Hémorragie du Post-Partum

(HPP)

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Conflits d'intérêt potentiels

- Laboratoire LFB (Clottafact®)
- Laboratoire Novonordisk (Novoseven®)
- Laboratoire Fresenius (Voluven®)

HPP : définition et incidence

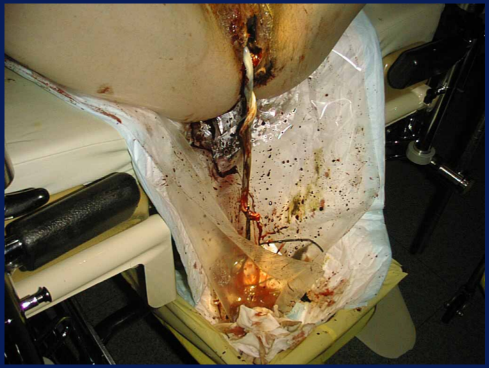
- HPP « immédiat » : pertes sanguines > 500 ml, dans les 24 h après l'accouchement
  - ➡ ≈ 5% des accouchements
- Sévère : > 1000 ml (voire 1500 ml)
  ou ↘ Hte > 10% (voire ↘ Hb > 4 g/dL)
  - ➡ ≈ 1% des accouchements

Diagnostic d'HPP : souvent pas si évident !

- **Saignement vaginal** souvent sous estimé :

  sac de recueil non utilisé

  - ➔ circonscrit dans l'utérus : AU
  - ➔ circonscrit derrière le placenta : HRP
  - ➔ hémopéritoine : RU
  - ➔ hématomes para vaginal ou pelvien : TG



- **Htc / Hb** (appareil portable) :

  ➔ varie selon le remplissage vasculaire et la vitesse du saignement

- **Instabilité hémodynamique** : trop tardive, voire absente en cas de réanimation précoce et énergique

Diagnostic d’HPP :

- Le saignement vaginal important extériorisé, la chute de l’Hb et l’hypoTA peuvent manquer

  ➔ peut induire en erreur l’**obstétricien !**

- Critères meilleurs = signes **indirects**
  - Besoins importants de remplissage vasculaire
    besoins de catécholamines
    besoins de transfusion
  - Troubles de l’hémostase

➔ évalués par l’**anesthésiste** !

➔ **communication** cruciale avec obstétricien !

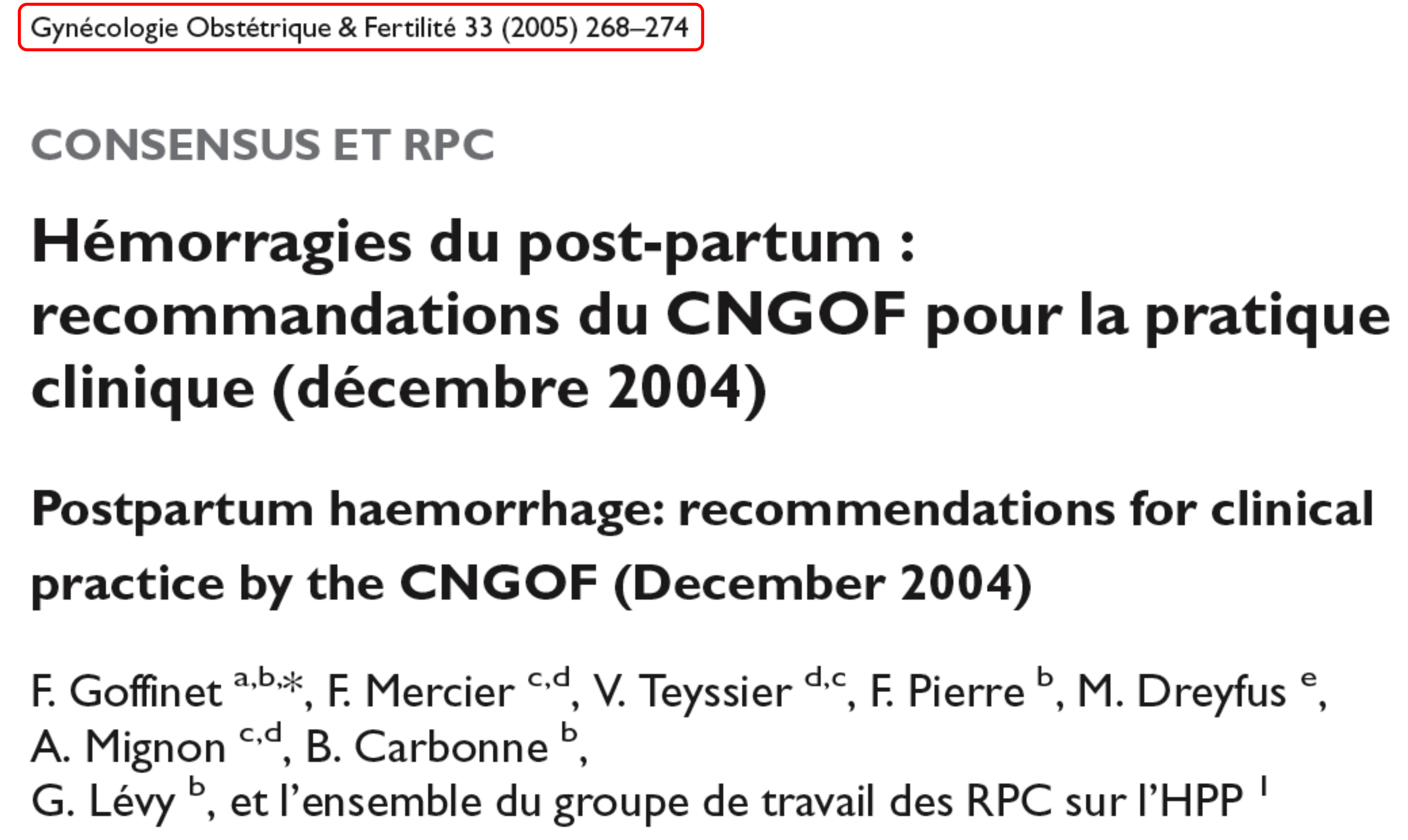
L’analyse des dossiers par le Comité National d’Experts sur la Mortalité Maternelle (CNEMM) montre que l’HPP :

- reste la 1ère cause de Mortalité Maternelle (MM)

- reste la cause de MM ayant le plus fort % d’évitabilité

(1er, 2nd et 3ème Rapports du CNEMM : 2000, 2006, 2010)

http://www.invs.sante.fr/publications/2010/mortalite_maternelle/rapport_mortalite_maternelle.pdf



Gynécologie Obstétrique & Fertilité 33 (2005) 268–274

CONSENSUS ET RPC

Hémorragies du post-partum : recommandations du CNGOF pour la pratique clinique (décembre 2004)

Postpartum haemorrhage: recommendations for clinical practice by the CNGOF (December 2004)

F. Goffinet [a,b,*], F. Mercier [c,d], V. Teyssier [d,c], F. Pierre [b], M. Dreyfus [e],
A. Mignon [c,d], B. Carbonne [b],
G. Lévy [b], et l'ensemble du groupe de travail des RPC sur l'HPP [1]

multidisciplinaire: CNGOF, CARO-SFAR, SFR, EFS, CNSF

Journées du CNGOF, déc 2004

J Gynecol Obstet Biol Reprod 2004, vol 33, supp N°8

1 - Fréquence, conséquences en termes de **santé** et FDR avant l'accouchement

2 - Gestion du risque **anténatal**

3 - FDR au cours du **travail** et prévention clinique et pharmacologique de l’HPP

4 & **5** - Prise en charge **obstétricale** / **anesthésique initiale** en cas d’HPP

6 & **7** - Prise en charge **obstétricale** / **anesthésique** en cas d’une HPP qui persiste malgré les mesures initiales ou qui est **grave** d'emblée

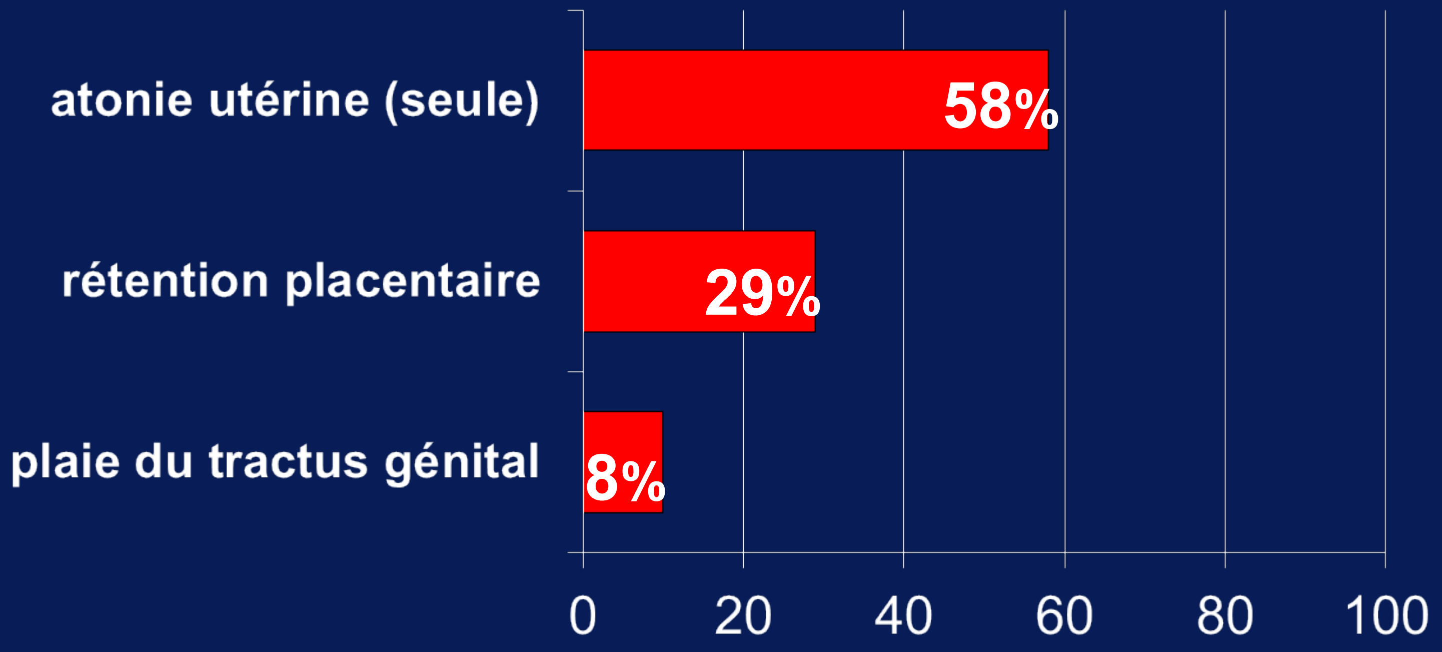
8 - Modalités d’un **transfert** maternel dans le cadre d’une HPP

9 - Prise en charge des HPP graves : indications et techniques de **l'embolisation** artérielle

10 - HPP immédiat : techniques et indications de la **chirurgie**

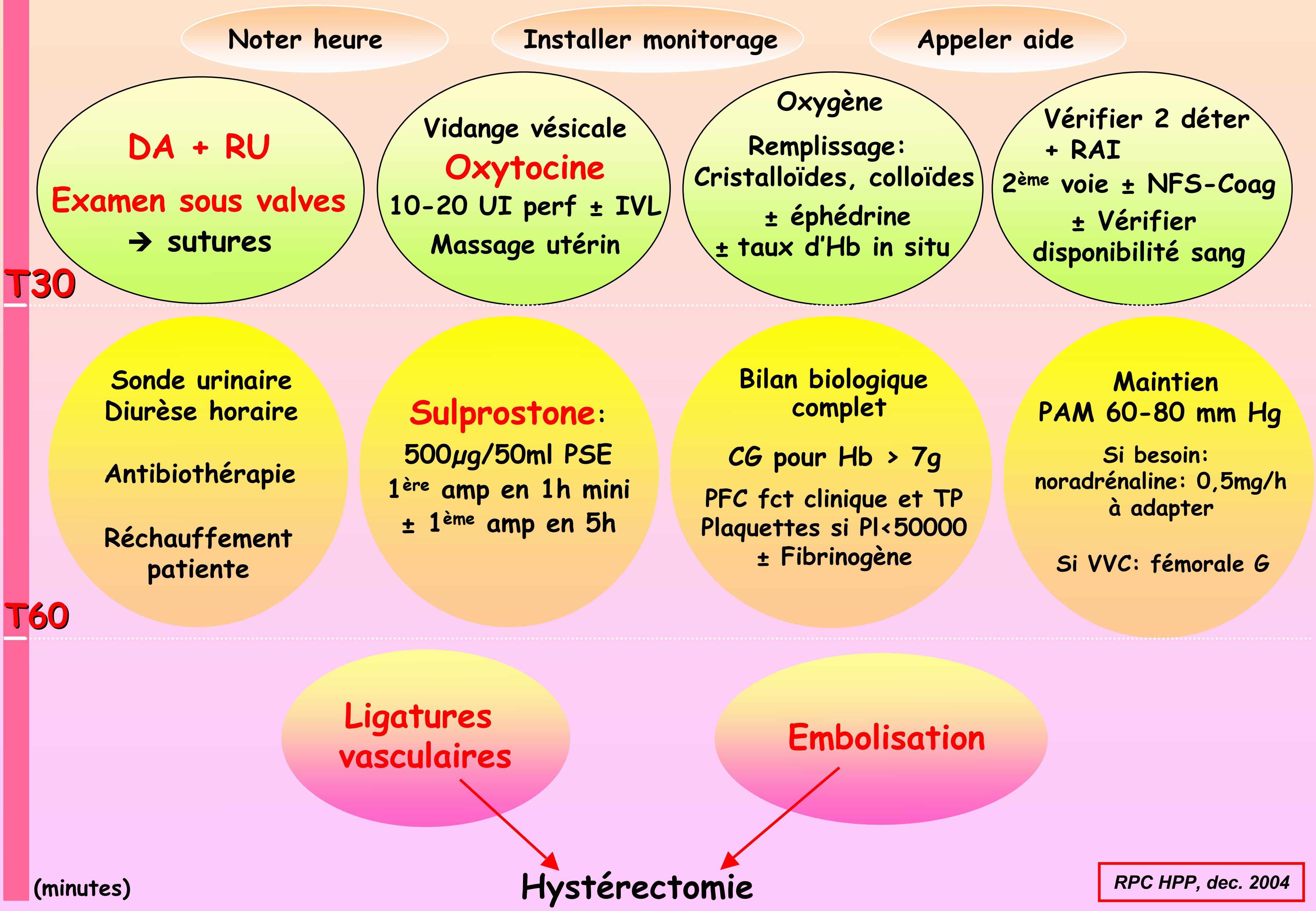
11 - Gestion des **PSL** dans le cadre des HPP immédiat

Les 3 étiologies les plus fréquentes d’HPP



➔ constituent 90 à 95% de l’ensemble des HPP

Hémorragie en salle de naissance



Noter heure

Installer monitorage

Appeler aide

DA + RU

Examen sous valves

→ sutures

Vidange vésicale

Oxytocine

10-20 UI perf ± IVL

Massage utérin

Oxygène

Remplissage:
Cristalloïdes, colloïdes

± éphédrine

± taux d'Hb in situ

Vérifier 2 déter
+ RAI

2ème voie ± NFS-Coag

± Vérifier
disponibilité sang

T30

Sonde urinaire
Diurèse horaire

Antibiothérapie

Réchauffement
patiente

Sulprostone:

500µg/50ml PSE

1ère amp en 1h mini

± 1ème amp en 5h

Bilan biologique
complet

CG pour Hb > 7g

PFC fct clinique et TP
Plaquettes si Pl<50000
± Fibrinogène

Maintien
PAM 60-80 mm Hg

Si besoin:
noradrénaline: 0,5mg/h
à adapter

Si VVC: fémorale G

T60

Ligatures vasculaires

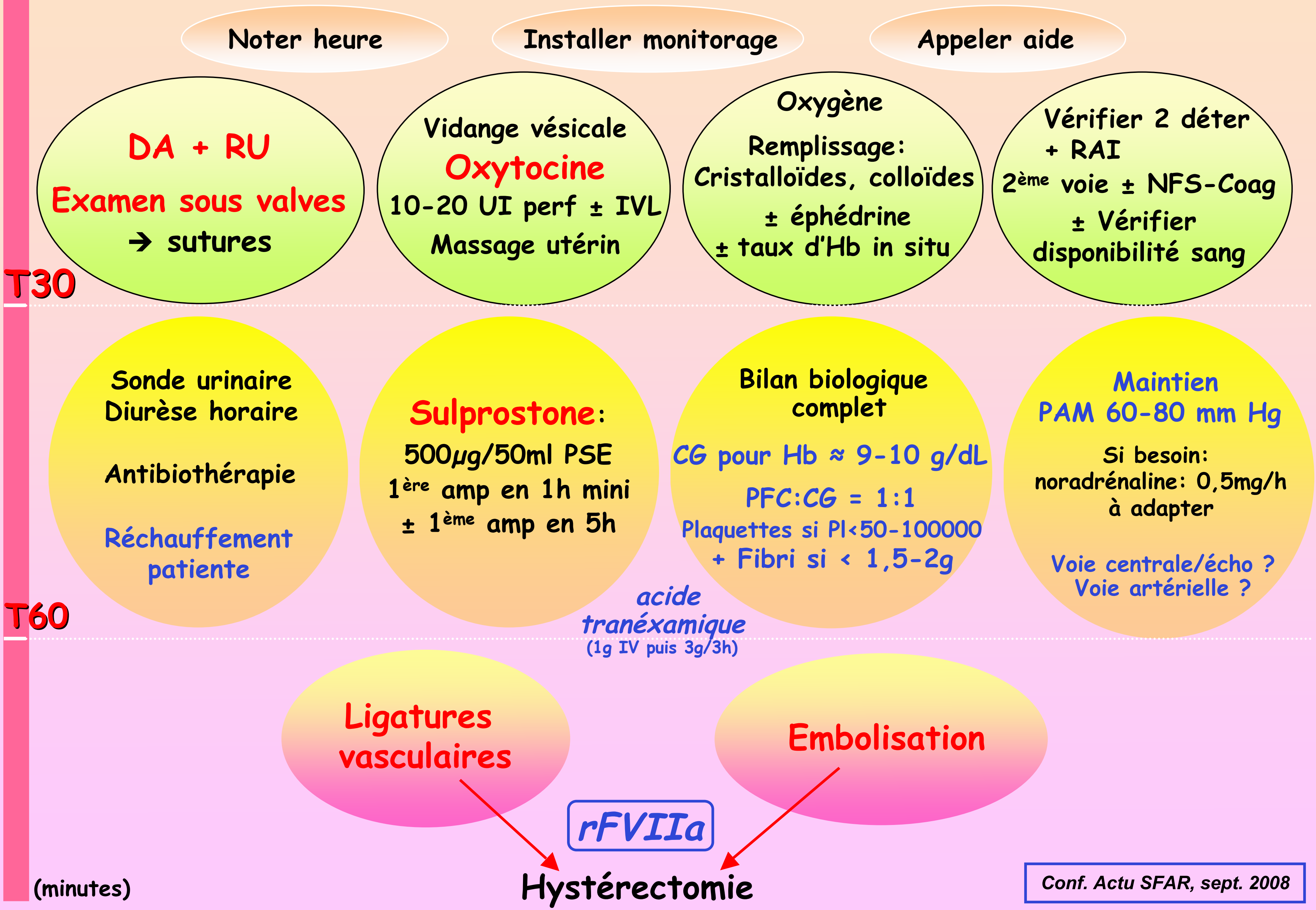
Embolisation

Hystérectomie

(minutes)

RPC HPP, dec. 2004

Hémorragie en salle de naissance



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Vérifier 2 déter
+ RAI

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± Vérifier disponibilité sang

T30

Sonde urinaire
Diurèse horaire

Antibiothérapie

Réchauffement patiente

Sulprostone:

500µg/50ml PSE

1ère amp en 1h mini

± 1ème amp en 5h

Bilan biologique complet

CG pour Hb ≈ 9-10 g/dL

PFC:CG = 1:1

Plaquettes si Pl<50-100000

+ Fibri si < 1,5-2g

Maintien
PAM 60-80 mm Hg

Si besoin:
noradrénaline: 0,5mg/h
à adapter

Voie centrale/écho ?
Voie artérielle ?

acide tranéxamique
(1g IV puis 3g/3h)

T60

Ligatures vasculaires

Embolisation

rFVIIa

Hystérectomie

(minutes)

Conf. Actu SFAR, sept. 2008

ELSEVIER
SAUNDERS

ANESTHESIOLOGY
CLINICS

Anesthesiology Clin
26 (2008) 53–66

Major Obstetric Hemorrhage

Frederic J. Mercier, MD, PhD[a,*],
Marc Van de Velde, MD, PhD[b]

[a]*Department of Anesthesia and Intensive Care, Hopital Antoine Beclere—APHP and Universite Paris-Sud, 157 rue de la Porte de Trivaux, 92141 Clamart Cedex BP 405, France*
[b]*Department of Anaesthesiology, University Hospitals Gasthuisberg, Katholieke Universiteit Leuven, Herestraat 49, B-3000 Leuven, Belgium*

Acide tranéxamique

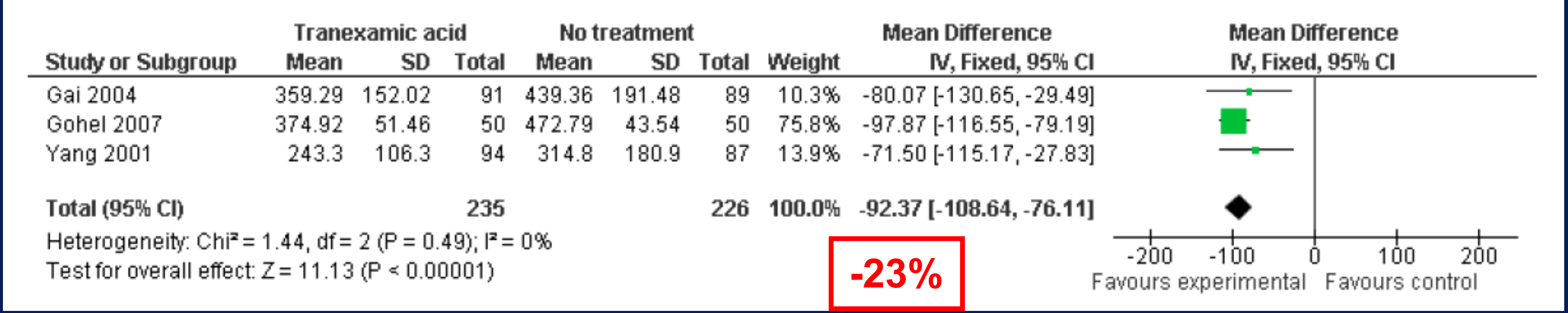
(Exacyl®)

Anti-fibrinolytic agents in post partum haemorrhage: a systematic review

Pili Ferrer, Ian Roberts*, Emma Sydenham, Karen Blackhall and Haleema Shakur

BMC Pregnancy and Childbirth 2009, **9**:29

Results: We identified three randomised controlled trials involving 461 participants. The trials compared tranexamic acid with no treatment and reported blood loss after delivery. In all three trials, allocation concealment was either inadequate or unclear. The administration of tranexamic acid was associated with a reduction in blood loss of 92 millilitres (95%CI 76 to 109). The most frequently reported adverse effect of tranexamic acid was nausea, although the increase was easily compatible with the play of chance (RR 4.63, 95%CI 0.23 to 95.14).



	Tranexamic acid			No treatment				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
Gai 2004	359.29	152.02	91	439.36	191.48	89	10.3%	-80.07 [-130.65, -29.49]
Gohel 2007	374.92	51.46	50	472.79	43.54	50	75.8%	-97.87 [-116.55, -79.19]
Yang 2001	243.3	106.3	94	314.8	180.9	87	13.9%	-71.50 [-115.17, -27.83]
Total (95% CI)			**235**			**226**	**100.0%**	**-92.37 [-108.64, -76.11]**

Heterogeneity: Chi² = 1.44, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 11.13 (P < 0.00001)

-23%

HPP > 4-500 ml : RR = 0.44 (95%CI 0.31 to 0.64).

Essai clinique randomisé contrôlé évaluant l'impact d'un traitement antifibrinolytique sur le volume de l'hémorragie du post-partum

étude prospective multicentrique
EXADELI

Crit Care Med 2011 : 15(2):R117. Epub 2011 Apr 15.

Anne-Sophie DUCLOY-BOUTHORS
Maternité Jeanne de Flandre
CHRU de LILLE

→ **4g** en 1h suivi de **1g/h** pendant 6h

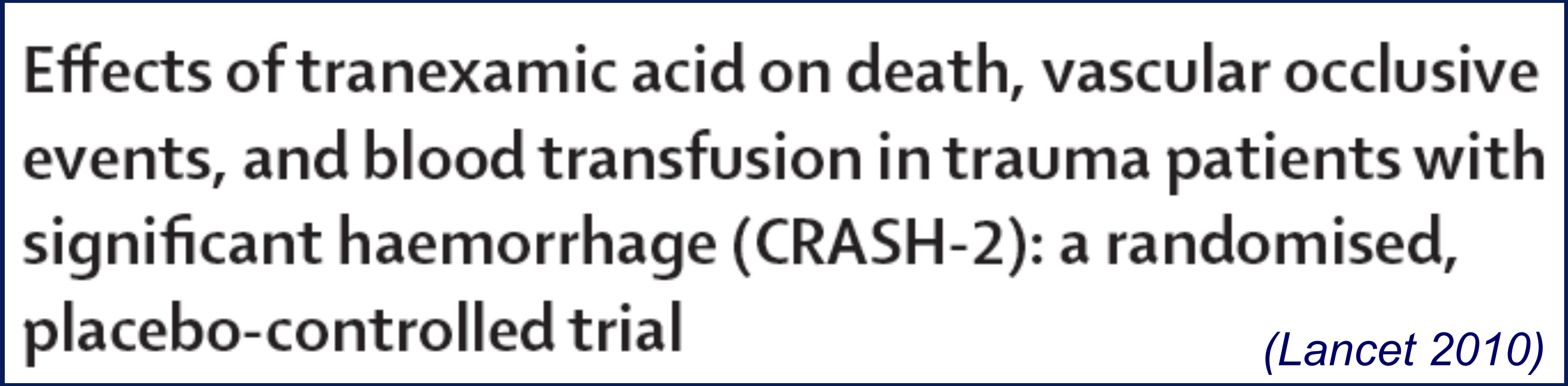
Efficacité

	Gr. Contrôle (n=74)	Gr. Exacyl (n=78)	*P*
↘ Hb > 4g	34	15	< 0,001
Total CG	62	28	< 0,001
Nalador®	36	34	NS
Embolisation	7	4	NS
Lig. / Hyst.	1 / 1	0 / 0	NS

Etude prospective multicentrique EXADELI

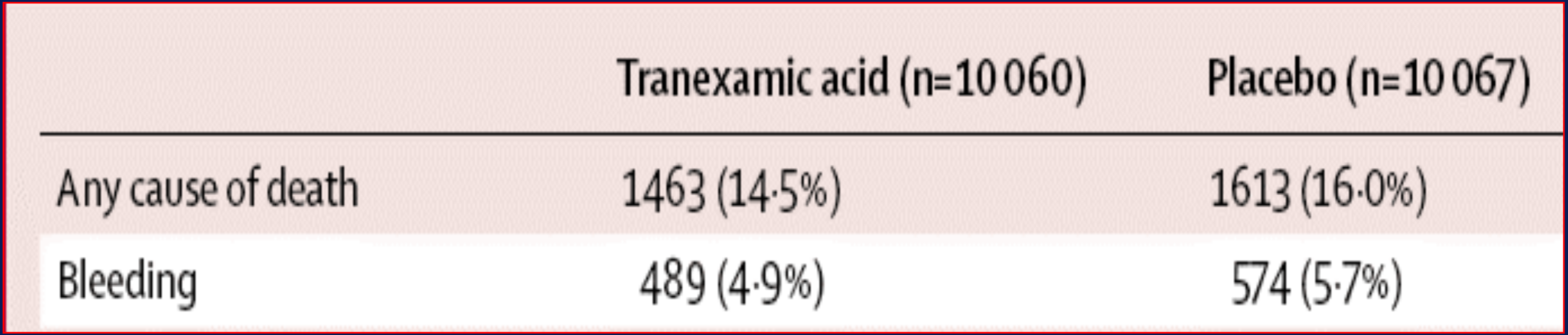
- réduit le volume de l’HPP de 25 à 50%
- Mais effets secondaires à type de troubles visuels et de nausées vomissements
- délai d’action de 30 minutes possible

→ réduire les doses de moitié et administrer dès le début des troubles de l’hémostase ?



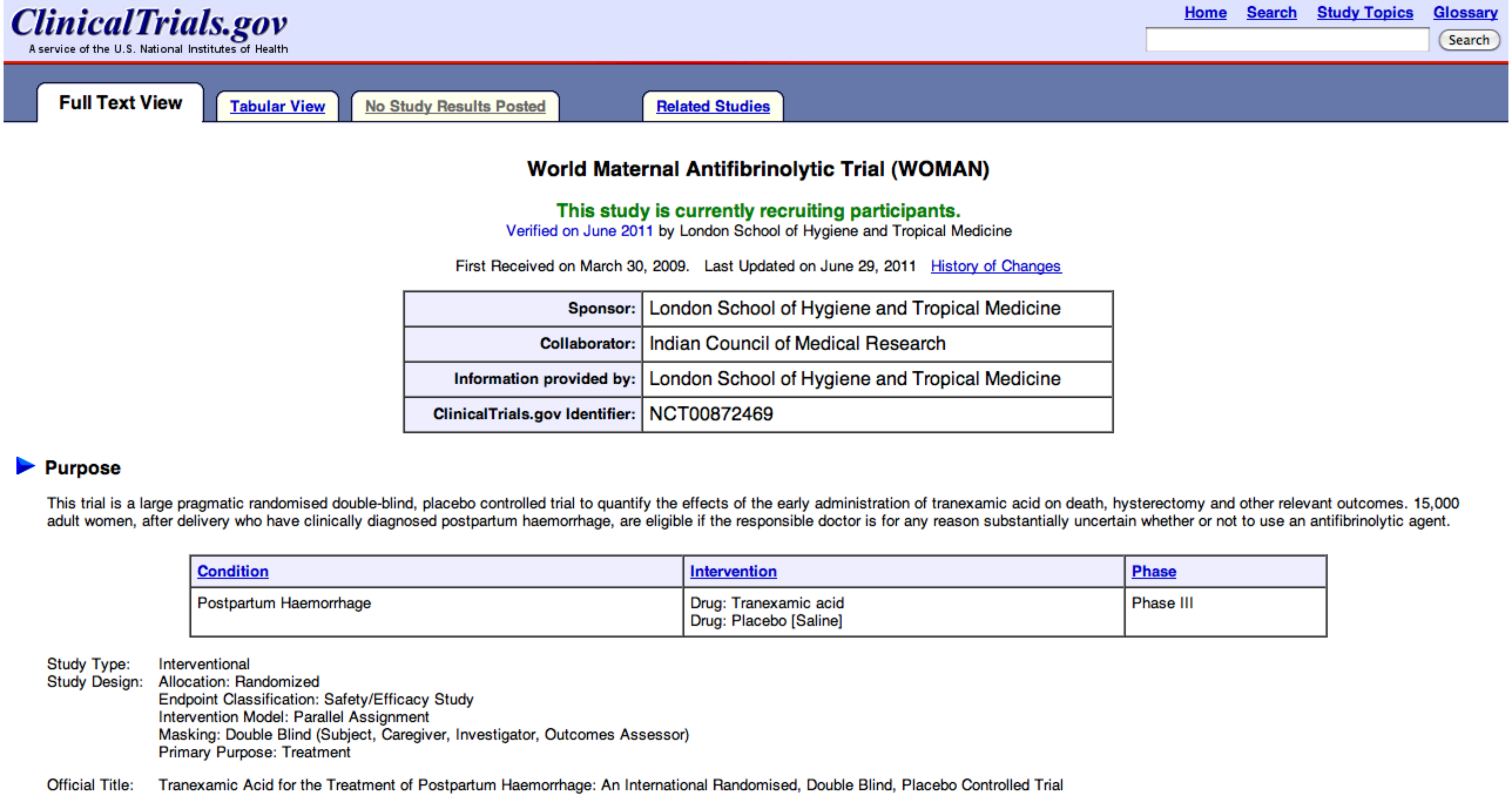
Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

(Lancet 2010)



	Tranexamic acid (n=10 060)	Placebo (n=10 067)
Any cause of death	1463 (14·5%)	1613 (16·0%)
Bleeding	489 (4·9%)	574 (5·7%)

→ **1g** IVL suivi de **1g** en perfusion IV sur 8h


ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Home
Search
Study Topics
Glossary
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Full Text View
Tabular View
No Study Results Posted
Related Studies

World Maternal Antifibrinolytic Trial (WOMAN)

This study is currently recruiting participants.
Verified on June 2011 by London School of Hygiene and Tropical Medicine

First Received on March 30, 2009. Last Updated on June 29, 2011 History of Changes

Sponsor:	London School of Hygiene and Tropical Medicine
Collaborator:	Indian Council of Medical Research
Information provided by:	London School of Hygiene and Tropical Medicine
ClinicalTrials.gov Identifier:	NCT00872469

Purpose

This trial is a large pragmatic randomised double-blind, placebo controlled trial to quantify the effects of the early administration of tranexamic acid on death, hysterectomy and other relevant outcomes. 15,000 adult women, after delivery who have clinically diagnosed postpartum haemorrhage, are eligible if the responsible doctor is for any reason substantially uncertain whether or not to use an antifibrinolytic agent.

Condition	Intervention	Phase
Postpartum Haemorrhage	Drug: Tranexamic acid Drug: Placebo [Saline]	Phase III

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: Tranexamic Acid for the Treatment of Postpartum Haemorrhage: An International Randomised, Double Blind, Placebo Controlled Trial

Acide tranéxamique (Exacyl®)

« Protocole Béclère » :

➔ 1g IVL en 5-10 min

± 0,5 g / h (1-2 g / 2-4 h)

Fibrinogène

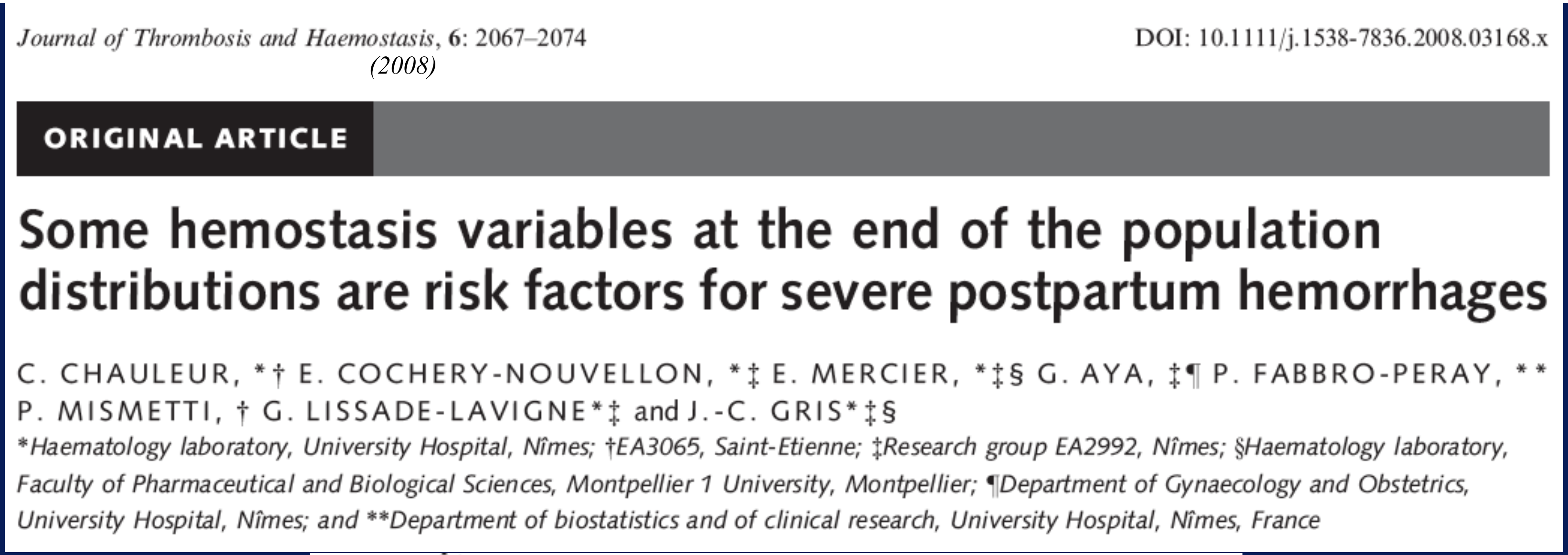
(Clottafact®)

RPC déc. 2004 : “L’intérêt d’un apport supplémentaire de fibrinogène dans le traitement de la CIVD est controversé”

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

Charbit et al, J Thromb Haemost 2007; 5: 266-73

- La fibrinogénémie est le seul paramètre indépendant qui soit associé avec une évolution sévère de l'HPP
- Taux FI > 4 g/l = VPN 79%
- Taux FI < 2 g/l = VPP 100%
- La valeur prédictive de ces résultats s'accentuent de H0 à H4



Journal of Thrombosis and Haemostasis, **6**: 2067–2074
(2008)

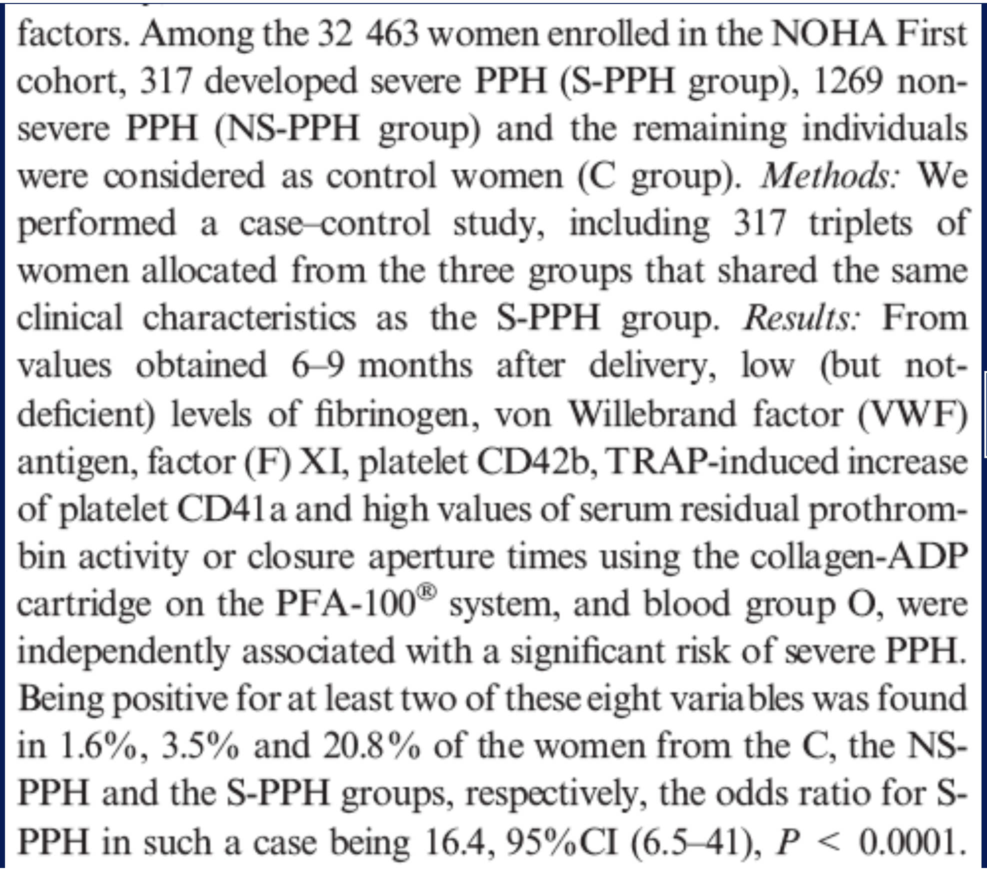
DOI: 10.1111/j.1538-7836.2008.03168.x

ORIGINAL ARTICLE

Some hemostasis variables at the end of the population distributions are risk factors for severe postpartum hemorrhages

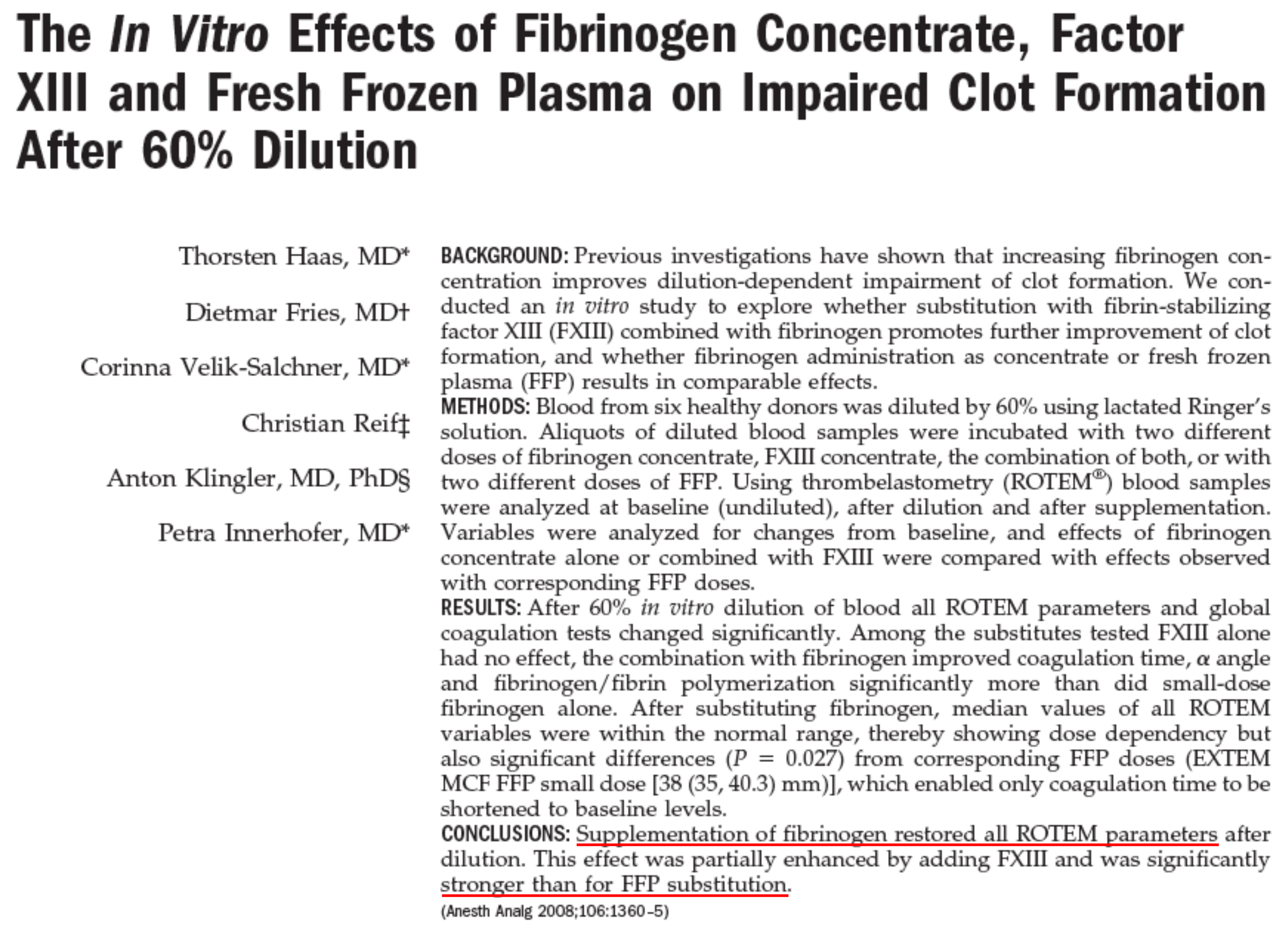
C. CHAULEUR,*† E. COCHERY-NOUVELLON,*‡ E. MERCIER,*‡§ G. AYA,‡¶ P. FABBRO-PERAY,** P. MISMETTI,† G. LISSADE-LAVIGNE*‡ and J.-C. GRIS*‡§

*Haematology laboratory, University Hospital, Nîmes; †EA3065, Saint-Etienne; ‡Research group EA2992, Nîmes; §Haematology laboratory, Faculty of Pharmaceutical and Biological Sciences, Montpellier 1 University, Montpellier; ¶Department of Gynaecology and Obstetrics, University Hospital, Nîmes; and **Department of biostatistics and of clinical research, University Hospital, Nîmes, France



factors. Among the 32 463 women enrolled in the NOHA First cohort, 317 developed severe PPH (S-PPH group), 1269 non-severe PPH (NS-PPH group) and the remaining individuals were considered as control women (C group). *Methods:* We performed a case–control study, including 317 triplets of women allocated from the three groups that shared the same clinical characteristics as the S-PPH group. *Results:* From values obtained 6–9 months after delivery, low (but not-deficient) levels of fibrinogen, von Willebrand factor (VWF) antigen, factor (F) XI, platelet CD42b, TRAP-induced increase of platelet CD41a and high values of serum residual prothrombin activity or closure aperture times using the collagen-ADP cartridge on the PFA-100® system, and blood group O, were independently associated with a significant risk of severe PPH. Being positive for at least two of these eight variables was found in 1.6%, 3.5% and 20.8% of the women from the C, the NS-PPH and the S-PPH groups, respectively, the odds ratio for S-PPH in such a case being 16.4, 95%CI (6.5–41), $P < 0.0001$.

Seuil fibri = 2 g / L



The *In Vitro* Effects of Fibrinogen Concentrate, Factor XIII and Fresh Frozen Plasma on Impaired Clot Formation After 60% Dilution

Thorsten Haas, MD*

Dietmar Fries, MD†

Corinna Velik-Salchner, MD*

Christian Reif‡

Anton Klingler, MD, PhD§

Petra Innerhofer, MD*

BACKGROUND: Previous investigations have shown that increasing fibrinogen concentration improves dilution-dependent impairment of clot formation. We conducted an *in vitro* study to explore whether substitution with fibrin-stabilizing factor XIII (FXIII) combined with fibrinogen promotes further improvement of clot formation, and whether fibrinogen administration as concentrate or fresh frozen plasma (FFP) results in comparable effects.

METHODS: Blood from six healthy donors was diluted by 60% using lactated Ringer's solution. Aliquots of diluted blood samples were incubated with two different doses of fibrinogen concentrate, FXIII concentrate, the combination of both, or with two different doses of FFP. Using thrombelastometry (ROTEM®) blood samples were analyzed at baseline (undiluted), after dilution and after supplementation. Variables were analyzed for changes from baseline, and effects of fibrinogen concentrate alone or combined with FXIII were compared with effects observed with corresponding FFP doses.

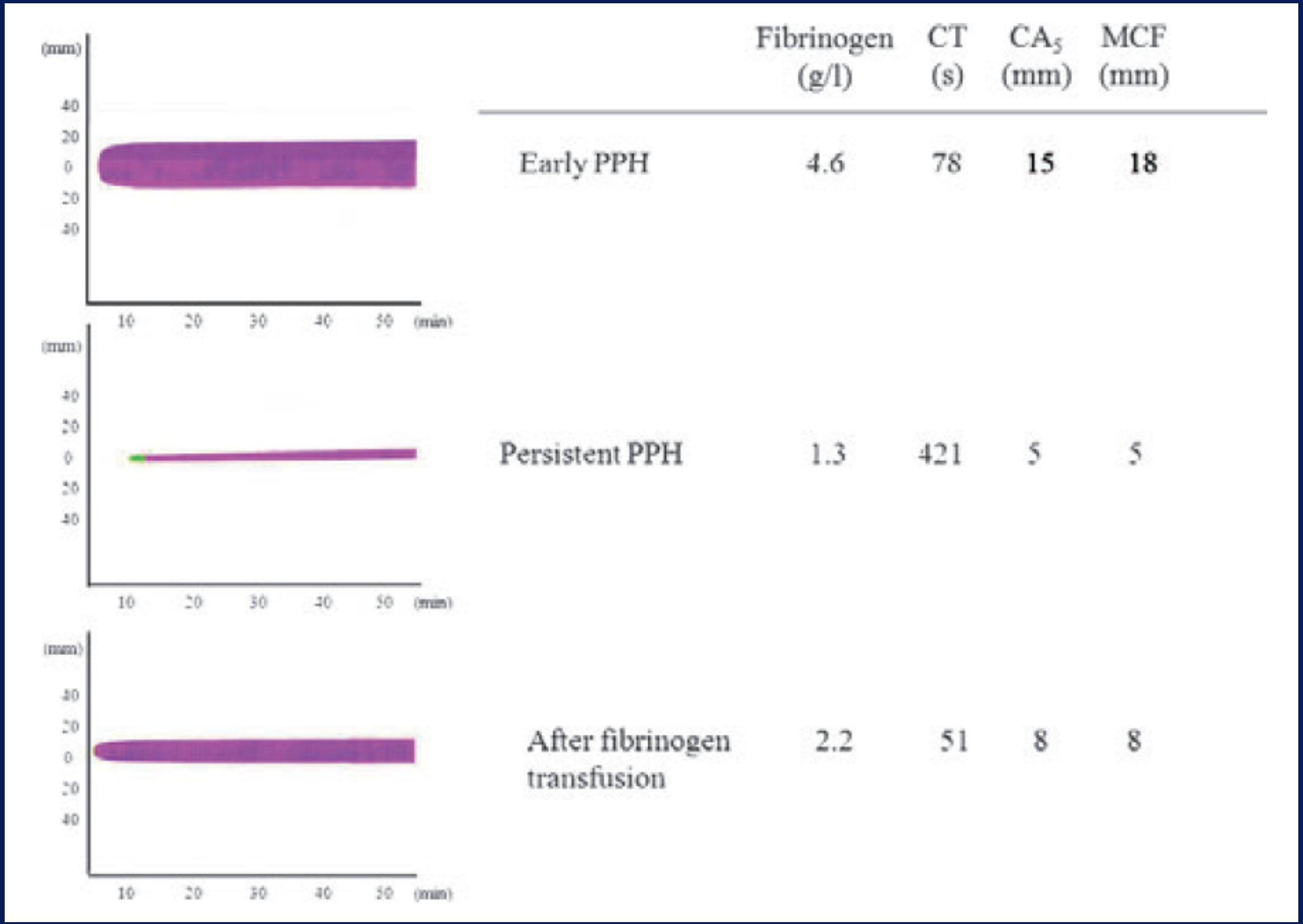
RESULTS: After 60% *in vitro* dilution of blood all ROTEM parameters and global coagulation tests changed significantly. Among the substitutes tested FXIII alone had no effect, the combination with fibrinogen improved coagulation time, α angle and fibrinogen/fibrin polymerization significantly more than did small-dose fibrinogen alone. After substituting fibrinogen, median values of all ROTEM variables were within the normal range, thereby showing dose dependency but also significant differences ($P = 0.027$) from corresponding FFP doses (EXTEM MCF FFP small dose [38 (35, 40.3) mm)], which enabled only coagulation time to be shortened to baseline levels.

CONCLUSIONS: Supplementation of fibrinogen restored all ROTEM parameters after dilution. This effect was partially enhanced by adding FXIII and was significantly stronger than for FFP substitution.

(Anesth Analg 2008;106:1360–5)

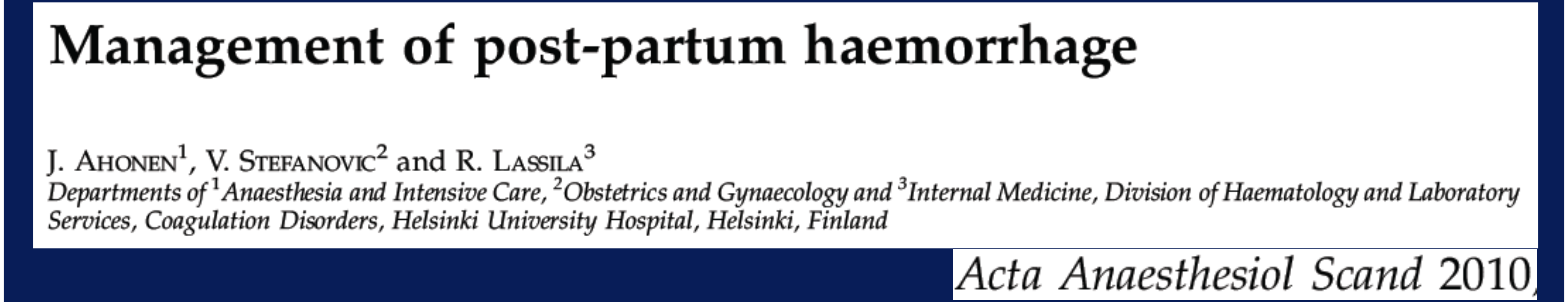
Beside assessment of fibrinogen level in PPH by thromboelastometry

Huissoud et al, BJOG 2009



	Fibrinogen (g/l)	CT (s)	CA_5 (mm)	MCF (mm)
Early PPH	4.6	78	**15**	**18**
Persistent PPH	1.3	421	5	5
After fibrinogen transfusion	2.2	51	8	8

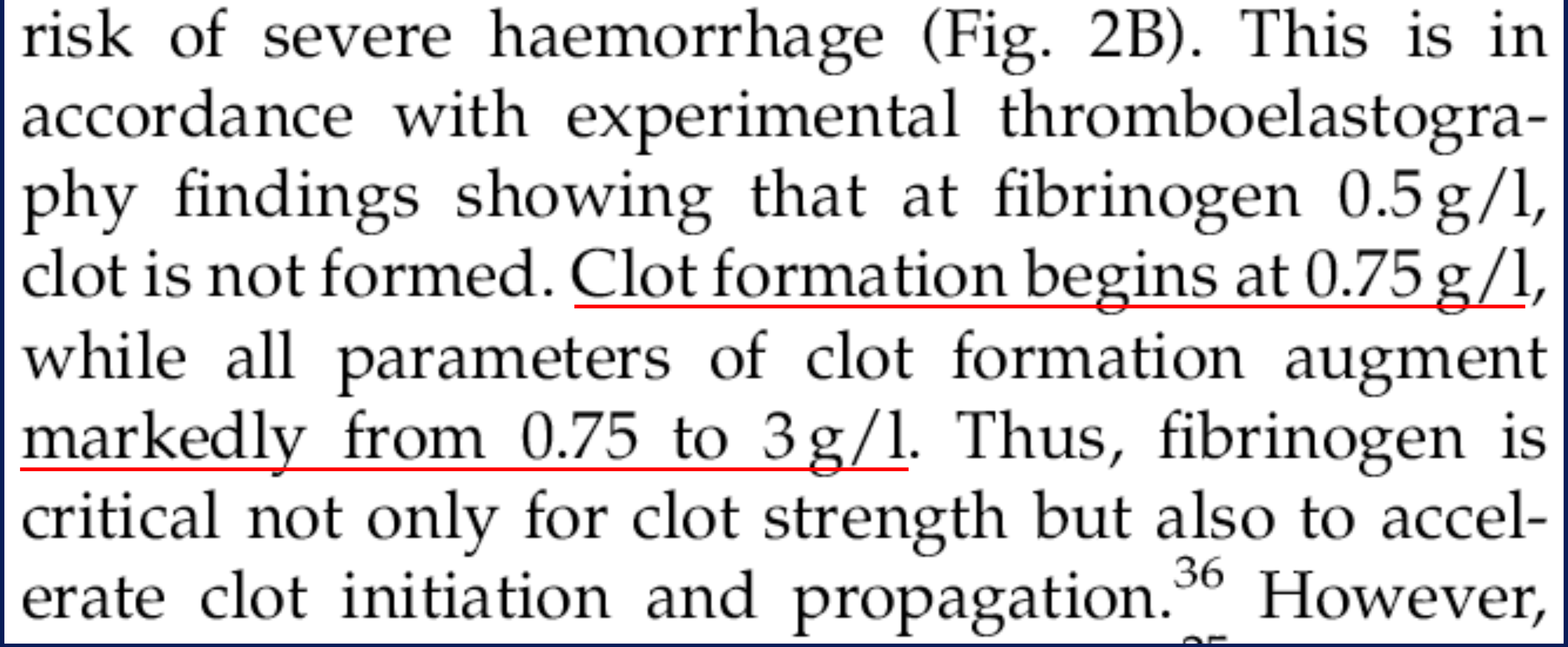
CA_{15} @ 6mm : valeur seuil pour détecter fibri < 1,5 g/l (Se = 100%, Spe = 88%)



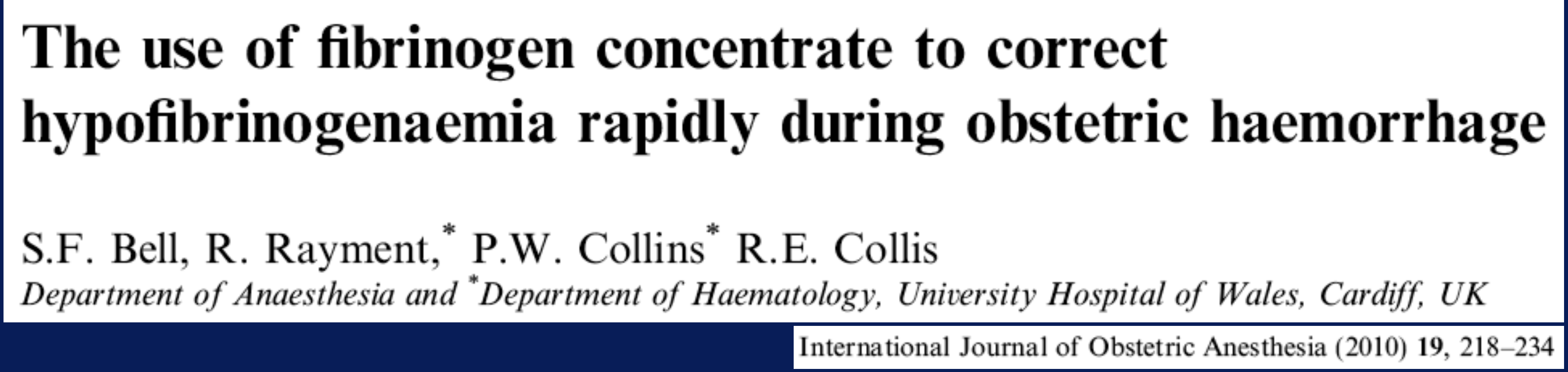
Management of post-partum haemorrhage

J. Ahonen[1], V. Stefanovic[2] and R. Lassila[3]
Departments of [1]Anaesthesia and Intensive Care, [2]Obstetrics and Gynaecology and [3]Internal Medicine, Division of Haematology and Laboratory Services, Coagulation Disorders, Helsinki University Hospital, Helsinki, Finland

Acta Anaesthesiol Scand 2010



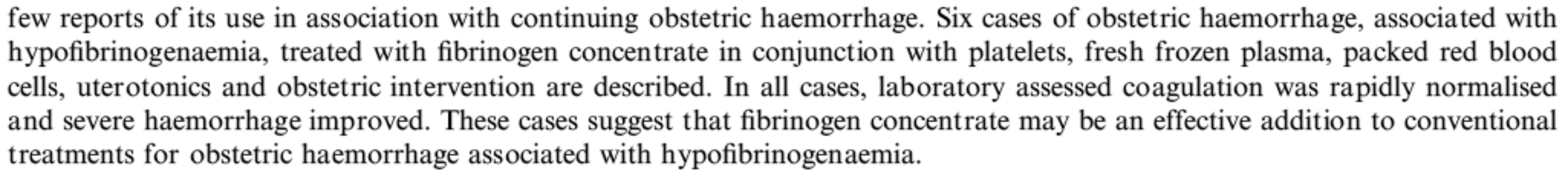
risk of severe haemorrhage (Fig. 2B). This is in accordance with experimental thromboelastography findings showing that at fibrinogen 0.5 g/l, clot is not formed. Clot formation begins at 0.75 g/l, while all parameters of clot formation augment markedly from 0.75 to 3 g/l. Thus, fibrinogen is critical not only for clot strength but also to accelerate clot initiation and propagation.[36] However,



The use of fibrinogen concentrate to correct hypofibrinogenaemia rapidly during obstetric haemorrhage

S.F. Bell, R. Rayment,* P.W. Collins* R.E. Collis
*Department of Anaesthesia and *Department of Haematology, University Hospital of Wales, Cardiff, UK*

International Journal of Obstetric Anesthesia (2010) **19**, 218–234



few reports of its use in association with continuing obstetric haemorrhage. Six cases of obstetric haemorrhage, associated with hypofibrinogenaemia, treated with fibrinogen concentrate in conjunction with platelets, fresh frozen plasma, packed red blood cells, uterotonics and obstetric intervention are described. In all cases, laboratory assessed coagulation was rapidly normalised and severe haemorrhage improved. These cases suggest that fibrinogen concentrate may be an effective addition to conventional treatments for obstetric haemorrhage associated with hypofibrinogenaemia.

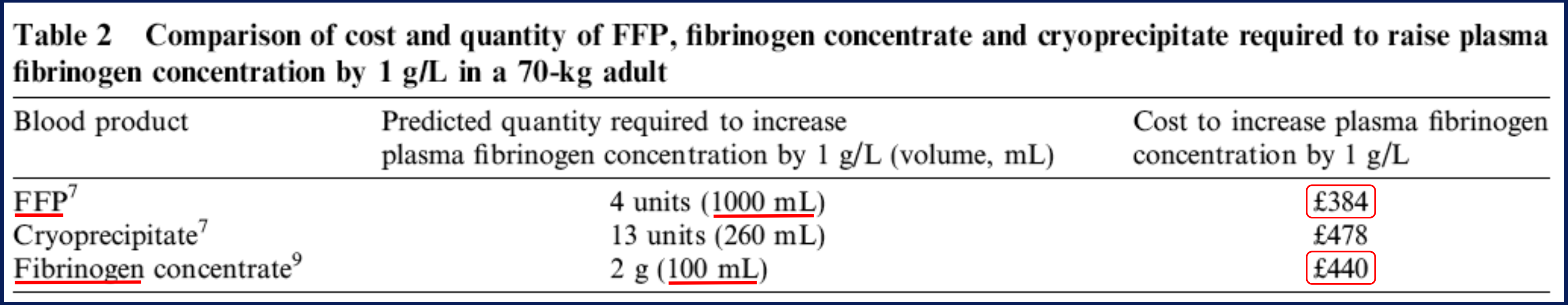
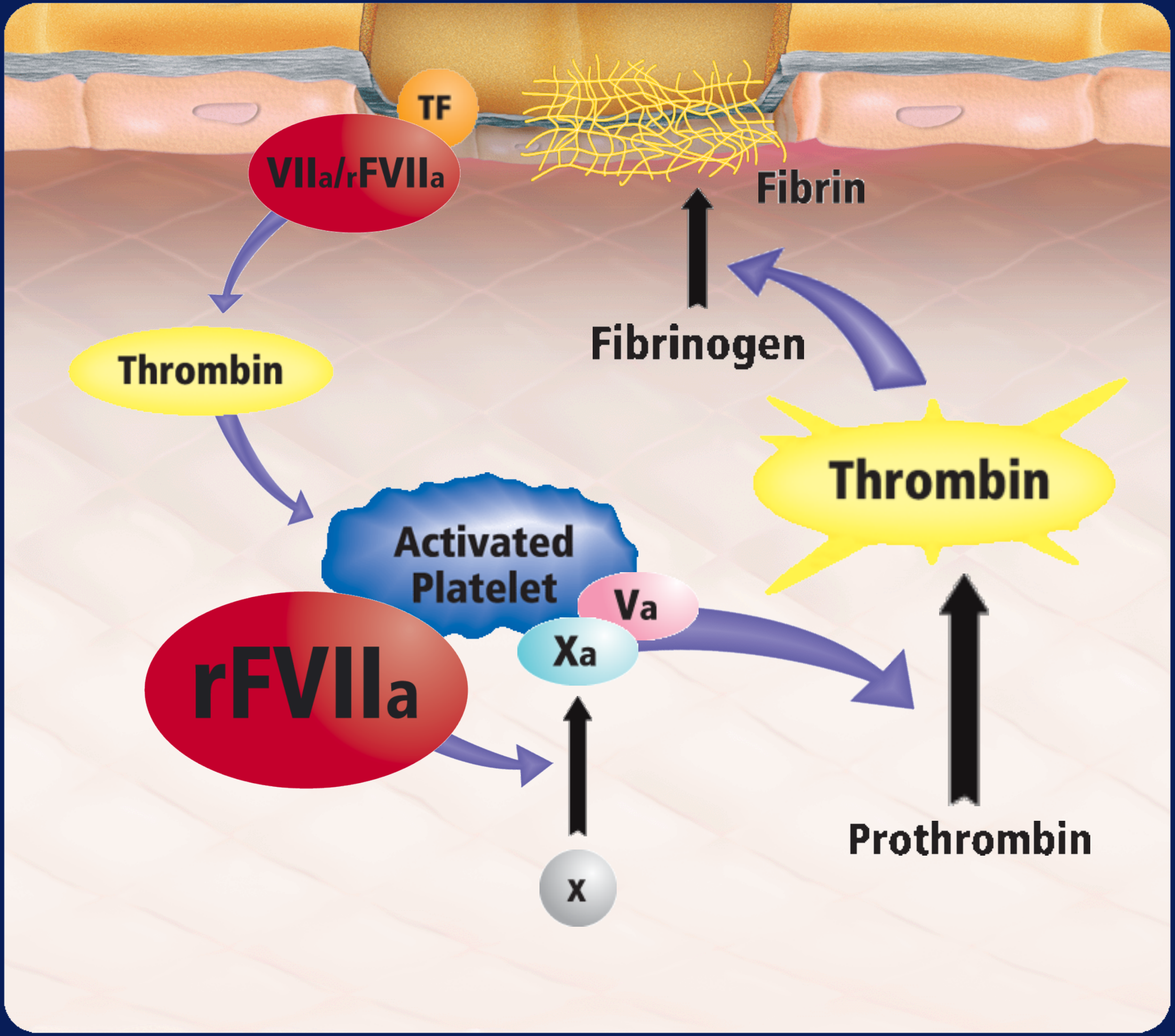


Table 2 Comparison of cost and quantity of FFP, fibrinogen concentrate and cryoprecipitate required to raise plasma fibrinogen concentration by 1 g/L in a 70-kg adult

Blood product	Predicted quantity required to increase plasma fibrinogen concentration by 1 g/L (volume, mL)	Cost to increase plasma fibrinogen concentration by 1 g/L
FFP[7]	4 units (1000 mL)	£384
Cryoprecipitate[7]	13 units (260 mL)	£478
Fibrinogen concentrate[9]	2 g (100 mL)	£440

Facteur VII activé recombinant

(FVIIa, Novoseven®)


TF
VIIa/rFVIIa
Fibrin
Fibrinogen
Thrombin
Thrombin
Activated Platelet
Va
Xa
rFVIIa
X
Prothrombin

Tissue factor (TF)/FVIIa, or TF/rFVIIa interaction, is necessary to initiatiate haemostasis

At pharmacological concentrations rFVIIa directly activates FX on the surface of locally activated platelets. **This activation will initiate the ”thrombin burst”** independently of FVIII and FIX. This step is independent of TF.

The thrombin burst leads to the formation of a stable clot

The use of rFVIIa in obstetric and GYN haemorrhage

Franchini et al., BJOG 2007; 114: 8-15

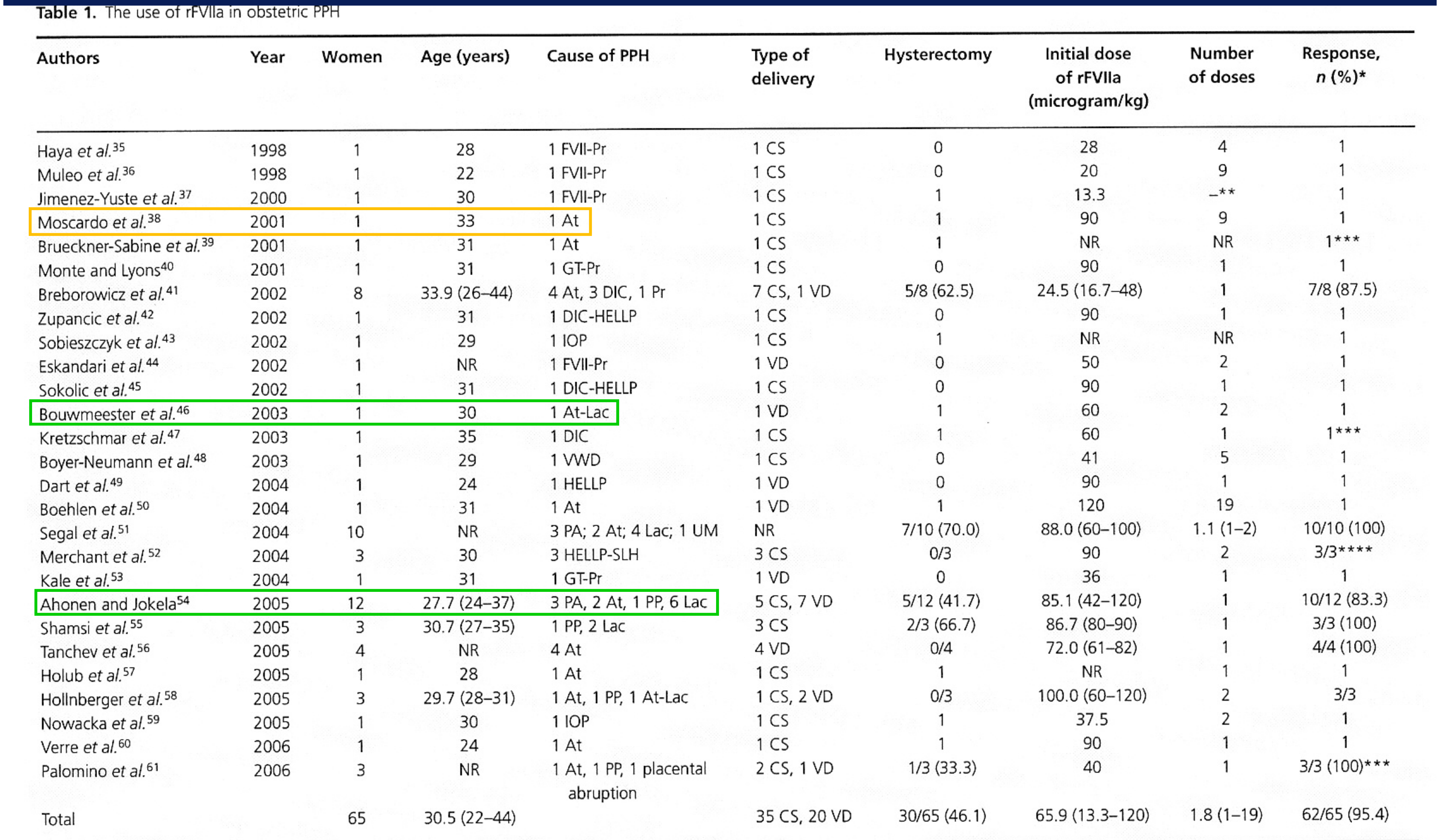


Table 1. The use of rFVIIa in obstetric PPH

Authors	Year	Women	Age (years)	Cause of PPH	Type of delivery	Hysterectomy	Initial dose of rFVIIa (microgram/kg)	Number of doses	Response, *n* (%)*
Haya *et al.*[35]	1998	1	28	1 FVII-Pr	1 CS	0	28	4	1
Muleo *et al.*[36]	1998	1	22	1 FVII-Pr	1 CS	0	20	9	1
Jimenez-Yuste *et al.*[37]	2000	1	30	1 FVII-Pr	1 CS	1	13.3	–**	1
Moscardo *et al.*[38]	2001	1	33	1 At	1 CS	1	90	9	1
Brueckner-Sabine *et al.*[39]	2001	1	31	1 At	1 CS	1	NR	NR	1***
Monte and Lyons[40]	2001	1	31	1 GT-Pr	1 CS	0	90	1	1
Breborowicz *et al.*[41]	2002	8	33.9 (26–44)	4 At, 3 DIC, 1 Pr	7 CS, 1 VD	5/8 (62.5)	24.5 (16.7–48)	1	7/8 (87.5)
Zupancic *et al.*[42]	2002	1	31	1 DIC-HELLP	1 CS	0	90	1	1
Sobieszczyk *et al.*[43]	2002	1	29	1 IOP	1 CS	1	NR	NR	1
Eskandari *et al.*[44]	2002	1	NR	1 FVII-Pr	1 VD	0	50	2	1
Sokolic *et al.*[45]	2002	1	31	1 DIC-HELLP	1 CS	0	90	1	1
Bouwmeester *et al.*[46]	2003	1	30	1 At-Lac	1 VD	1	60	2	1
Kretzschmar *et al.*[47]	2003	1	35	1 DIC	1 CS	1	60	1	1***
Boyer-Neumann *et al.*[48]	2003	1	29	1 VWD	1 CS	0	41	5	1
Dart *et al.*[49]	2004	1	24	1 HELLP	1 VD	0	90	1	1
Boehlen *et al.*[50]	2004	1	31	1 At	1 VD	1	120	19	1
Segal *et al.*[51]	2004	10	NR	3 PA; 2 At; 4 Lac; 1 UM	NR	7/10 (70.0)	88.0 (60–100)	1.1 (1–2)	10/10 (100)
Merchant *et al.*[52]	2004	3	30	3 HELLP-SLH	3 CS	0/3	90	2	3/3****
Kale *et al.*[53]	2004	1	31	1 GT-Pr	1 VD	0	36	1	1
Ahonen and Jokela[54]	2005	12	27.7 (24–37)	3 PA, 2 At, 1 PP, 6 Lac	5 CS, 7 VD	5/12 (41.7)	85.1 (42–120)	1	10/12 (83.3)
Shamsi *et al.*[55]	2005	3	30.7 (27–35)	1 PP, 2 Lac	3 CS	2/3 (66.7)	86.7 (80–90)	1	3/3 (100)
Tanchev *et al.*[56]	2005	4	NR	4 At	4 VD	0/4	72.0 (61–82)	1	4/4 (100)
Holub *et al.*[57]	2005	1	28	1 At	1 CS	1	NR	1	1
Hollnberger *et al.*[58]	2005	3	29.7 (28–31)	1 At, 1 PP, 1 At-Lac	1 CS, 2 VD	0/3	100.0 (60–120)	2	3/3
Nowacka *et al.*[59]	2005	1	30	1 IOP	1 CS	1	37.5	2	1
Verre *et al.*[60]	2006	1	24	1 At	1 CS	1	90	1	1
Palomino *et al.*[61]	2006	3	NR	1 At, 1 PP, 1 placental abruption	2 CS, 1 VD	1/3 (33.3)	40	1	3/3 (100)***
Total		65	30.5 (22–44)		35 CS, 20 VD	30/65 (46.1)	65.9 (13.3–120)	1.8 (1–19)	62/65 (95.4)

PLACE CHRONOLOGIQUE DE L'ADMINISTRATION DU FACTEUR VII ACTIVE RECOMBINANT EN SAUVETAGE MATERNEL DANS L'HEMORRAGIE SEVERE DU POST-PARTUM :

Avant ou après les gestes chirurgicaux de survie :

Embolisation, ligature vasculaire et hystérectomie d'hémostase

Inclusions terminées, analyse en cours !…

Investigateur Principal :
Dr Géraldine Lavigne

Investigateur coordonnateur :
Dr Guy Aya

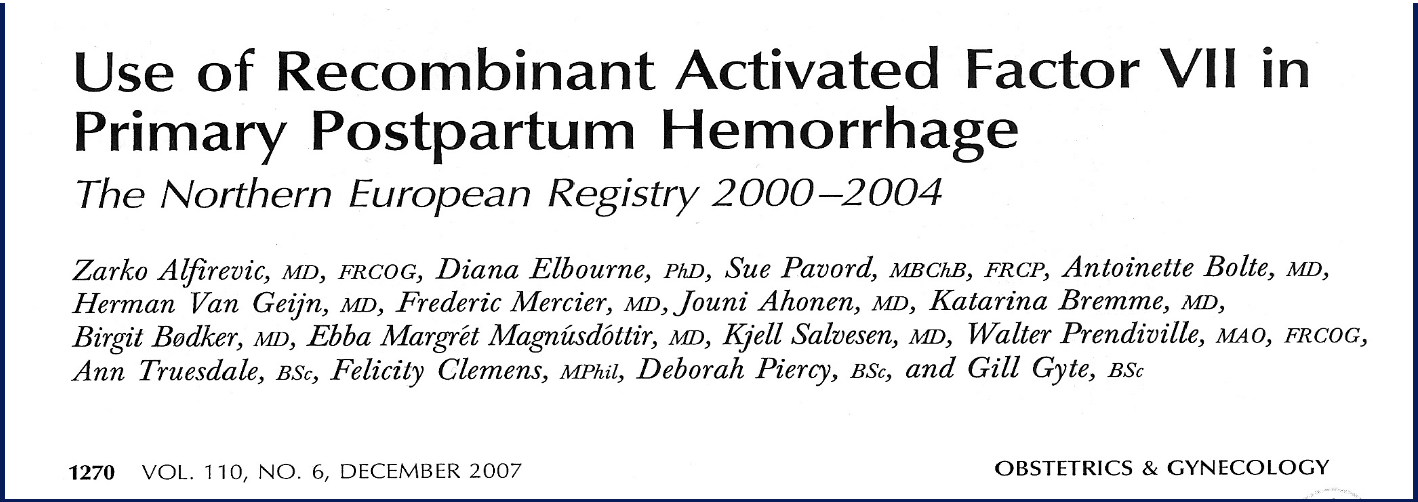
PHRC multicentrique

Promoteur : CHU Nîmes
(Nîmes, Clamart, Cochin, Lille, Nice, Montpellier, Genève, Saint Etienne)

42 patientes par groupe, **soit 84 patientes**

CJP : **❾ 30% du taux d'embolisation ou de ligature vasculaire** avec r**FVIIa**

ACJ : Nombre de sujets à traiter pour gagner une embolisation ou ligature, …



Use of Recombinant Activated Factor VII in Primary Postpartum Hemorrhage

The Northern European Registry 2000–2004

Zarko Alfirevic, MD, FRCOG, Diana Elbourne, PhD, Sue Pavord, MBChB, FRCP, Antoinette Bolte, MD, Herman Van Geijn, MD, Frederic Mercier, MD, Jouni Ahonen, MD, Katarina Bremme, MD, Birgit Bødker, MD, Ebba Margrét Magnúsdóttir, MD, Kjell Salvesen, MD, Walter Prendiville, MAO, FRCOG, Ann Truesdale, BSc, Felicity Clemens, MPhil, Deborah Piercy, BSc, and Gill Gyte, BSc

1270 VOL. 110, NO. 6, DECEMBER 2007 OBSTETRICS & GYNECOLOGY

NEFOH

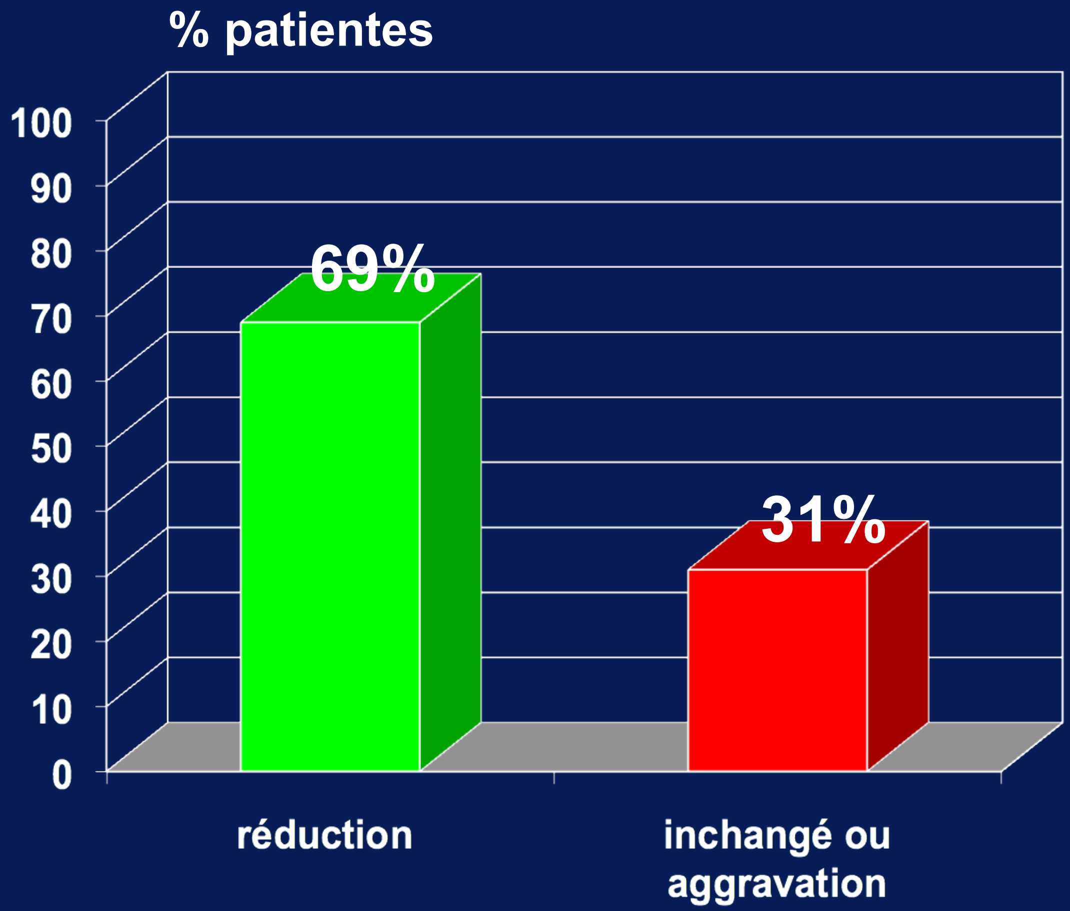
rVIIa ≈ 90 µg/kg

108 patients (65 maternités / 6 pays)

Amélioration	**83%**
Identique ou pire	**17%**

- **Embolie Pulmonaire (2)**
- **Thrombose veineuse bilatérale 4 semaines plus tard**
- **IDM après arrêt cardiaque**
- **Eruption cutanée**

OFFHO : 2005-2007



Effets indésirables	**Nombre de cas**
Thrombose veineuse membre supérieur	1
Thrombose veineuse membre inférieur	3
Thrombose veineuse ovarienne	2
Embolie pulmonaire	3

103 CRF

rFVIIa (Novoseven®) et HPP :

Protocole Thérapeutique Temporaire (PTT)

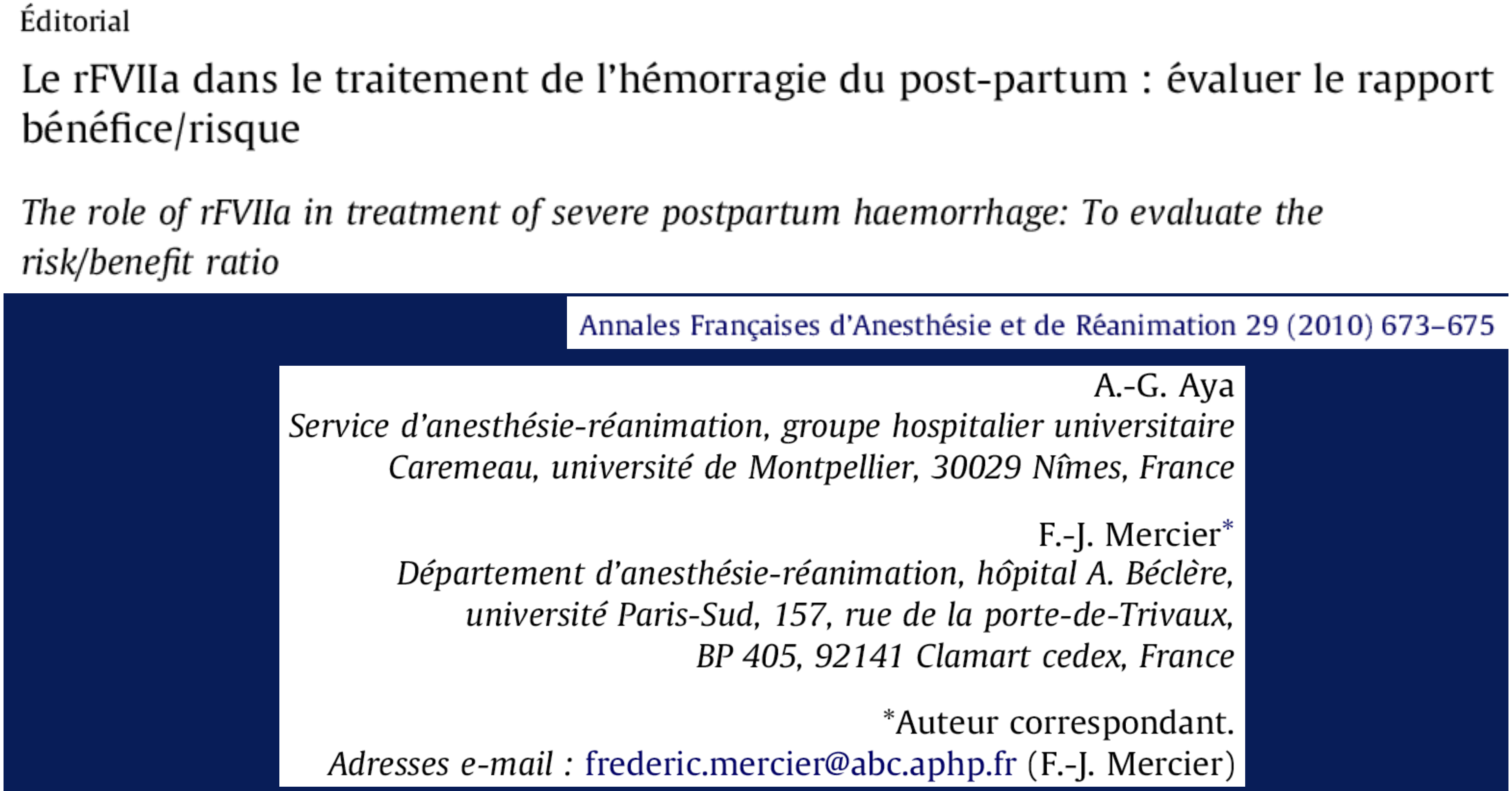
AFSSAPS mars 2008 (pour 4 ans)

(http://www.sante-ra.fr/doc/omedit/novoseven%20PTT%201.pdf)

- après procédure invasive (ligatures vasc. ou embolisation) :
  - si l'HPP continue
  - avant hystérectomie si possible

- dose ⇨ 90 µg/kg,
- renouvelable 1 fois (120 µg/kg)

+ normothermie, pH > 7,20, [Ca] ~ N^{al}
plaquettes > 30-50.000, fibrinogène > 0,5-1 g/L



Éditorial

Le rFVIIa dans le traitement de l’hémorragie du post-partum : évaluer le rapport bénéfice/risque

The role of rFVIIa in treatment of severe postpartum haemorrhage: To evaluate the risk/benefit ratio

Annales Françaises d’Anesthésie et de Réanimation 29 (2010) 673–675

A.-G. Aya
Service d’anesthésie-réanimation, groupe hospitalier universitaire Caremeau, université de Montpellier, 30029 Nîmes, France

F.-J. Mercier*
Département d’anesthésie-réanimation, hôpital A. Béclère, université Paris-Sud, 157, rue de la porte-de-Trivaux, BP 405, 92141 Clamart cedex, France

*Auteur correspondant.
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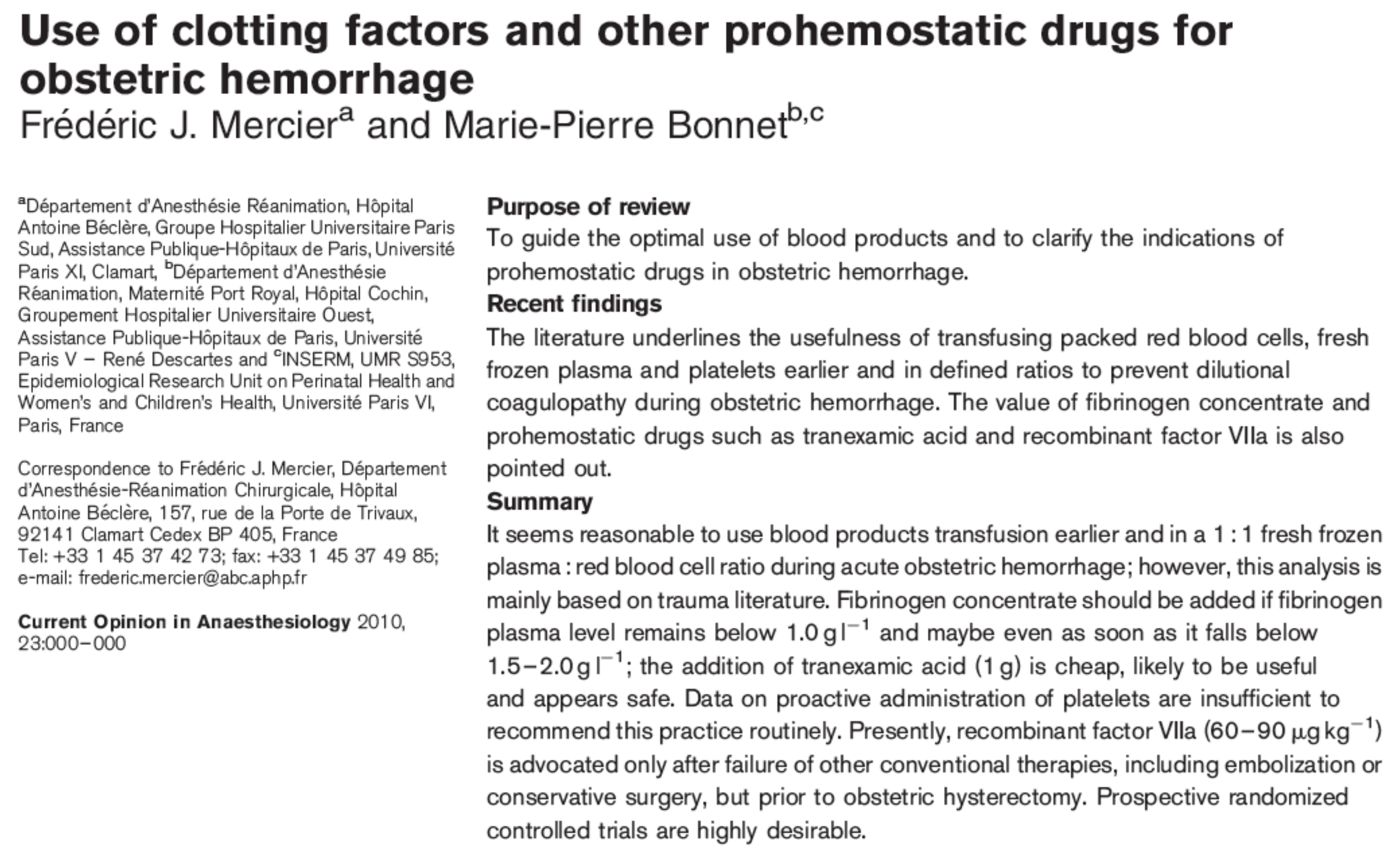


Use of clotting factors and other prohemostatic drugs for obstetric hemorrhage

Frédéric J. Mercier[a] and Marie-Pierre Bonnet[b,c]

[a]Département d'Anesthésie Réanimation, Hôpital Antoine Béclère, Groupe Hospitalier Universitaire Paris Sud, Assistance Publique-Hôpitaux de Paris, Université Paris XI, Clamart, [b]Département d'Anesthésie Réanimation, Maternité Port Royal, Hôpital Cochin, Groupement Hospitalier Universitaire Ouest, Assistance Publique-Hôpitaux de Paris, Université Paris V – René Descartes and [c]INSERM, UMR S953, Epidemiological Research Unit on Perinatal Health and Women's and Children's Health, Université Paris VI, Paris, France

Correspondence to Frédéric J. Mercier, Département d'Anesthésie-Réanimation Chirurgicale, Hôpital Antoine Béclère, 157, rue de la Porte de Trivaux, 92141 Clamart Cedex BP 405, France
Tel: +33 1 45 37 42 73; fax: +33 1 45 37 49 85;
e-mail: frederic.mercier@abc.aphp.fr

Current Opinion in Anaesthesiology 2010, 23:000–000

Purpose of review

To guide the optimal use of blood products and to clarify the indications of prohemostatic drugs in obstetric hemorrhage.

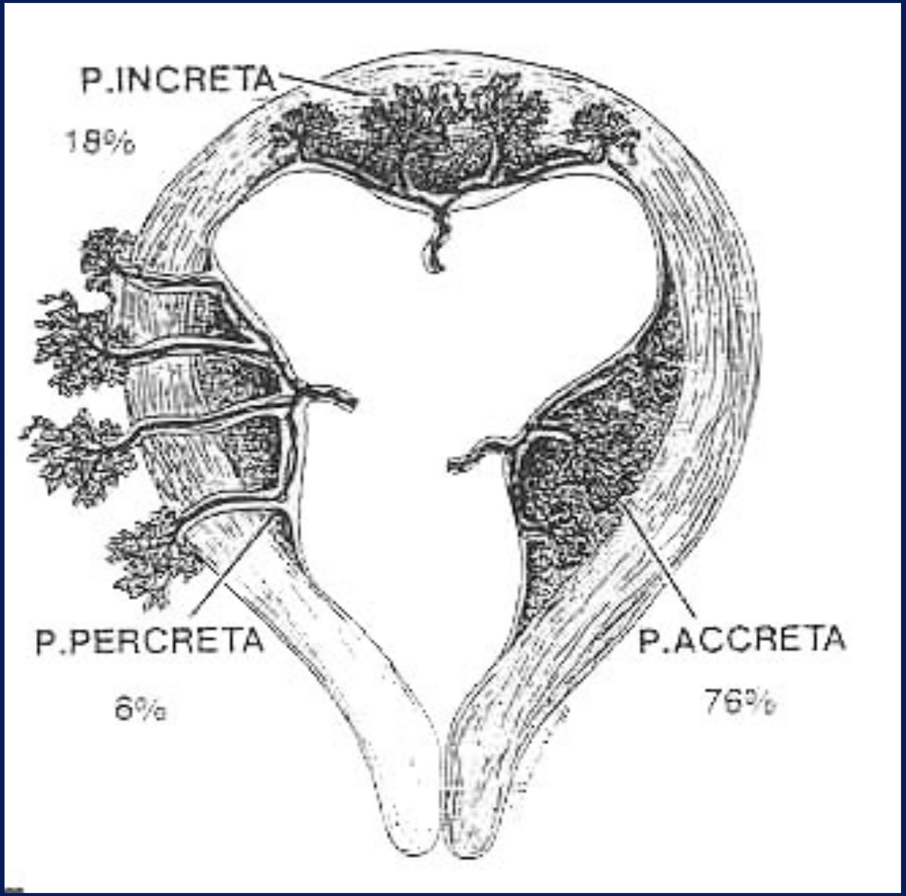
Recent findings

The literature underlines the usefulness of transfusing packed red blood cells, fresh frozen plasma and platelets earlier and in defined ratios to prevent dilutional coagulopathy during obstetric hemorrhage. The value of fibrinogen concentrate and prohemostatic drugs such as tranexamic acid and recombinant factor VIIa is also pointed out.

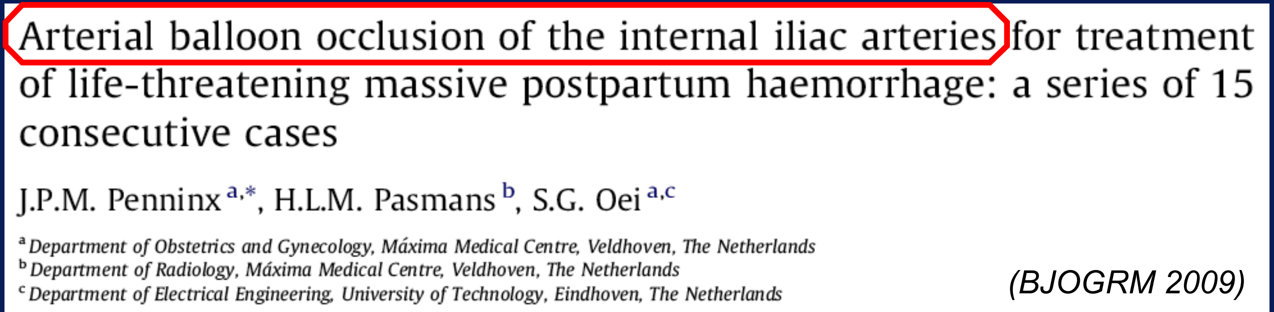
Summary

It seems reasonable to use blood products transfusion earlier and in a 1 : 1 fresh frozen plasma : red blood cell ratio during acute obstetric hemorrhage; however, this analysis is mainly based on trauma literature. Fibrinogen concentrate should be added if fibrinogen plasma level remains below $1.0\,\mathrm{g\,l^{-1}}$ and maybe even as soon as it falls below $1.5–2.0\,\mathrm{g\,l^{-1}}$; the addition of tranexamic acid (1 g) is cheap, likely to be useful and appears safe. Data on proactive administration of platelets are insufficient to recommend this practice routinely. Presently, recombinant factor VIIa ($60–90\,\mu\mathrm{g\,kg^{-1}}$) is advocated only after failure of other conventional therapies, including embolization or conservative surgery, but prior to obstetric hysterectomy. Prospective randomized controlled trials are highly desirable.

Pl. accreta


P.INCRETA
18%
P.PERCRETA
6%
P.ACCRETA
76%

adhésion et/ou pénétration
anormale du Pl.



Arterial balloon occlusion of the internal iliac arteries for treatment of life-threatening massive postpartum haemorrhage: a series of 15 consecutive cases

J.P.M. Penninx[a,*], H.L.M. Pasmans[b], S.G. Oei[a,c]

[a] Department of Obstetrics and Gynecology, Máxima Medical Centre, Veldhoven, The Netherlands
[b] Department of Radiology, Máxima Medical Centre, Veldhoven, The Netherlands
[c] Department of Electrical Engineering, University of Technology, Eindhoven, The Netherlands

(BJOGRM 2009)

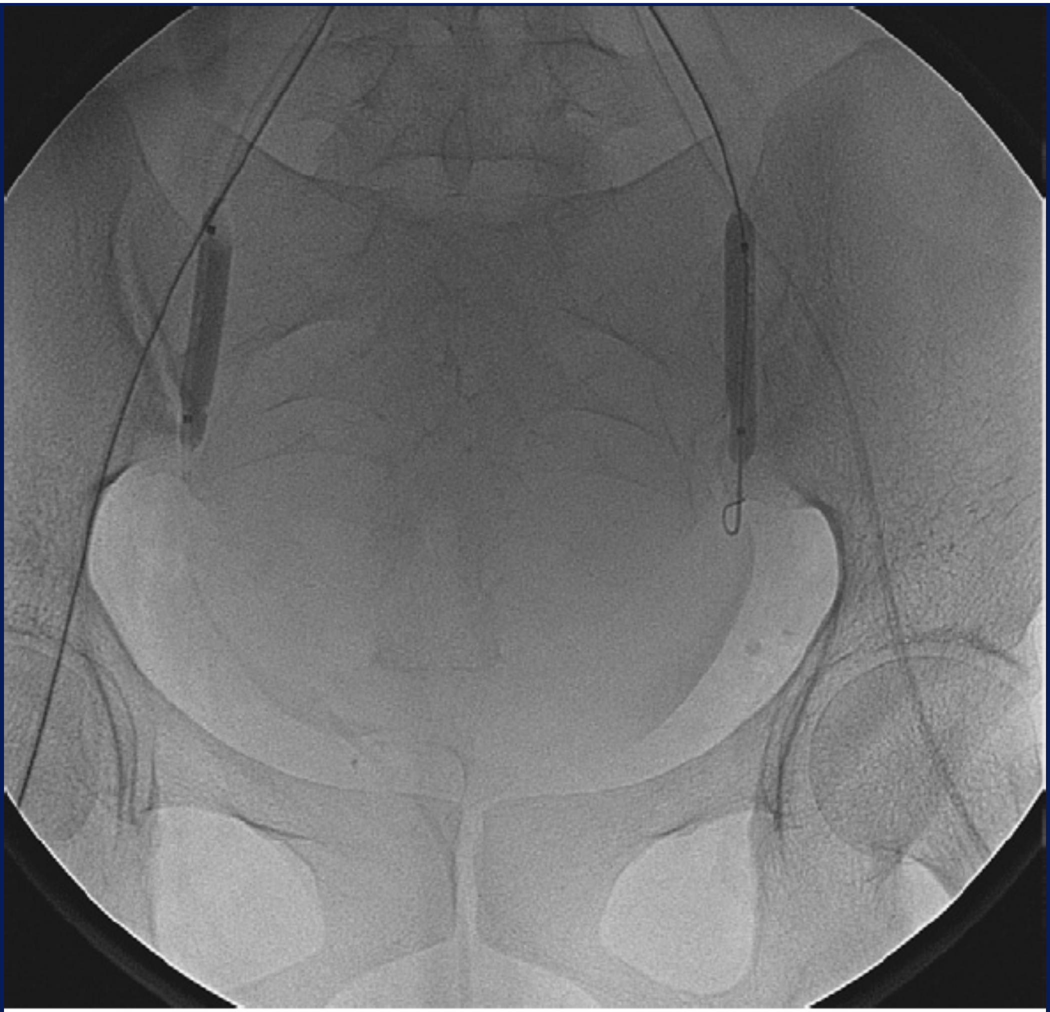
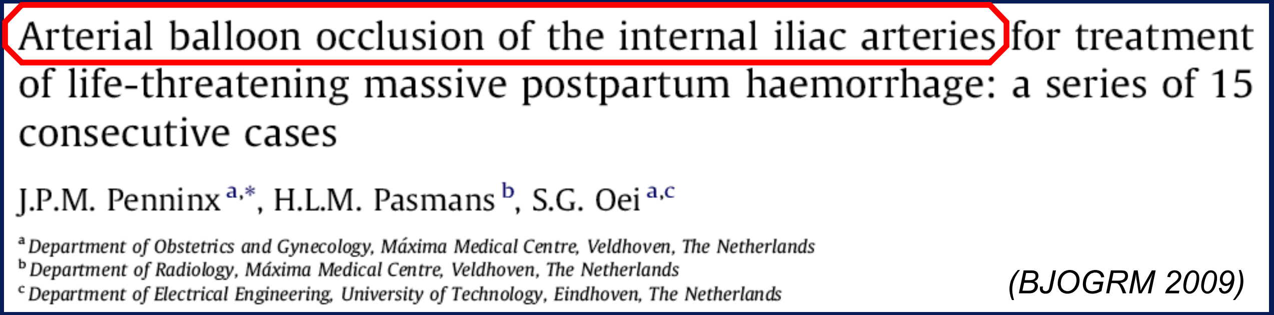


Fig. 1. Balloon occlusion of the internal iliac arteries.



Arterial balloon occlusion of the internal iliac arteries for treatment of life-threatening massive postpartum haemorrhage: a series of 15 consecutive cases

J.P.M. Penninx[a,*], H.L.M. Pasmans[b], S.G. Oei[a,c]

[a] *Department of Obstetrics and Gynecology, Máxima Medical Centre, Veldhoven, The Netherlands*
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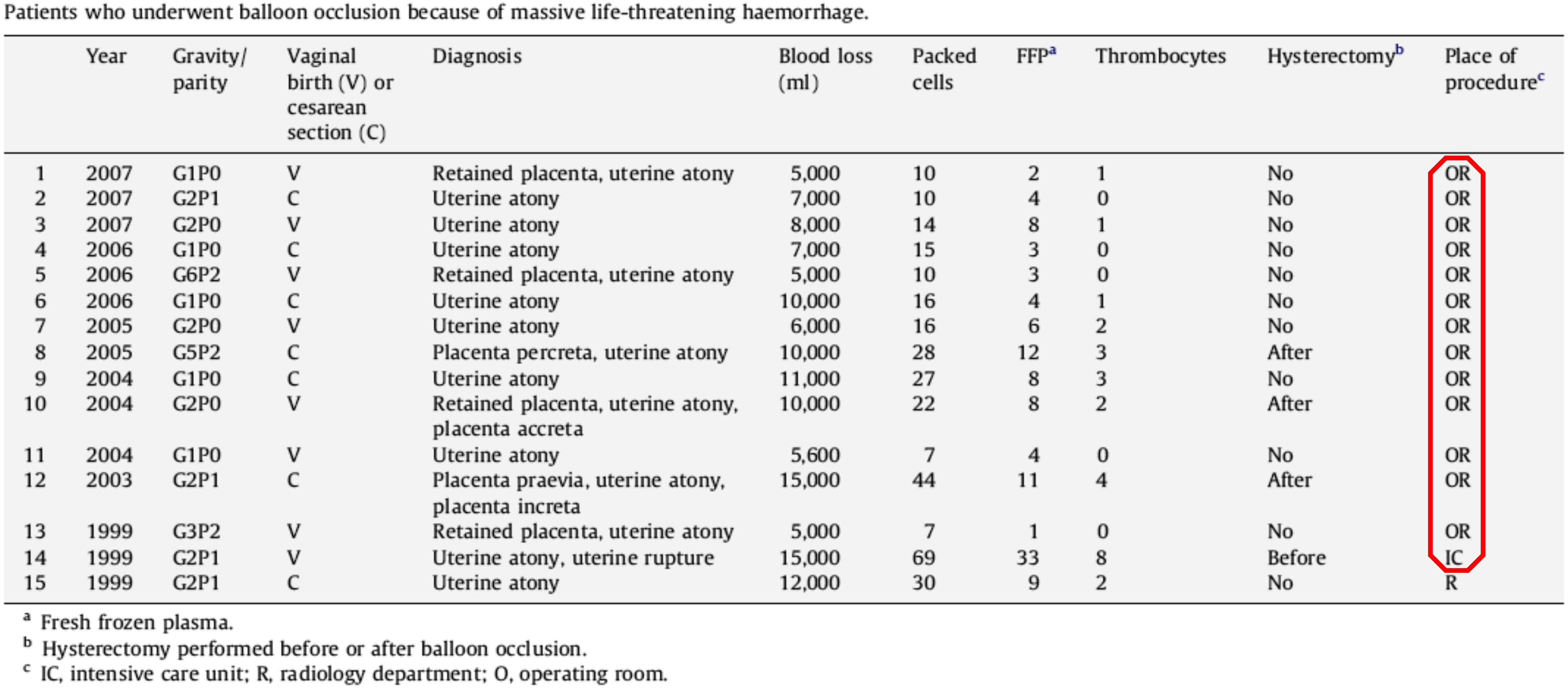
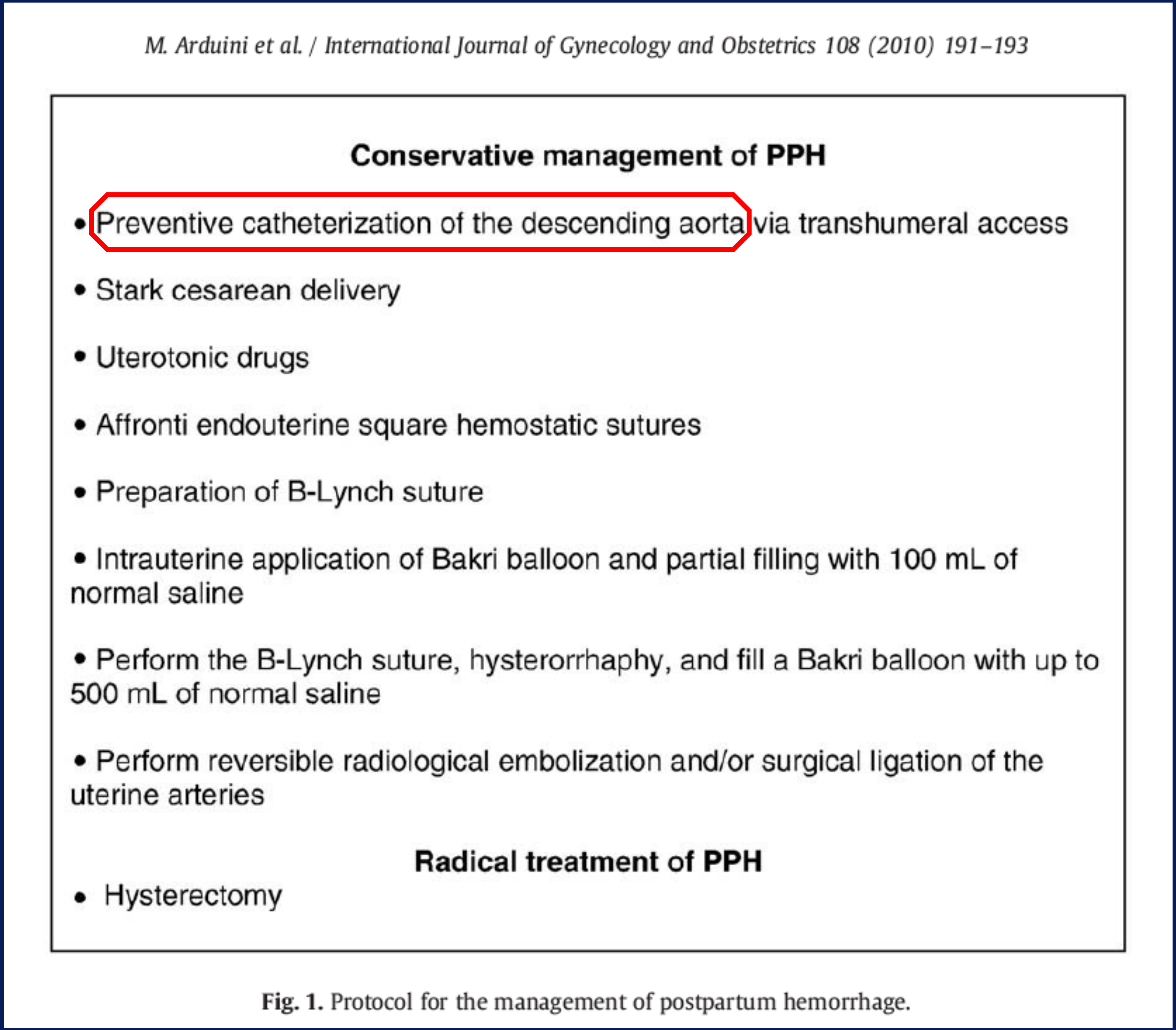
(BJOGRM 2009)



Patients who underwent balloon occlusion because of massive life-threatening haemorrhage.

	Year	Gravity/ parity	Vaginal birth (V) or cesarean section (C)	Diagnosis	Blood loss (ml)	Packed cells	FFP[a]	Thrombocytes	Hysterectomy[b]	Place of procedure[c]
1	2007	G1P0	V	Retained placenta, uterine atony	5,000	10	2	1	No	OR
2	2007	G2P1	C	Uterine atony	7,000	10	4	0	No	OR
3	2007	G2P0	V	Uterine atony	8,000	14	8	1	No	OR
4	2006	G1P0	C	Uterine atony	7,000	15	3	0	No	OR
5	2006	G6P2	V	Retained placenta, uterine atony	5,000	10	3	0	No	OR
6	2006	G1P0	C	Uterine atony	10,000	16	4	1	No	OR
7	2005	G2P0	V	Uterine atony	6,000	16	6	2	No	OR
8	2005	G5P2	C	Placenta percreta, uterine atony	10,000	28	12	3	After	OR
9	2004	G1P0	C	Uterine atony	11,000	27	8	3	No	OR
10	2004	G2P0	V	Retained placenta, uterine atony, placenta accreta	10,000	22	8	2	After	OR
11	2004	G1P0	V	Uterine atony	5,600	7	4	0	No	OR
12	2003	G2P1	C	Placenta praevia, uterine atony, placenta increta	15,000	44	11	4	After	OR
13	1999	G3P2	V	Retained placenta, uterine atony	5,000	7	1	0	No	OR
14	1999	G2P1	V	Uterine atony, uterine rupture	15,000	69	33	8	Before	IC
15	1999	G2P1	C	Uterine atony	12,000	30	9	2	No	R

[a] Fresh frozen plasma.
[b] Hysterectomy performed before or after balloon occlusion.
[c] IC, intensive care unit; R, radiology department; O, operating room.



M. Arduini et al. / International Journal of Gynecology and Obstetrics 108 (2010) 191–193

Conservative management of PPH

- Preventive catheterization of the descending aorta via transhumeral access
- Stark cesarean delivery
- Uterotonic drugs
- Affronti endouterine square hemostatic sutures
- Preparation of B-Lynch suture
- Intrauterine application of Bakri balloon and partial filling with 100 mL of normal saline
- Perform the B-Lynch suture, hysterorrhaphy, and fill a Bakri balloon with up to 500 mL of normal saline
- Perform reversible radiological embolization and/or surgical ligation of the uterine arteries

Radical treatment of PPH

- Hysterectomy

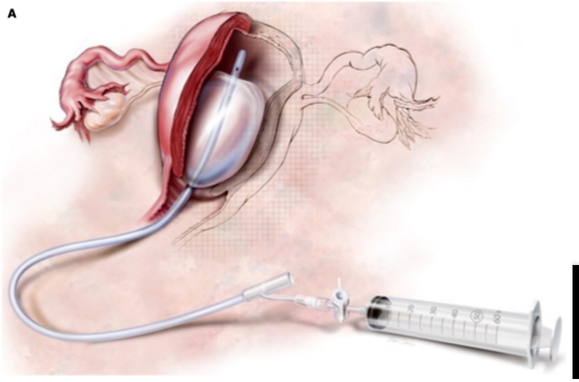
Fig. 1. Protocol for the management of postpartum hemorrhage.

ACOG

Table 1. Medical Management of Postpartum Hemorrhage

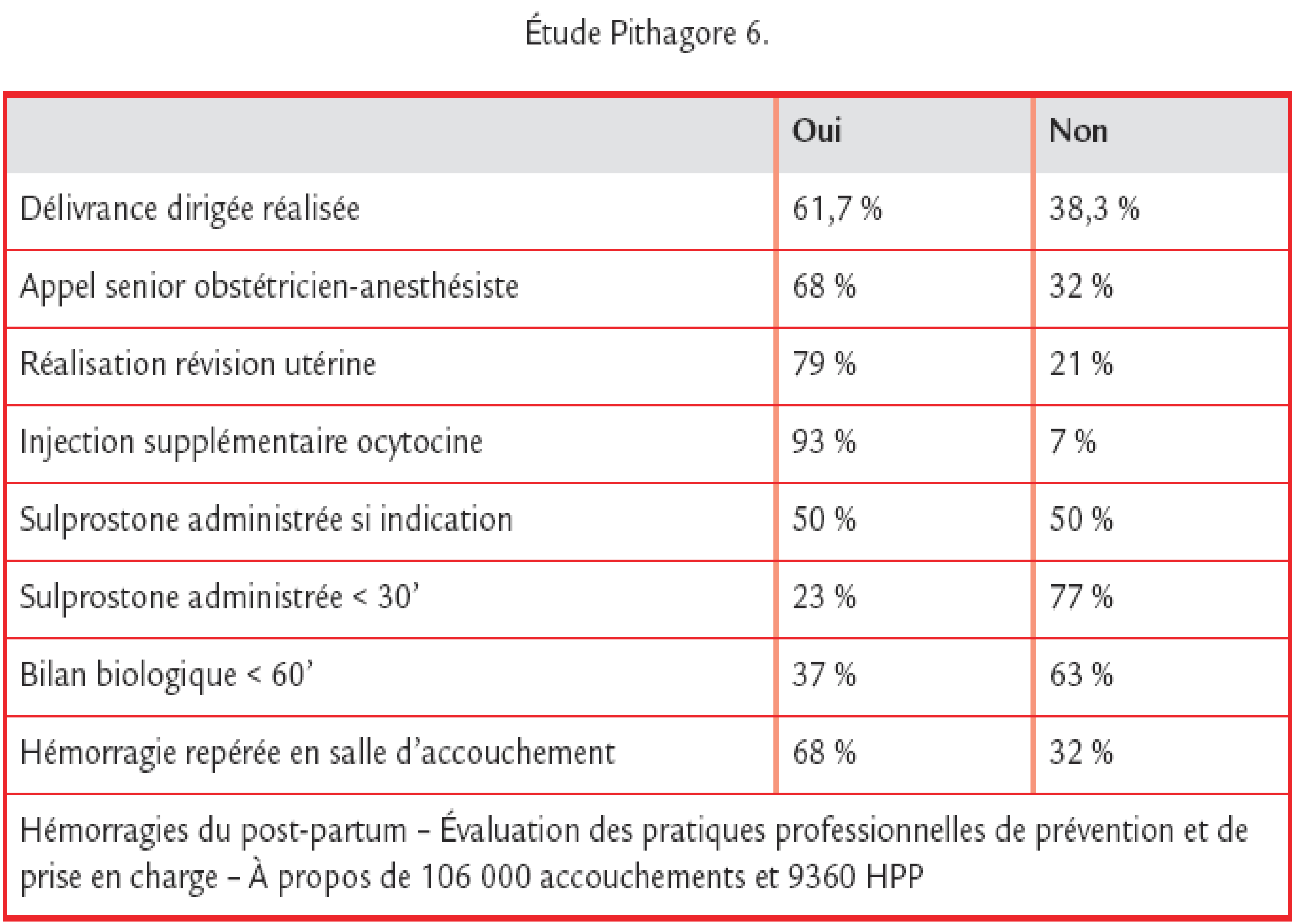
Table 2. Tamponade Techniques for Postpartum Hemorrhage

Technique	Comment
Uterine tamponade	
—Packing	—4-inch gauze; can soak with 5,000 units of thrombin in 5 mL of sterile saline
—Foley catheter	—Insert one or more bulbs; instill 60–80 mL of saline
—Sengstaken–Blakemore tube	
—SOS Bakri tamponade balloon	300–500 mL



(ACOG Committee Opinion, Oct 2006)

(Courtesy Ruth Landau)



Étude Pithagore 6.

	Oui	Non
Délivrance dirigée réalisée	61,7 %	38,3 %
Appel senior obstétricien-anesthésiste	68 %	32 %
Réalisation révision utérine	79 %	21 %
Injection supplémentaire ocytocine	93 %	7 %
Sulprostone administrée si indication	50 %	50 %
Sulprostone administrée < 30’	23 %	77 %
Bilan biologique < 60’	37 %	63 %
Hémorragie repérée en salle d’accouchement	68 %	32 %
Hémorragies du post-partum – Évaluation des pratiques professionnelles de prévention et de prise en charge – À propos de 106 000 accouchements et 9360 HPP		

Rapport du Comité national d'experts sur la mortalité maternelle (CNEMM)

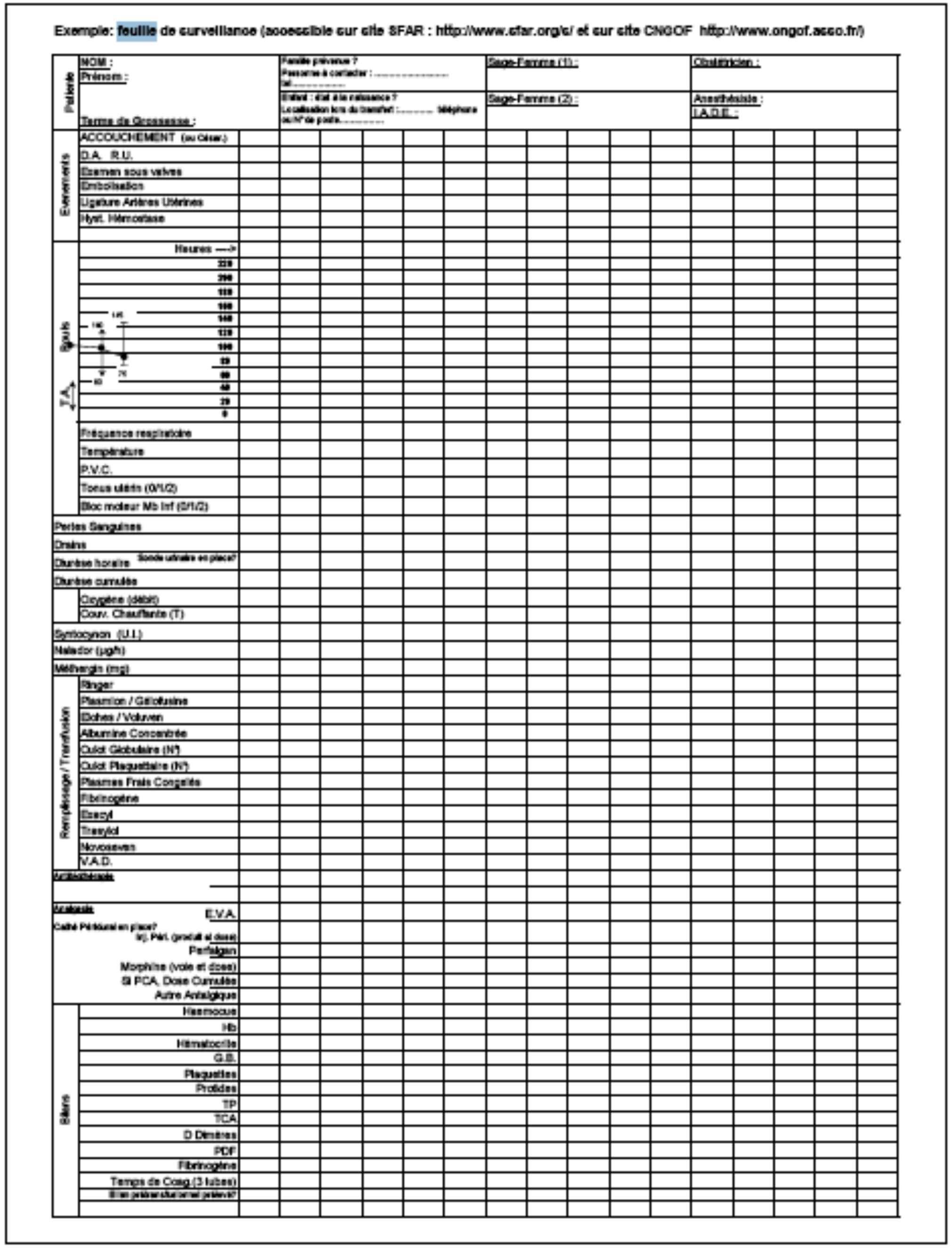
2001-2006

Instituts thématiques Inserm
Institut national de la santé et de la recherche médicale
Unité 953. Recherche épidémiologique en santé périnatale, santé des femmes et des enfants

Enquête nationale confidentielle sur les morts maternelles

InVS
Institut de veille sanitaire

FICHE DE SURVEILLANCE DE L'HÉMORRAGIE DE LA DÉLIVRANCE



Exemple: feuille de surveillance (accessible sur site SFAR : http://www.sfar.org/s/ et sur site CNGOF http://www.cngof.asso.fr/)

Patiente
NOM :
Prénom :
Terme de Grossesse :

Famille prévenue ?
Personne à contacter : ……………………
tel……………

Enfant : état à la naissance ?
Localisation lors du transfert : ……… téléphone ou n° de poste…………

Sage-Femme (1) :
Sage-Femme (2) :
Obstétricien :
Anesthésiste :
I.A.D.E. :

Evènements
ACCOUCHEMENT (ou César.)
D.A. R.U.
Examen sous valves
Embolisation
Ligature Artères Utérines
Hyst. Hémostase

Heures --->
Pouls
T.A.
220
200
180
160
140
120
100
80
60
40
20
0
Fréquence respiratoire
Température
P.V.C.
Tonus utérin (0/1/2)
Bloc moteur Mb Inf (0/1/2)

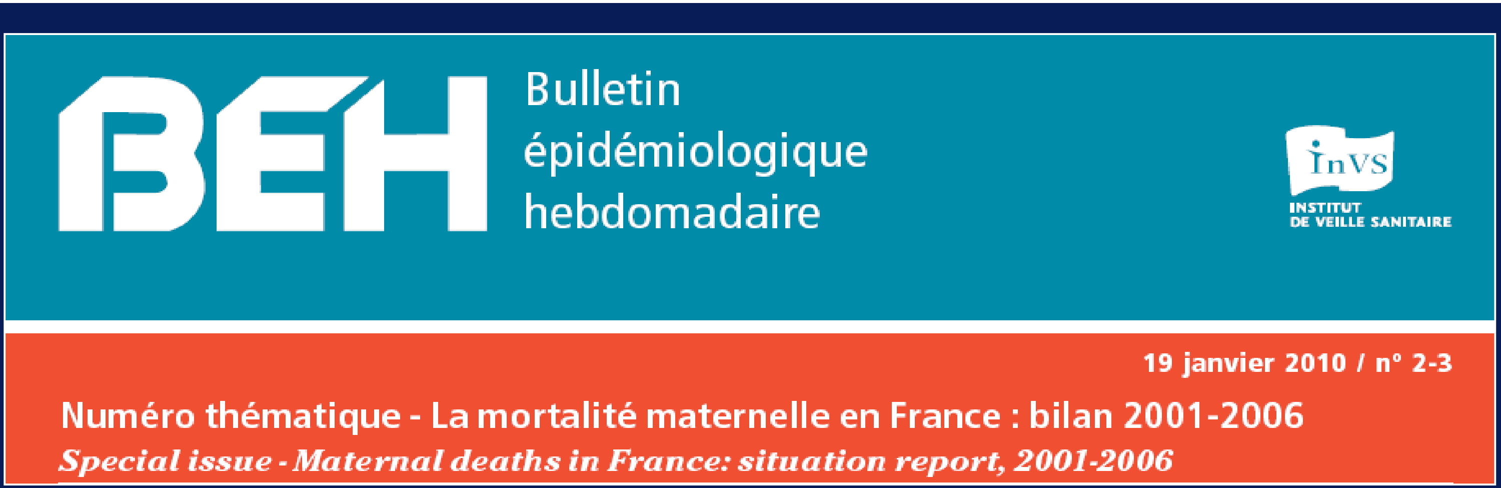
Pertes Sanguines
Drains
Diurèse horaire — Sonde urinaire en place?
Diurèse cumulée
Oxygène (débit)
Couv. Chauffante (T)
Syntocynon (U.I.)
Nalador (µg/h)
Méthergin (mg)

Remplissage / Transfusion
Ringer
Plasmion / Gélofusine
Elohes / Voluven
Albumine Concentrée
Culot Globulaire (N°)
Culot Plaquettaire (N°)
Plasmas Frais Congelés
Fibrinogène
Exacyl
Trasylol
Novoseven
V.A.D.

Antibiothérapie

Analgésie
E.V.A.
Cathé Péridural en place?
Inj. Péri. (produit et dose)
Perfalgan
Morphine (voie et dose)
Si PCA, Dose Cumulée
Autre Antalgique

Bilans
Haemocue
Hb
Hématocrite
G.B.
Plaquettes
Protides
TP
TCA
D Dimères
PDF
Fibrinogène
Temps de Coag (3 tubes)
Bilan prétransfusionnel prélevé?



BEH Bulletin épidémiologique hebdomadaire

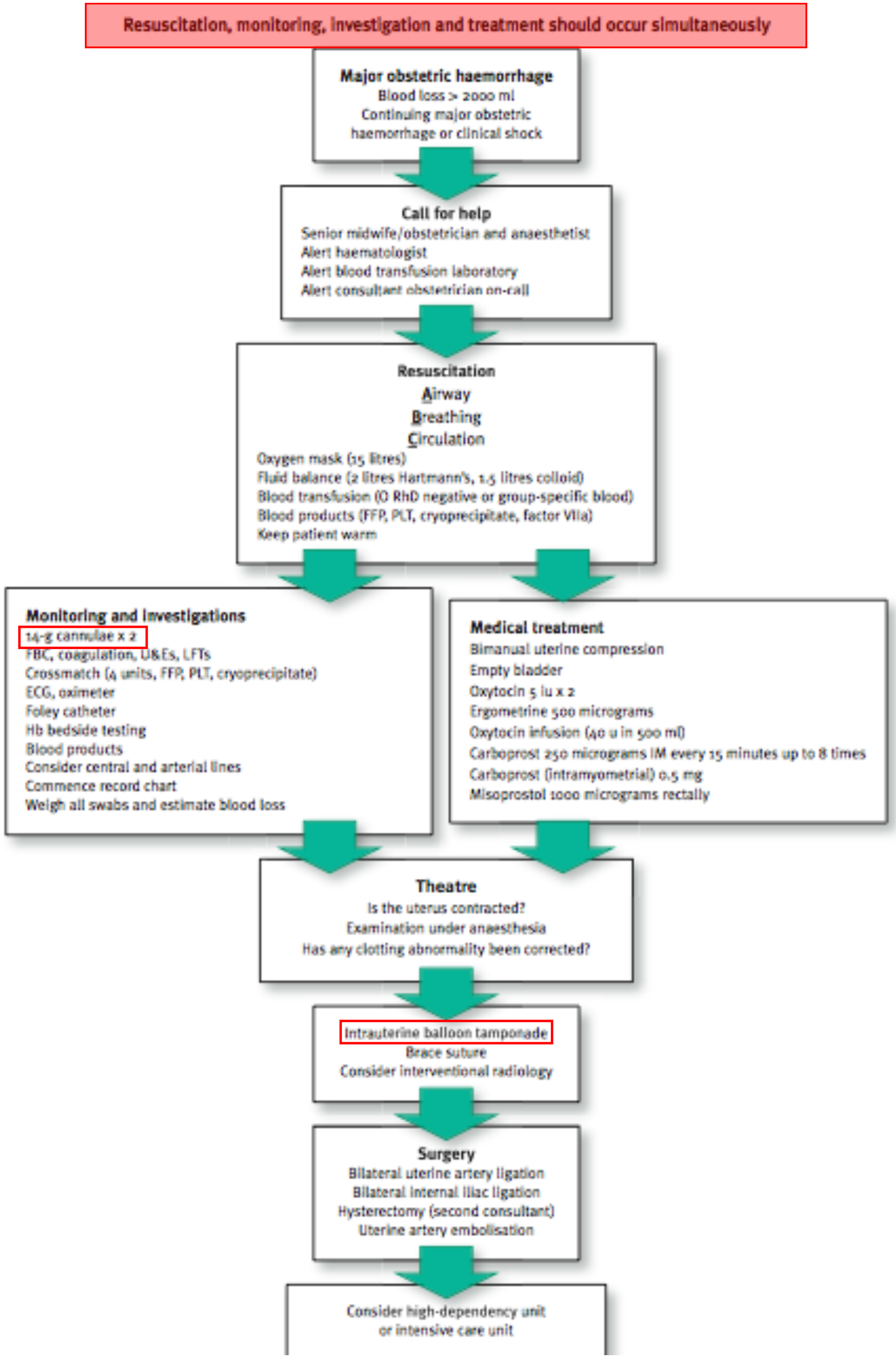
InVS INSTITUT DE VEILLE SANITAIRE

19 janvier 2010 / n° 2-3

Numéro thématique - La mortalité maternelle en France : bilan 2001-2006

Special issue - Maternal deaths in France: situation report, 2001-2006

- Feuille de surveillance de l'HPP : modèle
- Après échec du Nalador, effectuer rapidement les mesures invasives des RPC
- Toutes les maternités doivent prévoir dans leur organisation la venue sur place d'un chirurgien (GO ou non), lorsque le MDG n'en a pas la compétence
- Toute structure doit être organisée pour effectuer les premiers gestes d'hémostase sur place quand la gravité de l'hémorragie l'impose



Resuscitation, monitoring, investigation and treatment should occur simultaneously

Major obstetric haemorrhage
Blood loss > 2000 ml
Continuing major obstetric haemorrhage or clinical shock

Call for help
Senior midwife/obstetrician and anaesthetist
Alert haematologist
Alert blood transfusion laboratory
Alert consultant obstetrician on-call

Resuscitation
Airway
Breathing
Circulation
Oxygen mask (15 litres)
Fluid balance (2 litres Hartmann's, 1.5 litres colloid)
Blood transfusion (O RhD negative or group-specific blood)
Blood products (FFP, PLT, cryoprecipitate, factor VIIa)
Keep patient warm

Monitoring and investigations
14-g cannulae x 2
FBC, coagulation, U&Es, LFTs
Crossmatch (4 units, FFP, PLT, cryoprecipitate)
ECG, oximeter
Foley catheter
Hb bedside testing
Blood products
Consider central and arterial lines
Commence record chart
Weigh all swabs and estimate blood loss

Medical treatment
Bimanual uterine compression
Empty bladder
Oxytocin 5 iu x 2
Ergometrine 500 micrograms
Oxytocin infusion (40 u in 500 ml)
Carboprost 250 micrograms IM every 15 minutes up to 8 times
Carboprost (intramyometrial) 0.5 mg
Misoprostol 1000 micrograms rectally

Theatre
Is the uterus contracted?
Examination under anaesthesia
Has any clotting abnormality been corrected?

Intrauterine balloon tamponade
Brace suture
Consider interventional radiology

Surgery
Bilateral uterine artery ligation
Bilateral internal iliac ligation
Hysterectomy (second consultant)
Uterine artery embolisation

Consider high-dependency unit or intensive care unit

Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

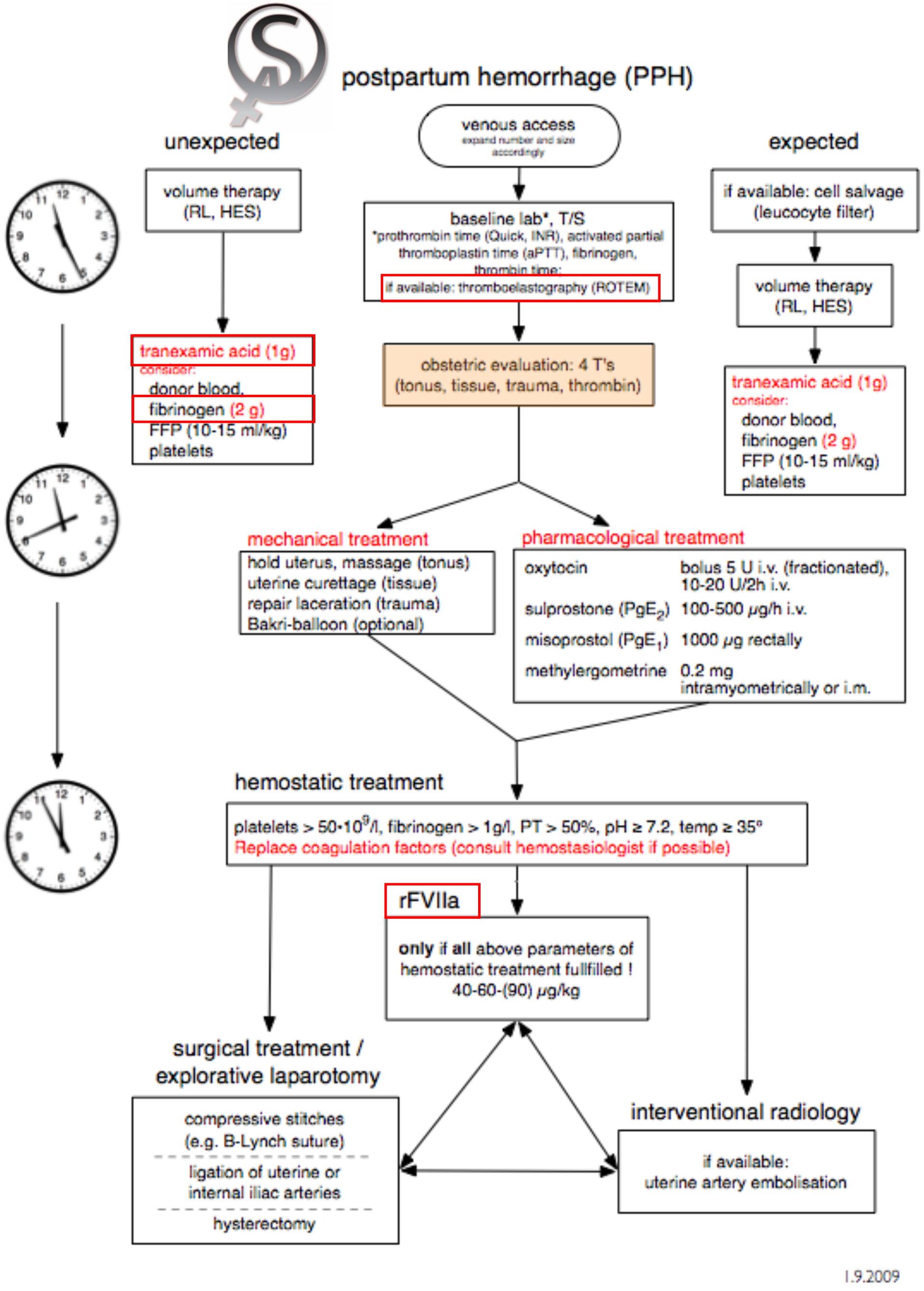
Green-top Guideline No. 52
May 2009
Minor revisions August 2009

PREVENTION AND MANAGEMENT OF POSTPARTUM HAEMORRHAGE

This is the first edition of this guideline.

gynécologie suisse
Société Suisse de Gynécologie et d'Obstétrique
Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe
Società Svizzera di Ginecologia e Ostetrica

SSAR SGAR



postpartum hemorrhage (PPH)

venous access
expand number and size accordingly

baseline lab*, T/S
*prothrombin time (Quick, INR), activated partial thromboplastin time (aPTT), fibrinogen, thrombin time;
if available: thromboelastography (ROTEM)

obstetric evaluation: 4 T's
(tonus, tissue, trauma, thrombin)

unexpected

volume therapy
(RL, HES)

tranexamic acid (1g)
consider:
donor blood,
fibrinogen (2 g)
FFP (10-15 ml/kg)
platelets

expected

if available: cell salvage
(leucocyte filter)

volume therapy
(RL, HES)

tranexamic acid (1g)
consider:
donor blood,
fibrinogen (2 g)
FFP (10-15 ml/kg)
platelets

mechanical treatment

hold uterus, massage (tonus)
uterine curettage (tissue)
repair laceration (trauma)
Bakri-balloon (optional)

pharmacological treatment

oxytocin	bolus 5 U i.v. (fractionated), 10-20 U/2h i.v.
sulprostone (PgE$_2$)	100-500 μg/h i.v.
misoprostol (PgE$_1$)	1000 μg rectally
methylergometrine	0.2 mg intramyometrically or i.m.

hemostatic treatment

platelets > 50·10^9/l, fibrinogen > 1g/l, PT > 50%, pH ≥ 7.2, temp ≥ 35°
Replace coagulation factors (consult hemostasiologist if possible)

rFVIIa

only if **all** above parameters of hemostatic treatment fullfilled !
40-60-(90) μg/kg

surgical treatment / explorative laparotomy

compressive stitches
(e.g. B-Lynch suture)

ligation of uterine or internal iliac arteries

hysterectomy

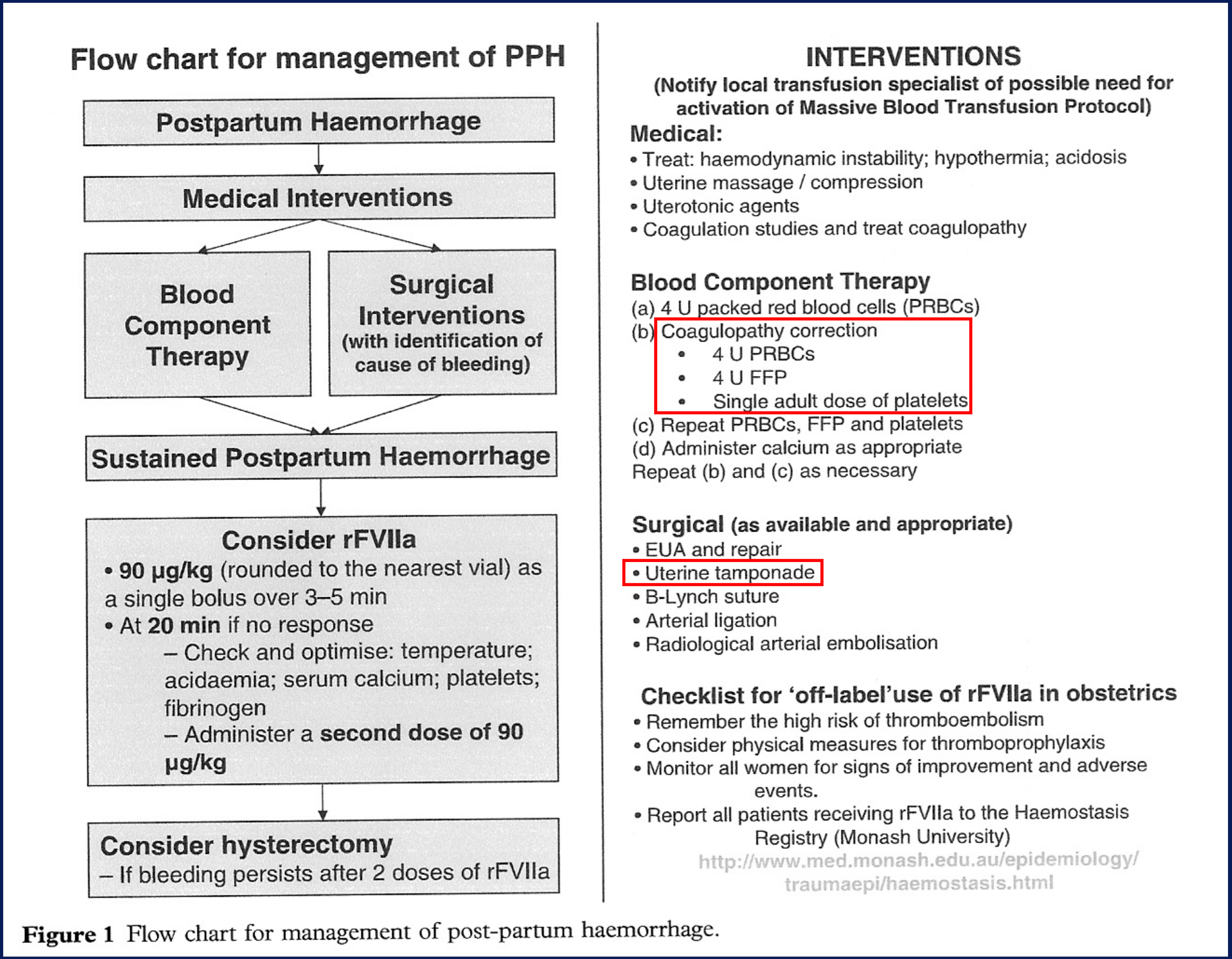
interventional radiology

if available:
uterine artery embolisation

1.9.2009

Guidelines for the use of rFVIIa in massive obstetric Haemorrhage

Welsh A et al, Aust N Z J Obstet Gynaecol 2008; 48: 12-16



Flow chart for management of PPH

Postpartum Haemorrhage

Medical Interventions

Blood Component Therapy

Surgical Interventions **(with identification of cause of bleeding)**

Sustained Postpartum Haemorrhage

Consider rFVIIa
- **90 µg/kg** (rounded to the nearest vial) as a single bolus over 3–5 min
- At **20 min** if no response
  - – Check and optimise: temperature; acidaemia; serum calcium; platelets; fibrinogen
  - – Administer a **second dose of 90 µg/kg**

Consider hysterectomy
– If bleeding persists after 2 doses of rFVIIa

INTERVENTIONS

(Notify local transfusion specialist of possible need for activation of Massive Blood Transfusion Protocol)

Medical:
- Treat: haemodynamic instability; hypothermia; acidosis
- Uterine massage / compression
- Uterotonic agents
- Coagulation studies and treat coagulopathy

Blood Component Therapy

(a) 4 U packed red blood cells (PRBCs)
(b) Coagulopathy correction
- 4 U PRBCs
- 4 U FFP
- Single adult dose of platelets

(c) Repeat PRBCs, FFP and platelets
(d) Administer calcium as appropriate
Repeat (b) and (c) as necessary

Surgical (as available and appropriate)
- EUA and repair
- Uterine tamponade
- B-Lynch suture
- Arterial ligation
- Radiological arterial embolisation

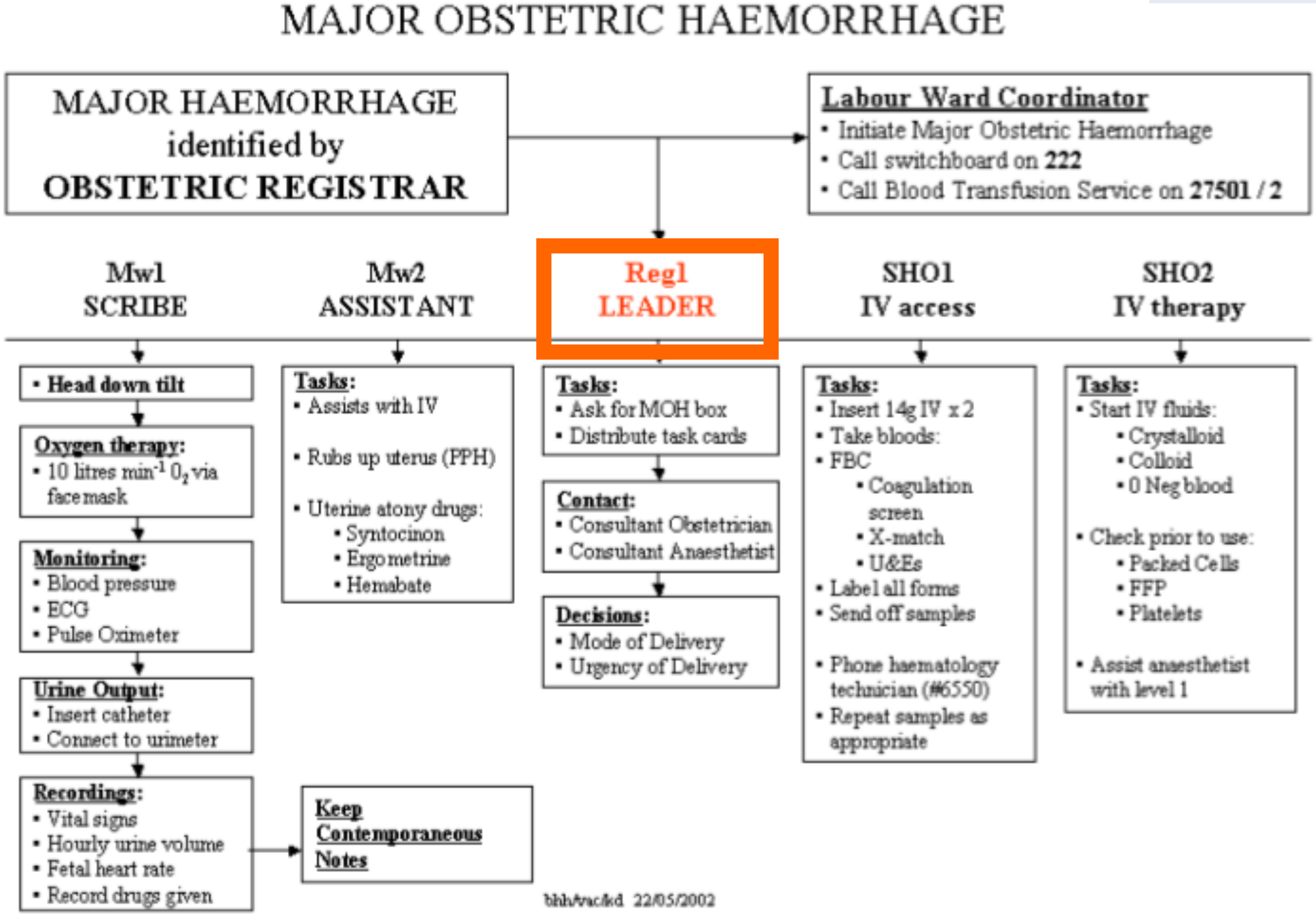
Checklist for 'off-label'use of rFVIIa in obstetrics
- Remember the high risk of thromboembolism
- Consider physical measures for thromboprophylaxis
- Monitor all women for signs of improvement and adverse events.
- Report all patients receiving rFVIIa to the Haemostasis Registry (Monash University)
  http://www.med.monash.edu.au/epidemiology/traumaepi/haemostasis.html

Figure 1 Flow chart for management of post-partum haemorrhage.

NHS Lothian

SIMPSON CENTRE FOR REPRODUCTIVE HEALTH
ROYAL INFIRMARY of EDINBURGH

Major Obstetric Haemorrhage Flow Chart



MAJOR OBSTETRIC HAEMORRHAGE

MAJOR HAEMORRHAGE
identified by
OBSTETRIC REGISTRAR

Labour Ward Coordinator
- Initiate Major Obstetric Haemorrhage
- Call switchboard on **222**
- Call Blood Transfusion Service on **27501 / 2**

Mw1
SCRIBE
- **Head down tilt**

Oxygen therapy:
- 10 litres min^{-1} O_2 via face mask

Monitoring:
- Blood pressure
- ECG
- Pulse Oximeter

Urine Output:
- Insert catheter
- Connect to urimeter

Recordings:
- Vital signs
- Hourly urine volume
- Fetal heart rate
- Record drugs given

Keep Contemporaneous Notes

Mw2
ASSISTANT

Tasks:
- Assists with IV
- Rubs up uterus (PPH)
- Uterine atony drugs:
  - Syntocinon
  - Ergometrine
  - Hemabate

Reg1
LEADER

Tasks:
- Ask for MOH box
- Distribute task cards

Contact:
- Consultant Obstetrician
- Consultant Anaesthetist

Decisions:
- Mode of Delivery
- Urgency of Delivery

SHO1
IV access

Tasks:
- Insert 14g IV x 2
- Take bloods:
- FBC
  - Coagulation screen
  - X-match
  - U&Es
- Label all forms
- Send off samples
- Phone haematology technician (#6550)
- Repeat samples as appropriate

SHO2
IV therapy

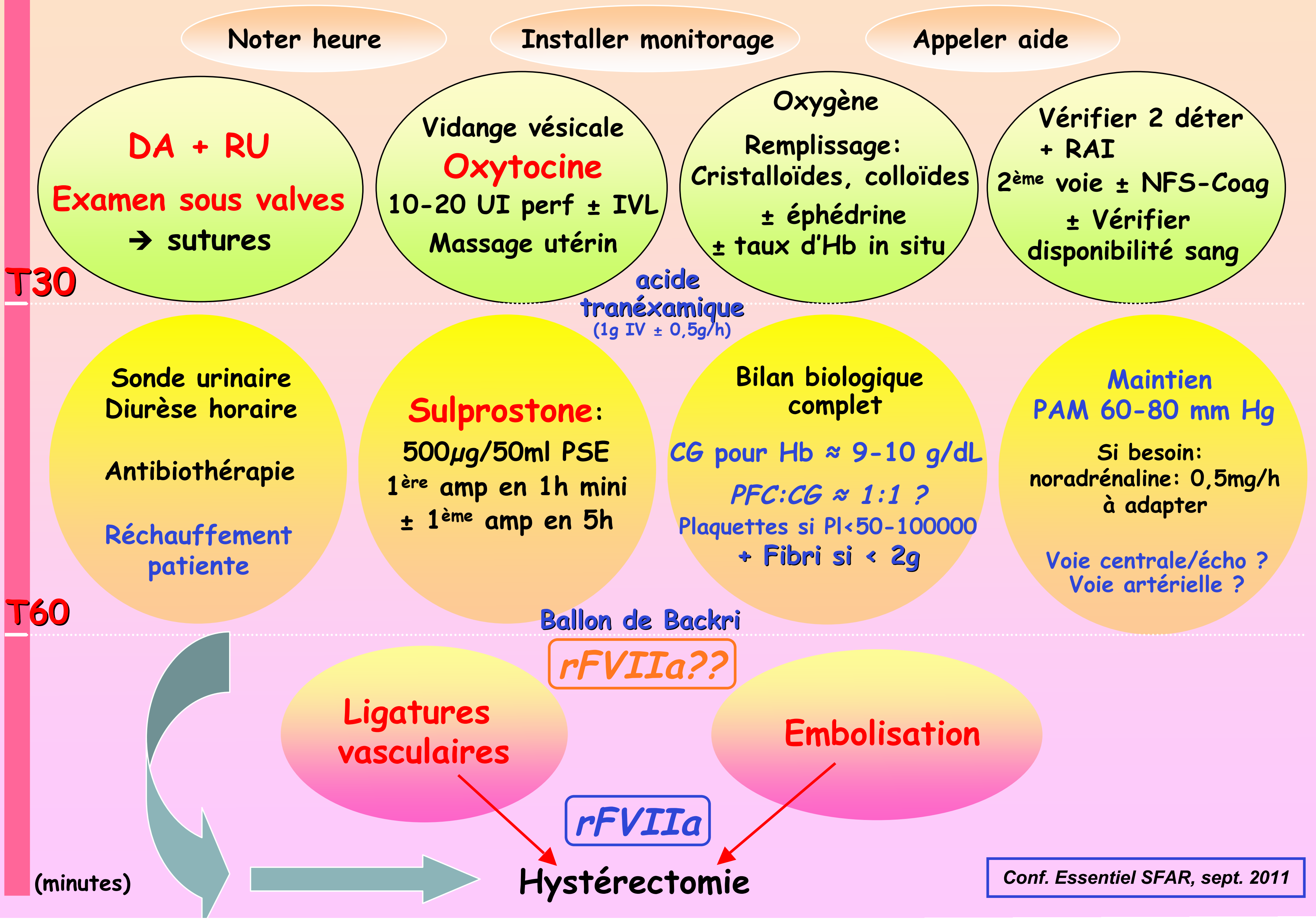
Tasks:
- Start IV fluids:
  - Crystalloid
  - Colloid
  - 0 Neg blood
- Check prior to use:
  - Packed Cells
  - FFP
  - Platelets
- Assist anaesthetist with level 1

bhh/rac/kd 22/05/2002

TASK

(Courtesy of Vicky Clark)

Hémorragie en salle de naissance



Noter heure

Installer monitorage

Appeler aide

DA + RU

Examen sous valves

→ sutures

Vidange vésicale

Oxytocine

10-20 UI perf ± IVL

Massage utérin

Oxygène

Remplissage:

Cristalloïdes, colloïdes

± éphédrine

± taux d'Hb in situ

Vérifier 2 déter + RAI

2ème voie ± NFS-Coag

± Vérifier disponibilité sang

T30

acide tranéxamique

(1g IV ± 0,5g/h)

Sonde urinaire

Diurèse horaire

Antibiothérapie

Réchauffement patiente

Sulprostone:

500µg/50ml PSE

1ère amp en 1h mini

± 1ème amp en 5h

Bilan biologique complet

CG pour Hb ≈ 9-10 g/dL

PFC:CG ≈ 1:1 ?

Plaquettes si Pl<50-100000

+ Fibri si < 2g

Maintien

PAM 60-80 mm Hg

Si besoin:

noradrénaline: 0,5mg/h

à adapter

Voie centrale/écho ?

Voie artérielle ?

T60

Ballon de Backri

rFVIIa??

Ligatures vasculaires

Embolisation

rFVIIa

Hystérectomie

(minutes)

Conf. Essentiel SFAR, sept. 2011

Conclusion

- Les règles de base des RPC sur l'HPP de déc. 2004 demeurent valables
- Nouveautés de ces dernières années :
  - transfusion massive et les hémostatiques (ATX, fibri & rFVIIa)
  - prise en charge réanimatoire plus précoce et plus « agressive »
  - réflexions encore « embryonnaires » sur :
    - la place des ballons intra-utérins, notamment avant transfert, ou transport au bloc opératoire ou en embolisation
    - une stratégie spécifique pour l'HPP survenant durant la césarienne
    - une stratégie spécifique pour le P. accreta / percreta
    - la place des ballons en iliaques internes, voire en ilaques communes ou dans l'aorte sous-rénale

BECAR 2011

Hôtel Pullman Montparnasse - PARIS

Mer 7 et Jeu 8 décembre :
→ Anesthésie-Réanimation Obstétricale

secret.anesthesieb@abc.aphp.fr

(ou 01 45 37 42 73)