.

J Thromb Haemost 2016; 14: 205–10.

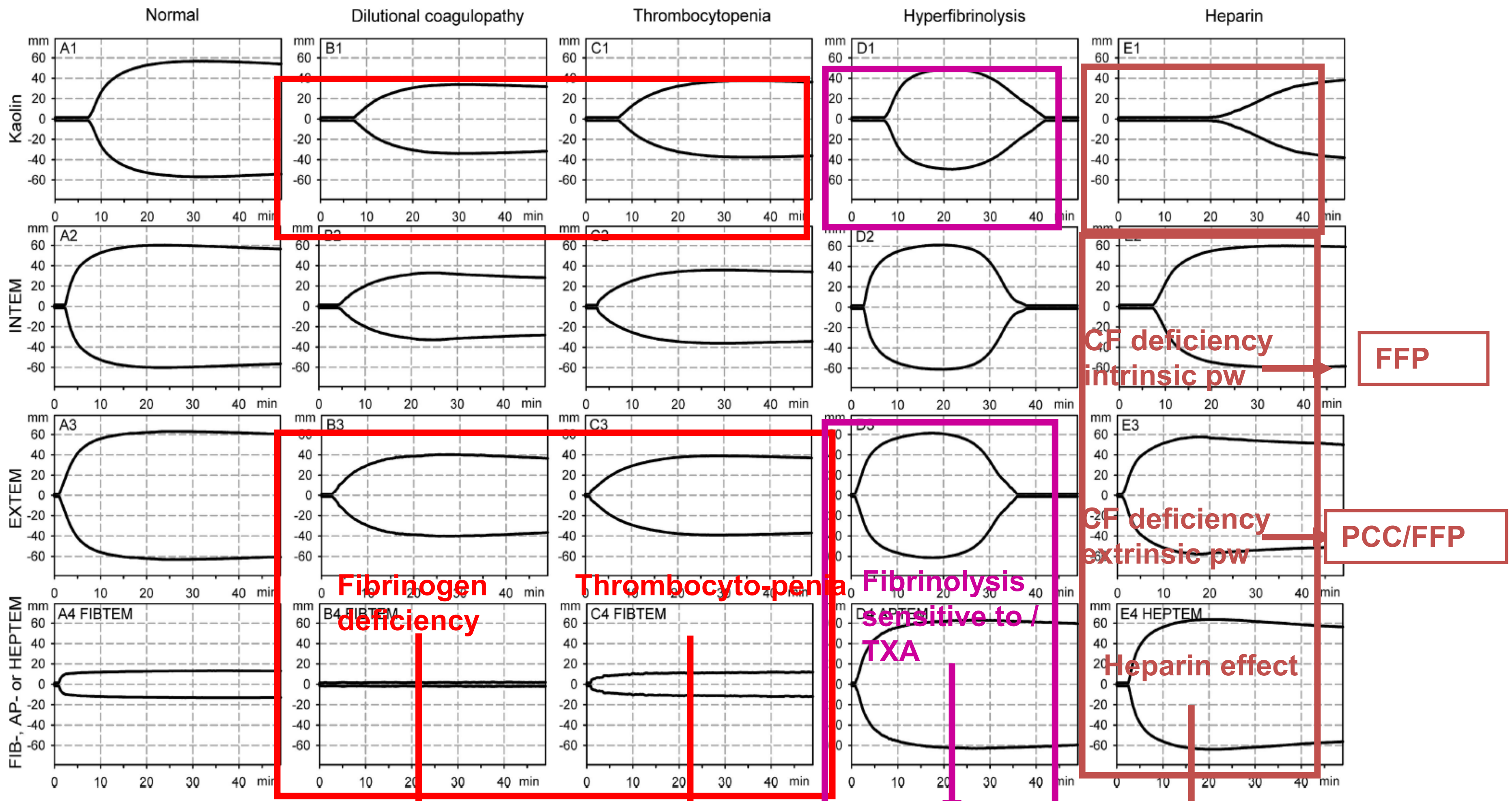
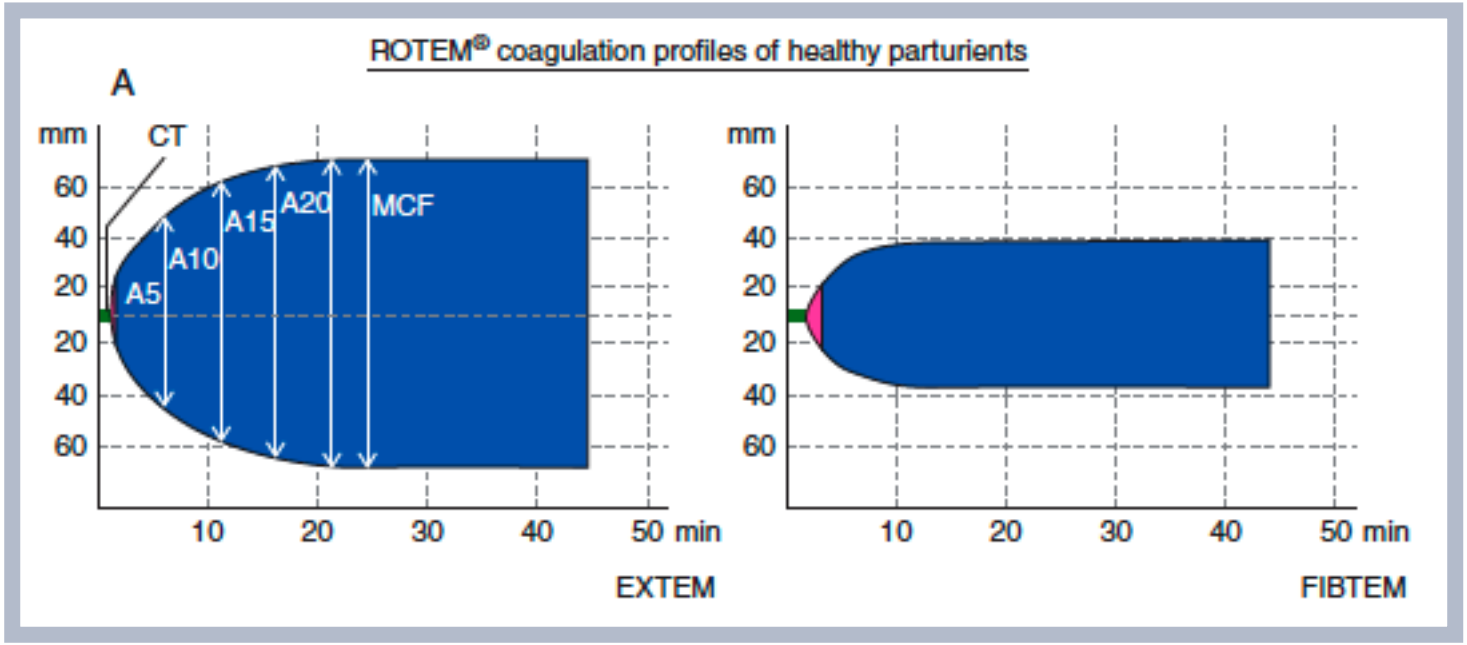


Fig. 2. Representative profiles of norma[illegible] control samples (*A*) and [illegible]odeled coagulop[illegible] thrombocy-
topenia (*C*), hyperfibrinolys[illegible]),
EXTEM (row 3), FIBTEM ([illegible]r;
FIBTEM = tissue factor an[illegible]ase; INTEM = ellagic acid.


ROTEM® coagulation profiles of healthy parturients
A
mm
CT
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40
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A5
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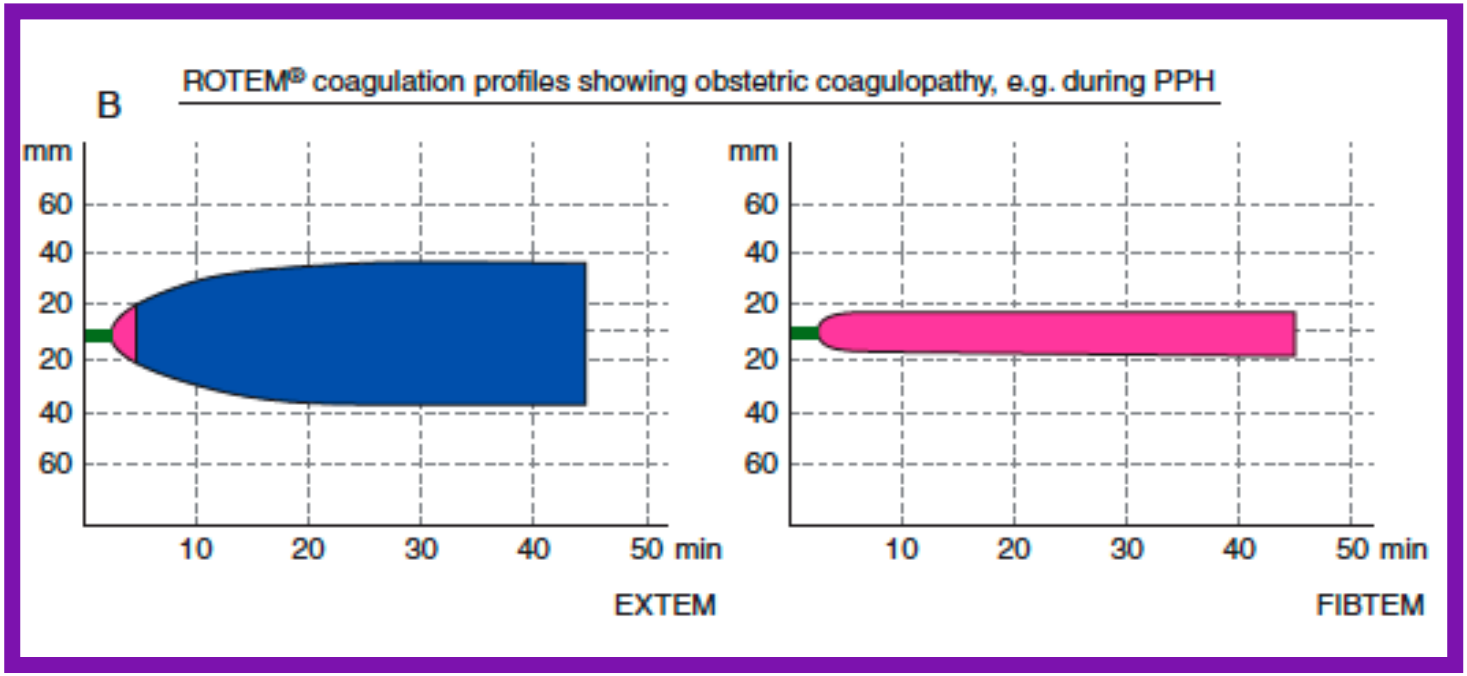
FIBTEM


B
ROTEM® coagulation profiles showing obstetric coagulopathy, e.g. during PPH
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20
30
40
50 min
FIBTEM

Table 3. Cut-off values for CA_5-FIBTEM in postpartum haemorrhage

Fibrinogen levels (g/l)	FIBTEM cut-off values (mm)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	*AUC*
Fibrinogen < 2	$CA_5 = 6$	100 (100–100)	87 (77–96)	50 (36–64)	100 (100–100)	0.97
Fibrinogen < 1.5	$CA_5 = 5$	100 (100–100)	85 (76–95)	30 (17–43)	100 (100–100)	0.96
Fibrinogen < 1	$CA_5 = 4$	100 (100–100)	86 (76–96)	13 (3–22)	100 (100–100)	0.96
Fibrinogen < 2	$CA_{15} = 8$	100 (100–100)	84 (75–94)	46 (32–60)	100 (100–100)	0.96
Fibrinogen < 1.5	$CA_{15} = 6$	100 (100–100)	88 (78–97)	33 (20–46)	100 (100–100)	0.97
Fibrinogen < 1	$CA_{15} = 5$	100 (100–100)	88 (79–97)	14 (5–24)	100 (100–100)	0.97

AUC, area under curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

PPH SITUAZIONE CLINICA

Blood loss>500mL vaginal
Blood loss>1000 mL cesarean
Blood loss>1500 mL severe

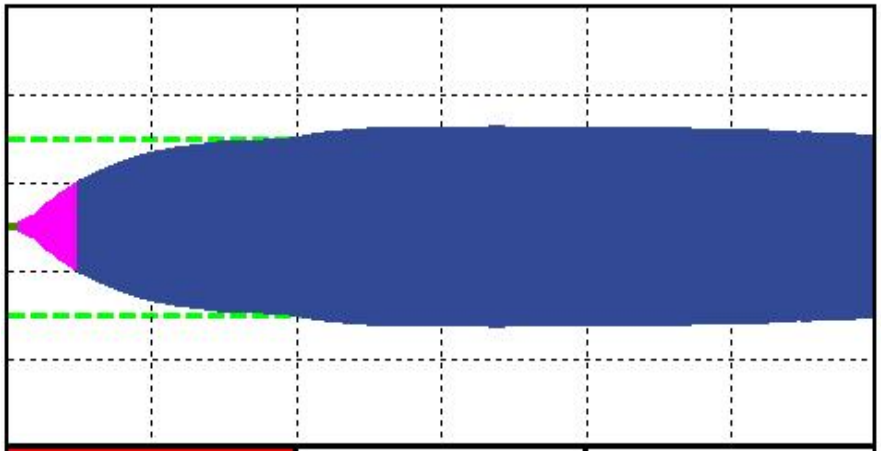
PPH GENERAZIONE DI TROMBINA

PPH CLOT FIRMNESS

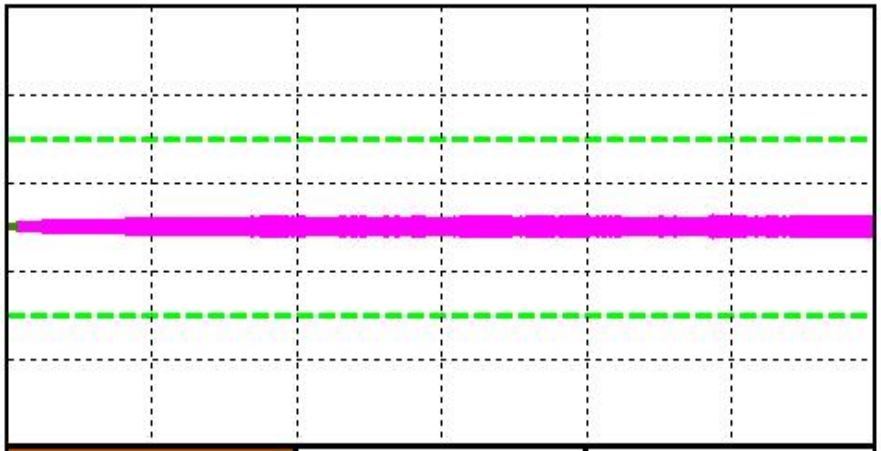
PPH IPERFIBRINOLISI

PPH RIVALUTAZIONE CLINICA/POC

IPOFIBRINOGENEMIA



EXTEM S	2012-10-12 11:31	2:
CT: 58s	CFT: 254s	α: 47°
A10: 34mm	A20: 40mm	MCF: 45mm



FIBTEM S	2012-10-12 11:31	2:
CT: 55s	CFT: - s	α: * 2°
A10: 4mm	A20: 4mm	MCF: 4mm

CLINICAL TRIALS AND OBSERVATIONS

Blood. 2014;124(11):1727-1736

Fibrin-based clot formation as an early and rapid biomarker for progression of postpartum hemorrhage: a prospective study

Peter W. Collins,[1,2] Graeme Lilley,[3] Daniel Bruynseels,[3] David Burkett-St. Laurent,[3] Rebecca Cannings-John,[4] Elizabeth Precious,[1] Vincent Hamlyn,[3] Julia Sanders,[4,5] Raza Alikhan,[1] Rachel Rayment,[1] Alexandra Rees,[5] Abigail Kaye,[5] Judith E. Hall,[2,3] Shantini Paranjothy,[6] Andrew Weeks,[7] and Rachel E. Collis[3]

Key Points

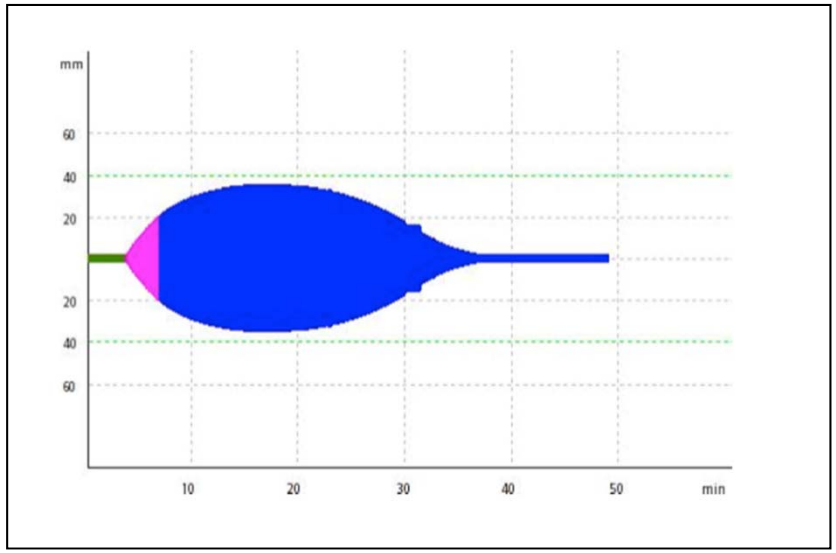
- Fibtem is an early and rapidly available biomarker for predicting progression of moderate to severe postpartum hemorrhage.
- Fibtem was predictive of need for blood transfusion and invasive procedures, bleeds >2500 mL, duration of bleed, and time in high dependency.

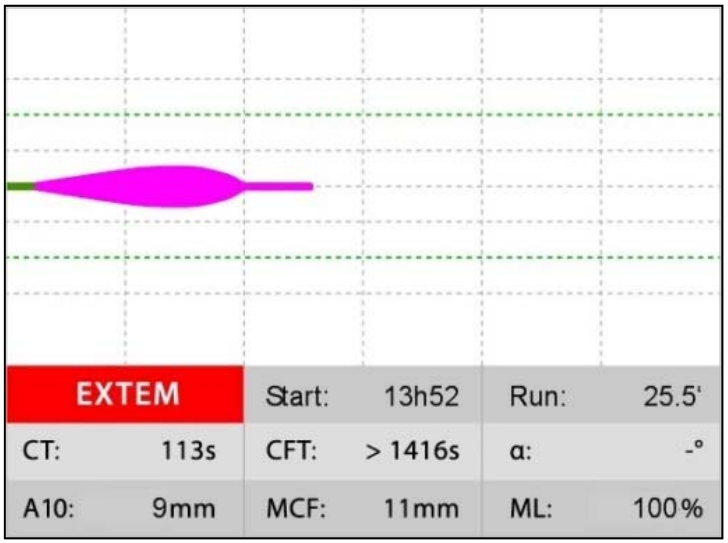
Women progressing to 8 U blood (RBCs + FFP + platelets) had a median (IQR) fibrinogen and **FIBTEM A5** of 2.1 (1.8-3.4) g/L and **12 (7-17) mm**, respectively, compared with 3.9 (3.2-4.5) g/L and **19 (17-23) mm** for those **not progressing.**

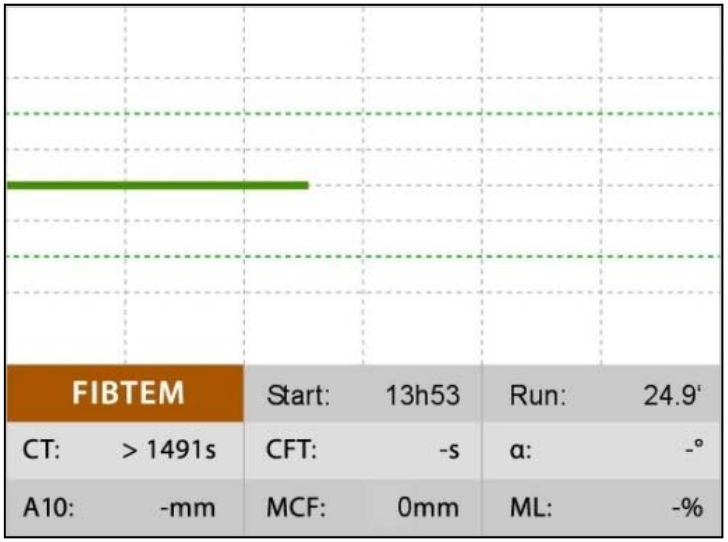
PPH	SITUAZIONE CLINICA
Blood loss>500mL vaginal Blood loss>1000 mL cesarean Blood loss>1500 mL severe	

PPH IPERFIBRINOLISI

IPERFIBRINOLISI







The use of viscoelastic haemostatic assays in the management of major bleeding

A British Society for Haematology Guideline

Recommendations

- **Viscoelastic haemostatic assays (VHA) are not usually helpful for predicting post-partum haemorrhage when taken during labour in a non-bleeding pregnant woman. Grade 2C.**
- **VHA may be used as part of an agreed algorithm to manage postpartum haemorrhage when the local institution's major obstetric haemorrhage protocol is activated. Grade 2C.**

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British Journal of Haematology, 2018, **182,** 789–806

TERAPIA EMOSTATICA

Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

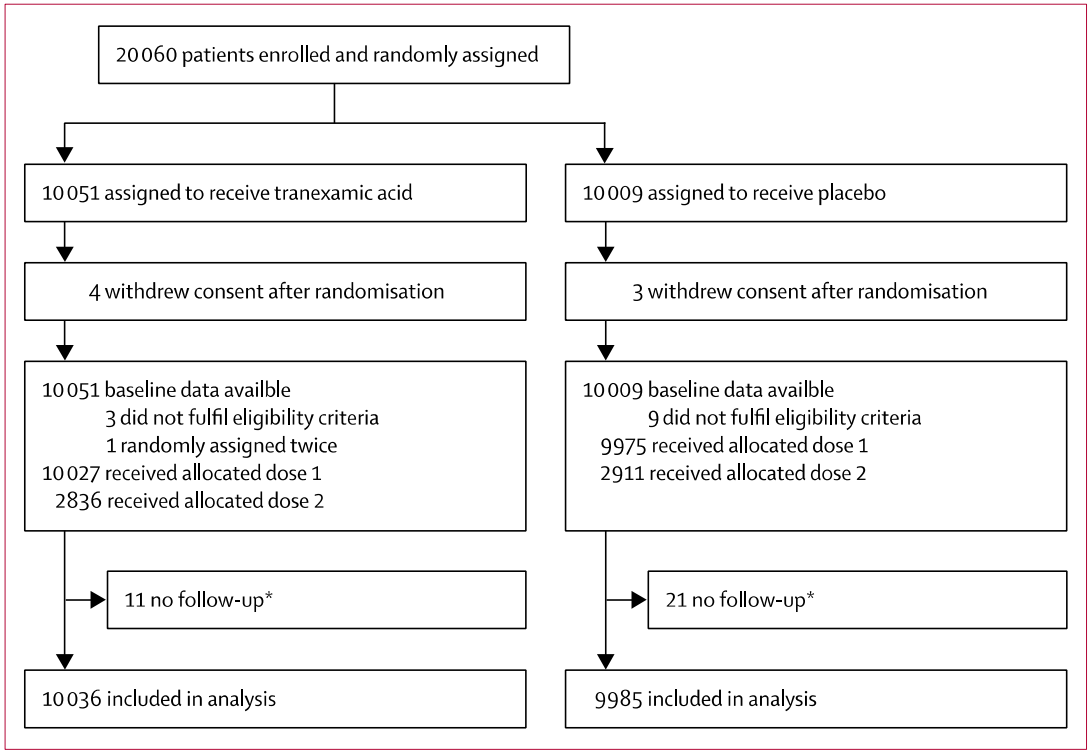
Green-top Guideline
No. 52
May 2009
Minor revisions November 2009 and April 2011

Crystalloid	**Up to 2 litres Hartmann's solution**
Colloid	**up to 1–2 litres colloid until blood arrives**
Blood	**Crossmatched** **If crossmatched blood is still unavailable, give uncrossmatched group-specific blood OR give 'O RhD negative' blood**
Fresh frozen plasma	**4 units for every 6 units of red cells or prothrombin time/activated partial thromboplastin time > 1.5 x normal (12–15 ml/kg or total 1 litres)**
Platelets concentrates	**if PLT count < 50 x 109**
Cryoprecipitate	**If fibrinogen < 1 g/l**

ANTIFIBRINOLITICI

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

WOMAN Trial Collaborators*



	Tranexamic acid group (n=10 051)	Placebo group (n=10 009)
Age at randomisation (years)		
<16	1 (<1%)	3 (<1%)
16–25	3445 (34%)	3407 (34%)
26–33	4580 (46%)	4608 (46%)
≥34	2022 (20%)	1987 (20%)
Unknown	3 (<1%)	4 (<1%)
Baby delivered in the randomising hospital		
Yes	8869 (88%)	8756 (88%)
No	1181 (12%)	1251 (13%)
Unknown	1 (<1%)	2 (<1%)
Type of delivery		
Vaginal	7093 (71%)	7126 (71%)
Caesarean section	2957 (29%)	2879 (29%)
Unknown	1 (<1%)	4 (<1%)
Time between delivery and randomisation (h)		
≤1	4852 (48%)	4733 (47%)
>1 to ≤3	2678 (27%)	2691 (27%)
>3	2517 (25%)	2574 (26%)
Unknown	4 (<1%)	11 (<1%)
Placenta fully delivered		
Yes	9089 (90%)	9016 (90%)
No	962 (10%)	990 (10%)
Primary cause of haemorrhage		
Uterine atony	6437 (64%)	6347 (63%)
Placenta praevia or accreta	943 (9%)	935 (9%)
Surgical trauma or tears	1834 (18%)	1857 (19%)
Other	720 (7%)	737 (7%)
Unknown	117 (1%)	133 (1%)
Systolic blood pressure (mm Hg)		
≥90	8138 (81%)	8065 (81%)
<90	1908 (19%)	1929 (19%)
Unknown	5 (<1%)	15 (<1%)
Estimated volume of blood lost (mL)		
≤500	295 (3%)	313 (3%)
>500 to ≤1000	4949 (49%)	4861 (49%)
>1000 to ≤1500	2832 (28%)	2882 (29%)
>1500	1973 (20%)	1953 (20%)
Unknown	2 (<1%)	0
Uterotonic prophylaxis given		
Yes	9687 (96%)	9618 (96%)
No	131 (1%)	139 (1%)
Unknown	233 (2%)	252 (3%)
Clinical signs of haemodynamic instability		
Yes	5961 (59%)	5898 (59%)
No	4090 (41%)	4110 (41%)

Table 1: **Baseline characteristics of participants before randomisation**

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

WOMAN Trial Collaborators*

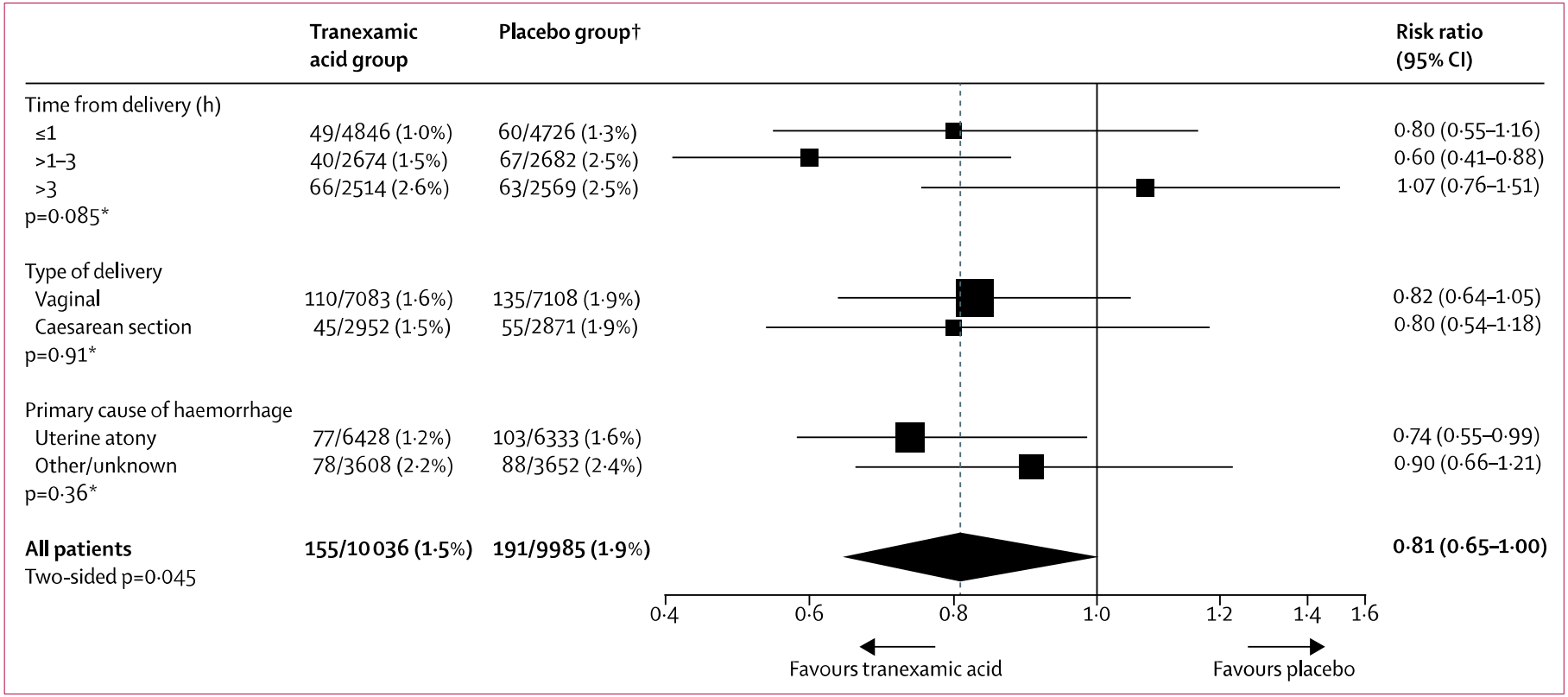


Figure 3: **Death from bleeding by subgroup**

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

WOMAN Trial Collaborators*

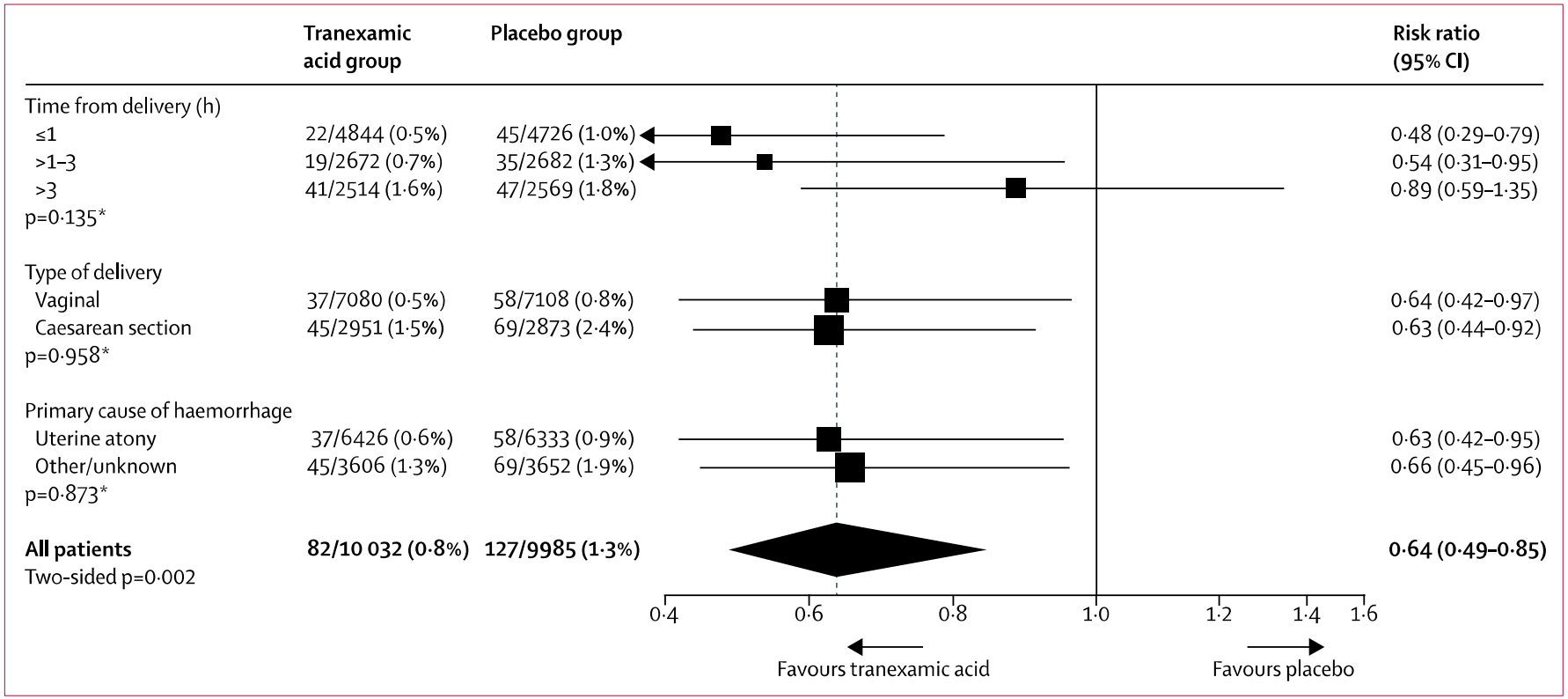


Figure 4: Laparotomy for bleeding by subgroup

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

WOMAN Trial Collaborators*

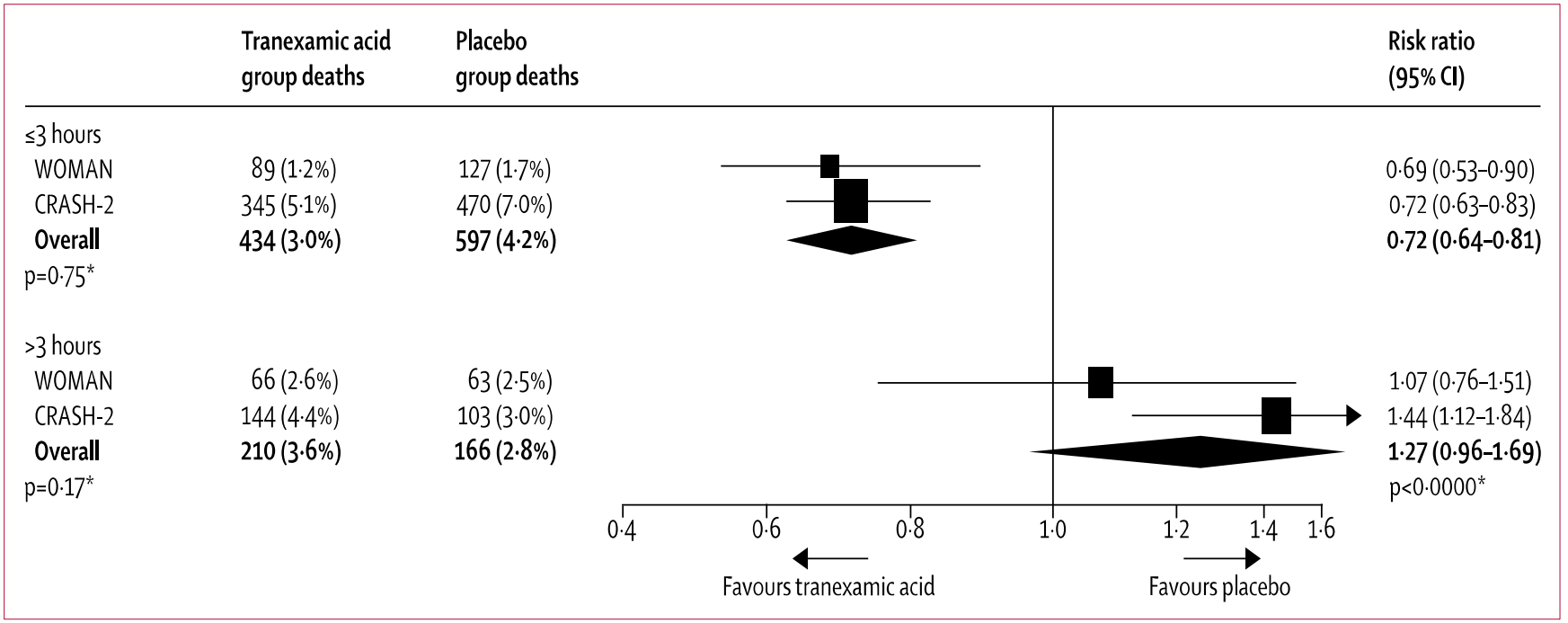
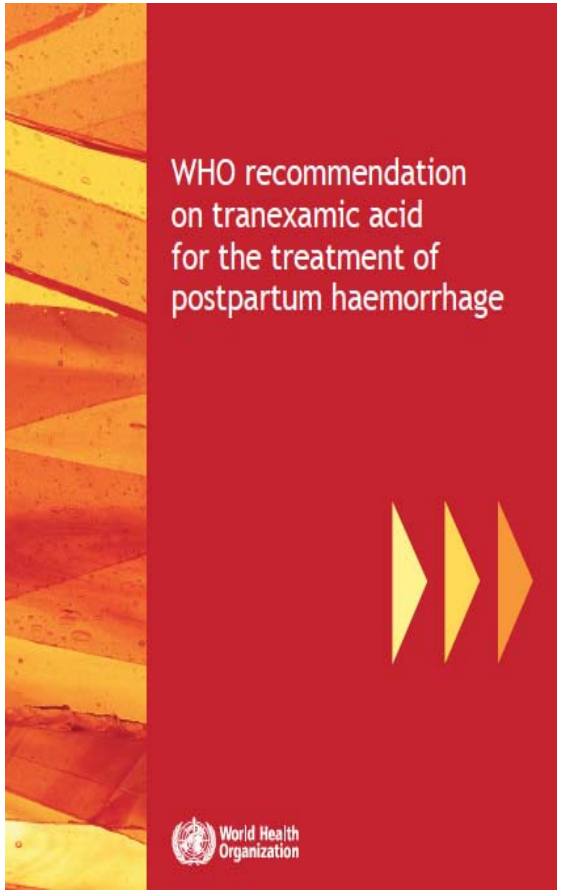


Figure 5: Time to treatment



Early use of intravenous tranexamic acid (within 3 hours of birth) in addition to standard care is recommended for women with clinically diagnosed postpartum haemorrhage following vaginal birth or caesarean section. *(Strong recommendation, moderate quality of evidence)*

Remarks

- Based on the dosing regimen used in the WOMAN trial, the GDG supports the administration of tranexamic acid (TXA) at a fixed dose of 1 g (100 mg/ml) intravenously (IV) at 1 ml per minute (i.e. administered over 10 minutes), with a second dose of 1 g IV if bleeding continues after 30 minutes, or if bleeding restarts within 24 hours of completing the first dose.
- The WOMAN trial defined "clinically diagnosed postpartum haemorrhage" as clinically estimated blood loss of more than 500 ml after a vaginal birth or 1000 ml after caesarean section, or any blood loss sufficient to compromise haemodynamic stability.
- Based on evidence from the WOMAN trial, the reference point for the start of the 3-hour window for starting TXA administration is time of birth. If time of birth is unknown, the best estimate of time of birth should be used as the reference point. As most deaths due to postpartum haemorrhage (PPH) occur within the first 2 to 3 hours after birth, it is critical that TXA is given as soon as possible to achieve clinical benefits.
- Analysis of the effects of timing of administration in the WOMAN trial, as well as an individual participant data (IPD) meta-analysis of 40 138 bleeding patients (including WOMAN trial participants), indicates that TXA administration beyond 3 hours does not confer any clinical benefit. Furthermore, the point estimates of effect of TXA use beyond 3 hours on death for trauma or after PPH were both in the direction of harm, albeit not statistically significant for women with PPH. In view of this evidence, the GDG does not support the use of TXA more than 3 hours after birth.
- Administration of TXA should be considered as part of the standard PPH treatment package. Standard care in the context of this recommendation includes routine care for PPH treatment, including fluid replacement, medical (uterotonics), monitoring of vital signs, nonsurgical (e.g. bimanual compression, intrauterine balloon tamponade, nonpneumatic antishock garment, aortic compression) and surgical interventions (e.g. brace sutures, arterial ligation, or hysterectomy) in accordance with WHO guidelines or adapted local PPH treatment protocols.
- TXA should be used in all cases of PPH, regardless of whether the bleeding is due to genital tract trauma or other causes.
- The use of TXA should be avoided in women with a clear contraindication to antifibrinolytic therapy (including TXA) (e.g. a known thromboembolic event during pregnancy).
- This recommendation applies only to IV use. The evaluation of benefits and potential harms of other routes of TXA administration is a research priority.
- Regardless of the level of health system resources, TXA should be recognized as a life-saving intervention and be made readily available for the management of PPH in settings where emergency obstetric care is provided.

FIBRINOGENO

RECOMMENDATIONS AND GUIDELINES

Management of coagulopathy associated with postpartum hemorrhage: guidance from the SSC of the ISTH

- We suggest that a fibrinogen of at least 2 g L^{-1} should be maintained during ongoing obstetric bleeding, even if PT and aPTT are normal. Either cryoprecipitate or fibrinogen concentrate may be used.
- We recommend against the use of fibrinogen concentrate in an unmonitored or pre-emptive manner.

J Thromb Haemost 2016; 14: 205–10.

The use of viscoelastic haemostatic assays in the management of major bleeding

A British Society for Haematology Guideline

Nicola S. Curry,[1,2] Ross Davenport,[3] Sue Pavord,[1,2] Susan V. Mallett,[4] Dianne Kitchen,[5] Andrew A. Klein,[6] Helena Maybury,[7] Peter W. Collins[8] and Mike Laffan[9]

During ongoing major postpartum haemorrhage, if the FIBTEM A5 is >12 mm fibrinogen replacement is unlikely to improve clinical haemostasis. Grade 2B.

During major postpartum haemorrhage, if FIBTEM A5 is <7 mm, or <12 mm with ongoing bleeding, fibrinogen replacement may improve clinical haemostasis. Grade 2C.

In a bleeding pregnant or post-partum patient, tranexamic acid should not be withheld based on the thromboelastography (TEG) or thromboelastometry (ROTEM)parameters. Grade 1B.

Viscoelastometric-guided early fibrinogen concentrate replacement during postpartum haemorrhage: OBS2, a double-blind randomized controlled trial

P. W. Collins[1,*], R. Cannings-John[2], D. Bruynseels[3], S. Mallaiah[4], J. Dick[5], C. Elton[6], A. D. Weeks[7], J. Sanders[8], N. Aawar[2], J. Townson[2], K. Hood[2], J. E. Hall[9] and R. E. Collis[3] on behalf the OBS2 study team[†]

Background: Postpartum haemorrhage (PPH) can be exacerbated by haemostatic failure. We hypothesized that early fibrinogen replacement, guided by viscoelastometric testing, reduces blood product usage and bleed size.

Methods: Women with PPH 1000–1500 ml were enrolled. If Fibtem A5 was ≤15 mm and bleeding continued, subjects were randomized to fibrinogen concentrate or placebo. The primary outcome compared the number of units of red blood cells, plasma, cryoprecipitate and platelets transfused.

Results: Of 663 women enrolled 55 were randomized. The adjusted incidence rate ratio (IRR) (95% CI) for the number of allogeneic units transfused in the fibrinogen group compared with placebo was 0.72 (0.3–1.7), P=0.45. In pre-specified subgroup analyses, subjects who had a Fibtem A5 ≤12 mm at the time of randomization and who received fibrinogen concentrate received a median (25th–75th centile) of 1 (0–4.5) unit of allogeneic blood products and had an additional 300 (100–350) ml blood loss whereas those who received placebo also received 3 (0–6) units of allogeneic blood products and had 700 (200–1550) ml additional blood loss; these differences were not statistically significantly different. There was one thrombotic event in each group.

Conclusions: Infusion of fibrinogen concentrate triggered by Fibtem A5 ≤15 mm did not improve outcomes in PPH. Pre-specified subgroup analyses suggest that fibrinogen replacement is not required if the Fibtem A5 is >12 mm or Clauss fibrinogen >2 g litre^{-1}, but an effect below these levels cannot be excluded. The raised fibrinogen at term appears to be a physiological buffer rather than required for haemostasis.

CONCENTRATI PIASTRINICI

RECOMMENDATIONS AND GUIDELINES

Management of coagulopathy associated with postpartum hemorrhage: guidance from the SSC of the ISTH

- We recommend that platelets should be transfused when the platelet count is $< 75 \times 10^9\ L^{-1}$ based on laboratory monitoring and against 1 : 1 : 1 RBC : FFP : platelet transfusion ratios.
- In cases of massive ongoing bleeding where women have been given 8 units of RBCs and 8 units of FFP and no coagulation results or platelet count are available then two pools of cryoprecipitate and one pool of platelets may be given.

J Thromb Haemost 2016; 14: 205–10.

PBM IN THE OBSTETRIC POPULATION

Effective implementation of PBM pathways into routine obstetric care can reduce antenatal anemia ad reduce peripartum transfusion rate.

This is particularly important when cesarean section is planned due to higher average blood loss compared with vaginal delivery.

Cesarean section results in calculated blood loss ranging from **440 mL to 800 mL-** this equates to surgery with moderate-to-high blood loss (>500mL) as defined by recent international consensus guidelines.




Catchement area of 1.128.570 inhabitants (25% regional population)

15 public hospitals and 14 private hospitals

4.691 beds

10.000 deliveries/year

3 Hospital Bank
1 Blood establishment (processed about 70.000 units)

Transfusion Medicine Reviews 31 (2017) 62–71

Contents lists available at ScienceDirect

Transfusion Medicine Reviews

journal homepage: www.tmreviews.com

Patient Blood Management Bundles to Facilitate Implementation

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ABSTRACT

More than 30% of the world's population are anemic with serious economic consequences including reduced work capacity and other obstacles to national welfare and development. Red blood cell transfusion is the mainstay to correct anemia, but it is also 1 of the top 5 overused procedures. Patient blood management (PBM) is a proactive, patient-centered, and multidisciplinary approach to manage anemia, optimize hemostasis, minimize iatrogenic blood loss, and harness tolerance to anemia. Although the World Health Organization has endorsed PBM in 2010, many hospitals still seek guidance with the implementation of PBM in clinical routine. Given the use of proven change management principles, we propose simple, cost-effective measures enabling any hospital to reduce both anemia and red blood cell transfusions in surgical and medical patients. This article provides comprehensive bundles of PBM components encompassing 107 different PBM measures, divided into 6 bundle blocks acting as a working template to develop institutions' individual PBM practices for hospitals beginning a program or trying to improve an already existing program. A stepwise selection of the most feasible measures will facilitate the implementation of PBM. In this manner, PBM represents a new quality and safety standard.

PBM multidisciplinarity team (March 2018)

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA Azienda Unità Sanitaria Locale della Romagna DIREZIONE SANITARIA	ELENCO DEI COMPONENTI DEL GRUPPO DI LAVORO PER LA REDAZIONE DELLA PROCEDURA	Rev. 00 del 25/02/2019 S PA194_01 Pagina 1 di 1

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SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA Azienda Unità Sanitaria Locale della Romagna DIREZIONE SANITARIA	**PATIENT BLOOD MANAGEMENT** **I PILASTRO** **Gestione dell'anemia nel preoperatorio**	**P 194** Pagina 1 di 11

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA Azienda Unità Sanitaria Locale della Romagna DIREZIONE SANITARIA	**PREVENZIONE E TRATTAMENTO EMORRAGIA POST- PARTUM** **PROTOCOLLO TRASFUSIONALE**	Rev. 00 del 06/11/2018 **S PA148 _04** Pagina 1 di 6

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA Azienda Unità Sanitaria Locale della Romagna DIREZIONE SANITARIA	**PATIENT BLOOD MANAGEMENT** **SECONDO PILASTRO**	Rev. 00 del XX/XX/20XX **P codice XX** Pagina 1 di 11

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA Azienda Unità Sanitaria Locale della Romagna Direzione Sanitaria Aziendale	**Modalità di funzionamento del Sistema Integrato Assistenza Grandi Traumi S.I.A.T.**	Rev. 00 del 01/01/2018 **PA110** Pagina 52 di 59

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Emergency room

Operating room

Interventional radiology

ICU

Blood components

Coagulation Factor Concentrates

SERVER

BLOOD BANK FIXED MONITOR

ROTATIONAL THROMBOELASTOMETRY

Clin Ter 2017; 168 (5):e307-316. doi: 10.7417/T.2017.2026

The daily-practiced post-partum hemorrhage management: an Italian multidisciplinary attended protocol

G. Affronti[1], V. Agostini[2], A. Brizzi[3], L. Bucci[4], E. De Blasio[5], M.G. Frigo[6], C. Giorgini[7], M. Messina[8], A. Ragusa[9], F. Sirimarco[10], A. Svelato[9]

Long EXTEM CT →	FFP 20-30 ml/kg	
EXTEM ML > 15% →	Normal APTEM →	TXA 1 g
EXTEM A10 < 40 mm →	FIBTEM A5 ≤ 6 mm or A15 ≤ 8 mm→	Fibrinogen concentrate 2-4 g
	FIBTEM A5 ≥ 6 mm or A15 ≥ 8 mm→	Platelet concentrate
→ NO RESPONSE		
→ GO BACK TO FIGURE 2		

A10 = Clot firmness (mm) 10 minutes after CT; A5 = Clot firmness (mm) 5 minutes after CT; CT = Clotting time; FFP = Fresh Frozen Plasma; ML = Maximum lysis; TXA = Tranexamic acid

Fig. 3. Protocol: Point B. Transfusion therapy guided by ROTEM

Administer PLT Monitor coagulation: repeat INR, PPT, fibrinogen, PLT and TEG every 60-90 minutes Possible request for additional blood products				
R > 1 →	Deficiency of coagulation factors→	Plasma / Cryoprecipitate		
R > 0 < 1 → MA > 54 < 72 →	Surgical bleeding →	Experienced surgeon		
MA < 54 →	Functional fibrinogen (FF) →	MA > 9 < 29 →	Shortage of platelets →	Platelets
		MA < 9→	Deficiency of fibrinogen →	Fibrinogen
→ NO RESPONSE				
→ GO BACK TO FIGURE 2				

In ogni protocollo trasfusionale **deve** essere previsto l'impiego di **acido tranexamico** da somministrare alla dose di 1 gr in bolo ripetibile dopo 30 min o entro 24 ore dalla prima dose, in caso di ripresa del sanguinamento. Le raccomandazioni della WHO suggeriscono una somministrazione precoce dell'antifibrinolitico, possibilmente entro le 3 ore dal parto.

La scelta della strategia trasfusionale dipende in larga misura dalla disponibilità di strumenti Point of Care per il monitoraggio della coagulazione e di fibrinogeno concentrato.

1. **Strategia goal-directed con impiego di fattori (CF*)**: prevede il monitoraggio sequenziale della coagulazione con tecniche viscoelastiche e il rapido ripristino di valori fisiologici di fibrinogeno ove si evidenzi un deficit. Tenuto conto che la fibrinogenemia fisiologica a termine di gravidanza è molto elevata (4,5-5,8 g/L), gli abituali criteri di "allarme" devono essere adattati. Una riduzione del fibrinogeno Clauss al di sotto dei 2 gr impone una rapida correzione in caso di sanguinamento attivo. La somministrazione di concentrato di fibrinogeno deve essere associata a trasfusione di emazie e se necessario, di piastrine. Il vantaggio della strategia CF è quello di consentire un intervento molto precoce unitamente al ripristino effettivo dei valori di fibrinogeno. Lo svantaggio è relativo al fatto che per garantire un adeguato supporto volemico è spesso necessario ricorrere all'infusione di volumi importanti di cristalloidi. Le infusioni massive di cristalloidi favoriscono l'edema tissutale, il danno endoteliale e la diluizione degli altri fattori della coagulazione. Per questo motivo, qualora l'emorragia non dovesse essere controllata, è opportuno ricorrere anche all'impiego di plasma.

2. **Strategia con "pacchetti trasfusionali":** prevede la trasfusione di plasma ed emazie (ed eventualmente piastrine) in un rapporto fisso tra plasma fresco congelato (PFC) ed emazie concentrate (EC) pari a 1:1, 2:3 o 4:6. Per la definizione del rapporto ottimale tra gli emocomponenti si fa riferimento a protocolli, mutuati dalla traumatologia, anche se non sono disponibili prove solide in caso di emorragia ostetrica. Le più recenti linee guida sulla gestione della emorragia ostetrica, basate sul consenso tra esperti, promuovono tuttavia un uso precoce del PFC, con un rapporto tra PFC ed EC pari a 4:6. **Nella AUSL della Romagna i volumi medi delle unità di plasma da aferesi e di emazie concentrate leucodeplete sono rispettivamente di 700Ml e 260Ml, pertanto il rapporto 1:1 corrisponde a 1 unità di plasma e 3 di emazie**.

L'uso di rFVIIa, in pazienti non affetti da emofilia, per ridurre il sanguinamento post operatorio in pazienti sottoposti a interventi di chirurgia maggiore e in pazienti con gravi traumi, è stato valutato da alcuni studi con risultati promettenti.

Un protocollo per la gestione dell'EPP basato su un approccio pragmatico prevede la distinzione di due categorie di pazienti sulla base della stima della perdita e delle condizioni emodinamiche:

1. pazienti con perdita tra 500 e 1000 mL senza segni di instabilità emodinamica che richiedono un monitoraggio di base e l'allerta del personale (**scenario A**)
2. pazienti con perdita >1000 mL e segni di instabilità emodinamica che richiedono un supporto precoce della coagulazione (**scenario B**)

SCENARIO A

CHIEDERE AIUTO

Ginecologo e un secondo esperto in ostetricia
Allertare l'anestesista, la medicina trasfusionale, la sala operatoria e la radiologia interventistica (se disponibile)

↓

GARANTIRE GLI ACCESSI VENOSI

Agocannula da 16 G o 14 G
Catetere vescicale

↓

RICHIEDERE ESAMI EMOCOAGULATIVI

Test pretrasfusionali (gruppo sanguigno e ricerca anticorpi irregolari), emocromo, PT,aPTT, fibrinogeno Clauss
Se disponibili strumenti per il monitoraggio viscoelastico (tromboelastometro/elastografo) iniziare il monitoraggio

↓

RICHIEDERE EMAZIE CONCENTRATE

4 unità di emazie concentrate

↓

SOMMINISTRARE TERAPIA FARMACOLOGICA

Ossitocina (20 UI in 500 mL di soluzione salina in 2 ore); se dopo 20 min non si osserva nessuna risposta, usare un uterotonico di seconda linea
Somministrare a c. tranexamico 1 gr in bolo

↓

EVITARE: ipotermia, acidosi (lattati>2mmol/L)

↓

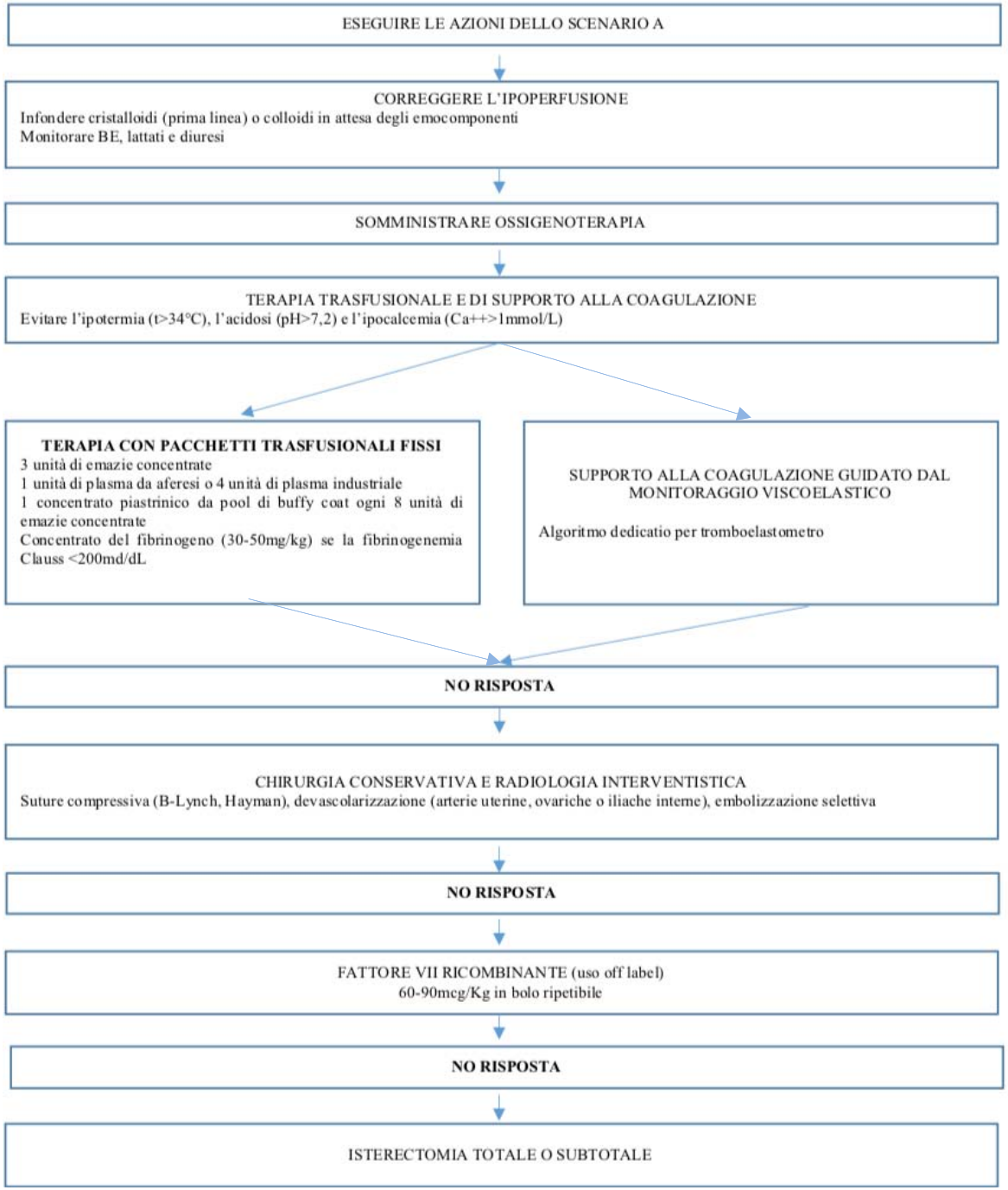
STABILIRE E RISOLVERE LE CAUSE DEL SANGUINAMENTO (4T)

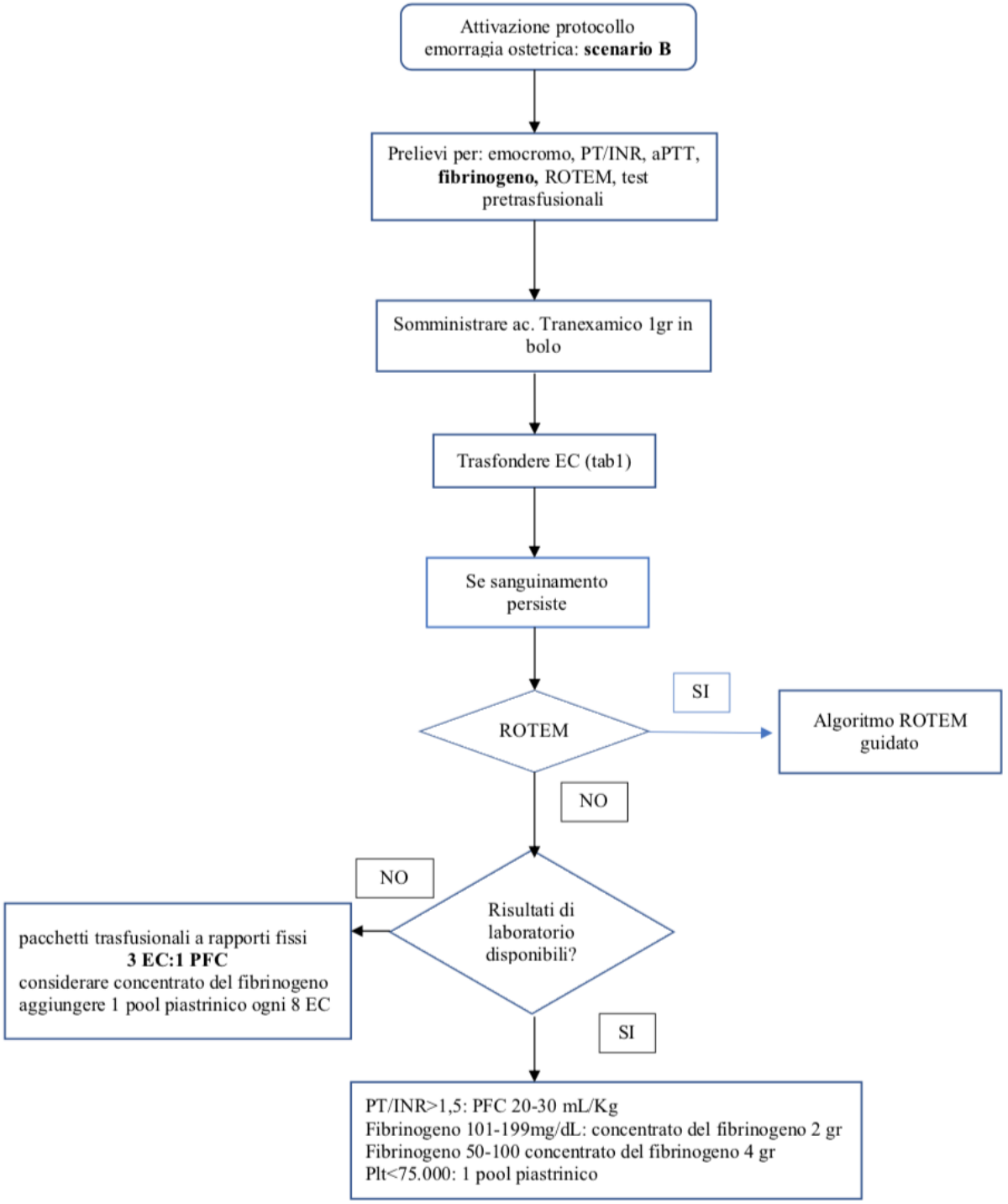
↓

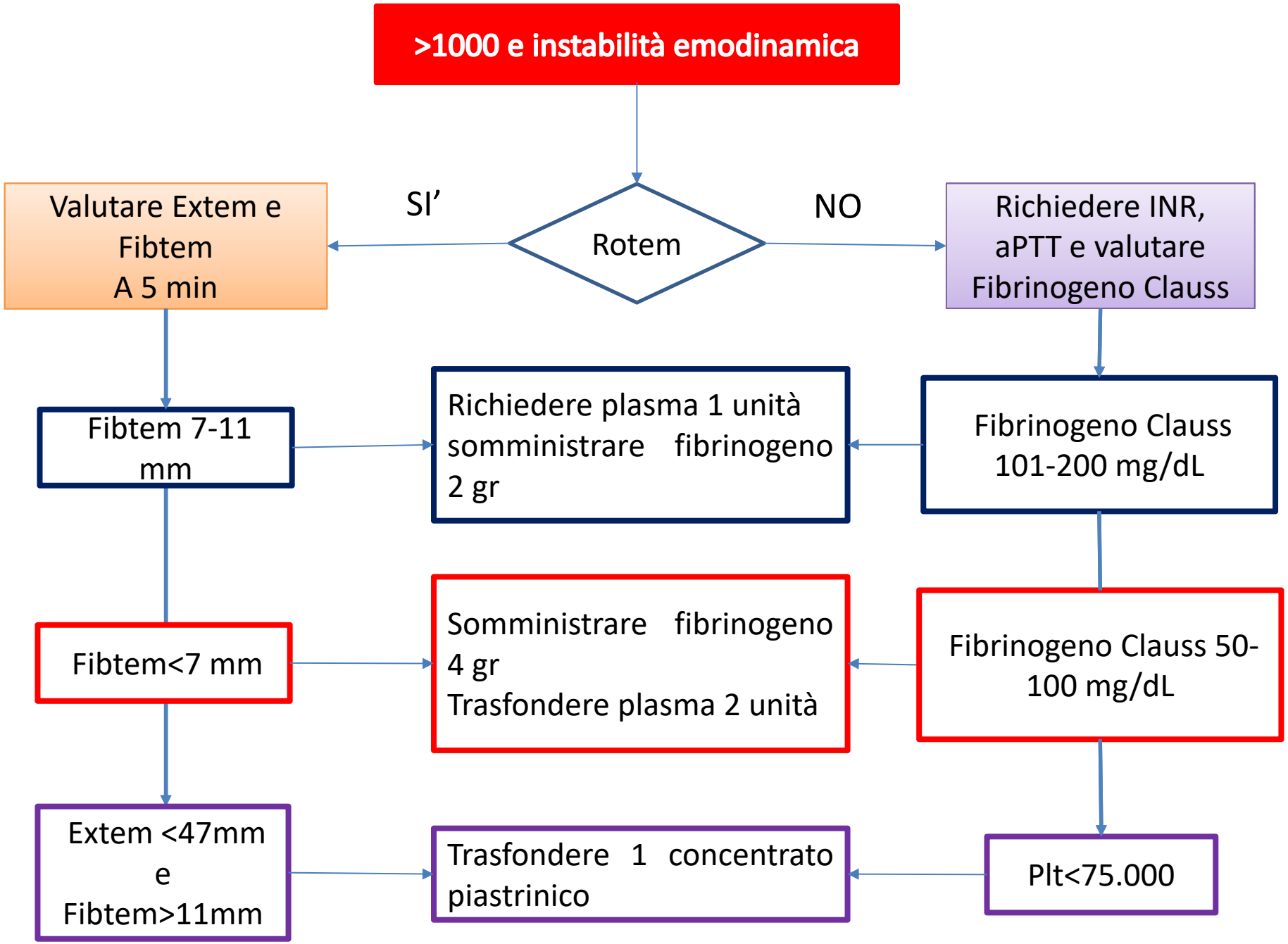
Se il sanguinamento persiste e non si è trovata la causa del sanguinamento procedere come da scenario B

SCENARIO

B


ESEGUIRE LE AZIONI DELLO SCENARIO A
CORREGGERE L'IPOPERFUSIONE
Infondere cristalloidi (prima linea) o colloidi in attesa degli emocomponenti
Monitorare BE, lattati e diuresi
SOMMINISTRARE OSSIGENOTERAPIA
TERAPIA TRASFUSIONALE E DI SUPPORTO ALLA COAGULAZIONE
Evitare l'ipotermia (t>34°C), l'acidosi (pH>7,2) e l'ipocalcemia (Ca++>1mmol/L)
TERAPIA CON PACCHETTI TRASFUSIONALI FISSI
3 unità di emazie concentrate
1 unità di plasma da aferesi o 4 unità di plasma industriale
1 concentrato piastrinico da pool di buffy coat ogni 8 unità di emazie concentrate
Concentrato del fibrinogeno (30-50mg/kg) se la fibrinogenemia Clauss <200md/dL
SUPPORTO ALLA COAGULAZIONE GUIDATO DAL MONITORAGGIO VISCOELASTICO
Algoritmo dedicatio per tromboelastometro
NO RISPOSTA
CHIRURGIA CONSERVATIVA E RADIOLOGIA INTERVENTISTICA
Suture compressiva (B-Lynch, Hayman), devascolarizzazione (arterie uterine, ovariche o iliache interne), embolizzazione selettiva
NO RISPOSTA
FATTORE VII RICOMBINANTE (uso off label)
60-90mcg/Kg in bolo ripetibile
NO RISPOSTA
ISTERECTOMIA TOTALE O SUBTOTALE


Attivazione protocollo emorragia ostetrica: **scenario B**
Prelievi per: emocromo, PT/INR, aPTT, **fibrinogeno,** ROTEM, test pretrasfusionali
Somministrare ac. Tranexamico 1gr in bolo
Trasfondere EC (tab1)
Se sanguinamento persiste
ROTEM
SI
Algoritmo ROTEM guidato
NO
Risultati di laboratorio disponibili?
NO
pacchetti trasfusionali a rapporti fissi
3 EC:1 PFC
considerare concentrato del fibrinogeno
aggiungere 1 pool piastrinico ogni 8 EC
SI
PT/INR>1,5: PFC 20-30 mL/Kg
Fibrinogeno 101-199mg/dL: concentrato del fibrinogeno 2 gr
Fibrinogeno 50-100 concentrato del fibrinogeno 4 gr
Plt<75.000: 1 pool piastrinico


>1000 e instabilità emodinamica
Rotem
SI'
NO
Valutare Extem e Fibtem A 5 min
Richiedere INR, aPTT e valutare Fibrinogeno Clauss
Fibtem 7-11 mm
Richiedere plasma 1 unità somministrare fibrinogeno 2 gr
Fibrinogeno Clauss 101-200 mg/dL
Fibtem<7 mm
Somministrare fibrinogeno 4 gr
Trasfondere plasma 2 unità
Fibrinogeno Clauss 50-100 mg/dL
Extem <47mm e Fibtem>11mm
Trasfondere 1 concentrato piastrinico
Plt<75.000

SUMMARY

1. Successful management of PPH requires early intervention at the bedside from a multidisciplinary team
2. Coagulation studies should be performed ASAP or the use of POCT should be considered
3. Tranex 1 gr i.v. ASAP; 3h windows
4. Women with a fibrinogen of <2g/L are at high risk of severe PPH and need urgent coagulation product replacement (cryo, fib concentrate)
5. Most women who have PPH have normal clotting and fibrinogen: early FFP IS NOT NECESSARY