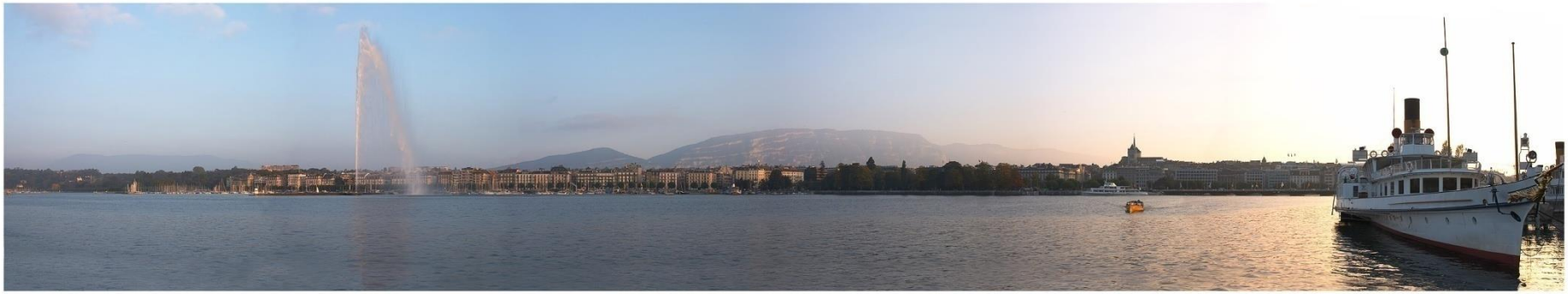


Jet d'eau, Genève

am

Tests d'évaluation de la fonction plaquettaire délocalisés : un guide pour la transfusion de plaquettes ?

Dre Fanny Bonhomme

XIIe Congrès National d'Hémovigilance et de Sécurité Transfusionnelle

Hôpitaux Universitaires Genève

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Déclaration de conflits d'intérêts

Nom :

☐ **J'ai, ou ai eu** durant les trois dernières années, une affiliation, des intérêts financiers ou autres intérêts avec un organisme industriel ou commercial de type :

- ☐ Rémunération / Bourse / Honoraires
  - ☐ Orateur / Consultant
- ☐ Autre :

Nom de l'organisme / des organismes :

✔ **Je n'ai pas de conflit d'intérêt**

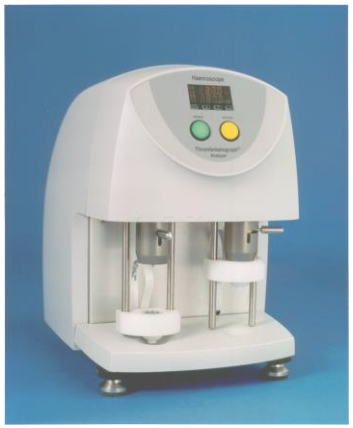
Tests

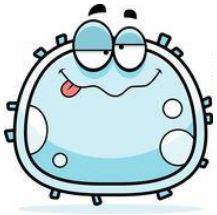
Pratiqués "A côté / Au lit" du patient

En dehors d'un laboratoire de biologie (bloc opératoire, soins intensifs, etc.)

Par du personnel sans formation de laboratoire

Sans préparation de l'échantillon : en sang total





POC platelet function analysis (whole blood)

- Based on shear stress
  - PFA 100/200®

- Based on clot strength
  - TEG Platelet Mapping®

- Based on aggregation
  - Platelet count Plateletworks®

  - Light transmission Verify Now®

  - Impedance aggregometry Multiplate®, Rotem platelet®

Adapted with courtesy of Dr. G Casso

GUIDELINES

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Kozek-Langenecker, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa Alvarez Santullano, Edoardo De Robertis, Daniela C. Filipescu, Dietmar Fries, Klaus Görlinger, Thorsten Haas, Georgina Imberger, Matthias Jacob, Marcus Lancé, Juan Llau, Sue Mallett, Jens Meier, Niels Rahe-Meyer, Charles Marc Samama, Andrew Smith, Cristina Solomon, Philippe Van der Linden, Anne Juul Wikkelsø, Patrick Wouters and Piet Wyffels

We suggest that preoperative platelet function testing be used to identify decreased platelet function caused by medical conditions and antiplatelet medication. **2C**

Eur J Anaesthesiol 2013;30:270-382

Expert position paper on the management of antiplatelet therapy in patients undergoing coronary artery bypass graft surgery

EUROPEAN SOCIETY OF CARDIOLOGY®

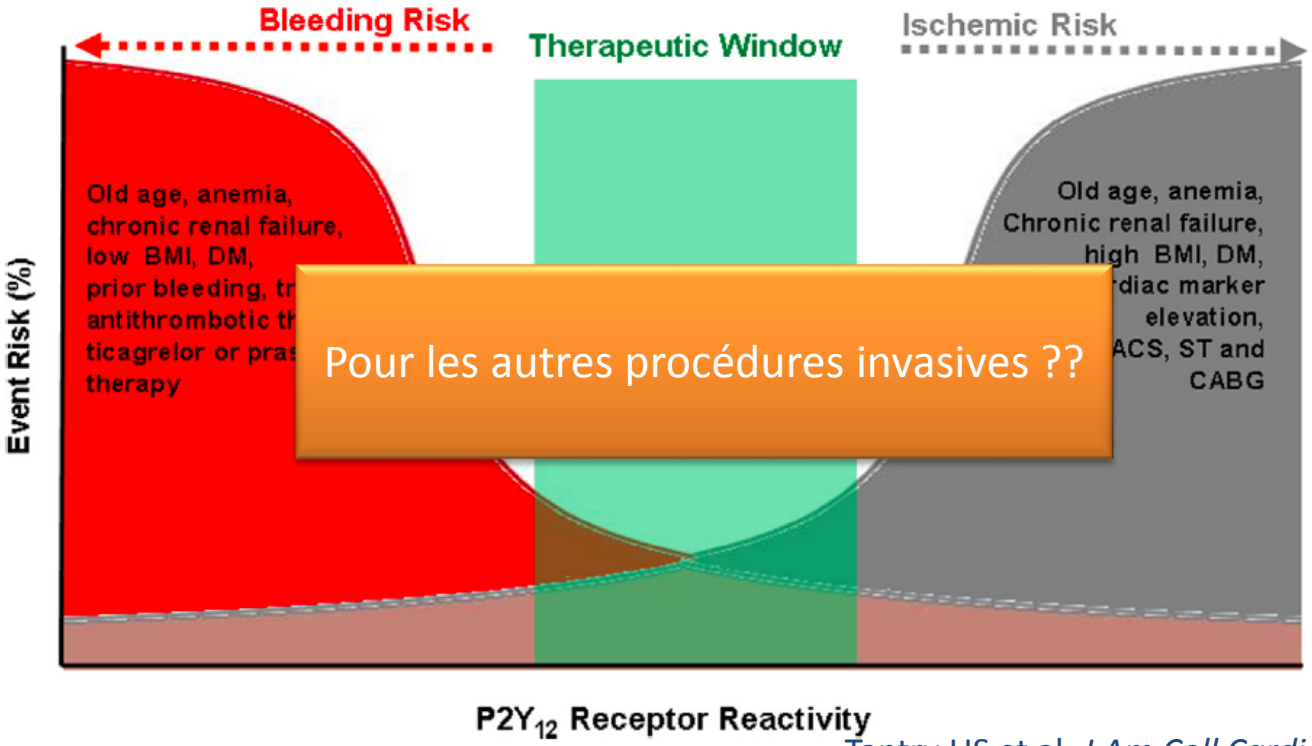
Table 2 Bridging therapies and platelet function monitoring

The risks of bleeding and thrombosis and decision-making regarding DAPT and timing of surgery should be assessed by the heart team prior to CABG surgery	I	C	
Bridging with cangrelor, if available, is recommended in high-risk patients	I	B	43
Bridging with short-acting intravenous GPIIb/IIIa inhibitors may be considered in patients at high risk for ischaemic events	IIb	C	44
It is reasonable to base timing of surgery on **platelet function monitoring** rather than arbitrary use of a specified period of delay in patients on DAPT.	IIa	B	45

Sousa-Uva M, et al. *Eur Heart J* 2014;35:1510-14

Fonction plaquettaire pour prédire le risque hémorragique ?

Consensus and Update on the Definition of On-Treatment Platelet Reactivity to Adenosine Diphosphate Associated With Ischemia and Bleeding



Pour les autres procédures invasives ??

Tantry US et al. *J Am Coll Cardiol* 2013;62:2261-73

Platelet inhibition assessed with VerifyNow, flow cytometry and PlateletMapping in patients undergoing heart surgery

Conclusion: We found a modest agreement between the methods for preoperative platelet inhibition, though not for PlateletMapping-MA_{ADP}. There was a correlation between preoperative platelet inhibition measured by VerifyNow$P2Y_{12}$ and surgical blood loss or transfusion requirements. However, for the individual patient, preoperative use of VerifyNow$P2Y_{12}$ as an instrument to decide bleeding and transfusion risk does not seem helpful.

	VerifyNow (percent	VASP (IPP)	Platelet mapping	24h pertes sanguines
Poursu (n=41)				nL
Stop cl veille (n				nL
Stop clopi 48h avant (n=7)	20%	65%	18%	1902 mL

	VerifyNow$P2Y_{12}$ n = 60	VASP-assay n = 48	PlateletMapping—MAADP n = 58
Total blood loss			
r	0.29	0.1	0.01
p-value	0.03	0.52	0.98
Total RBC transfusion			
r	0.43	0.04	0.05
p-value	<0.01	0.78	0.69

Alström U et al, *Thrombosis Research* 2009;124:572–7

Test de fonction plaquettaire pour prédire le risque hémorragique ?

Degré de concordance modéré entre les tests

Pas de consensus sur la méthode à utiliser

Valeurs seuils à définir, à adapter en fonction du risque hémorragique (patient, procédures invasives)

Platelet function testing and guidance of transfusion management in CABG p

Study	Platelet function test	Design	Surgery type	Result
Görlinger et al. [138]	Multiplate (ADP-, COL-, ASPI-, TRAPtest) ROTEM (EX-, IN-, FIB-, HEPTEM)	Retrospective cohort study of ROTEM & Multiplate guided protocol (P)[a] vs historical control (H)	CABG, VS, complex cardiac surgery	Significant decrease in overall amount of transfusion requirements, median number of transfused PRBCs and FFP, and re-exploration rate
Chen et al. [130]	LTA (2 μmol/L ADP) PFA-100 (COL/ADP)	Prospective LTA and PFA-100 guided strict protocol (P) vs historical control (H)	Primary CABG	Significantly reduced transfusions of PLT and FFP, but not of PRBCs, in patients without clopidogrel in P vs H. Significantly reduced use of PRBCs in patients with clopidogrel in P vs H
Spiess et al. [139]	TEG	Prospective TEG guided non-strict protocol (P) vs historical control (H)	CABG (798), complex or open ventricle surgery	Significantly lower incidence of overall transfusion during hospitalization and total transfusion in the operating room in P vs H. Mediastinal re-exploration for hemorrhage also lower in P vs H
Shore-Lesserson et al. [140]	TEG (celite/TF-activated ± heparinase)	Randomization: TEG guided protocol (T) vs control (C)	VR, combined CABG + VS, cardiac reoperation, aortic surgery	No significant difference in post-operative CT drainage, but significantly less administration of blood and blood components in T vs C.
Royston et al. [141]	TEG (celite activated)	Randomization: TEG guided protocol (T) vs control (C)	Cardiac surgery (50% CABG)	Significantly fewer patients received blood components and a significant reduction in the amount of product used in T vs C. No difference in CT drainage volume.
Westbrook et al. [142]	TEG (including platelet mapping)	Randomization: TEG guided protocol (T) vs control (C)	Cardiac surgery	No significant differences in either blood loss, re-exploration or other clinical parameters.
Ak et al. [143]	TEG (kaolin-activated ± heparinase)	Randomization between TEG guided protocol (T) vs control (C)	Primary CABG	No differences in blood loss, re-exploration for bleeding, and early clinical outcome, but significantly lower median units of packed cells and blood products, FFP and platelet transfused in T vs C.
Weber et al. [26]	Multiplate (ADPtest/ TRAPtest/ASPItest) ROTEM (EX-, IN-, FIB-, HEPTEM)	Randomization between ROTEM & Multiplate guided protocol (T) vs control (C)	CABG + VS, 2–3 VS, aortic surgery or redo surgery	Significantly lower erythrocyte transfusion rate in T vs C. FFP and platelet transfusion rates, post-operative mechanical ventilation time, length of intensive care unit stay, and 6 mo mortality significantly lower in T vs C
Avidan et al. [144]	PFA-100 (COL/EPI, COL/ADP) TEG	Randomization: strict PFA-100, TEG, and Hepcon guided protocol (T) vs control (C). Additional historical control (H).	Primary CABG	No difference in median blood loss. Significantly greater amount of transfusion of PRBCs and blood components in H vs T or C. No difference in the transfusion of PRBCs and blood components in T vs C.

Janssen PW et al. *Blood Rev* 2014;28:109-21

Clopidogrel and bleeding in patients undergoing elective coronary artery bypass grafting

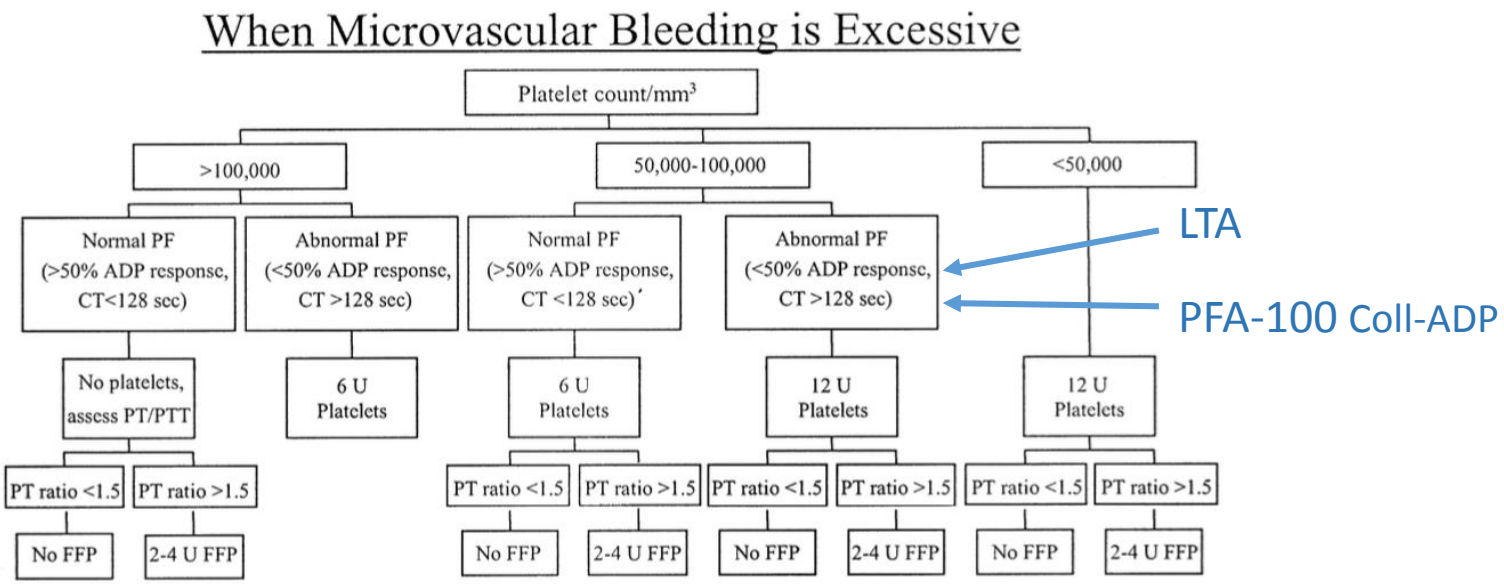


Figure 1. Bleeding management algorithm used for treatment of excessive microvascular bleeding. *PF*, Platelet function; *ADP*, adenosine diphosphate; *CT*, closure time; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *FFP*, fresh frozen plasma.

Chen L, et al. *J Thorac Cardiovasc Surg* 2004 Sep;128(3):425-31

Clopidogrel and bleeding in patients undergoing elective coronary artery bypass grafting

TABLE 2. Component transfusion in prospective and retrospective patients undergoing CABG

	Prospective		Retrospective (historical)	
	Clopidogrel group (n = 45)	Control group (n = 45)	Clopidogrel group (n = 53)	Control group (n = 428)
PLT, U	9.0 ± 1.7*	1.2 ± 0.5	12.5 ± 2.1*	2.3 ± 0.3‡
PRBC, U	4.3 ± 0.6*	2.3 ± 0.5	6.4 ± 0.8*,†	2.3 ± 0.1
FFP, U	1.0 ± 0.6	0.5 ± 0.3	2.9 ± 1.0*	1.0 ± 0.1‡

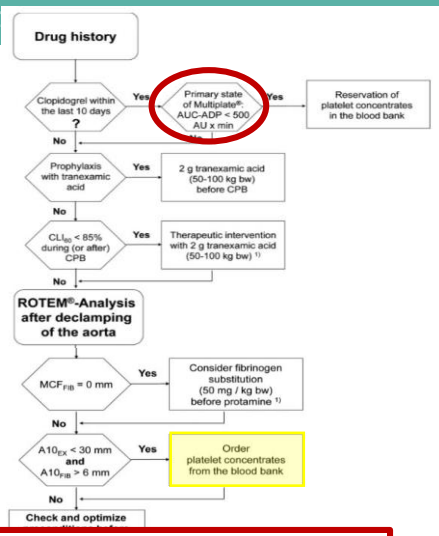
PFA-100 analysis in both the preheparin and postprotamine periods
not predictive of who would bleed and require platelet or PRBC transfusions

‡$P < .05$ compared with prospective control subjects.

Chen L, et al. *J Thorac Cardiovasc Surg* 2004;128:425-31

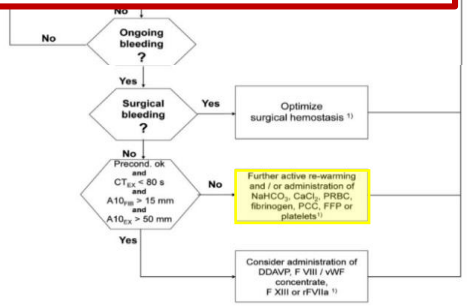
First-line Therapy with Coagulation Factor Concentrates Combined with Point-of-Care Coagulation Testing Is Associated with Decreased Allogeneic Blood Transfusion in Cardiovascular Surgery

A Retrospective, Single-center Cohort Study



n=1718 n=2147

	Before Implementation of Point-of-care-supported Coagulation Management (2004)	After Implementation of Point-of-care-supported Coagulation Management (2009)	*P* Value	Relative Risk of Cohort 2009 Compared with Cohort 2004
Primary binary endpoints: Incidence of transfusion				
Any allogeneic blood product transfusion (n, %)	902/1,718 (52.5%)	906/2,147 (42.2%)	<0.0001	0.804 (0.752–0.859)
PRBC transfusion (n, %)	854/1,718 (49.7%)	868/2,147 (40.4%)	<0.0001	0.813 (0.758–0.872)
FFP transfusion (n, %)	333/1,718 (19.4%)	24/2,147 (1.1%)	<0.0001	0.058 (0.038–0.087)
Platelet transfusion (n, %)	173/1,718 (10.1%)	280/2,147 (13%)	0.0041	1.295 (1.083–1.548)
Massive transfusion (≥10 units of PRBC) (n, %)	43/1,718 (2.50%)	27/2,147 (1.26%)	0.0057	0.502 (0.312–0.81)



Görlinger K, et al. *Anesthesiology* 2011;115:1179-91

Point-of-Care Testing

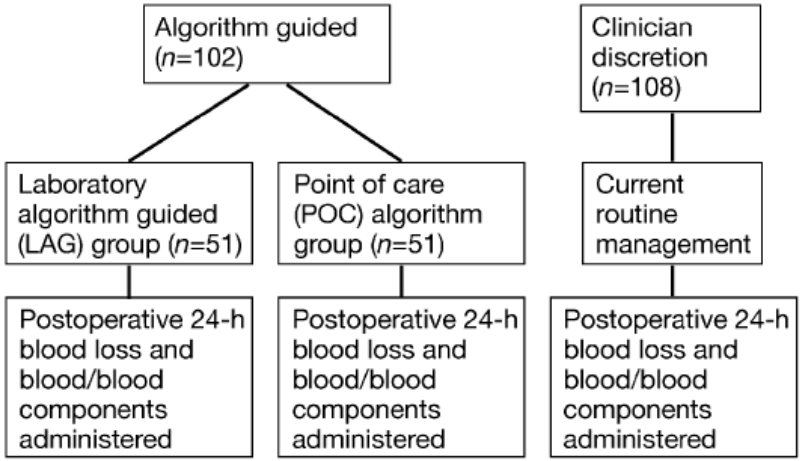
A Prospective, Randomized Clinical Trial of Efficacy in Coagulopathic Cardiac Surgery Patients

Conventional : Algorithme basé sur ACT et tests de labo ; n=50
POCT : Algorithme basé sur POCT (ROTEM + Multiplate) ; n=50

	Intraoperative			Postoperative			Cumulative		
	Conventional Group	POC Group	*P* Value	Conventional Group	POC Group	*P* Value	Conventional Group	POC Group	*P* Value
Packed erythrocytes	—	—	—	—	—	—	—	—	—
Transfused patients	45 (90)	33 (66)	0.007	41 (82)	32 (64)	0.07	49 (98)	42 (84)	0.031
Units transfused [U]	3 (2; 5)	2 (0; 3)	<0.001	2 (1; 4)	2 (0; 2)	0.041	5 (4; 9)	3 (2; 6)	<0.001
FFP	—	—	—	—	—	—	—	—	—
Transfused patients	39 (78)	16 (32)	<0.001	19 (38)	7 (14)	0.011	40 (80)	20 (40)	<0.001
Units transfused [U]	4 (2; 5)	0 (0; 3)	<0.001	0 (0; 2)	0 (0; 0)	0.016	5 (3; 8)	0 (0; 3)	<0.001
PC	—	—	—	—	—	—	—	—	—
Transfused patients	24 (48)	10 (20)	0.006	26 (52)	23 (46)	0.689	33 (66)	28 (56)	0.412
Units transfused [U]	0 (0; 3)	0 (0; 0)	0.001	1 (0; 2)	0 (0; 2)	0.402	2 (0; 5)	2 (0; 2)	0.010

Weber C, et al. *Anesthesiology* 2012; 117:351-47

Comparison of structured use of routine laboratory tests or near-patient assessment with clinical judgement in the management of bleeding after cardiac surgery

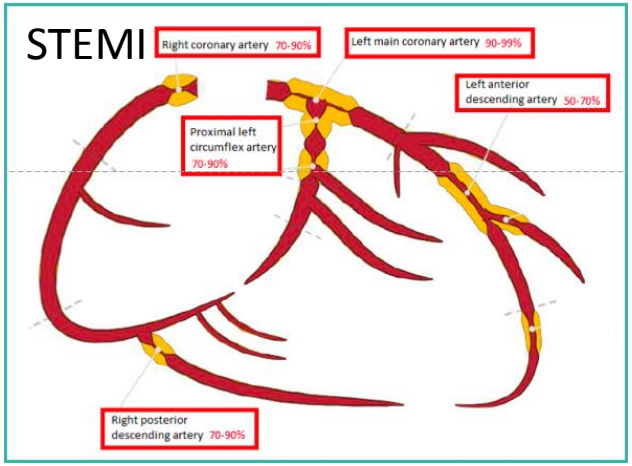


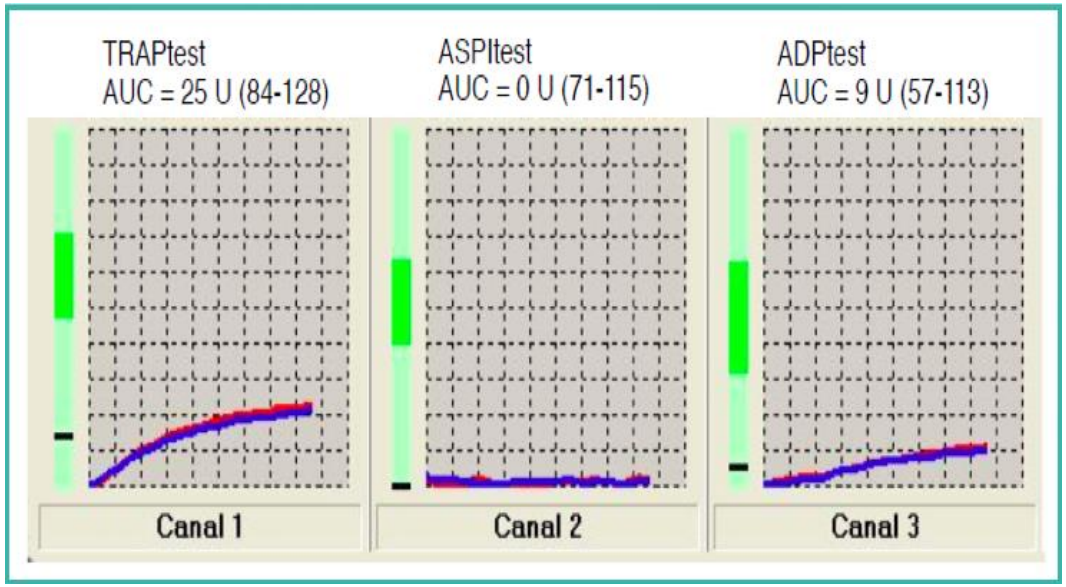
Variable	LAG group (*n*=51	POC group (*n*=51)	CD group (*n*=108)
Postoperative 24 h blood loss (ml)	850 (688–1095)	755 (606–975)	810 (550–1295)

Blood component	LAG group (*n*=51)	POC group (*n*=51)	CD group (*n*=108)	*P* (χ^2 test)
Packed red blood cells	35 (69)	34 (68)	92 (85)	0.01
Fresh frozen plasma	0	2 (4)	16 (15)	0.003
Platelets	1 (2)	2 (4)	14 (13)	0.02

Avidan MS, et al. *Br J Anaesth 2004:92:178–86*

Dans la pratique





Unité plaquettaire (UP) = 0.5 10^{11} plaquettes
Concentré plaquettaire (CP) = 6 à 8 UP

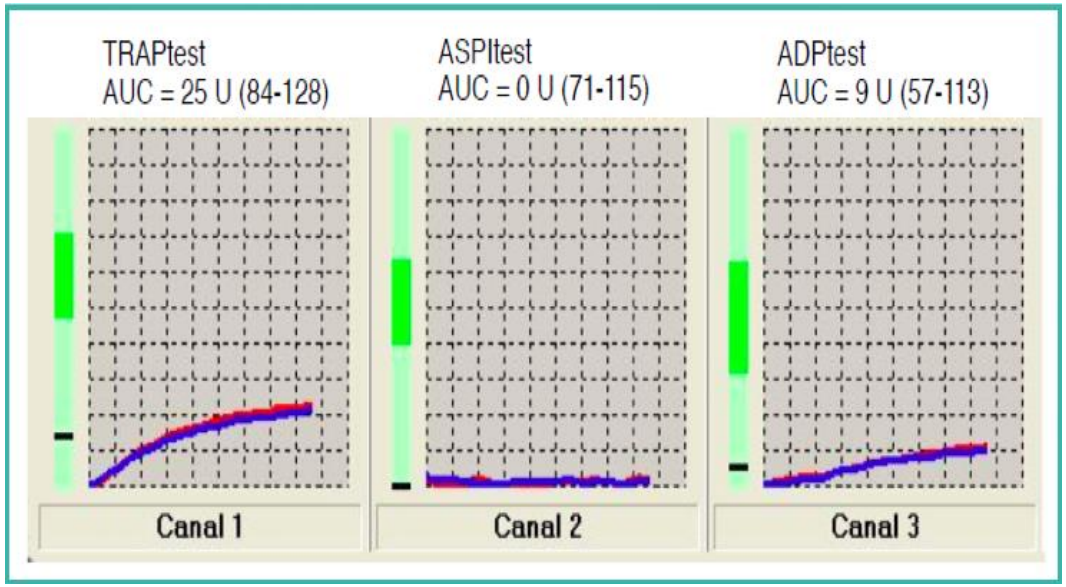
Dans la pratique

A. Pour éviter un saignement excessif peropératoire et la transfusion de plaquettes, vous discutez avec le chirurgien d'attendre 5 jours.

B. Vous opérez le patient le jour même, et transfusez 2 concentrés plaquettaires dès son arrivée au bloc.

C. Vous transfusez un concentré plaquettaire, refaites une analyse des fonctions plaquettaires, et poursuivez la transfusion selon les résultats.

D. Vous attendez que le chirurgien commence son intervention, et déciderez plus tard…



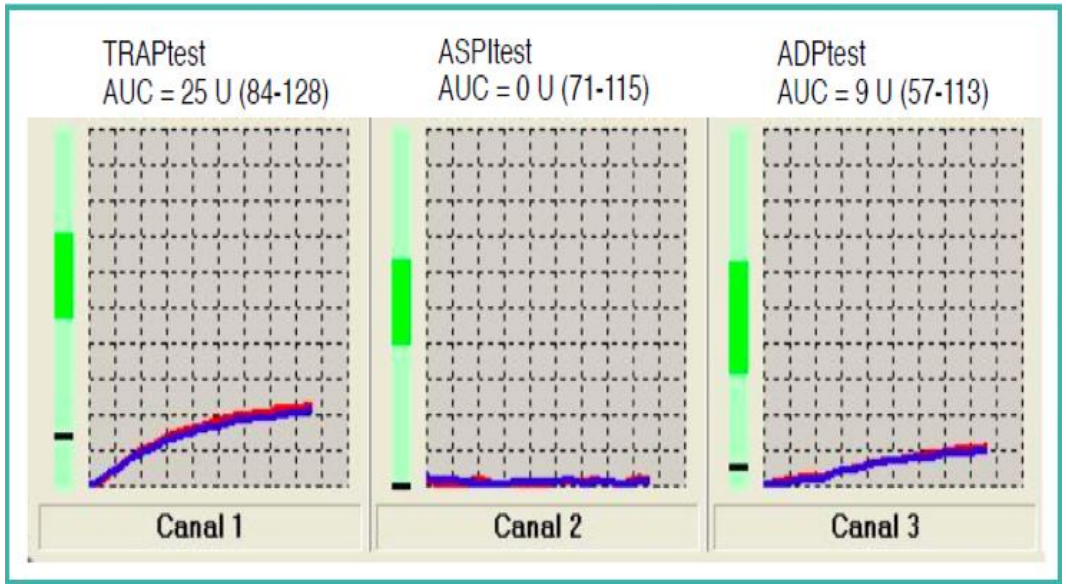
Dans la pratique

A. Pour éviter un saignement excessif peropératoire et la transfusion de plaquettes, vous discutez avec le chirurgien d'attendre 5 jours.

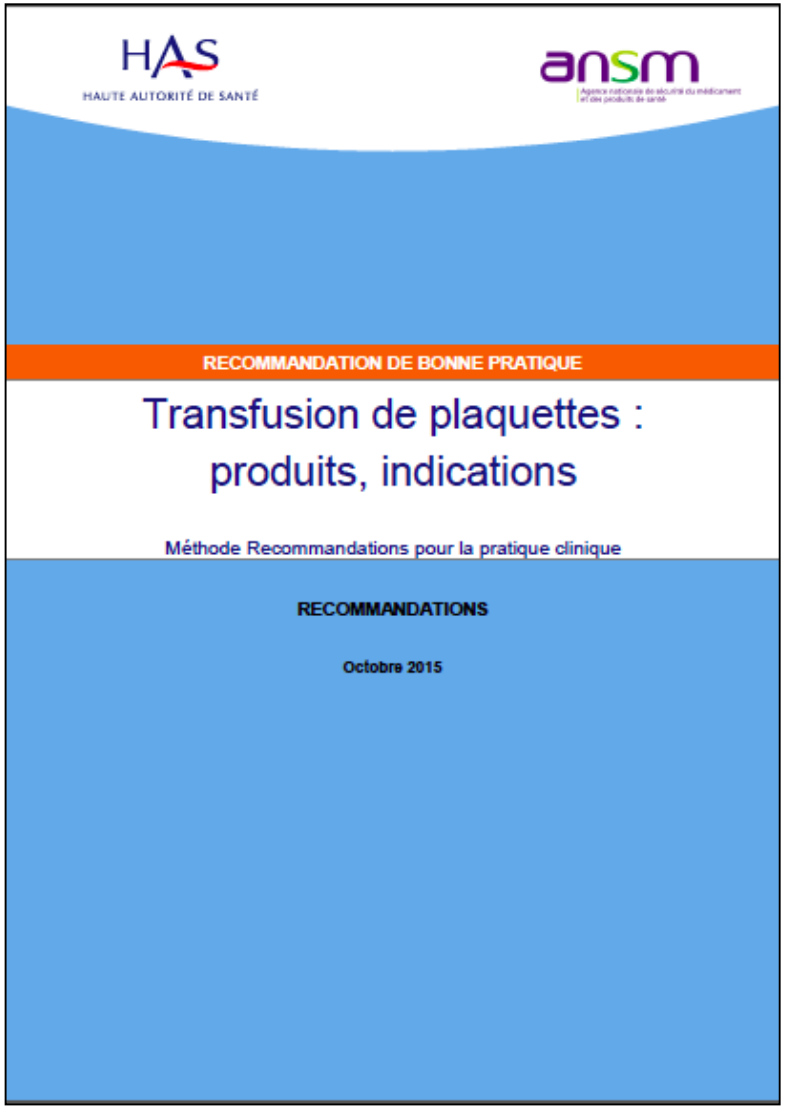
B. Vous opérez le patient le jour même, et transfusez 2 concentrés plaquettaires dès son arrivée au bloc.

C. Vous transfusez un concentré plaquettaire, refaites une analyse des fonctions plaquettaires, et poursuivez la transfusion selon les résultats.

D. Vous attendez que le chirurgien commence son intervention, et déciderez plus tard…



Pas de place aux tests de fonction plaquettaire dans l'indication de transfusion de plaquettes, y compris en chirurgie cardiaque


HAS
HAUTE AUTORITÉ DE SANTÉ

ansm

RECOMMANDATION DE BONNE PRATIQUE

Transfusion de plaquettes : produits, indications

Méthode Recommandations pour la pratique clinique

RECOMMANDATIONS

Octobre 2015

http://www.has-sante.fr/portail/upload/docs/application/pdf/2015-11/recommandations_-_transfusion_de_plaquettes.pdf

Take home messages

- Peu d'études, limitées aux patients de chirurgie cardiaque avec traitement antiplaquettaire
- Place des tests de fonction plaquettaire pour guider la transfusion reste à valider scientifiquement que ce soit en chirurgie cardiaque ou dans d'autres situations
- Pas d'algorithme communément accepté

- Associés au contexte clinique (SAIGNEMENT) et à d'autres résultats biologiques, ces tests pourraient être une aide à la compréhension de la physiopathologie du saignement et sa prise en charge.