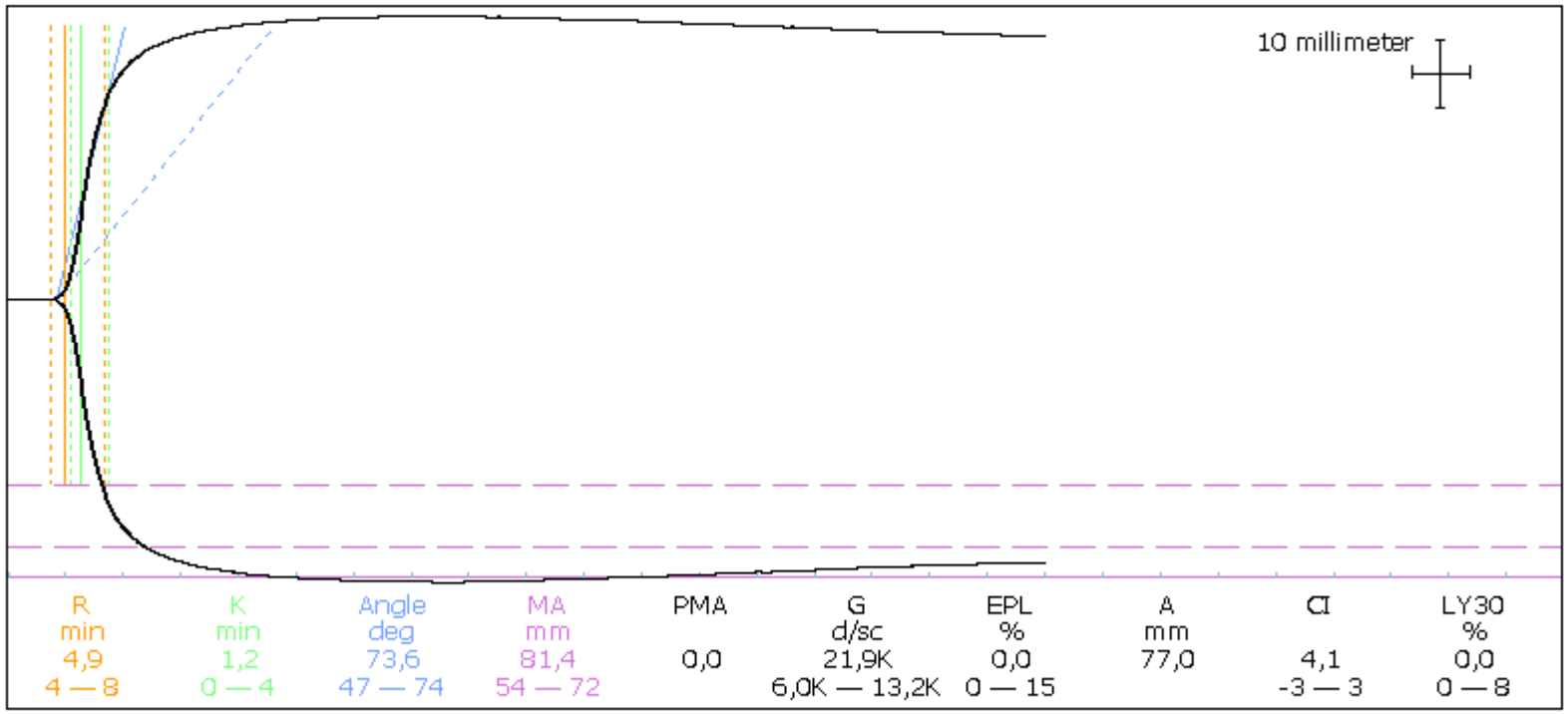
1 Kaolin

Prov: 2010-03-03 03:08PM-04:38PM



Hemostas under graviditet och förlossning

Ove Karlsson

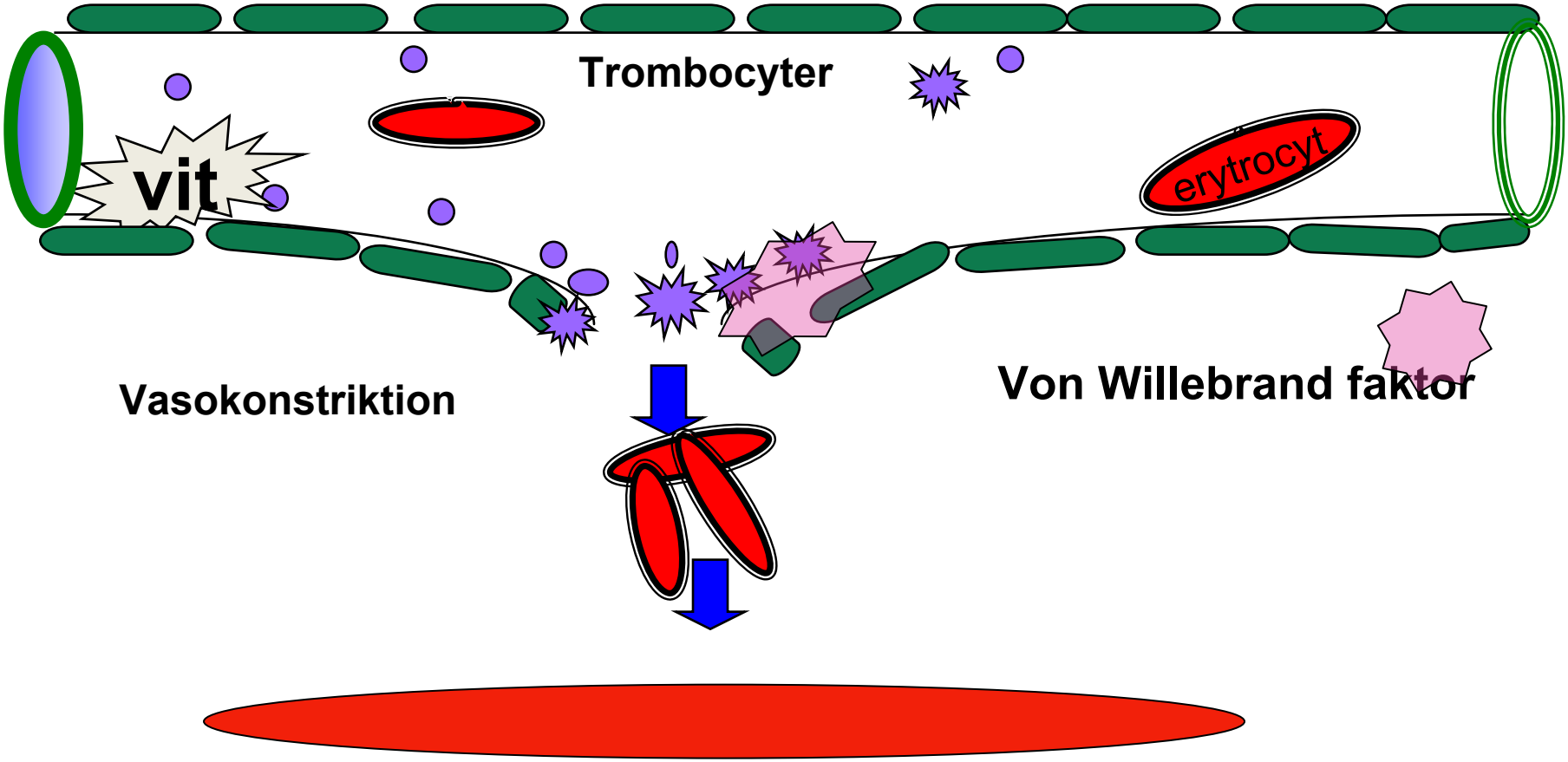
Sahlgrenska Universitetssjukhuset

Handledare

- Margareta Hellgren, professor
  Obstetriska kliniken, Område 1
  Sahlgrenska Universitetssjukhuset

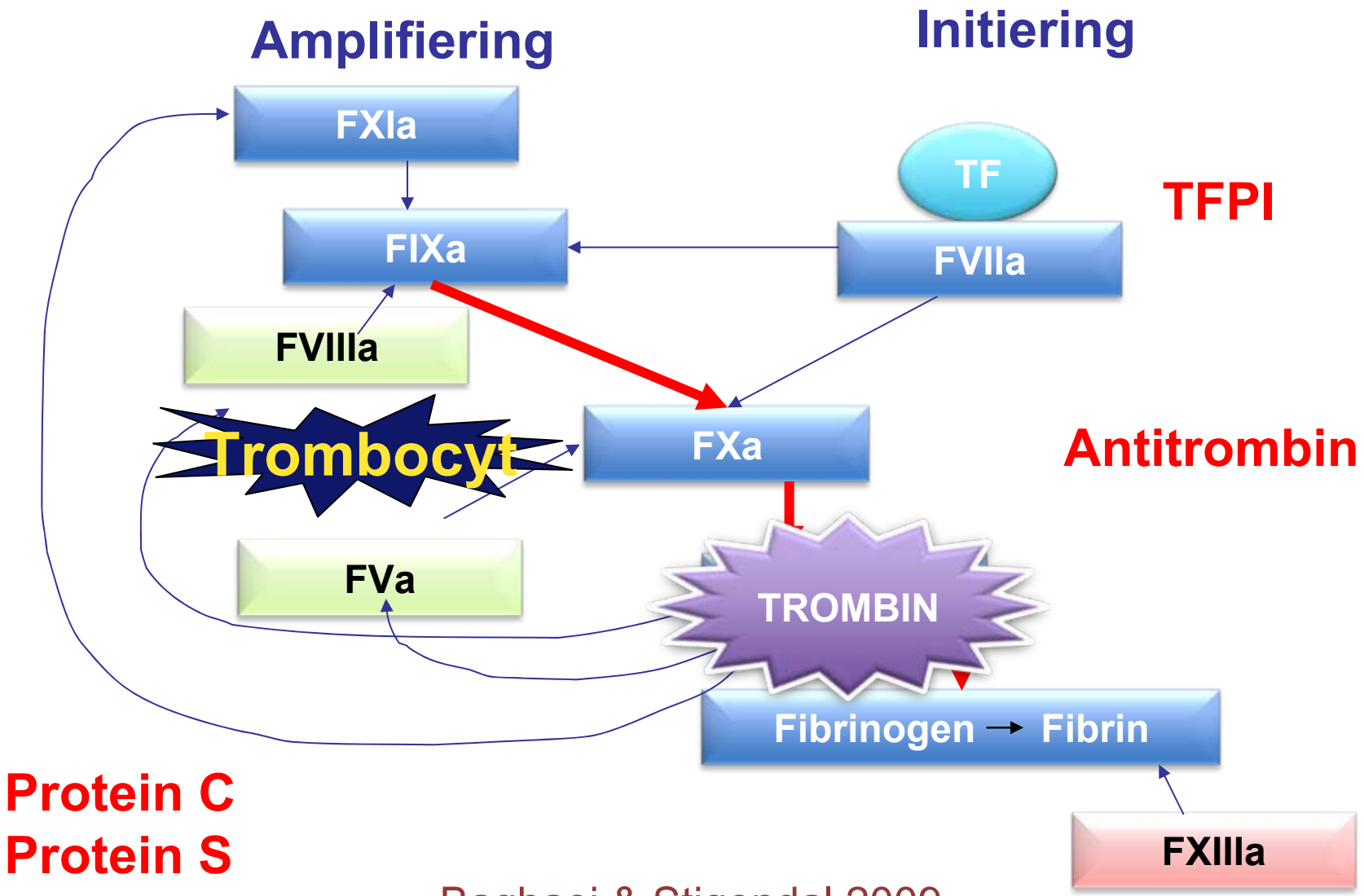
- Anders Jeppsson, professor
  Thorax kliniken, Område 6
  Sahlgrenska Universitetssjukhuset

VAD HÄNDER VID EN KÄRLSKADA?



Baghaei & Stigendal 2009

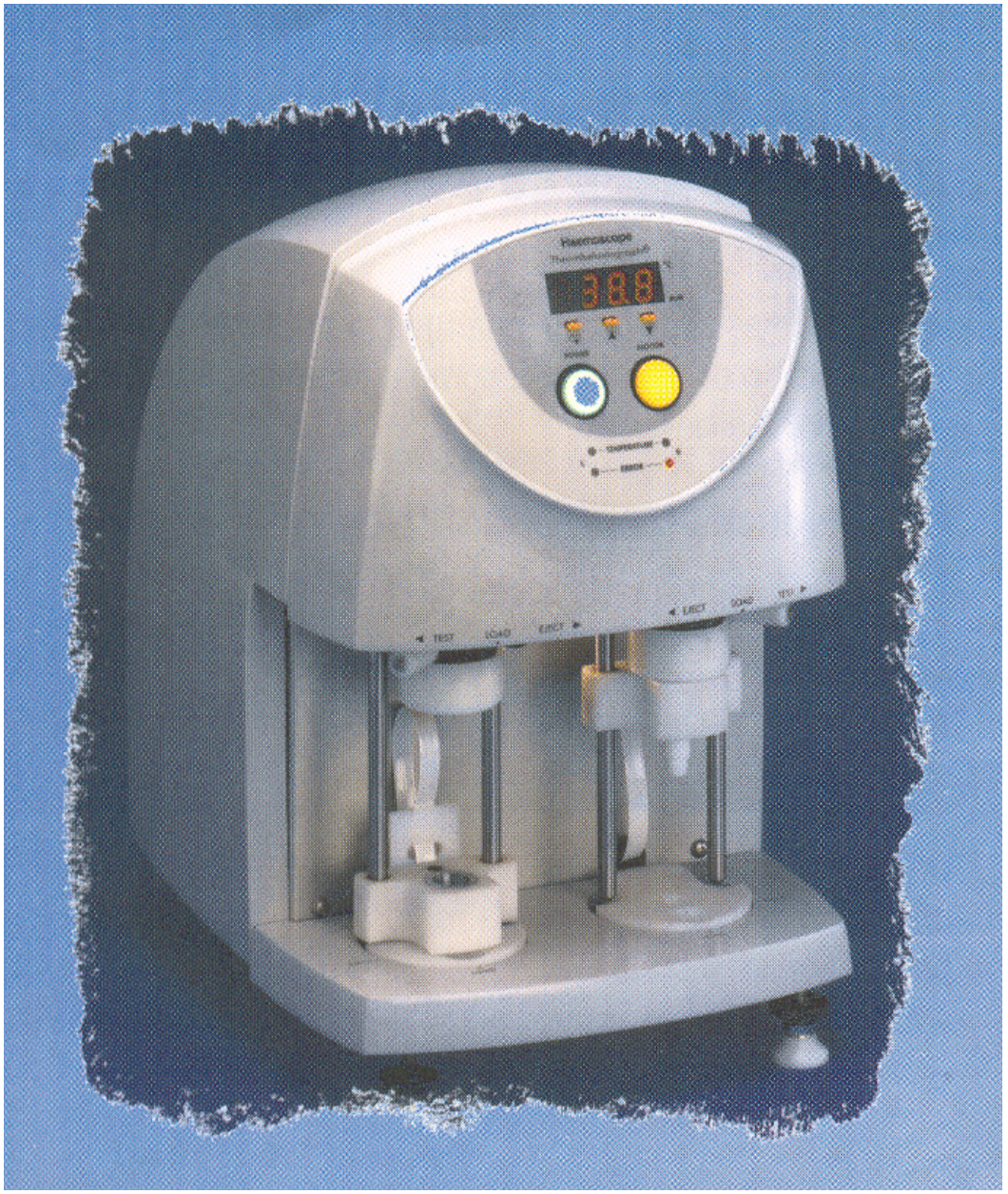
KOAGULATIONEN

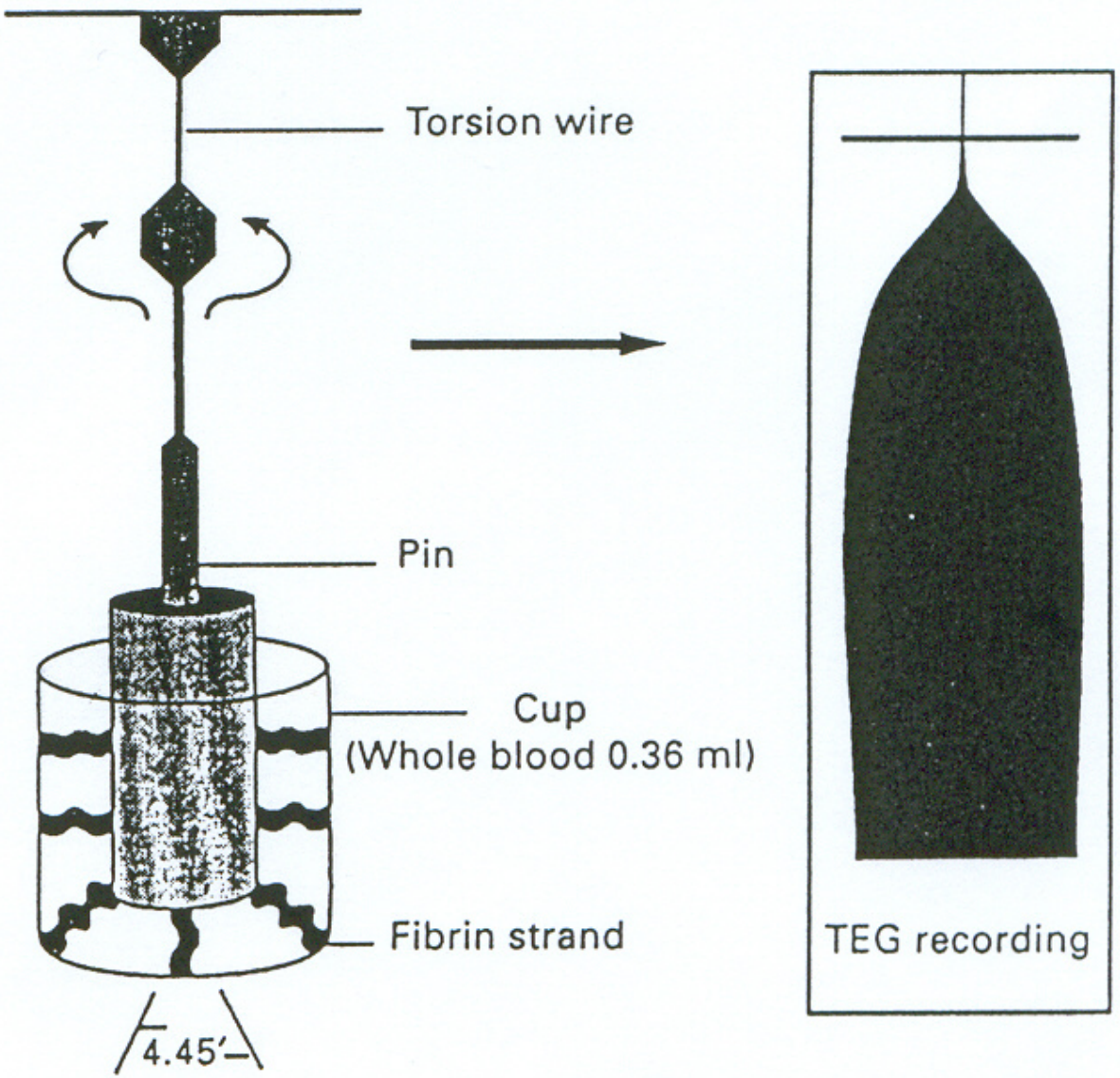


Baghaei & Stigendal 2009

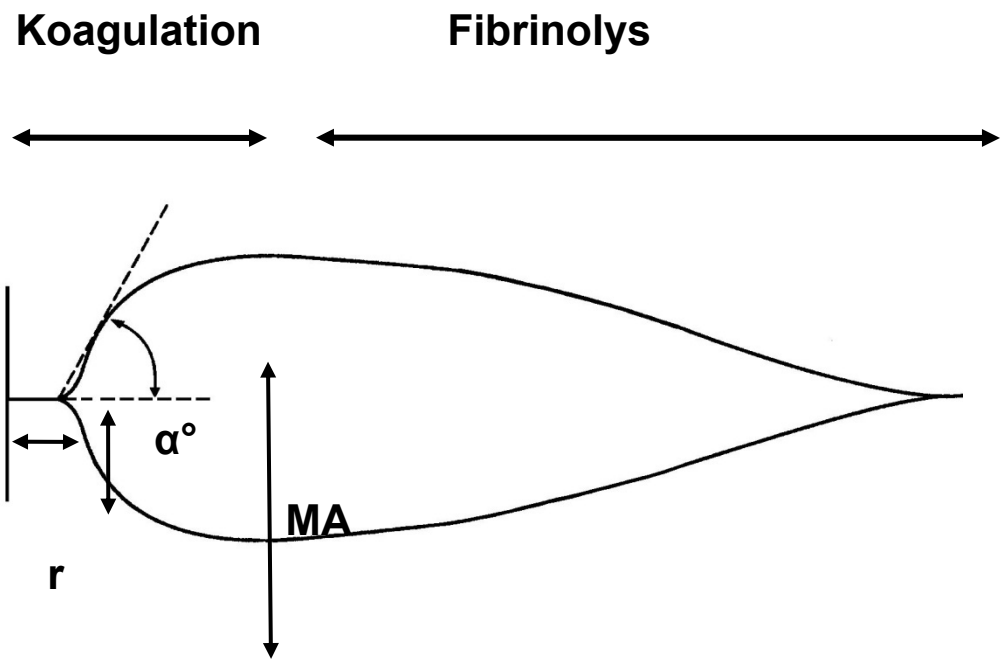
Under graviditet

- Faktorer ↗
  - Fibrinogen
  - Faktor VII, VIII, X, XII
  - vWF
- Faktorer ➔
  - Protein C
  - Antitrombin ev ↘
- Faktorer ↘
  - Faktor XI, XIII
  - Protein S
- Fibrinolysen ↘
  - Plasminogen ↗
  - PAI-1 ↗↗
  - PAI-2 ↗↗


Haemascope
Thrombelastograph
388
TEST
LOAD
EJECT
EJECT
LOAD
TEST


Torsion wire
Pin
Cup
(Whole blood 0.36 ml)
Fibrin strand
4.45'
TEG recording

TEG



Normalvärden

r = reaktionstid 6-9 min

MA = maximal amplitud 50-70 mm

α° = koagelbildningshastighet > 50°

Kang et al: Anesth Analg 1985:64:888-896

Society for Obstetric Anesthesia and Perinatology

Section Editor: Cynthia A. Wong

Prospective Longitudinal Study of Thromboelastography and Standard Hemostatic Laboratory Tests in Healthy Women During Normal Pregnancy

Ove Karlsson, MD,* Tommy Sporrong, MD, PhD,† Andreas Hillarp, PhD,† Anders Jeppsson, MD, PhD,‖¶ and Margareta Hellgren, MD, PhD†#

BACKGROUND: Hemostatic disorders are common in obstetric complications. Thromboelastography (TEG®) simultaneously measures coagulation and fibrinolysis within 10 to 20 minutes. Our primary aim in this prospective longitudinal study was to obtain knowledge about physiological changes in TEG® variables during normal pregnancy and 8 weeks postpartum. The secondary aims were to compare TEG® variables during pregnancy with TEG® variables 8 weeks postpartum and gestational weeks 10 to 15 and to correlate TEG® variables to standard laboratory analyses.

METHODS: Blood samples were collected from 45 healthy pregnant women at gestational weeks 10 to 15, 20 to 22, 28 to 30, and 38 to 40, and at 8 weeks postpartum. The following TEG® analyses were performed: time until start of clotting (TEG®-R), time until 20-mm clot firmness (TEG®-K), angle of clotting (TEG®-Angle), maximum amplitude (TEG®-MA), and lysis after 30 minutes (TEG®-LY30). Activated partial thromboplastin time, prothrombin time, soluble fibrin, antithrombin, D-dimer, and platelet count were analyzed.

RESULTS: Compared to 8 weeks postpartum TEG®-R was at least 0.9 minutes shorter (upper limit 99% confidence intervals) until gestational weeks 28 to 30 and the mean reduction varied between 23%–26%. TEG®-K was at least 0.1 minutes shorter throughout pregnancy and the mean reduction varied between 18%–35%. TEG®-Angle was at least 2.5 degrees greater during pregnancy and the mean increase varied between 12%–20%. TEG®-MA was also at least 0.4 mm greater during pregnancy and the mean increase varied between 6%–8%. TEG®-LY30 was at least 0.03% lower during gestational weeks 28 to 30 and 38 to 40 and the mean reduction varied between 67%–73%. The routine coagulation laboratory values were within normal pregnant limits. There were no or weak correlations between TEG® and the laboratory variables.

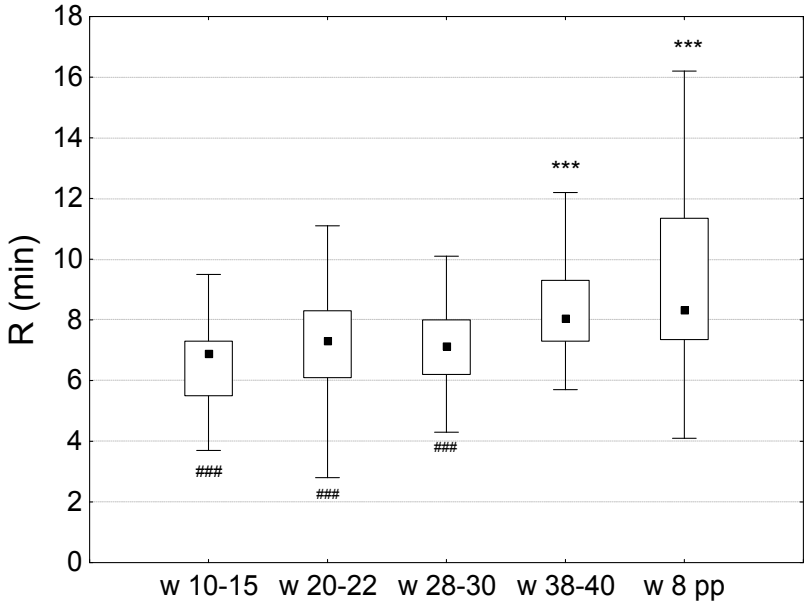
CONCLUSIONS: TEG® demonstrates increased coagulability and decreased fibrinolysis during pregnancy. There was a faster initiation of hemostasis, with a minor increase in clot strength. Fibrinolysis decreased during late pregnancy. Alternative cutoff limits for TEG® variables may be required during pregnancy. Standard hemostatic laboratory tests were as expected during pregnancy. Future studies are needed to ascertain whether viscoelastic methods are preferable to standard hemostatic tests for the diagnosis of coagulopathy during obstetric hemorrhage. (Anesth Analg 2012;115:890–8)

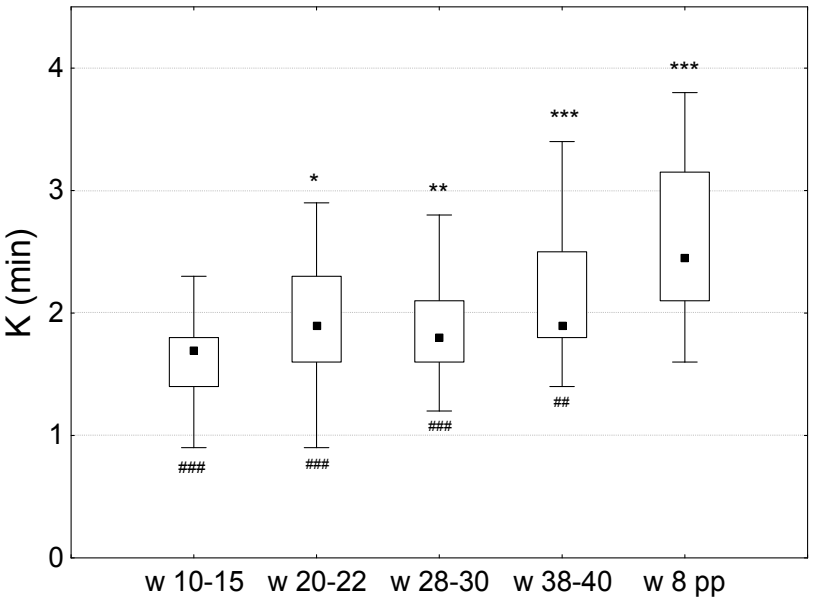
Aims

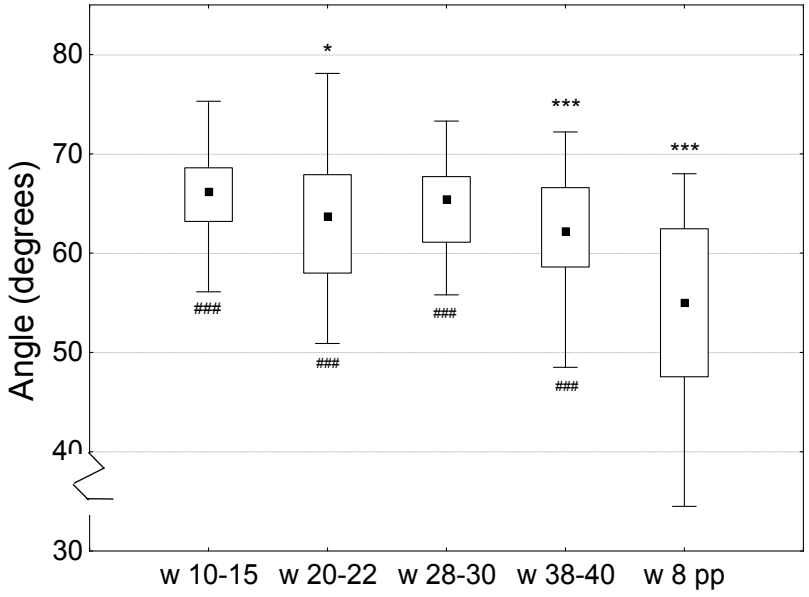
- To obtain knowledge about changes in TEG variables during normal pregnancy and at 8 weeks' postpartum
- Assess laboratory analyses, including APTT, PT, platelet count, antithrombin, soluble fibrin and D-dimer
- To evaluate if correlations exist between these parameters and the TEG variables during normal pregnancy and 8 weeks' postpartum

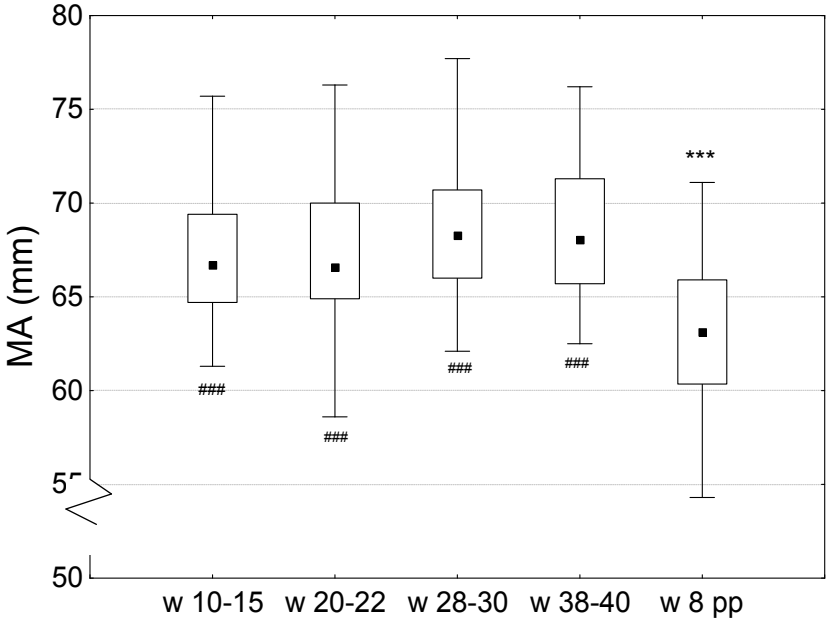
Methods

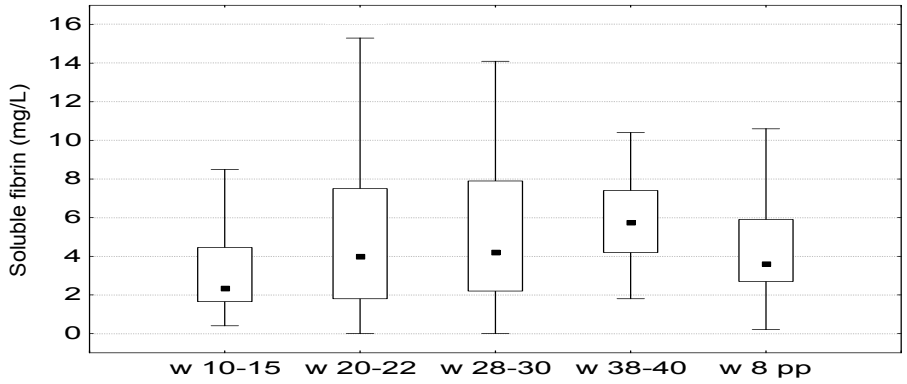
- Blood samples were collected from 45 pregnant women at gestational weeks' 10-15, 20-22, 28-30 and 38-40 and at 8 weeks' postpartum
- TEG analyses: time until start of clotting (TEG-R), time until 20 mm clot firmness (TEG-K), angle of clotting (TEG-Angle), maximum amplitude (TEG-MA) and lysis after 30 minutes (TEG-LY30)
- Activated partial thromboplastin time (APTT), prothrombin time (PT), soluble fibrin, antithrombin, D-dimer and platelet count

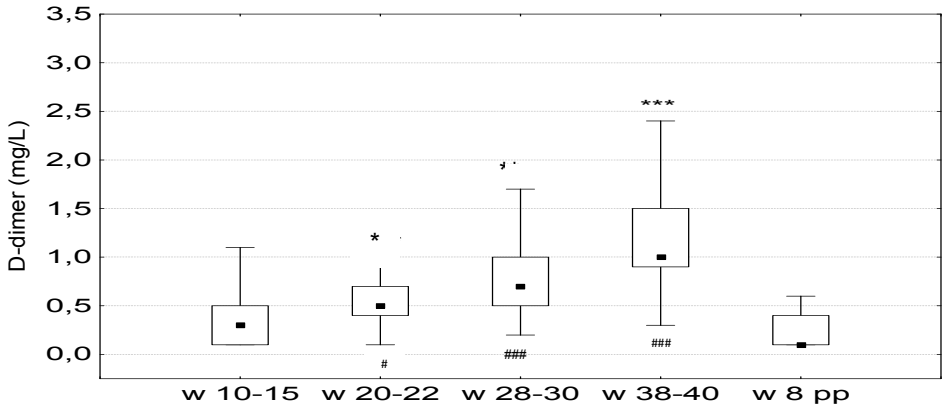

R (min)
18
16
14
12
10
8
6
4
2
0
***
***
###
###
###
w 10-15
w 20-22
w 28-30
w 38-40
w 8 pp

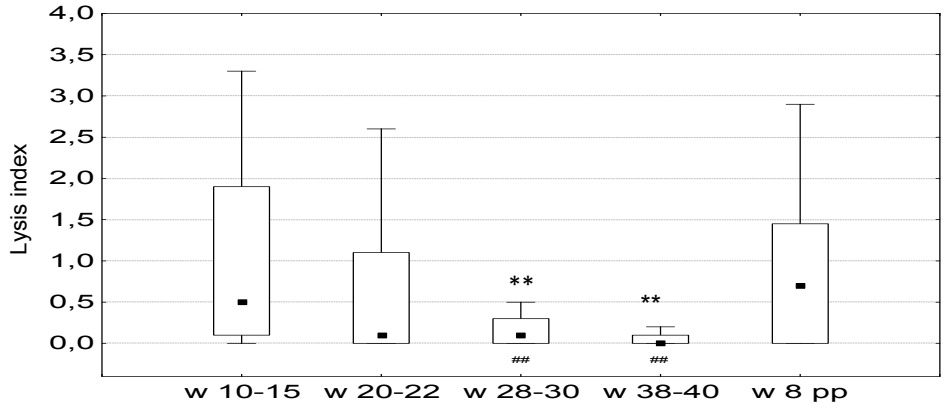

K (min)
4
3
2
1
0
*
**
***
***
###
###
###
##
w 10-15
w 20-22
w 28-30
w 38-40
w 8 pp


Angle (degrees)
80
70
60
50
40
30
*
***
***
###
###
###
###
w 10-15
w 20-22
w 28-30
w 38-40
w 8 pp


MA (mm)
80
75
70
65
60
50
***
###
###
###
###
w 10-15
w 20-22
w 28-30
w 38-40
w 8 pp


Soluble fibrin (mg/L)
16
14
12
10
8
6
4
2
0
w 10-15
w 20-22
w 28-30
w 38-40
w 8 pp


D-dimer (mg/L)
3,5
3,0
2,5
2,0
1,5
1,0
0,5
0,0
*
***
#
###
###
w 10-15
w 20-22
w 28-30
w 38-40
w 8 pp


Lysis index
4,0
3,5
3,0
2,5
2,0
1,5
1,0
0,5
0,0
**
**
##
##
w 10-15
w 20-22
w 28-30
w 38-40
w 8 pp

Conclusions

- TEG demonstrates increased coagulability and decreased fibrinolysis during pregnancy
- There was a faster initiation of hemostasis, with a minor increase in clot strength
- Alternative cutoff limits for TEG-K, TEG-Angle and TEG-MA may be required during pregnancy
- Future studies are needed to ascertain whether viscoelastic methods are preferable to standard hemostatic tests in cases of bleeding complications

International Journal of Obstetric Anesthesia (2014) 23, 10–17
0959-289X/$ - see front matter
http://dx.doi.org/10.1016/j.ijoa.2013.07.003

ORIGINAL ARTICLE

ELSEVIER
www.obstetanesthesia.com

Major obstetric haemorrhage: monitoring with thromboelastography, laboratory analyses or both?

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[b] *Department of Cardiovascular Surgery and Anaesthesia, Sahlgrenska University Hospital and Department of Molecular and Clinical Medicine, University of Gothenburg, Gothenburg, Sweden*
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ABSTRACT
Background: Haemorrhage is a common cause of morbidity and mortality in the obstetric population. The aim of this study was to compare the use of thromboelastography and laboratory analyses to evaluate haemostasis during major obstetric haemorrhage. A secondary aim was to evaluate correlations between the results of thromboelastography, laboratory analyses and estimated blood loss.
Methods: Forty-five women with major obstetric haemorrhage and 49 women with blood loss <600 mL were included. The following thromboelastography analyses were performed: time to start of clotting (TEG-R), time to 20 mm of clot firmness (TEG-K), rate of clot growth (TEG-Angle), maximum amplitude of clot (TEG-MA) and lysis after 30 min (TEG-LY30). In addition, platelet count, activated partial thromboplastin time, prothrombin time, fibrinogen, antithrombin and D-dimer were measured.
Results: Thromboelastography variables reflecting clot stability and fibrinolysis were decreased in women with massive obstetric haemorrhage compared to women with normal bleeding, while clot initiation was accelerated. Laboratory analyses also showed impaired haemostasis with the most pronounced differences in platelet count, fibrinogen concentration and antithrombin activity. The strongest correlations existed between fibrinogen and TEG-MA and between estimated blood loss and TEG-MA, fibrinogen and antithrombin, respectively.
Conclusions: Impaired haemostasis, demonstrated by thromboelastography and laboratory analyses, was found after an estimated blood loss of 2000 mL. Thromboelastography provides faster results than standard laboratory testing which is advantageous in the setting of on-going obstetric haemorrhage. However, laboratory analyses found greater differences in coagulation variables, which correlated better with estimated blood loss.

Aims

- To evaluate the use of thromboelastography and laboratory analyses during major obstetric haemorrhage
- To evaluate whether there were any correlations between thromboelastography, laboratory analyses and estimated blood loss

Methods

- Forty-five women with major obstetric haemorrhage and 49 women with normal deliveries were included
- Thromboelastography analyses: time until start of clotting (TEG-R), time until 20 mm of clot firmness (TEG-K), rate of clot growth (TEG-Angle), maximum amplitude of clot (TEG-MA) and lysis after 30 minutes (TEG-LY30).
- Platelet count, activated partial thromboplastin time, prothrombin time, fibrinogen, antithrombin and D-dimer

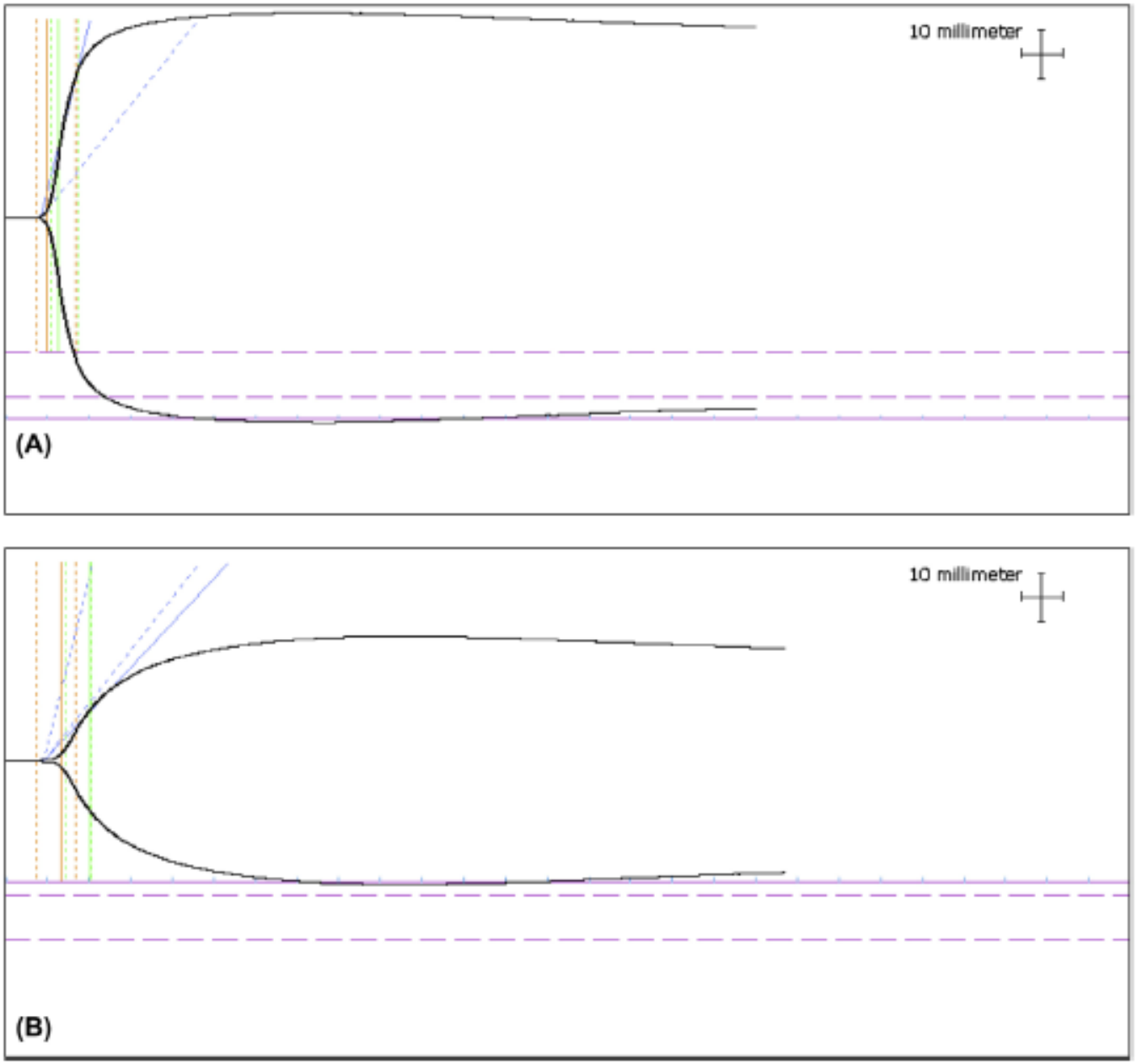


Fig. 1 Two thromboelastographic profiles. (A) TEG profile in a woman with normal bleeding postpartum. Estimated blood loss 250 mL, TEG-R 4.9 min, TEG-MA 81.4 mm, platelets 239×10^9/L, fibrinogen 6.0 g/L and antithrombin 0.98 kIU/L. (B) TEG profile in a woman with major obstetric haemorrhage. Estimated blood loss 2500 mL, TEG-R 6.6 min, TEG-MA 48.9 mm, platelets 55×10^9/L, fibrinogen 1.7 g/L, antithrombin 0.37 kIU/L.

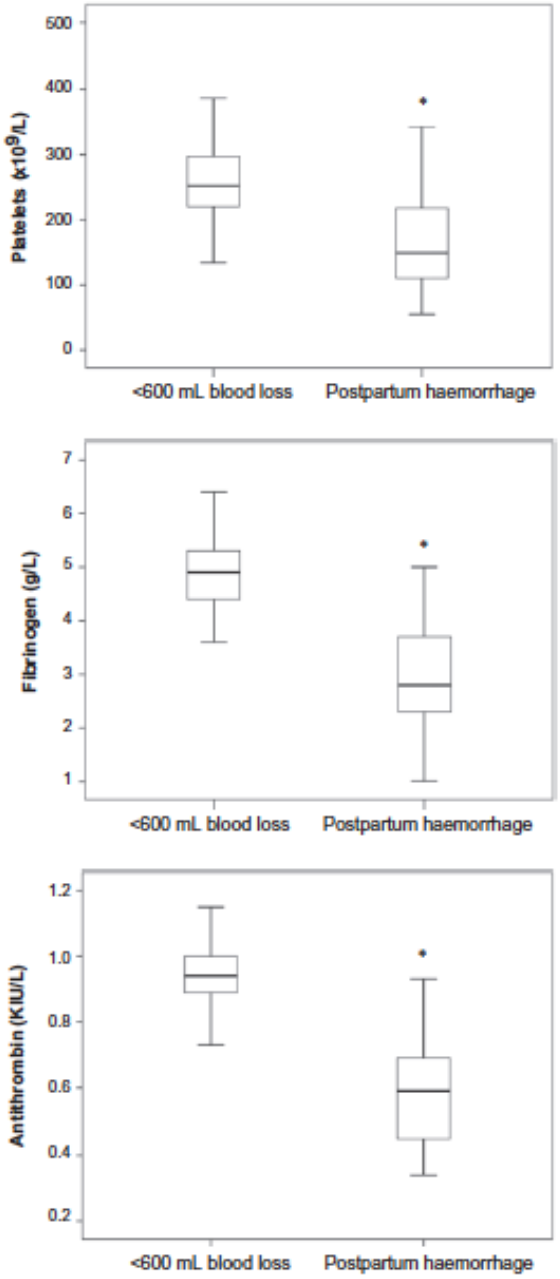


Fig. 2 Platelets, fibrinogen and antithrombin in women with normal bleeding postpartum and in women with major obstetric haemorrhage. Box-whisker plots with median, 25%–75% percentile, minimum and maximum. *$P < 0.0001$.

TEG		Normal bleeding	Major obstetric haemorrhage, all	Major obstetric haemorrhage, <3L	Major obstetric haemorrhage, ≥3L
	Women, n	49	45	35	10
R, min	Mean	6.3	**5.1 ****	5.2	4.5
	95% CI	5.8 to 6.9	4.5 to 5.7	4.5 to 5.9	3.2 to 5.9
	Range	1.8 – 13.4	1.3 – 9.6	1.6 – 9.6	1.3 – 6.7
K, min	Mean	1.8	2.0	2.0	2.1
	95% CI	1.6 to 2.1	1.8 to 2.2	1.8 to 2.2	1.6 to 2.6
	Range	1.0 – 5.3	1.2 – 3.7	1.2 – 3.7	1..3 – 3.3
Angle, degree	Mean	65.2	**61.3 ***	61.4	60.8
	95% CI	62.7 to 67.6	58.7 – 63.8	58.4 to 64.3	55.0 to 66.7
	Range	38.6 – 77.1	42.1 – 72.1	42.1 – 72.1	48.5 – 71.8
MA, mm	Mean	72.9	**64.8 ******	65.1	63.8
	95% CI	71.4 to 74.4	62.4 to 67.3	62.2 to 68.1	59.7 to 67.9
	Range	54.2 – 81.6	38.0 – 79.4	38.0 – 79.4	55.4 – 74.6
LY 30, %	Mean	1.5	**0.4 ****	0.4	0.2
	95% CI	0.9 to 2.2	0.1 to 0.7	0.1 to 0.8	-0.06 to 0.4
	Range	0.0 – 9.3	0 – 5.9	0.0 – 5.9	0.0 – 0.9

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

Sample		Normal bleeding	Major obstetric haemorrhage, all	Major obstetric haemorrhage, <3L	Major obstetric haemorrhage, ≥3L
	Women, n	48-49	41-44	31-34	9-10
Platelet count, $x10^9$	Mean 95% CI Range	260.1 242 to 278 134 – 461	**167.8** **** 145 to 190 55 – 343	179.5 154 to 205 55 - 343	128.1 84 to 172 68 - 285
APTT, s	Mean 95% CI Range	31.4 30.8 to 31.9 28 – 36	**36.1** **** 34.7 to 37.4 30 – 49	35.5 33.9 to 37.1 30 - 49	37.9 35.0 to 40.8 30 - 43
PT (INR)	Mean 95% CI Range	0.95 0.9 to 1.0 0.8 – 1.1	**1.07** **** 1.0 to 1.1 0.8 – 1.4	1.06 1.0 to 1.1 0.8 – 1.4	1.10 1.0 to 1.2 0.9 – 1.2
Fibrinogen, g/L	Mean 95% CI Range	4.8 4.6 to 5.0 3.6 – 6.7	**3.0** **** 2.7 to 3.3 1.0 – 5.0	3.1 2.8 to 3.5 1.0 – 5.0	2.5 1.9 to 3.0 1.8 – 4.1
Anti-thrombin, kIU/L	Mean 95% CI Range	0.96 0.93 to 0.99 0.73 – 1.19	**0.60** **** 0.54 to 0.65 0.34 – 1.10	0.62 0.55 to 0.69 0.34 – 1.10	0.53 0.45 to 0.61 0.40 – 0.78
D-dimer, mg/L	Mean 95% CI Range	4.1 3.1 to 5.1 1.3 – 21.0	**8.1** **** 6.1 to 10.2 1.1 – 21.0	8.3 5.9 to 10.7 1.1 – 21.0	7.6 2.8 to 12.4 1.6 – 21.0

**** $p<0.0001$

Conclusions

- Impaired haemostasis, demonstrated by thromboelastography and laboratory analyses, was found after an estimated blood loss of 2000 mL
- Thromboelastography provides faster results than standard laboratory testing which is advantageous in the setting of ongoing obstetric haemorrhage
- Laboratory analyses found greater differences in coagulations variables and correlated better with estimated blood loss

A longitudinal study of Factor XIII activity, fibrinogen concentration, platelet count and clot strength during normal pregnancy

Submitted Trombosis Research

Aims

- To describe longitudinal changes in factor XIII activity, fibrinogen concentration and platelet count during normal pregnancy
- Their potential associations with clot strength and to bleeding volume during delivery.

Methods

- A longitudinal observational study was undertaken in 44 healthy pregnant women
- Blood samples were collected during gestational weeks 10 to 15, 20 to 22, 28 to 30 and 38 to 40 and at 8 weeks postpartum
- Factor XIII activity, fibrinogen concentration, platelet count and clot strength (TEG-MA) were analysed at all time points
- Bleeding volume during delivery was registered

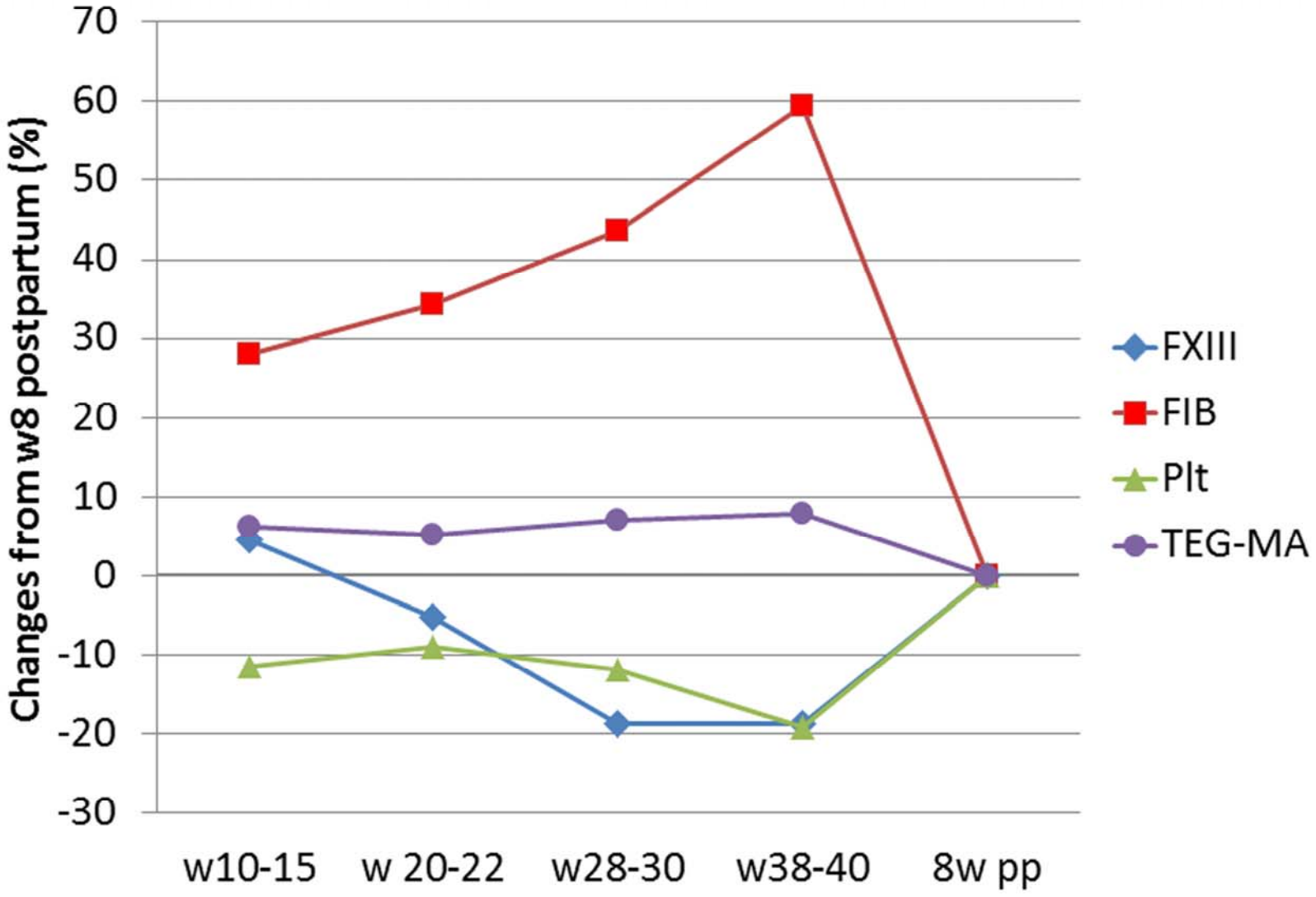

70
60
50
40
30
20
10
0
-10
-20
-30
Changes from w8 postpartum (%)
w10-15
w 20-22
w28-30
w38-40
8w pp
FXIII
FIB
Plt
TEG-MA

Table 2: Correlations between Factor XIII, fibrinogen and clot strength (TEG-MA) and between Factor XIII and fibrinogen in healthy women during normal pregnancy and at 8 weeks postpartum

Gestational weeks		Factor XIII/ TEG-MA	Fibrinogen/ TEG-MA	Factor XIII/ Fibrinogen
10-15	r	0.17	0.32	0.42
	r^2	0.03	0.10	0.18
	p	0.32	0.06	0.01
20-22	r	0.25	0.36	0.53
	r^2	0.06	0.13	0.28
	p	0.15	0.03	0.001
28-30	r	0.20	0.12	0.43
	r^2	0.04	0.01	0.18
	p	0.26	0.50	0.01
38-40	r	0.13	0.53	0.46
	r^2	0.02	0.29	0.21
	p	0.48	0.001	0.007
8 weeks postpartum	r	0.21	0.41	0.43
	r^2	0.05	0.17	0.19
	p	0.21	0.01	0.007

TEG-MA = maximum amplitude, r = Pearson's correlation coefficient, r^2 = coefficient of determination

Conclusions

- Factors influencing clot strength respond differently during normal pregnancy
- Factor XIII activity and platelet count were lower while fibrinogen concentrations was higher than at 8 weeks postpartum
- The resulting clot strength is increased during pregnancy compared to 8 weeks postpartum
- None of the investigated variables were associated with bleeding volume at delivery

Fibrinogen – predictor for major obstetric haemorrhage?

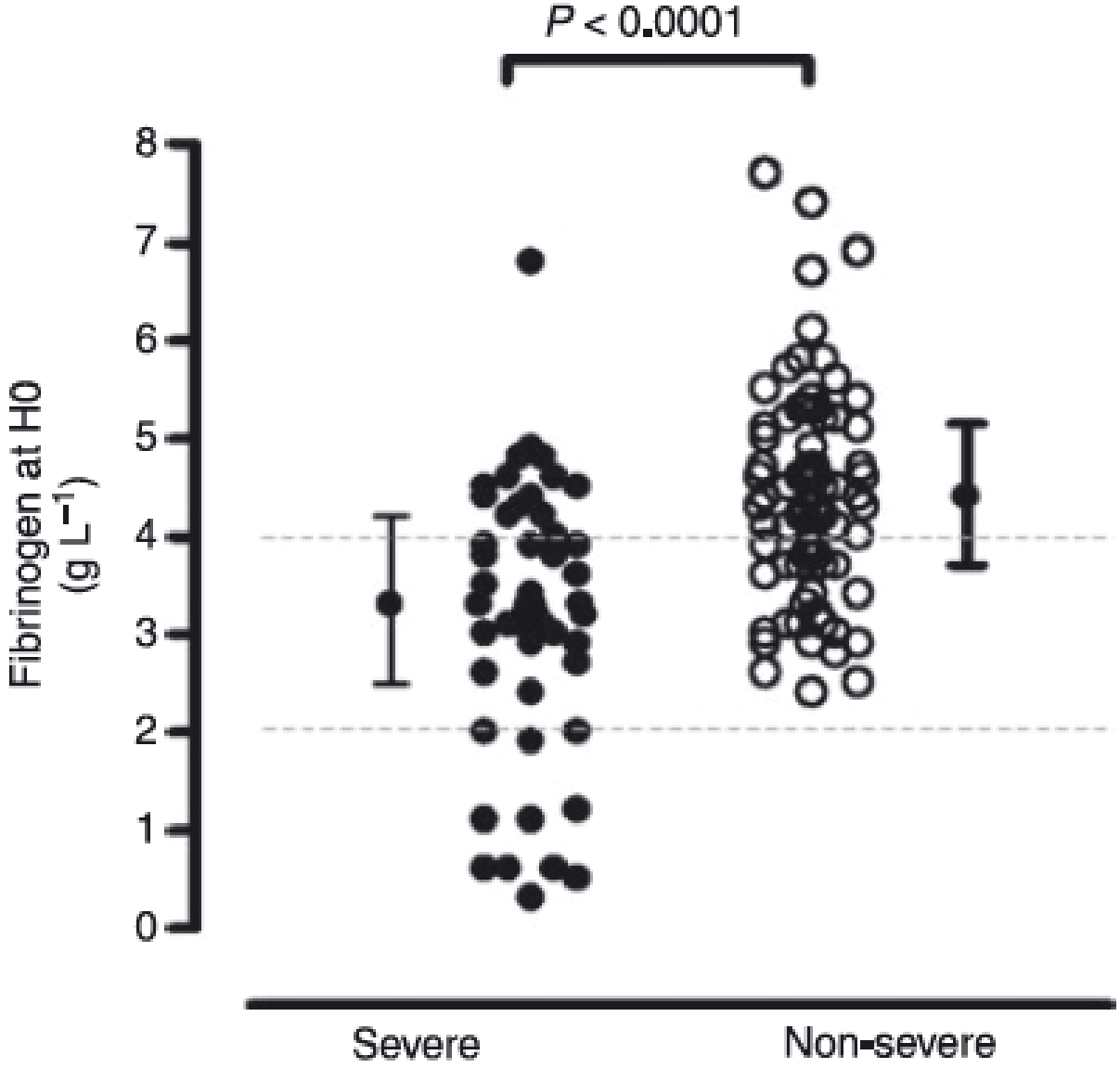
Manuscript

Journal of Thrombosis and Haemostasis, **5**: 266–273

ORIGINAL ARTICLE

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

B. CHARBIT,*† L. MANDELBROT,‡ E. SA
O. SIBONY,** D. MAHIEU-CAPUTO,¶ M
M. H. DENNINGER,†‡‡ and D. DE PROST
*AP-HP, Hôpital Saint-Antoine, Clinical Investigation Ce
§Hôpital Jean Minjoz, Besançon; ¶AP-HP, Hôpital Bichat
PhenoGen, Paris, France



British Journal of Anaesthesia **108** (6): 984–9 (2012)
Advance Access publication 6 April 2012 · doi:10.1093/bja/aes096

BJA

OBSTETRICS

Association between fibrinogen level and severity of postpartum haemorrhage: secondary analysis of a prospective trial

M. Cortet[1,2,3,4*], C. Deneux-Tharaux[5], C. Dupont[6,7], C. Colin[8], R.-C. Rudigoz[9], M.-H. Bouvier-Colle[5] and C. Huissoud[2,9,10]

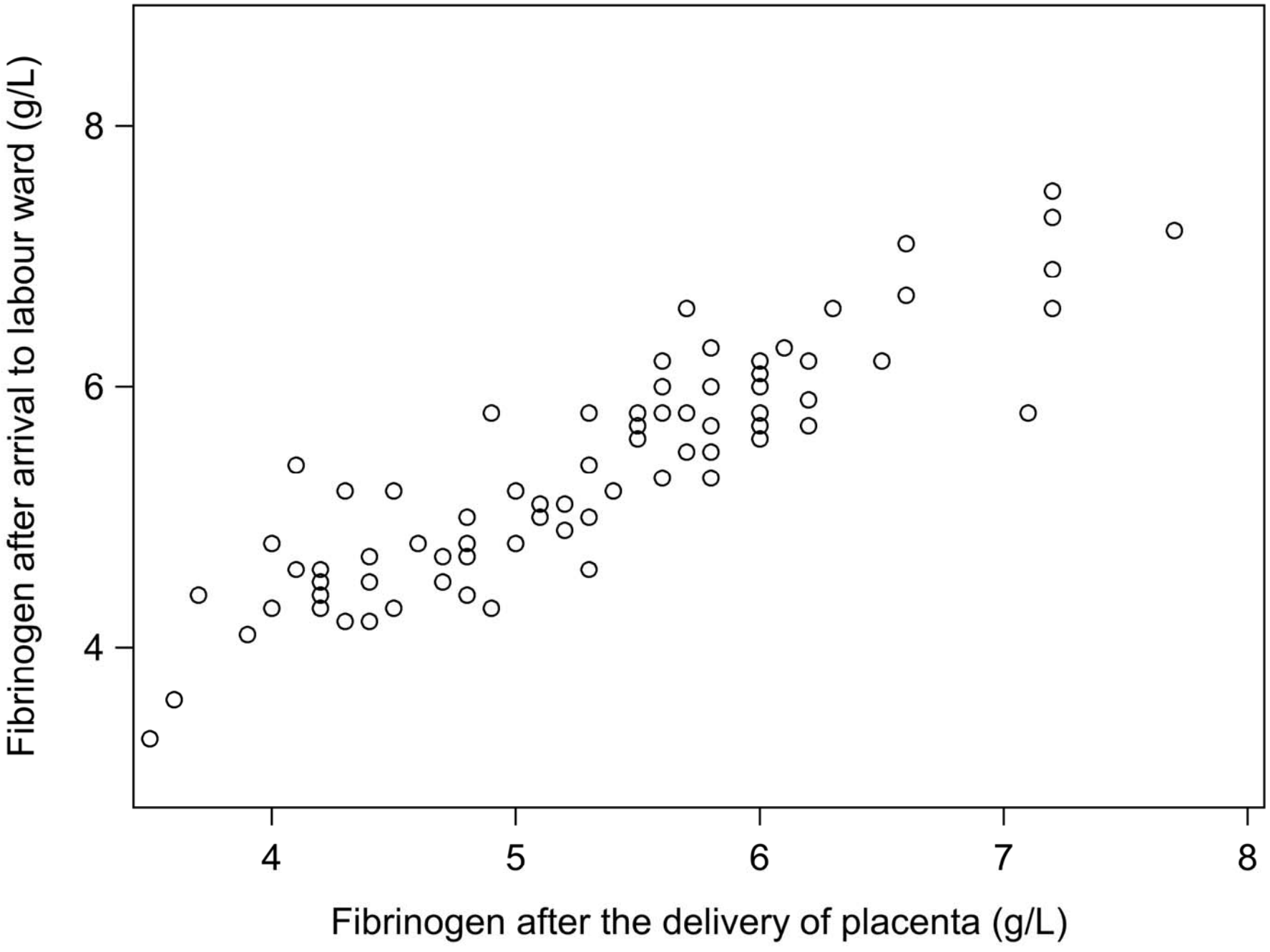
[1] Hospices civils de Lyon, Service de Biostatistique, F-69003, Lyon, France

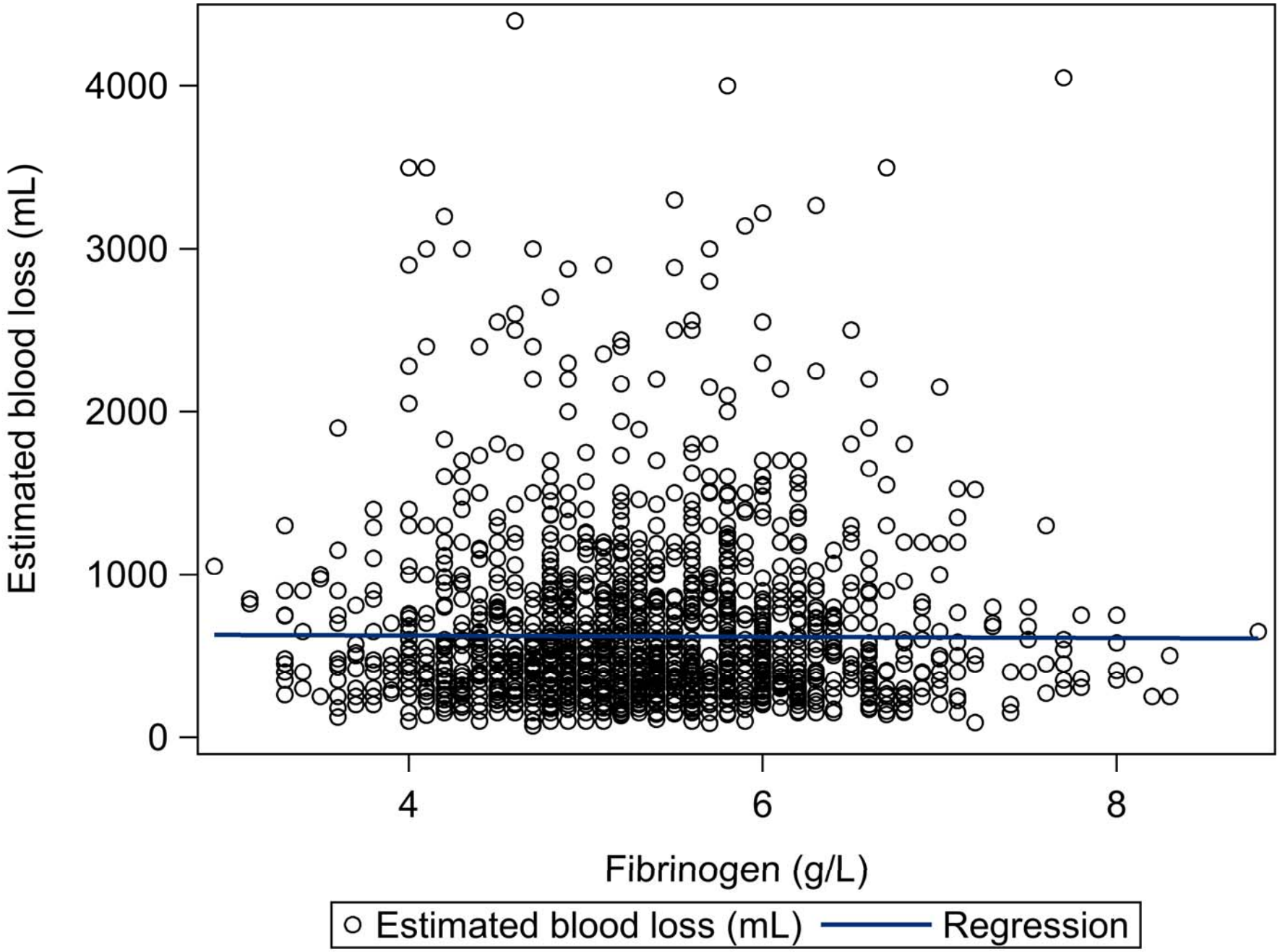
Aims

- To evaluate if there is associations between fibrinogen concentration, taken after arrival to labour ward and the severity of bleeding postpartum
- To study what happens with fibrinogen during labour

Methods

- All women asked, after arrival to labour ward, to participate in the study until 2000 women were included
- Blood sample for fibrinogen concentration was performed
- Bleeding postpartum was determined by weighing surgical sponges and pads and by measuring collected blood


Fibrinogen after arrival to labour ward (g/L)
8
6
4
4
5
6
7
8
Fibrinogen after the delivery of placenta (g/L)


Estimated blood loss (mL)
4000
3000
2000
1000
0
4
6
8
Fibrinogen (g/L)
Estimated blood loss (mL)
Regression

Disputation 24 oktober

International Journal of Obstetric Anesthesia

On the Cover

Current Issue

February 2014, Vol. 23, No. 1

Issue Highlights

Geraldine O'Sullivan
February 2014(Vol. 23 | No. 1 | Pages 8-9)
Robin Russell
Full Text | PDF (166 KB)

Major obstetric haemorrhage: monitoring with thromboelastography, laboratory analyses or both?
February 2014(Vol. 23 | No. 1 | Pages 10-17)
O. Karlsson, A. Jeppsson, M. Hellgren
Abstract | Full Text | PDF (628 KB)

Impact of a third stage of labor oxytocin protocol on cesarean delivery outcomes
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A.I. Lee, C.A. Wong, L. Healy, P. Toledo
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