Tromboembolismo Durante a Gravidez de Mulheres Cardiopatas

Simpósio Coração e Mulher
Antigo desafio, Novos conhecimentos
IDPC – 2016

Sem conflito de interesse

Tromboembolismo na Gestante Cardiopata

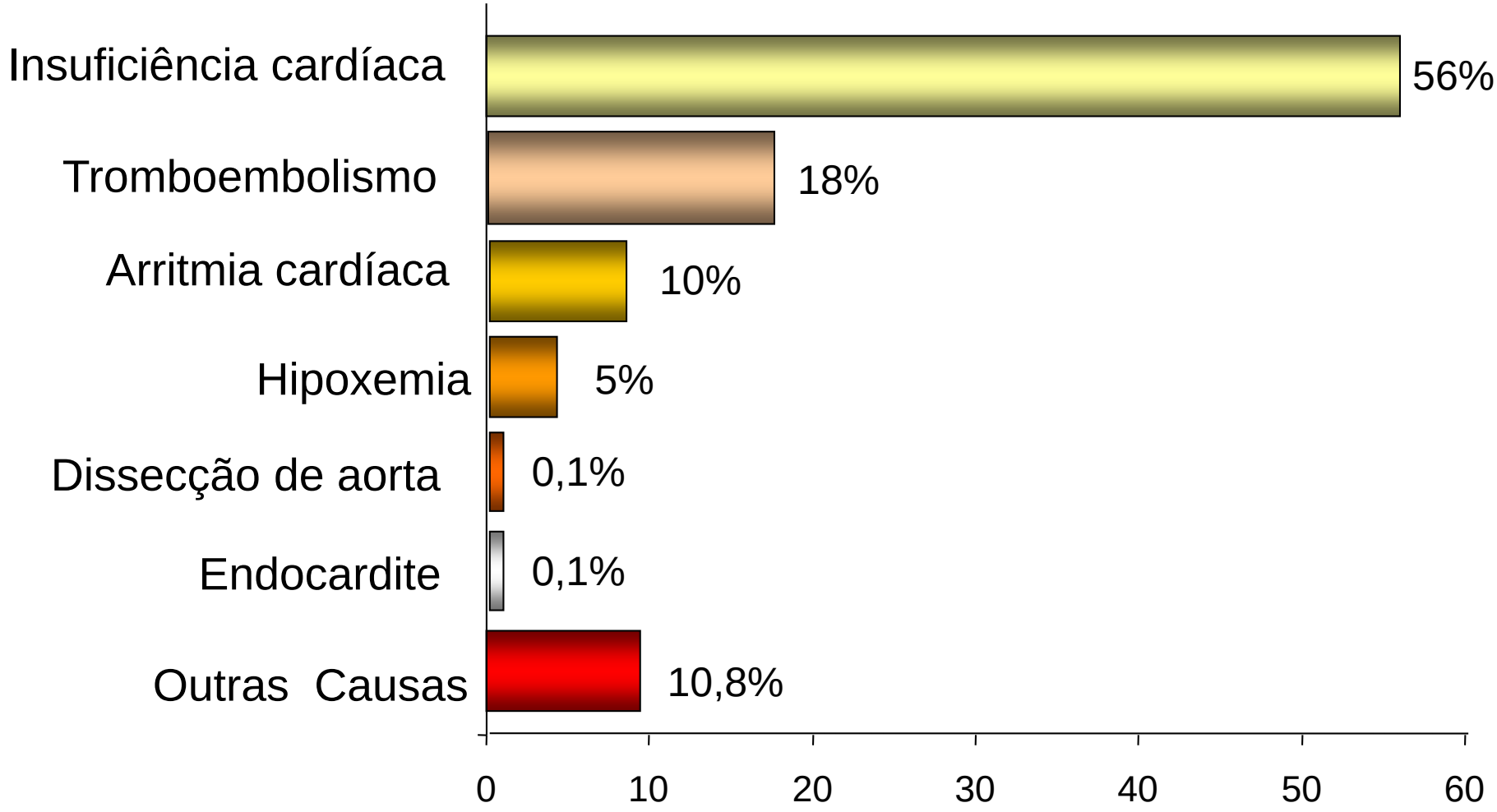
Considerações sobre:

Anticoagulantes - características do uso

Situações clínicas que exigem anticoagulante

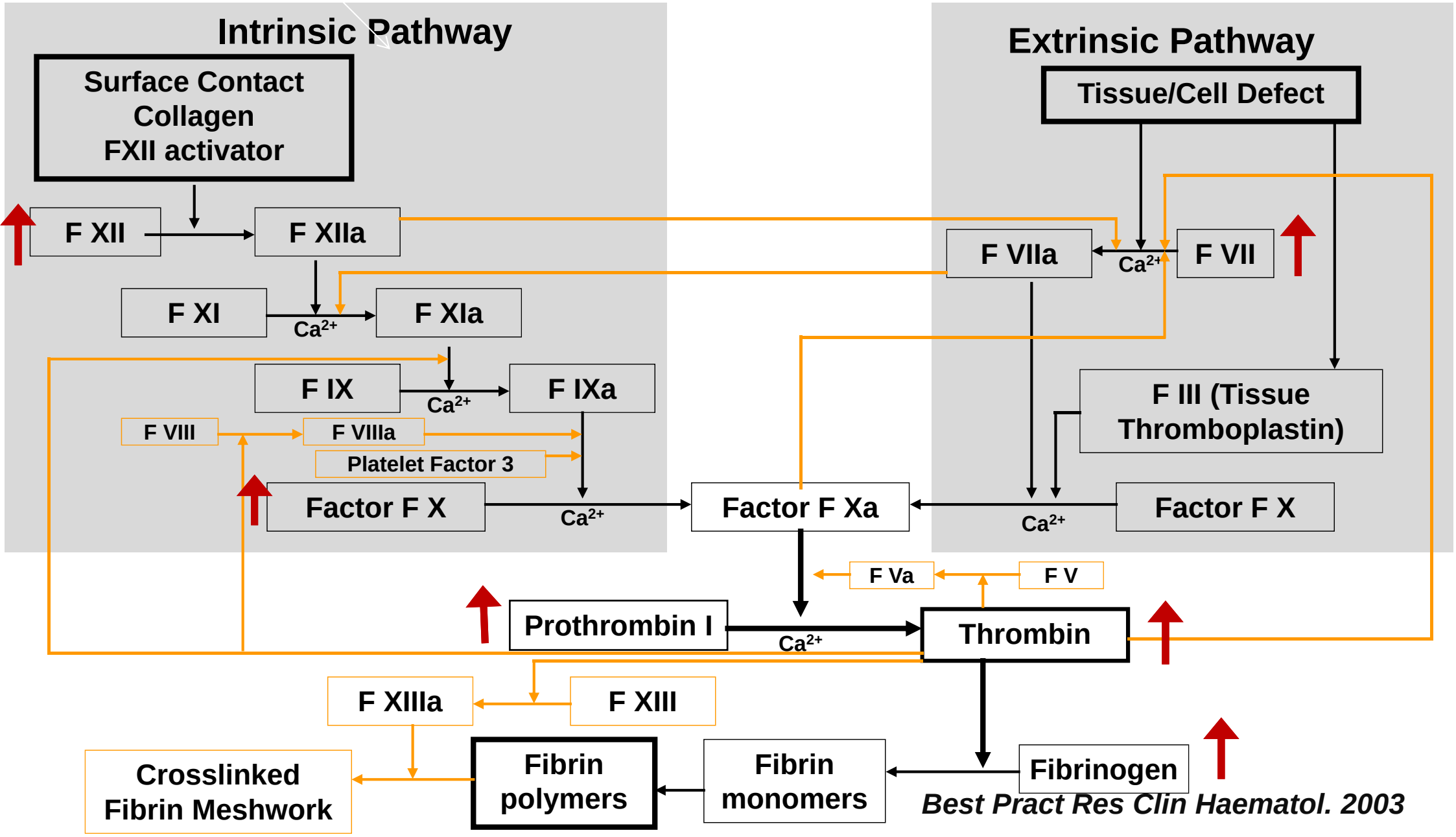
Propostas para prevenção

Complicações Cardíacas que Causaram Morte Materna Gravidez - Análise de 1000 Gestações Mortalidade 2,7%



Avila W S et al Clinical Cardiol, 2003

Ativação dos fatores de Coagulação Durante a Gravidez

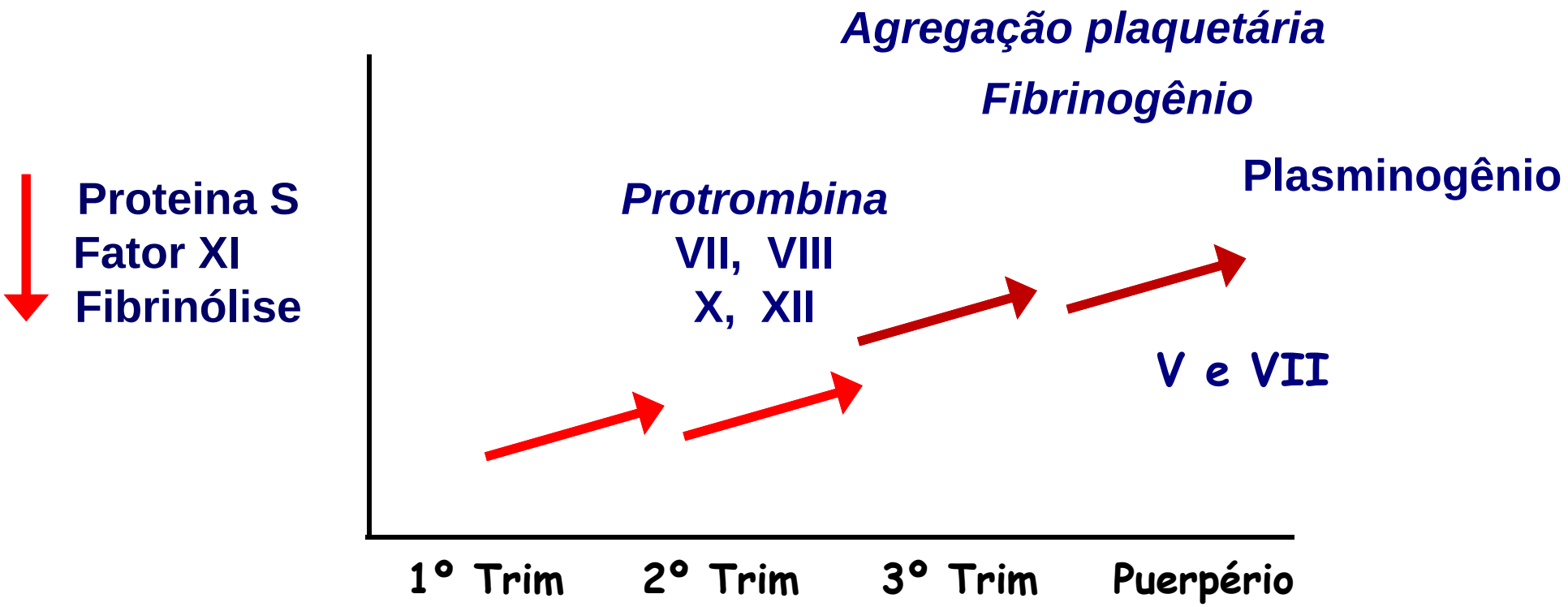


Best Pract Res Clin Haematol. 2003

Gravidez é Fator de Risco à Mulher Portadora de Cardiopatia

Hipercoagulabilidade

Aumento da ativação dos fatores de coagulação na gravidez



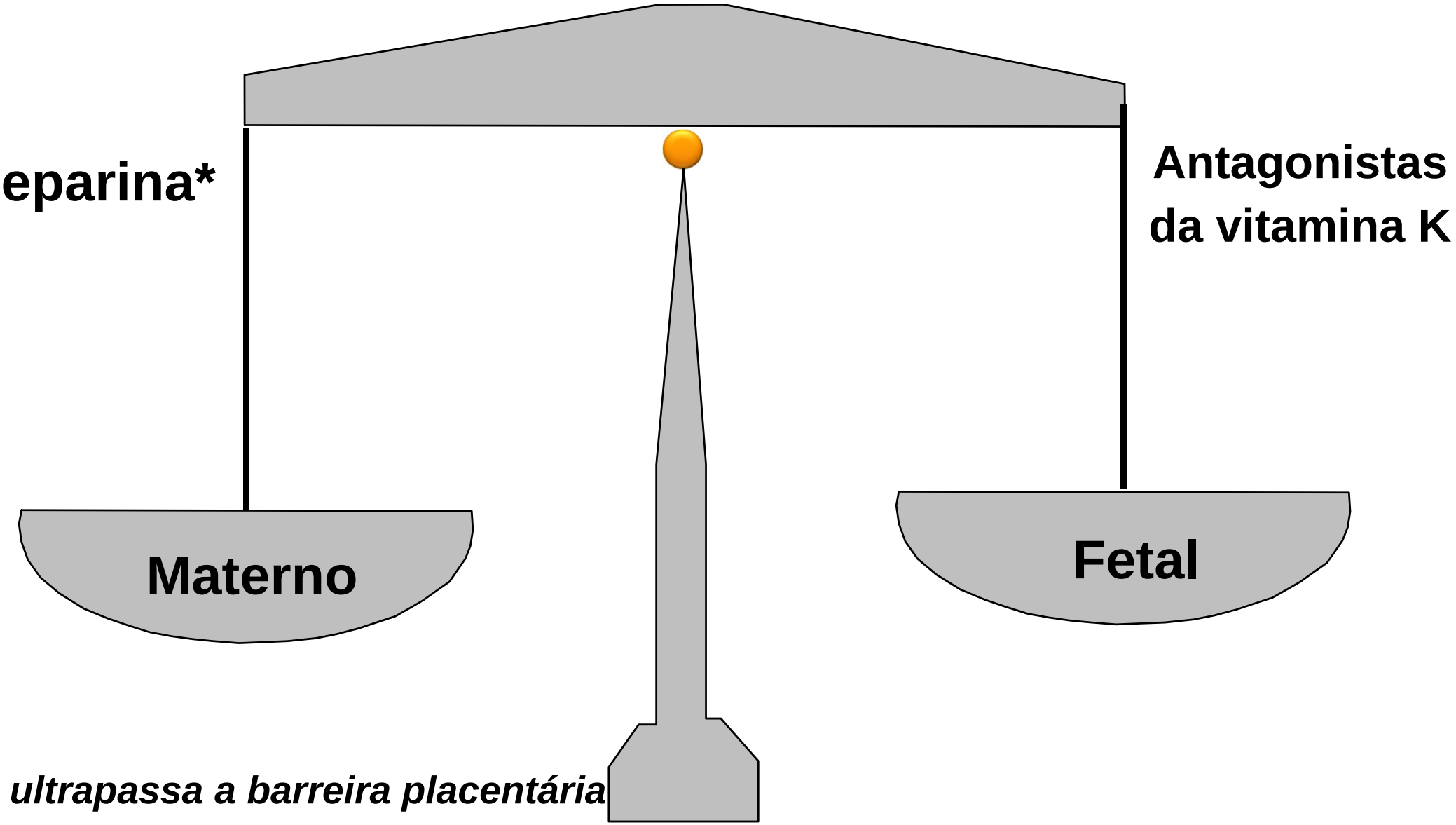
Bremme KA et al Best Pract Res Clin Haematol. 2003;16(2):153.

Tromboembolismo na Gestante Cardiopata

Considerações sobre:

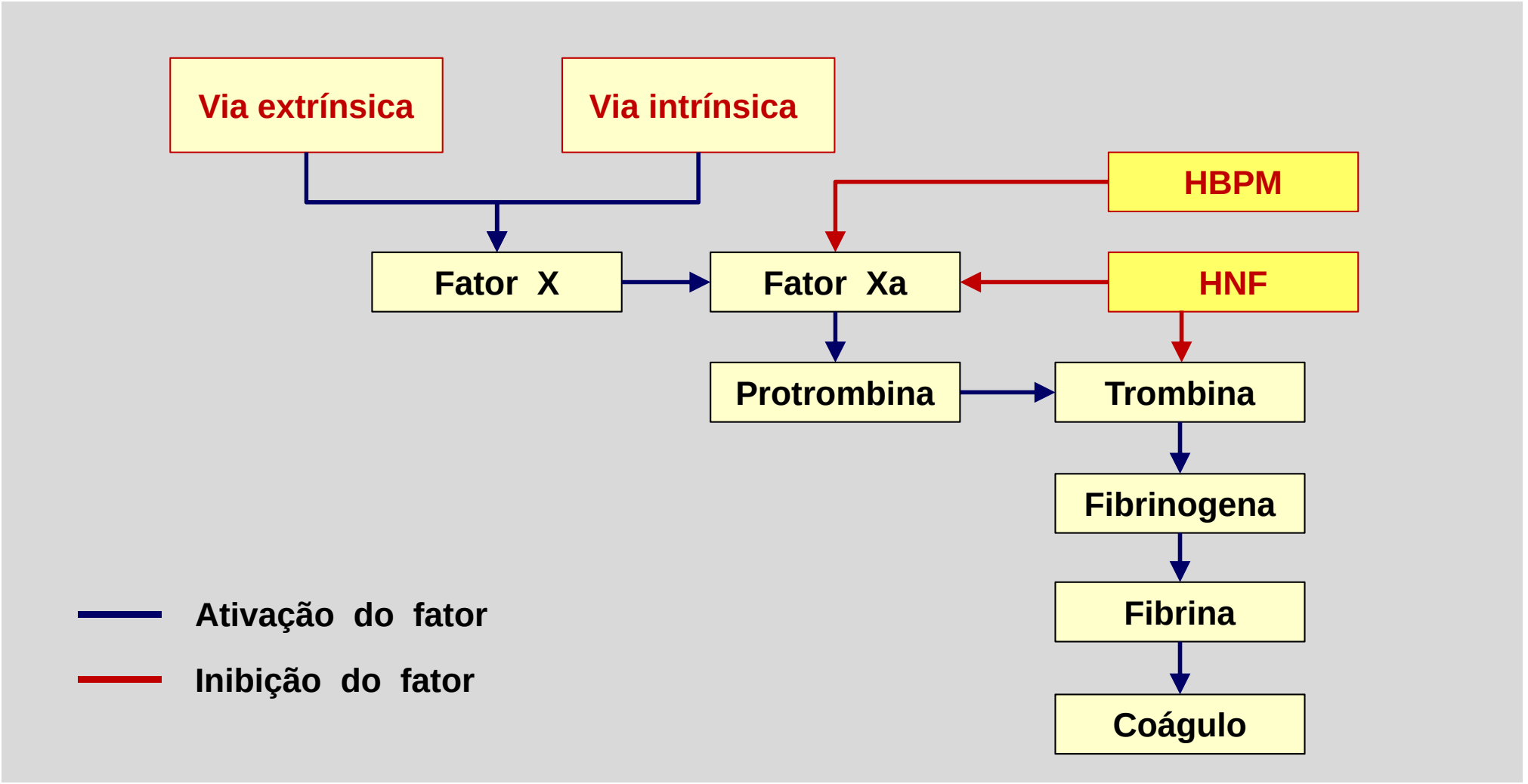
Anticoagulantes : peculiaridades do uso na gravidez

Escolha da Anticoagulação Permanente Durante a Gravidez :Riscos materno-fetais



** Não ultrapassa a barreira placentária*

Anticoagulação durante a Gravidez
HBPM e Não fracionada HNF



Comparação entre Heparina Não Fracionada e de Baixo Peso Molecular

Propriedades	HNF	HBPM
Peso molecular	12.000 - 14.000	4.000 - 6.000
Ação anticoagulante	Trombina e Xa	Xa
Bio-disponibilidade	30%	100%
Meia-vida após aplicação	45-60 min	12 h
Absorção após injeção SC	Variável	100%
Trombocitopenia	27%	0%
Monitorização	TTPA	Fator anti-Xa
Custo	Baixo	Alto
Periodicidade de controle	Maior	Menor
Controle	11/2 a 2 X	07-12 u/ml

Ginsberg JS et al Arch Intern Med. 2003;163:694

Heparina FDA C
(Não atravessa placenta)

❖ ***Complicações – Anticoagulação permanente***

Obstétricas **Hemorragia placentária**

Maternas **Hemorragia - 2%**
Osteoporose - 30% (> 1 mês)
Fraturas (< 2%)
Trombocitopenia (5%-15%)
Trombose de prótese mecânica- (12 a 24%)

❖ ***Limitação***

Desconforto da aplicação
Controle adequado da anticoagulação
Custo mensal

Ginsberg JS et al Arch Intern Med. 2003;163:694

Protese valvar em idade fértil

Journal of Perinatology

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Journal of Perinatology (2010) 30, 253–257

0743-8346/10 $32

www.nature.com/jp

ORIGINAL ARTICLE

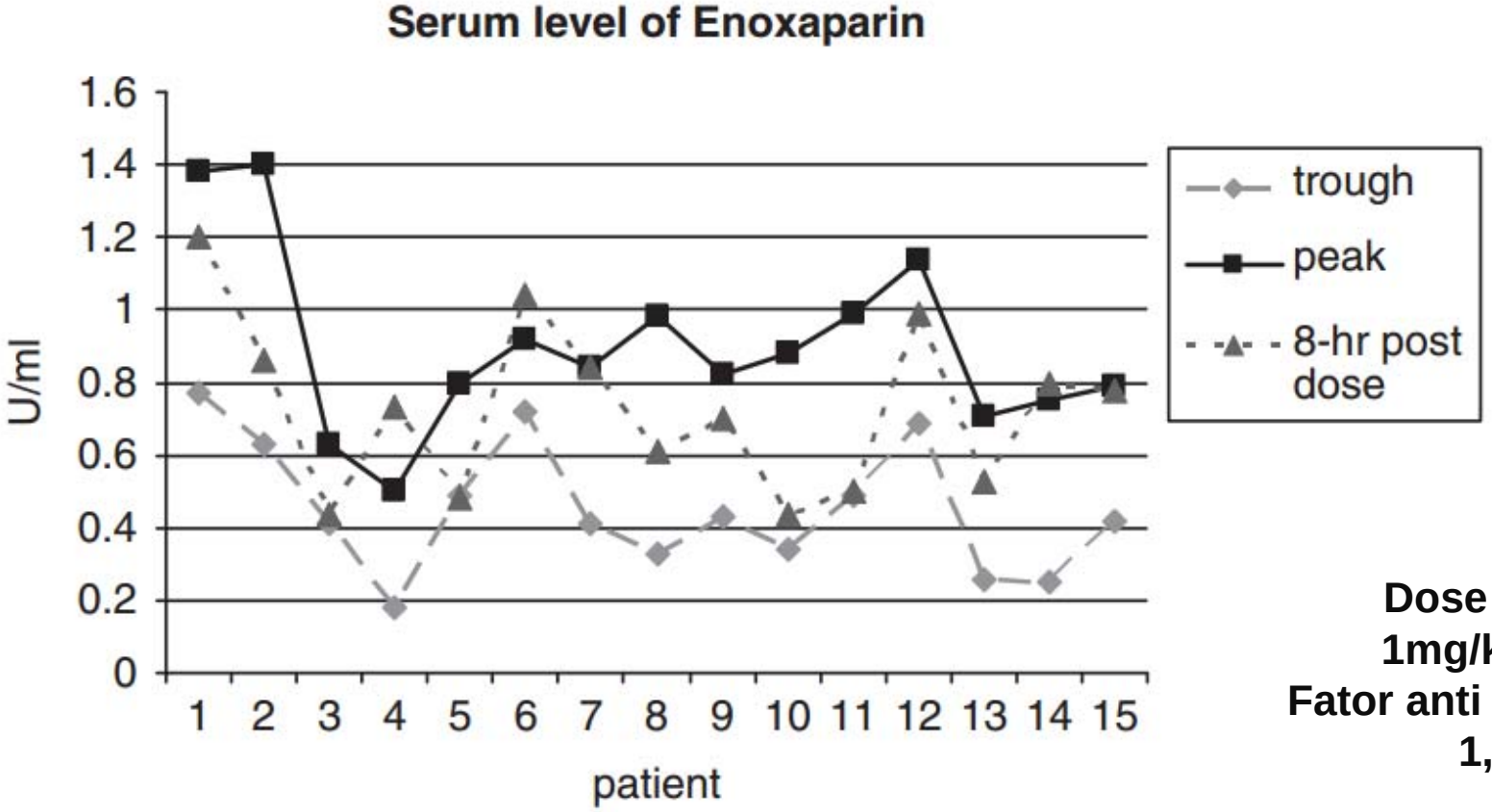
Fluctuations in anti-factor Xa levels with therapeutic enoxaparin anticoagulation in pregnancy

E Friedrich and AB Hameed

Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of California, Irvine, Orange, CA, USA and Long Beach Memorial Medical Center/Miller Children's Hospital, Long Beach, CA, USA

Anticoagulação na gravidez em Protese valvar mecanica

Trough, peak and 8-h post-dose anti-factor Xa activity levels for individual subjects



Dose diária SC
1mg/kg/12/12hs
Fator anti Xa – 0,6 U/ml a 1,2 U/ml

Friedrich and Hameed. J Perinatol. 2010;30:253-7

Vitamin K antagonists and pregnancy outcome

A multi-centre prospective study

N= 666 vs 1098

Christof Schaefer[1], Doreen Hannemann[1], Reinhard Meister[2], Elisabeth Eléfant[3], Wolfgang Paulus[4], Thierry Vial[5], Minke Reuvers[6], Elisabeth Robert-Gnansia[7], Judy Arnon[8], Marco De Santis[9], Maurizio Clementi[10], Elvira Rodriguez-Pinilla[11], Alla Dolivo[12], Paul Merlob[13]

[1]Pharmakovigilanz- und Beratungszentrum für Embryonaltoxikologie, Berlin, Germany; [2]Department of Mathematics, Technische Fachhochschule Berlin, Germany; [3]Centre Renseignements sur les Agents Teratogènes, Hôpital Armand-Trousseau, Paris, France; [4]Institut für Reproduktionstoxikologie, Ravensburg, Germany; [5]Centre Antipoison – Centre de Pharmacovigilance, Hospices Civils, Lyon, France; [6]Teratology Information Service, National Institute of Public Health and Environment, Bilthoven, The Netherlands; [7]Institut Européen des Génomutations, Lyon, France; [8]Israel Teratogen Information Service, Israel Ministry of Health, Israel; [9]Telefono Rosso – Teratology Information Service, Department of Obstetrics and Gynecology, Catholic University of Sacred Heart, Rome, Italy; [10]Servizio di Informazione Teratologica, Genetica Clinica ed Epidemiologica, University of Padua, Padua, Italy; [11]Servicio de Informacion Telefonica sobre Teratogenos Español, Centro de Investigación sobre Anomalías Congénitas, Instituto de Salud Carlos III, Madrid, Spain; [12]Swiss Teratogen Information Service, Lausanne, Switzerland; [13]Beilinson Teratology Information Service, Department of Neonatology, Rabin Medical Centre, Tel Aviv, Israel

The rate of major birth defects after 1st trimester exposure was significantly increased (OR 3.86, 95% CI 1.86-8.00). However, there were only two coumarin embryopathies (0.6%; both phenprocoumon). Prematurity was more frequent (16.0% vs. 7.6%, OR 2.61, 95% CI 1.76-3.86), mean gestational age at delivery (37.9 vs.39.4, p<0.001), and mean birth weight of term infants (3,166 g vs. 3,411 g; p < 0.001) were lower compared to the controls. Using the methodology of survival analysis, miscarriage rate reached 42% vs. 14% (hazard ratio 3.36; 95% CI 2.28-4.93). In conclusion, use of VKA during pregnancy increases the risk of structural defects and other adverse pregnancy outcomes.

Thromb Haemost. 2006;95(6):949-57.

Síndrome Varfarínica - Embriopatia – 4 a 10%

6ª e 12ª semana de gestação

- *Acometimento ósseo/cartilagen (Condrodisplasia punctata)*
- *Hipoplasia de extremidades (Nanismo e distrofia óssea)*

Defeito óptico - cegueira, atrofia óptica, microftalmia

- *SNC - retardo mental, surdez*
- *Restrição de crescimento intrauterino*
- *Escoliose*
- *Cardiopatia congênita*
- *Morte*

(OR 3.86, 95% CI 1.86-8.00).

Schaefer C Thromb Haemost, 2006;95(6):949.

Birth Defects Research Part A | Clinical and Molecular Teratology

Brief Report
Low-Dose Maternal Warfarin Intake Resulting in Fetal Warfarin Syndrome: In Search for a Safe Anticoagulant Regimen during Pregnancy

Sriparna Basu*, Priyanka Aggarwal, Neha Kakani, and Ashok Kumar

Background: Fetal exposure to maternal ingestion of warfarin is known to produce certain dysmorphic features in the neonate, known as fetal warfarin syndrome (FWS). There is a general consensus that maternal intake of warfarin at a daily dose of 5 mg or less is safe both for the infant and the mother. Methods: We report four cases of FWS born to mothers with rheumatic heart disease on warfarin prophylaxis during pregnancy at a dose less than 5 mg/day. Results: Along with typical facial features of FWS and multiple epiphyseal stippling in skeletal x-ray, Case 1 had Dandy-Walker malformation and Case 2 had laryngo-tracheomalacia and patent ductus arteriosus. Conclusion: We emphasize the need for optimizing the choice and dosage schedule of anticoagulants during pregnancy, least harmful for the mother and her developing fetus.

Birth Defects Research (Part A) 106:142–147, 2016.

Key words: anticoagulants; fetal warfarin syndrome; heart valve prosthesis; neonate; pregnancy; warfarin

Novos Anticoagulantes Orais

Inbidores Diretos da Trombina

Dabigatran

Inibidores do Fator Xa

Rivaroxaban

Apixaban

Edoxaban

CONTRA - INDICAÇÃO NA GESTAÇÃO

Tromboembolismo na Gestante Cardiopata

Considerações sobre:

Situações clínicas que exigem anticoagulante

Doença Cardíaca

I. Alto risco

- **Prótese valvar mecânica**
  - *POSIÇÃO DA PRÓTESE*
  - *TIPO DE PRÓTESE*
  - *DISFUNÇÃO VENTRICULAR*
- **Valvopatia mitral e Fibrilação atrial permanente**

II. Risco menor

- *FIBRILAÇÃO/FLUTER ATRIAL PERMANENTE*
- *ICC e CARDIOMIOPATIA DILATADA*
- *CARDIOPATIAS CONGÊNITAS COMPLEXAS*
- *SÍNDROME DE EISENMENGER*
- *HIPERTENSÃO ARTERIAL PULMONAR PRIMÁRIA*
- *ANTECEDENTES DE AVC*

Diretrizes da SBC - Arq Bras Cardiol 72, 1999

Trombose de Prótese Valvar Mecânica

- Incidência de trombose

  Aórtica: 0,1/100 pt/ano; Mitral: 0,35/100pt/ano

  Anticoagulação inadequada - 3 a 6 vezes maior

- Gravidez predispõe ao tromboembolismo

  Estado hipercoagulabilidade da gravidez e puerpério

  Dificuldades na anticoagulação adequada

- Incidência dos riscos na gravidez
  - **Hemorragia - 5% (2,5 a 17%)**
  - **Tromboembolismo - 10 a 15%**

Cannergier SC et al Circulation. 1994;89:635.

Circulation

American Heart Association

Valvular Heart Disease

Pregnancy in Women With a Mechanical Heart Valve

Data of the European Society of Cardiology Registry of Pregnancy and Cardiac Disease (ROPAC)

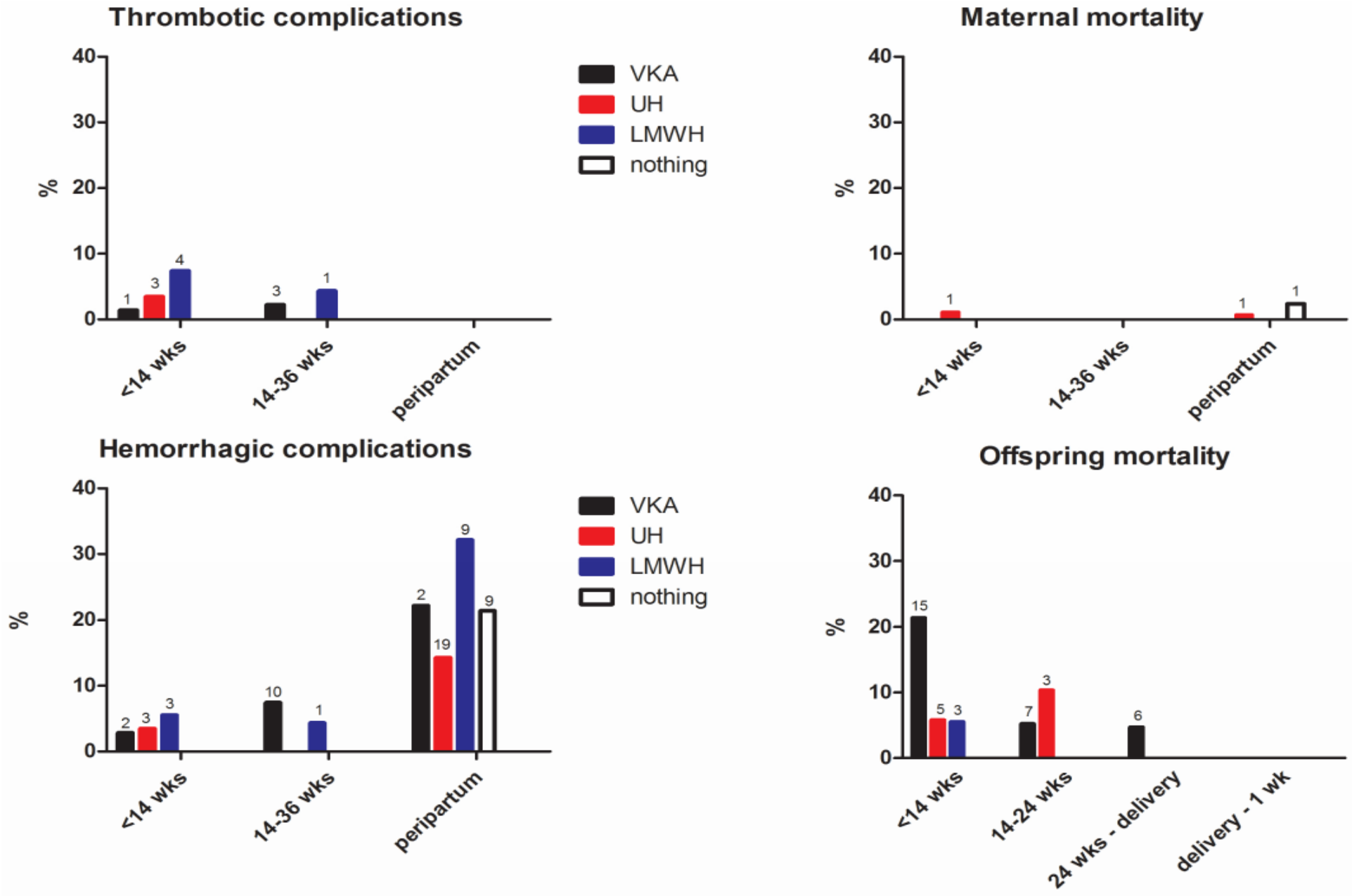
Iris M. van Hagen, MD; Jolien W. Roos-Hesselink, MD, PhD; Titia P.E. Ruys, MD, PhD; Waltraut M. Merz, MD, PhD; Sorel Goland, MD; Harald Gabriel, MD; Malgorzata Lelonek, MD, PhD; Olga Trojnarska, MD; Wael Abdulrahman Al Mahmeed, MD; Hajnalka Olga Balint, MD; Zeinab Ashour, MD; Helmut Baumgartner, MD, PhD; Eric Boersma, MD, PhD; Mark R. Johnson, MD, PhD; Roger Hall, MD, FRCP; on behalf of the ROPAC Investigators and the EURObservational Research Programme (EORP) Team*

	Prótese mecânica 212	vs	Prótese biológica 134
Morte materna	1,4%	vs	1,5%
Trombose	10 (4,7%)	vs	0 (5 na transição com heparina)
Hemorragia	23,1%	vs	5,1% (p < 0.001)
Abortamento	28,6%	vs	9,2% (p < 0.001)
Perda fetal	7,1%	vs	0,7% (p = 0.016)

Somente 58% das PM foram livres de eventos vs 79% PB (p<0.001)

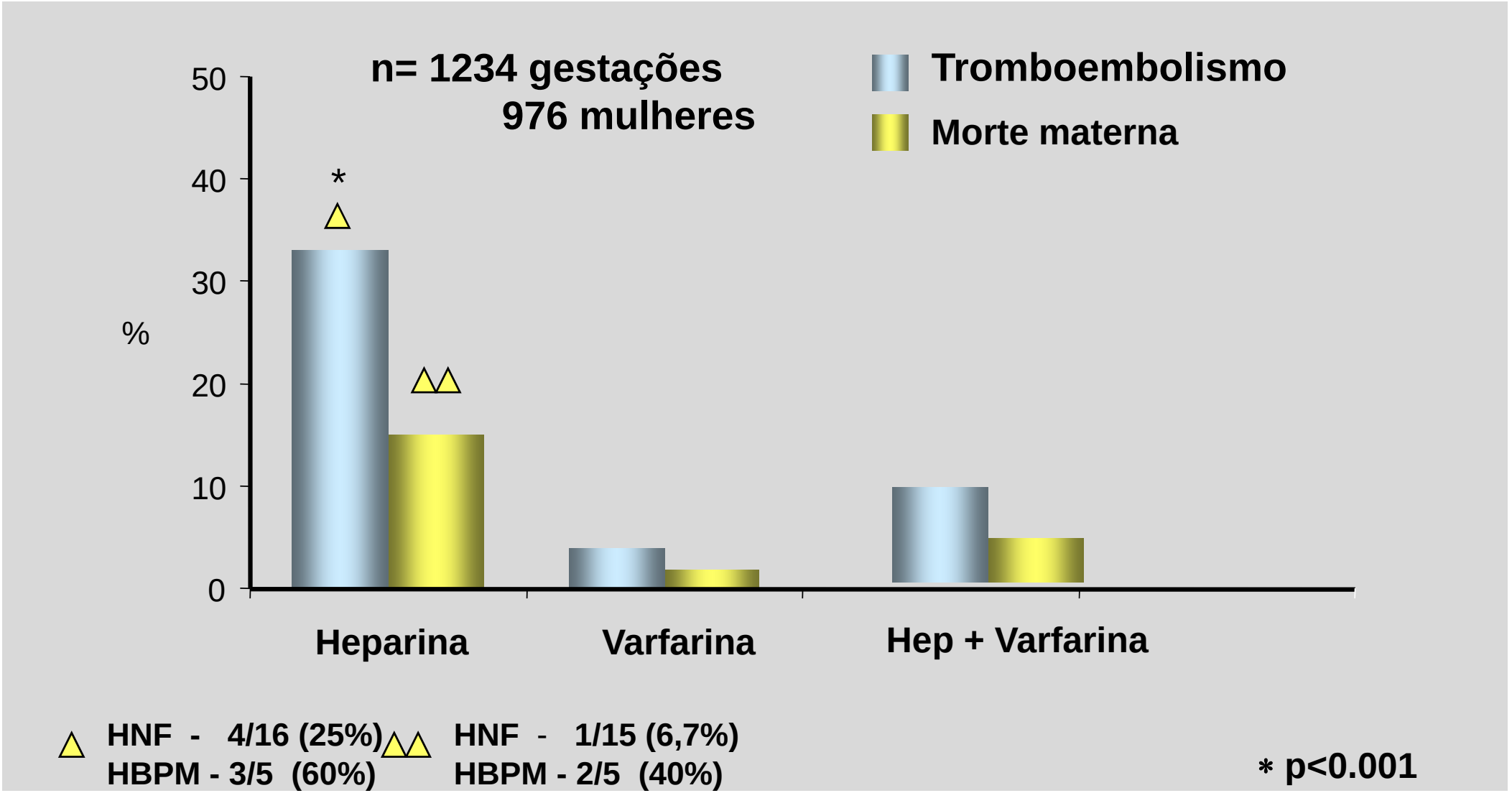
Circulation. 2015;132:132-42.

CoAnticoagulation / related events – ROPAC



Circulation. 2015;132:132-42.

Frequência de Complicações Maternas de acordo com o esquema de anticoagulação – Próteses Mecânicas



Chan WS et al, Arch Intern Med 2000;160:191

Tromboembolismo na Gestante Cardiopata

Considerações sobre:

Propostas para prevenção

Pregnancy and Heart Disease

Carole A. Warnes and Thomas H. Lee

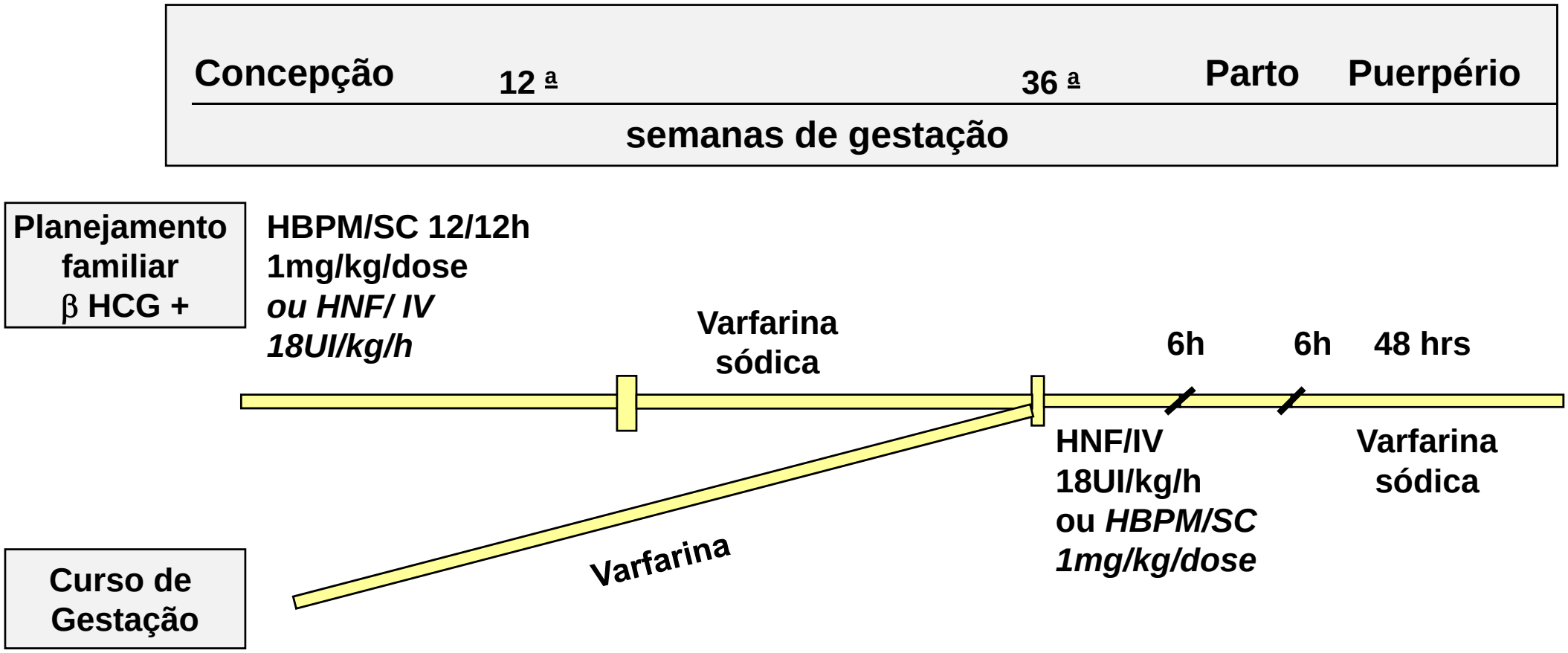
TABLE 78G-5 ACC/AHA Recommendations for Anticoagulation Regimens in Pregnant Patients with Mechanical Prosthetic Valves

CLASS	INDICATION	LEVEL OF EVIDENCE
Class I (indicated)	Continuous therapeutic anticoagulation with frequent monitoring	B
	If warfarin is discontinued between weeks 6 and 12 of gestation, replace with continuous intravenous UFH, dose-adjusted UFH, or dose-adjusted subcutaneous LMWH.	C
	Up to 36 weeks of gestation, the therapeutic choice of continuous intravenous or dose-adjusted subcutaneous UFH, dose-adjusted LMWH, or warfarin should be discussed fully.	C
	If dose-adjusted LMWH is used, the LMWH should be administered twice daily subcutaneously to maintain the anti-Xa level between 0.7 and 1.2 units/mL 4 hours after administration.	C
	If dose-adjusted UFH is used, the aPTT should be at least twice control levels.	C
	If warfarin is used, the INR goal should be 3.0 (range, 2.5 to 3.5).	C
	Warfarin should be discontinued starting 2 to 3 weeks before planned delivery and continuous intravenous UFH given instead.	C
Class IIa (strong supportive evidence)	It is reasonable to avoid warfarin between weeks 6 and 12 of gestation because of the high risk of fetal defects.	C
	It is reasonable to resume UFH 4 to 6 hours after delivery and begin oral warfarin in the absence of significant bleeding.	C
	It is reasonable to give low-dose aspirin (75 to 100 mg/day) in the second and third trimesters of pregnancy, in addition to anticoagulation with warfarin or heparin.	C
Class III (not indicated)	LMWH should not be administered unless anti-Xa levels are monitored 4 to 6 hours after administration.	C
	Dipyridamole should not be used instead of aspirin as an alternative antiplatelet agent because of its harmful effects on the fetus.	B

aPTT = activated partial thromboplastin time; INR = international normalized ratio; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin.

Prevenção do Tromboembolismo em Cardiopatias de alto risco

Anticoagulação Permanente



HBPM - heparina de baixo peso
HNF - heparina não fracionada

Controle de dose: HBPM - anti Xa
HNF- TTPA: 1,5 X vn
Varfarina sódica: INR 2,5 - 3,0

Tromboembolismo na Gestação

Tromboembolismo é causa importante de morte materna.

A seleção da anticoagulação é fundamentada no risco de trombose materna.

Prótese mecânica e valvopatia mitral + fibrilação atrial são situações clínicas de maior risco

Anticoagulação plena e permanente deve respeitar a rotina de cada serviço.

Os dilemas sobre a conduta devem ser expostas para o casal, idealmente no planejamento familiar.