Optimisation de la CEC: vers une CEC biocompatible

Pr Christophe Baufreton, CHU Angers
Cours du DU de CEC (Bordeaux), 21 février 2025

CEC conventionnelle

- Préparation
  - → Circuit de CEC débullé
  - → Dose héparine IV: 300 UI/Kg (par le chirurgien dans l'OD)
  - → 5000 UI dans liquide d'amorçage
  - → Check-list
- Anticoagulation: ACT > 480s
- Monitorage: Hémochron ou HMS
- Neutralisation: Protamine dose pour dose
- **Suivi morbidité immédiate**
  - → **Saignement (± reprise au bloc)**
  - → **Transfusion**

CEC optimale ?

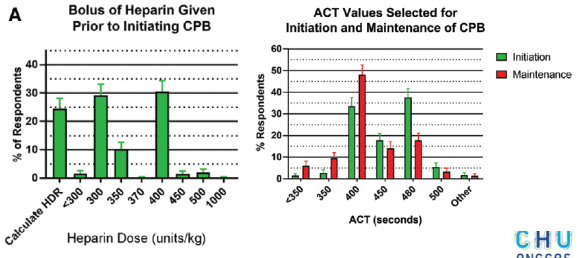

Optimal Perfusion During Cardiopulmonary Bypass: An Evidence-Based Approach

- Management des variables physiologiques et des composants de la machine cœur-poumon
- **Mais rien sur la gestion de l'anticoagulation !**

Murphy GS, Hessel EA, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. Anesth Analg. 2009;108(5):1394-417.

Gestion dans le monde de l'anticoagulation en CEC en 2018

For those respondents who used an activated clotting time to determine adequate anticoagulation for CPB initiation, an activated clotting time value of 480 or 400 seconds was used by 70.7%



Sniecinski RM, Bennett-Guerrero E, Shore-Lesserson L. Anticoagulation Management and Heparin Resistance During Cardiopulmonary Bypass. Anesth Analg. 2018 Dec;:1.

Sur quoi reposent les recommandations pour l'anticoagulation en CEC ? Faiblesse du niveau de preuve pour le gold-standard !

Heparin therapy during extracorporeal circulation

I. Problems inherent in existing heparin protocols

8 patients
Computer simulation

Brian S. Bull, M.D.,* Ralph A. Korpman, M.D.,* Wilfred M. Huse, M.D.,** and Bernard D. Briggs, M.D.,*** *Loma Linda, Calif.*

Heparin therapy during extracorporeal circulation

II. The use of a dose-response curve to individualize heparin and protamine dosage

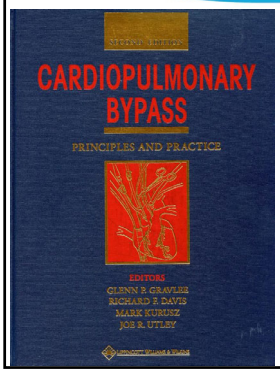
25 patients

Brian S. Bull, M.D.,* Wilfred M. Huse, M.D.,** Floyd S. Brauer, M.D.,*** and Ralph A. Korpman, M.D.,* *Loma Linda, Calif.*

According to Bull (1975) ACT value:

- *< 180 seconds: life threatening*
- *180-300 seconds: questionable*
- *> 300 seconds: safe*
- *> 600 seconds: unwise*

Que peut-on lire dans les ouvrages de référence ?



Bull et al. also recommended attaining an ACT of 480 seconds before initiating CPB, suggesting that this particular ACT value provides a safety margin over the believed minimum safe ACT of 300 seconds.

It appears that many practitioners have misinterpreted *their recommendation by assuming that an ACT of 480 seconds represents the minimum safe level for CPB anticoagulation, when the authors were simply offering* ***a suggestion without scientific validation***

EDITORIAL

Patient blood management during cardiac surgery: Do we have enough evidence for clinical practice?

Factor	Limitations of current evidence	Issues for future research
Anticoagulation measurement	Optimal measure and threshold unclear	Which is the optimal method with which to monitor anticoagulation? What are the minimum acceptable target threshold levels?
Reduced systemic heparinization	Heparin dose and target ACT not clearly defined; lack of high-level evidence	Does reduction of systemic heparinization in the setting of biocompatible circuits decrease bleeding and transfusion rate?

Ranucci M, Aronson S, Dietrich W, Dyke CM, Hofmann A, Karkouti K, et al. Patient blood management during cardiac surgery: do we have enough evidence for clinical practice? J Thorac Cardiovasc Surg. Elsevier; 2011 Aug;142(2):249.e1-32.

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Guidelines US 2018 pour l'anticoagulation en CEC

CLINICAL PRACTICE GUIDELINES

The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines[1]—Anticoagulation During Cardiopulmonary Bypass

Linda Shore-Lesserson, MD, Robert A. Baker, PhD, CCP, Victor A. Ferraris, MD, PhD, Philip R. Greilich, MD, David Fitzgerald, MPH, CCP, Philip Roman, MD, MPH, and John W. Hammon, MD

It is reasonable to maintain activated clotting time above 480 seconds during CPB. However, this minimum threshold value is an approximation and may vary based on the bias of the instrument being used (Level of Evidence C)

To maintain a margin of safety above 400 seconds, the minimum acceptable ACT value of approximately 480 seconds became a "standard of care" that was used in numerous future studies and in clinical practice, but was ***based on limited evidence***

Options for calculating the initial heparin bolus include a fixed, weight-based dose, (eg, 300 IU/kg), or use of point-of-care tests that measure the whole blood sensitivity to heparin using an associated dose response.

Depuis 1975 les patients ont changé !

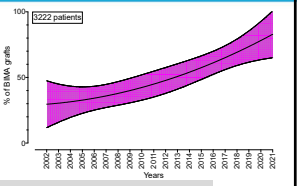
Changing Volumes, Risk Profiles, and Outcomes of Coronary Artery Bypass Grafting and Percutaneous Coronary Interventions

Gabriel S. Aldea, MD, Nahush A. Mokadam, MD, Rayland Melford, Jr, MD, Douglas Stewart, MD, Charles Maynard, PhD, Mark Reisman, MD, and Richard Gess, MD, MPH

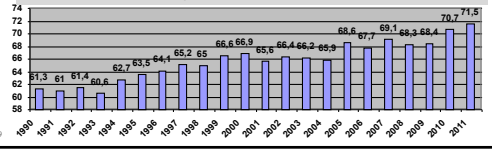
Fifteen-Year Outcome Trends for Valve Surgery in North America

Richard Lee, MD, Shuang Li, MS, J. Scott Rankin, MD, Sean M. O'Brien, PhD, James S. Gammie, MD, Eric D. Peterson, MD, Patrick M. McCarthy, MD, and Fred H. Edwards, MD, for The Society of Thoracic Surgeons Adult Cardiac Surgical Database

Aldea GS, et al. Ann Thorac Surg. 2009 Jun 1;87(6):1828-38.
Lee R, et al. Ann Thorac Surg. 2011 Mar 1;91(3):677-84.



Evolution de l'âge des patients et des modes de revascularization sur 20 ans au CHU d'Angers



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Impact de la double anti-aggrégation plaquettaire sur le saignement post-opératoire

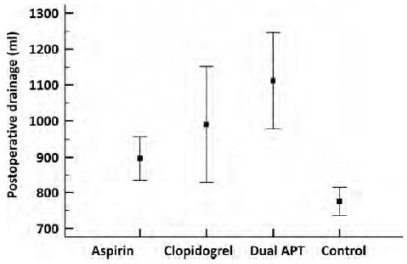
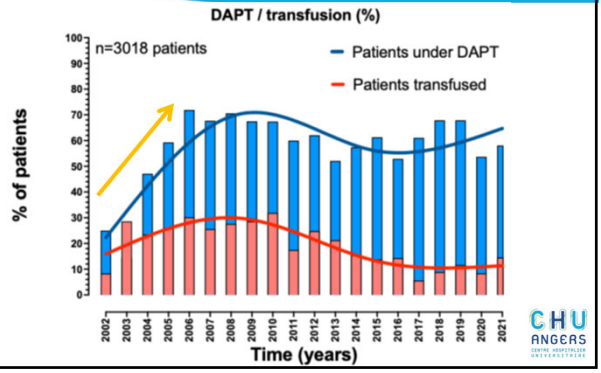


Figure 3: Postoperative chest tube drainage volumes, by antiplatelet treatment (mean and 95% CI). Matched patients.

Kremke M, et al. Antiplatelet therapy at the time of coronary artery bypass grafting: a multicentre cohort study. Eur J Cardiothorac Surg. 2013 Jul 11;44(2):e133-40.

10

Impact de la double anti-aggrégation plaquettaire sur la transfusion post-opératoire (Angers)



2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery

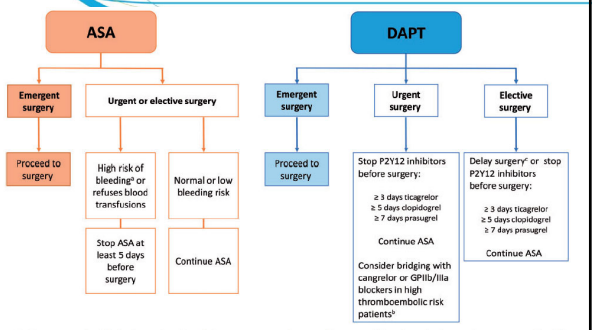


Figure 1: Management of antiplatelet therapy in patients having coronary artery bypass grafting surgery. [a]Complex and redo operations, severe renal insufficiency, haematological diseases and hereditary deficiencies in platelet function. [b]Recent stent implantation, recent thromboembolic event and alarming angiographic results. [c]Until the recommended DAPT period is completed. ASA: acetylsalicylic acid; DAPT: dual antiplatelet therapy; GPIIb/IIIa: glycoprotein IIb/IIIa.

Authors/Task Force Members. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery: The Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA). Eur J Cardiothorac Surg. 2017 Oct 3.

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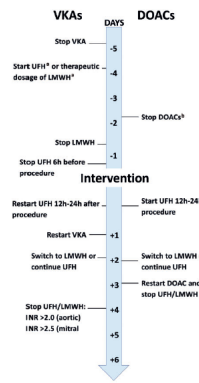
2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery



AVK et AOD

Figure 2: Management of oral anticoagulation in patients with an indication for pre- and/or postoperative bridging (reproduced with permission from Sousa-Uva, Stuart J. Head, Milan Milojevic, Jean-Philippe Collet, Giovanni Landoni, Manuel Castella *et al.* 2017 EACTS Guidelines on Perioperative Medication in Adult Cardiac Surgery. *Eur J Cardiothorac Surg* 2017; doi:10.1093/ejcts/ezx314). [a]Bridging with UFH/LMWH should start when INR values are below specific therapeutic ranges. [b]Discontinuation should be prolonged to >72 h if creatinine clearance is 50–79 ml/min/1.73 m^2 or ≥96 h if creatinine clearance is <50 ml/min/1.73 m^2. DOACs: direct oral anticoagulants; INR: international normalized ratio; LMWH: low-molecular-weight heparin; UFH: unfractionated heparin; VKAs: vitamin K antagonists.

Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA), Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):88-120.

Original paper

Perfusion

Prevalence of preoperative anaemia in patients having first-time cardiac surgery and its impact on clinical outcome. A retrospective observational study

Perfusion 1–7
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DOI: 10.1177/0267659114542457
prf.sagepub.com
SAGE

CJ Kim,[1] H Connell,[2] AD McGeorge[2] and R Hu[3]

28% patients anémiques
80% vs 38% transfusion

Abstract

The prevalence of anaemia is increasing globally. It has a close association with perioperative blood transfusion which, in turn, results in an increased risk of postoperative complications. Undesirable effects are not only limited to short-term, but also have long-term implications. Despite this, many patients undergo cardiac surgery with undiagnosed and untreated anaemia. We designed a retrospective, observational study to estimate the prevalence of anaemia in patients having cardiac surgery in Auckland District Health Board, blood transfusion rates and associated clinical outcome. Two hundred of seven hundred and twelve (28.1%) patients were anaemic. Red blood cell (RBC) transfusion rates were significantly higher in the anaemic group compared to the non-anaemic group (160 (80%) vs. 192 (38%), p-value <0.0001, RR (CI 95%) 2.133 (1.870-2.433)). Transfusion rates for fresh frozen plasma (FFP), cryoprecipitate and platelets were also higher in the anaemic group. Anaemia was significantly associated with the development of new infection (14 (7%) vs. 15 (2.9%), p-value 0.0193, RR (CI 95%) 2.389 (1.175-4.859)), prolonged ventilation time (47.01 hours vs. 23.59 hours, p-value 0.0076) and prolonged intensive care unit (ICU) stay (80.23 hours vs. 50.27, p-value 0.0011). Preoperative anaemia is highly prevalent and showed a clear link with significantly higher transfusion rates and postoperative morbidity. It is vital that a preoperative management plan for the correction of anaemia should be sought to improve patient safety and outcome.

JAMA®

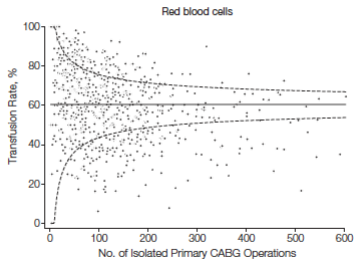
Online article and related content current as of October 19, 2010.

Variation in Use of Blood Transfusion in Coronary Artery Bypass Graft Surgery

Elliott Bennett-Guerrero; Yue Zhao; Sean M. O'Brien; et al.

JAMA. 2010;304(14):1568-1575 (doi:10.1001/jama.2010.1406)

Figure 1. Observed Variation in Hospital-Specific Transfusion Rates for Primary Isolated CABG Surgery With Cardiopulmonary Bypass During 2008 (N=798 Sites)



Définition universelle du saignement péri-opératoire

Clinical significance and determinants of the universal definition of perioperative bleeding classification in patients undergoing coronary artery bypass surgery

Eeva-Maija Kinnunen, MS,[a] Tatu Juvonen, MD, PhD,[a] Kari Eino Juhani Airaksinen, MD, PhD,[b] Jouni Heikkinen, MD, PhD,[a] Ulla Kettunen, RN,[a] Giovanni Mariscalco, MD, PhD,[c] and Fausto Biancari, MD, PhD[a]

Independent predictors of high UDPB classes

- Increased age
- Low hemoglobin
- **On-pump surgery *(full anticoagulation protocol)***
- Potent antiplatelet drug pause of <5 days
- Warfarin pause <2 days

Conclusions: High UDPB classes were associated with significantly poorer immediate and late outcomes. The UDPB classification seems to be a valuable research tool to estimate the severity of bleeding and its prognostic impact affect after coronary surgery. (J Thorac Cardiovasc Surg 2014;148:1640-6)

Kinnunen E-M, et al. Clinical significance and determinants of the universal definition of perioperative bleeding classification in patients undergoing coronary artery bypass surgery. J Thorac Cardiovasc Surg 2014;148(4):1640-2.

Que peut-on faire ?

Comment gérer de façon optimale l'anticoagulation en CEC au 21ème siècle?

Les guidelines !

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful and effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/ opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence/general agreement that the given treatment/procedure is not useful/effective and may sometimes be harmful.	Is not recommended

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	The consensus of expert opinion and/or small studies, retrospective studies, registries.

Recommendations	Class[a]	Level[b]	Ref[c]
Implementation of institutional measures to reduce haemodilution by fluid infusion and CPB during cardiac surgery to reduce the risk of bleeding and the need for transfusions is recommended.	I	C	
The use of a closed extracorporeal circuit may be considered to reduce bleeding and transfusions.	IIb	B	[112, 113]
The use of a biocompatible coating to reduce perioperative bleeding and transfusions may be considered.	IIb	B	[114–116]
The routine use of cell salvage should be considered to prevent transfusions.	IIa	B	[117–119]
(Modified) ultrafiltration may be considered as part of a blood conservation strategy to minimize haemodilution.	IIb	B	[120–122]
Retrograde and antegrade autologous priming should be considered as part of a blood conservation strategy to reduce transfusions.	IIa	A	[123–125]
Normothermia during CPB (temperature >36°C) and maintenance of a normal pH (7.35–7.45) may contribute to a reduced risk of postoperative bleeding.	IIb	B	[126, 127]

Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA), Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):88-120.

Interactive CardioVascular and Thoracic Surgery 19 (2014) 788–794
doi:10.1093/icvts/ivu266 Advance Access publication 14 August 2014

ORIGINAL ARTICLE – ADULT CARDIAC

A structured blood conservation programme reduces transfusions and costs in cardiac surgery

Lisa Ternström[a,b], Monica Hyllner[c], Erika Backlund[a], Henrik Schersten[a] and Anders Jeppsson[a,b,*]

[a] Department of Cardiothoracic Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden
[b] Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[c] Department of Cardiothoracic Anaesthesia and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden

The programme included:
- Education risk/benefit
- Guidelines respect
- Transfusion log
  - → Indication
  - → Patient status
  - → Prescribing physician

But heparin 350 IU/Kg and protamine 1:1

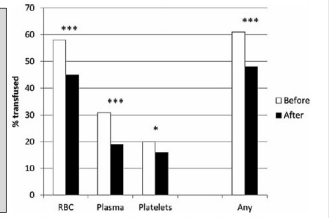
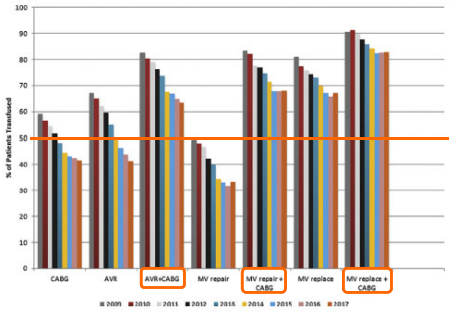


Figure 2: Percentage of patients transfused with red blood cells (RBCs), plasma, platelets and any blood product before (white bars) and after (black bars) the blood conservation programme was started. *P <0.05, ***P <0.001.

Où en sommes-nous dans la vie réelle ?



D'Agostino RS et al. The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2019 Update on Outcomes and Quality. Ann Thorac Surg. 2019;107(1):24-32.

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Deux stratégies différentes

1. Réduction de la dose d'héparine
2. Réduction ciblée de l'anticoagulation

1. Réduction de la dose d'héparine

- Habituellement la moitié de la dose habituelle d'héparine
- 150 UI/Kg au lieu de 300 UI/Kg
- Gestion de la CEC inchangée par ailleurs, excepté l'utilisation systématique de circuits pré-héparinés

Sans changer le seuil d'anticoagulation
Possibilité de réduire la dose d'héparine

A starting dose of 200 IU/kg of heparin and if necessary one 50 IU/kg increment achieved target ACT in 81.5% of patients.

Excess of heparin dose to reach ACT>480s

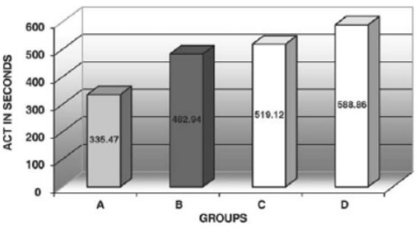

Fig. 2. Mean ACT after the initial dose of heparin in different groups.

Shuhaibar MN, et al. How much heparin do we really need to go on pump? A rethink of current practices. Eur J Cardiothorac Surg. 2004;26(5):947-50.

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Plus grande expérience en réduction d'héparine combinée à l'utilisation de CEC préhéparinée

Øvrum et al — Acquired Cardiovascular Disease

Heparinized cardiopulmonary bypass circuits and low systemic anticoagulation: An analysis of nearly 6000 patients undergoing coronary artery bypass grafting

Eivind Øvrum, MD, PhD, Geir Tangen, MD, Stein Tøløfsrud, MD, PhD, Bjørn Skeie, MD, PhD, Mari Anne L. Ringdal, CCP, Reidar Istad, CCP, and Rolf Øystese, CCP

Objective: Heparin coating of cardiopulmonary bypass circuits reduces the inflammatory response and increases the thromboresistance during extracorporeal circulation. These properties enables a lower systemic heparin dose, which has been shown to reduce the need for blood transfusions. Experience with this technique accumulated over 11 years has been analyzed.

Methods: All patients underwent on-pump coronary artery bypass grafting with heparin-coated circuits. Apart from some patients receiving a high intraoperative dose of aprotinin, the systemic heparin dose was reduced, with a lower level of an activated clotting time of 250 seconds during extracorporeal circulation. The overall strategy aimed at a fast-track regimen, with early extubation, minimal use of blood transfusions, and rapid postoperative recovery.

Results: Altogether, 5954 patients were included; 1131 (19.0%) were female (median age, 70 years), and 4823 were male (median age, 65 years). The median additive EuroSCORE was 3 (range, 0–14; mean 3.5 ± 2.5). No significant signs of clotting were seen in any part of the extracorporeal circuit. Bank blood products were given to 427 (7.2%) patients. Median extubation time was 1.7 hours. The stroke rate was 1.0%, transient neurologic deficits occurred in 0.7%, and perioperative myocardial infarction occurred in 1.2%. On the fifth day, 88.1% of the patients were physically rehabilitated and ready for discharge. Thirty-day mortality was 0.9% (54 patients).

Conclusions: The experience with this patient cohort including mostly low- to medium-risk patients with a relatively short cardiopulmonary bypass time indicates that coronary artery bypass grafting performed with heparin-coated circuits and reduced level of systemic heparinization is safe and results in a very satisfactory clinical course. No signs of clotting or other technical incidents were recorded. (J Thorac Cardiovasc Surg 2010;■:1-5)

2. Réduction ciblée du niveau d'anticoagulation

- Détermination d'un ACT cible
- *Reduced Goal Directed Anticoagulation*
- Pratique non fondée sur le poids du patient pour administrer une dose initiale d'héparine
- Pratique d'anticoagulation adaptée à chaque patient selon les circonstances
  Recours à un monitorage dédié

Les 10 commandements

1. ACT cible @ 250s pour les cœurs fermés. ACT cible @ 350s pour cœurs ouverts et redux
2. Utilisation d'un monitorage dédié permettant une titration précise de l'héparine et de la protamine (ratio protamine:heparine @ 0.3:1)
3. Utilisation d'un antifibrinolytique (ac. tranexamique)
4. CEC en normothermie
5. Contrôle des aspiration chirurgicales péricardiques et utilisation d'un Cell-Saver

Les 10 commandements

6. CEC préhéparinée avec oxygénateur à membrane réduisant l'interface air-sang (circuit clos, décharge VG par déclivité dans réservoir souple: pas de retour veineux actif)
7. Limiter l'hémodilution autant que possible (attention au remplissage préopératoire, rétropriming)
8. Les purges cavitaires au CO_2 sont hautement thrombogéniques et doivent être évitées
9. Eviter la stagnation de sang dans le circuit, rincer et recirculer après arrêt de la CEC
10. Respecter une hémostase chirurgicale rigoureuse !

1. ACT cible @ 250 s
Cœurs fermés

Effect of Anticoagulation Protocol on Outcome in Patients Undergoing CABG With Heparin-Bonded Cardiopulmonary Bypass Circuits

Gabriel S. Aldea, MD, Paul O'Gara, CCP, Oz M. Shapira, MD, Patrick Treanor, CCP, Ashraf Osman, MD, Eva Patalis, MD, Charles Arkin, MD, Rhea Diamond, PhD, Viken Babikian, MD, Harold L. Lazar, MD, and Richard J. Shemin, MD

Departments of Cardiothoracic Surgery, Pathology, and Neurology, Boston University Medical Center, Boston, Massachusetts

Essai clinique randomisé prospectif : ACT @ 250s *vs* ACT @ 450s

- Moins de transfusion: **24.2%** *vs* 35.8% (p<0.05)
- Moins d'évènements emboliques: **0.81%** *vs* 5.0% (p<0.05)
- Pas de corrélation entre production de thrombine et anticoagulation
- Pas de différence sur embolisation cérébrale et fonction cognitive

Aldea GS, et al. Effect of anticoagulation protocol on outcome in patients undergoing CABG with heparin-bonded cardiopulmonary bypass circuits. Ann Thorac Surg. 1998;65(2):425-33.

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1. ACT cible @ 350 s
Cœurs ouverts et redux

- Valeur empirique !
- Prend en compte l'impact de l'interface air-sang sur l'activation de la coagulation
- Dérive en partie de l'étude de Schönberger

Un circuit clos/circuit ouvert:
1. **Réduit l'activation de**
   - **complément**
   - **neutrophiles**
   - **plaquettes**
   - **fibrinolyse**
2. **Diminue l'hémolyse et le saignement post-op.**
3. **Améliore la clearance de l'endotoxine**

Schönberger JP, Everts PA, Hoffmann JJ. Systemic blood activation with open and closed venous reservoirs. Ann Thorac Surg. 1995 Jun 1;59(6):1549-55.

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2. Monitorage adapté pour l'héparine et la protamine
Diminuer le ratio protamine/héparine

- Identifier la réponse individuelle à l'héparine pour atteindre un ACT cible
- Calcul de la dose initiale en mettant le sang du patient au contact de deux doses d'héparine afin d'établir une courbe dose -réponse
- En fin de procédure, détermination de l'héparine résiduelle en vue de sa neutralisation par la dose adéquate de protamine

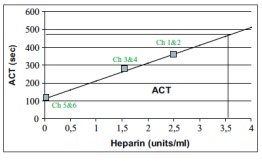

Figure 1. Heparin dose response (HDR) curve

Noui N et al. Anticoagulation monitoring during extracorporeal circulation with the Hepcon/HMS device. Perfusion 2012;27(3):214-20.

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2. Monitorage adapté pour l'héparine et la protamine
Diminuer le ratio protamine/héparine

44 pts: PAC ou RVA ACT@400s	HMS (n=22)	Hémocron (n=22)
Durée fermeture (min)	42 ± 15	68 ± 27 *
Durée clampage (min)	56 ± 30	62 ± 28
Ratio protamine/héparine	0,62 ± 0,13	1 ± 0.11 *
Saignement (mL)	804 ± 729	1416 ± 1103 *
Transfusion (U/Pt)	1,04 ± 1,5	2,1 ± 1,87 *

*HMS: Heparin Management System ; *:p<0,05*

Noui N et al. Anticoagulation monitoring during extracorporeal circulation with the Hepcon/HMS device. Perfusion 2012;27(3):214-20.

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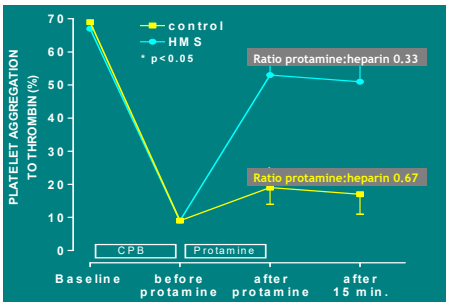
2. Monitorage adapté pour l'héparine et la protamine
Effet de la protamine en excès sur les plaquettes



Shigeta O, et al. Low-dose protamine based on heparin-protamine titration method reduces platelet dysfunction after cardiopulmonary bypass. J Thorac Cardiovasc Surg. 1999;118(2):354-60.

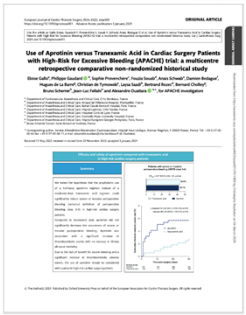
3. Anti-fibrinolytique

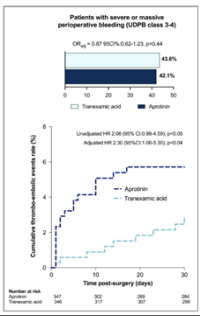
- Acide tranexamique: antifibrinolytique synthétique bon marché, qui inhibe le t-PA et l'activité de la plasmine, entrainant une réduction du saignement postopératoire
- Aprotinine: inhibiteur non spécifique de protéases, issue du poumon bovin, qui interagit avec les sites actifs de la plasmine, et de la kallikréine. Couteux, surtout en protocole dit de Royston (>8 MU), anti-inflammatoire à doses élevées seulement.
- Aprotinine retirée du marché à la fin des années 2000, puis réintroduit récemment
- Augmentation de la mortalité avec l'aprotinine *vs* acide tranexamique alors que peu d'effet supplémentaire sur la réduction du saignement
- Les équipes ont appris à s'en passer dans la grande majorité des cas !

Fergusson DA et al. N Engl J Med. 2008;358(22):2319-31.
Takagi H et al. Interact Cardiovasc Thorac Surg. 2009;9(1):98-101. Benedetto U et al. J Am Heart Assoc. 2018;7(5):e007570.

33

3. Anti-fibrinolytique
Aprotinine vs Ac Tranexamique (APACHE)


Use of Aprotinin versus Tranexamic Acid in Cardiac Surgery Patients with High-Risk for Excessive Bleeding (APACHE) trial: a multicentre retrospective comparative non-randomised historical study



Gallo, E. *et al.* Use of Aprotinin Versus Tranexamic Acid in Cardiac Surgery Patients with High-Risk for Excessive Bleeding (APACHE trial): A multicentre retrospective comparative non-randomised historical study. *Eur. J. Cardio-Thorac. Surg.* ezae001 (2024) doi:10.1093/ejcts/ezae001

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4. Normothermie


Benefits and Risks of Maintaining Normothermia during Cardiopulmonary Bypass in Adult Cardiac Surgery: A Systematic Review

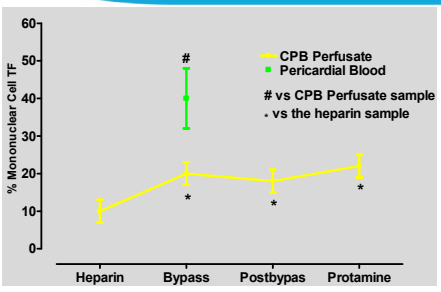
TAKE HOME MESSAGE
The current evidence suggests that maintaining hypothermia during cardiopulmonary bypass in adult cardiac surgery is associated with an increased risk of bleeding and allogeneic blood transfusion but without significant benefits in reducing the risk of stroke, cognitive decline, atrial fibrillation, use of inotropic support or intra-aortic balloon pump, myocardial infarction, all- cause infections, and acute kidney injury after cardiac surgery.

Normothermia during CPB (temperature >36°C) and maintenance of a normal pH (7.35–7.45) may contribute to a reduced risk of postoperative bleeding.	IIb	B

Ho KM, Tan JA. Benefits and Risks of Maintaining Normothermia during Cardiopulmonary Bypass in Adult Cardiac Surgery: A Systematic Review. Cardiovasc Ther. 2009;29(4):260-79.

35

5. Gestion des aspirations
Cavité péricardique et voie tissulaire de la coagulation

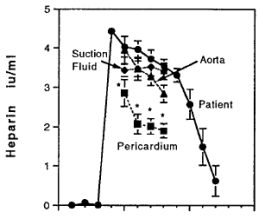


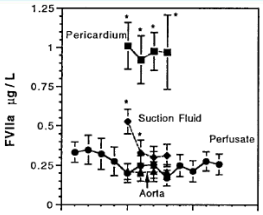
Facteur tissulaire exprimé par les monocytes

Chung JH, Gikakis N, Rao AK, Drake TA, Colman RW, Edmunds LH. Pericardial blood activates the extrinsic coagulation pathway during clinical cardiopulmonary bypass. Circulation 1996;93(11):2014-8.

5. Gestion des aspirations

Héparine et activation voie tissulaire dans le péricarde





1. Voie veineuse centrale
2. Aorte (outflow coronaire de CPG rétrograde)
3. Péricarde
4. Aspirations CEC

Philippou H, et al. Two-chain factor VIIa generated in the pericardium during surgery with cardiopulmonary bypass : relationship to increased thrombin generation and heparin concentration. Arterioscler Thromb Vasc Biol. 1999 Feb 1;19(2):248-54.

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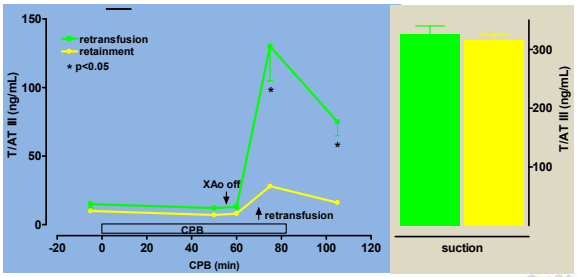
5. Gestion des aspirations

Impact de la gestion des aspirations du sang péricardiques sur l'activation de la coagulation dans le sang circulant



de Haan J et al. Retransfusion of suctioned blood during cardiopulmonary bypass impairs hemostasis. Ann Thorac Surg. 1995 Apr;59(4):901-7.

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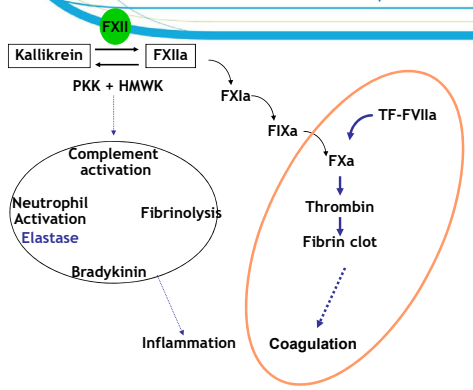
Activation de la coagulation en CEC

Place de la voie extrinsèque / intrinsèque



5. Gestion des aspirations et embolies

Comparaison cell-saver et filtres artériels

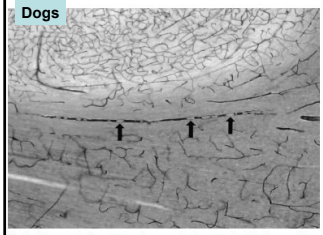


Fig 1. Representative photomicrograph of canine brain tissue with SCADs, indicating by arrows, after CPB and return of scavenged blood (alkaline phosphatase-stained, 100 µm thick).

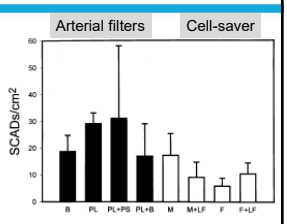


Fig 2. Mean SCAD density ± standard error by filter or cell saver group. Closed bars represent arterial filter group; open bars represent cell saver group. p < 0.05 for cell saver versus arterial filter groups; p > 0.05 for all other intergroup comparisons. (B = Bentley Duraflo II AF-1025D; PL = Pall LeukoGuard AL; PS = Pall SmartPrime; M = Medtronic autoLog cell saver, LF = Pall RCXL 1 leukocyte removal filter; F = Fresenius Continuous autotransfusion System.)

SCAD: Small capillary and arteriolar dilations

Kincaid EH, Jones TJ, Stump DA, Brown WR, Moody DM, Deal DD, et al. Processing scavenged blood with a cell saver reduces cerebral lipid microembolization. Ann Thorac Surg. 2000;70(4):1296-300.

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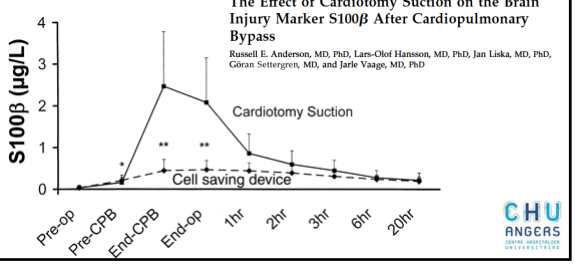
5. Gestion des aspirations

Cell-Saver et réponse inflammatoire

Réduction des concentrations circulantes:

- **hémoglobine libre** ***(Reents Ann Thorac Surg 1999)***
- **cytokines** ***(Reents Ann Thorac Surg 1999)***
- **protéine S100b** ***(Anderson Ann Thorac Surg 2000)***



Source lipidique extra cérébrale de la protéine s100β (non spécifique)

7 patients (*Part II*)		s100β en µg/L
Champ opératoire	Incision cutanée	12 ± 5
	Après sternotomie	42 ± 18
Réservoir du cell-saver	Avant lavage	33 ± 12
	Après lavage	1,9 ± 0,9
Sérum	préopératoire	0,03 ± 0,04
	postopératoire	0,44 ± 0,17

Le recours à un *cell-saver* permet de limiter la transfusion de particules lipidiques à partir du champ opératoire

Anderson RE, Hansson LO, Liska J, Settergren G, Vaage J. The effect of cardiotomy suction on the brain injury marker S100beta after cardiopulmonary bypass. The Annals of Thoracic Surgery 2000;69:847-50.

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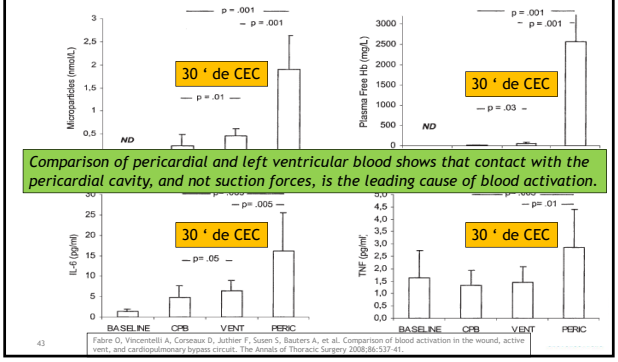
Le péricarde comme source d'activation inflammatoire et d'hémolyse



Comparison of pericardial and left ventricular blood shows that contact with the pericardial cavity, and not suction forces, is the leading cause of blood activation.

Fabre O, Vincentelli A, Corseaux D, Juthier F, Susen S, Bauters A, et al. Comparison of blood activation in the wound, active vent, and cardiopulmonary bypass circuit. The Annals of Thoracic Surgery 2008;86:537-41.

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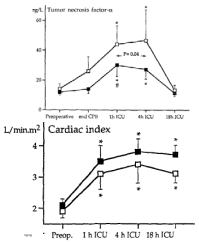
La production de TNF varie avec l'âge et altère la performance myocardique

MYOCARDIAL PERFORMANCE IN ELDERLY PATIENTS AFTER CARDIOPULMONARY BYPASS IS SUPPRESSED BY TUMOR NECROSIS FACTOR

<55 ans vs >65 ans



The aim of this study was to determine whether elderly patients (aged ≥65 years, *n* = 20) in comparison with younger patients (aged ≤55 years, *n* = 23) demonstrate a different biochemical and hemodynamic response to coronary artery bypass operations. In the elderly group, we calculated a smaller body surface area ($p < 0.01$) than that in the younger group, and more female patients were included in this group ($p < 0.05$). During cardiopulmonary bypass, the elderly had higher endotoxin plasma concentrations ($p < 0.01$) than the younger patients, and significantly more circulating tumor necrosis factor-alpha was found after operation ($p < 0.04$). In the intensive care unit, the elderly patients had a significantly higher pulmonary capillary wedge pressure ($p < 0.001$), a higher mean pulmonary artery pressure ($p < 0.01$), and a lower calculated left ventricular stroke work index ($p < 0.05$). Multivariate analysis for the postoperative outcome showed that the intergroup differences in tumor necrosis factor-alpha, mean pulmonary artery pressure, and pulmonary capillary wedge pressure could be explained mainly by the difference in age between the groups and that the calculated left ventricular stroke work index difference could be explained by the difference in circulating tumor necrosis factor-alpha levels. Thus in elderly patients higher circulating endotoxin and tumor necrosis factor-alpha concentrations were detected than in younger patients, which clinically resulted in a suppressed myocardial performance. (J Thorac Cardiovasc Surg 1995;110:1663-9)

Henk te Velthuis, PhD,[a] Piet G. M. Jansen, MD, PhD,[a] Heleen M. Oudemans-van Straaten, MD,[a] Augueste Sturk, PhD,[b] Leon Eijsman, MD, PhD,[a] and Charles R. H. Wildevuur, MD, PhD,[a] *Amsterdam and Leiden, The Netherlands*

Velthuis H te, Jansen PGM, Straaten HMO, Sturk A, Eijsman L, Wildevuur CRH. Myocardial performance in elderly patients after cardiopulmonary bypass is suppressed by tumor necrosis factor. The Journal of Thoracic and Cardiovascular Surgery 1995;110:1663-9.

Hémolyse: la pompe ou les aspirations ?

standard roller pump (STD, n = 20),
dynamically set nonocclusive roller pump (DYN, n = 20)
centrifugal pump (CEN, n = 20).

La réinjection du sang des aspirations de cardiotomie est la principale source d'hémoglobine libre plasmatique

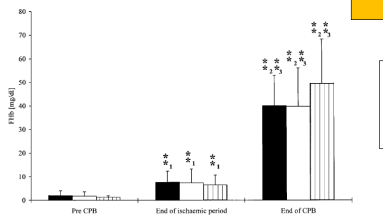


Figure 4 FHb, CEN group (solid bars), STD group (open bars) and DYN group (hatched bars). **1 $p < 0.001$ for all groups at the end of the ischaemic phase of CPB compared to pre-CPB. **2 $p < 0.001$ for all groups at the end of CPB compared to pre-CPB. **3 $p < 0.001$ for all groups at the end of CPB compared to the end of the ischaemic phase.

Hansbro SD, Sharpe DA, Catchpole R, Welsh KR, Munsch CM, McGoldrick JP, et al. Haemolysis during cardiopulmonary bypass: an in vivo comparison of standard roller pumps, nonocclusive roller pumps and centrifugal pumps. Perfusion. 1999;14(1):3-10.

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Qualité du sang récupéré
Aspirations de cardiotomie *vs* cell-saver

Table 1. Concentration of Proinflammatory Cytokines, Hemostasis Factors, Free Hemoglobin, Leukocyte Count, and Hematocrit

Variables	Patient Preop	Patient Intraop	Patient Postop	Cardiotomy Suction Intraop	avant Harem 1	après process Harem 2
IL-6 (pg/L)	2 (1–6)	10 (8–30)	113 (38–357)	52* (19–89)	178 (77–643)	9 (2–30)
IL-8 (pg/L)	13 (10–19)	20 (16–29)	29 (20–43)	26* (24–42)	95 (54–106)	50* (27–43)
TNF-α (pg/L)	0 (0–4)	1 (0–5)	0 (0–2)	24* (20–33)	22 (0–33)	0 (0–4)
TAT (µg/L)	5 (3–15)	43 (32–73)	81 (60–108)	115* (99–153)	693 (586–870)	175* (20–313)
PAP (µg/L)	427 (285–595)	489 (393–607)	653 (496–773)	566* (505–658)	899 (644–965)	20 (14–34)
Thrombocytes (10^9/µL)	195 (154–220)	137 (123–158)	134 (113–151)	127 (114–144)	60 (49–66)	14 (11–17)
CD62$^+$	3	6	20	2	NA	NA
Thrombocytes (%)	(0–4)	(1–13)	(7–46)	(1–6)		
Free Hb (mg/dL)	24 (18–34)	30 (27–32)	38 (31–43)	67* (50–70)	500 (542–452)	50* (45–62)
Leukocytes (10^3/µL)	4.6 (4.0–6.1)	7.1 (5.2–8.9)	9.6 (8.9–32.0)	6.0 (4.8–8.0)	3.7 (2.8–4.0)	5.2 (5.4–6.3)
Hematocrit (%)	37.0 (35.3–40.4)	25.3 (21.7–24.3)	25.2 (24.5–26)	25 (25.6–25.3)	16 (12.7–10.3)	26.8 (24.1–29.1)

* Value significantly different from patients intraop value; [b] Value above the reference range in the processed blood.
Data are presented as medians with the lower and upper quartiles in parentheses.
Patient preop, intraop, and postop samples taken from the arterial catheter in the course of the operation.
Cardiotomy suction intraop samples taken from the cardiotomy suction. Haem 1 and Haem 2 samples taken from blood collected with the Haemonetics system before (Haem 1) and after processing (Haem 2).
Hb = hemoglobin; IL = interleukin; NA = not analyzed; PAP = plasmin-antiplasmin complex; TAT = thrombin-antithrombin complex; TNF-α = tumor necrosis factor-α.

Réduction paramètres
- SIRS Cytokines
- Coagulation
- Fibrinolyse
- Hémolyse

Contamination bactérienne:
- Fréquente 90%
- Faible charge (<10/mL)

Reents W, Babin-Ebell J, Misoph MR, Schwarzkopf A, Elert O. Influence of different autotransfusion devices on the quality of salvaged blood. The Annals of Thoracic Surgery 1999;68:58-62.

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Qualité du sang récupéré au cell-saver
Contamination bactérienne

Table 1. *Bacterial and endotoxin assay of patient and Cell Saver System blood and priming fluid during cardiac operations*

	Bacterial culturer No. positive/No. of tests (%)	Endotoxin assay No. positive/No. of tests (%)
Blood		
Preoperative	4/37 (10.8)	0/35 (0)
Intraoperative	11/36 (30.6)	5/35 (14.3)
Cell Saver System	30/31 (96.8)	7/29 (24.1)
Postoperative	1/28 (3.6)	5/25 (20)
All blood	46/132 (34.8)	17/124 (13.7)
Priming fluid	0/38 (0)	0/35 (0)
Total	46/169 (27.2)	17/159 (10.7)

- Etude prospective chez 38 patients
- Contamination bactérienne du réservoir de cell-saver fréquente
- Germes contaminants en provenance de l'air ambiant, de la flore cutanée, ou des surfaces environnementales
- 79,5% staph. coag. neg. et 20,5% diphtéroïdes
- Aucun épisode de sepsis postopératoire

Bland LA, Villarino ME, Arduino MJ, McAllister SK, Gordon SM, Uyeda CT, et al. Bacteriologic and endotoxin analysis of salvaged blood used in autologous transfusions during cardiac operations. J Thorac Cardiovasc Surg 1992;103:582-8.

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Hemodynamic effects of cardiotomy suction blood

Martin Westerberg, MD, PhD,[a] Jakob Gäbel, MD,[a] Anders Bengtsson, MD, PhD,[b] Johan Sellgren, MD, PhD,[c] Ola Eidem, ECCP,[a] and Anders Jeppsson, MD, PhD[a]

Dr Westerberg

J Thorac Cardiovasc Surg 2006;131:1352-7

Objective: Cardiac surgery induces a systemic inflammatory activation, which in severe cases is associated with peripheral vasodilation and hypotension. Cardiotomy suction blood contains high levels of inflammatory mediators, but the effect of cardiotomy suction blood on the vasculture is unknown. We investigated the effect of cardiotomy suction blood on systemic vascular resistance in vivo and whether cell-saver processing of suction blood affects the vascular response.

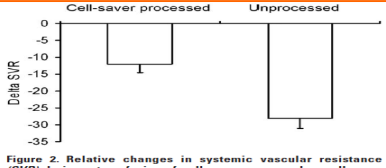

Figure 2. Relative changes in systemic vascular resistance (SVR) during retransfusion of cell-saver processed or cell-saver unprocessed cardiotomy suction blood (mean ± standard error of the mean). There was a significant difference between the 2 groups ($P = .001$).

Conclusions: The results suggest cardiotomy suction blood is vasoactive and might influence vascular resistance and blood pressure during cardiac surgery. The observed vasodilation is proportional to the inflammatory activation of suction blood and can be reduced by processing suction blood with a cell-saving device before retransfusion.

Hemodynamic effects of cardiotomy suction blood

Martin Westerberg, MD, PhD,[a] Jakob Gäbel, MD,[a] Anders Bengtsson, MD, PhD,[b] Johan Sellgren, MD, PhD,[c] Ola Eidem, ECCP,[a] and Anders Jeppsson, MD, PhD[a]

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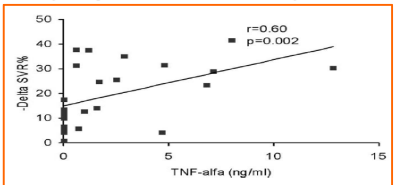
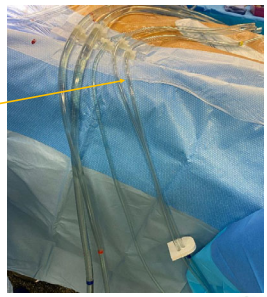


Figure 3. Correlation between plasma levels of TNF-α in retransfused cardiotomy suction blood and relative changes in systemic vascular resistance.

Conclusions: The results suggest cardiotomy suction blood is vasoactive and might influence vascular resistance and blood pressure during cardiac surgery. The observed vasodilation is proportional to the inflammatory activation of suction blood and can be reduced by processing suction blood with a cell-saving device before retransfusion.

En pratique comment faire ?

- Utiliser systématiquement un cell-saver
- Conserver l'installation de la ligne d'aspiration de cardiotomie en place (*rescue*)
- Dans l'urgence, se souvenir que si le sang aspiré n'a séjourné que quelques secondes dans le péricarde, il n'a pas eu le temps de subir une activation importante
- Le sang de la décharge VG n'est pas soumis à la même activation



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6. Traitements de surfaces

- Standard CPB + Cardiotomy suction
- Heparin-coated CPB + Cardiotomy suction
- Heparin-coated CPB No cardiotomy suction

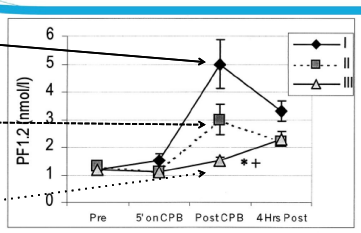

Figure 1. Comparison of thrombin generation (PF-1.2) for different treatment strategies. *Diamonds*, Group I; *squares*, group II; *triangles*, group III. *Asterisk* indicates $P < .001$ for group I versus group III; *plus sign* indicates $P = .042$ for group II versus group III, by ANOVA and Scheffé test.

ACT @ 450s using Hepcon® HMS

Aldea GS et al. Limitation of thrombin generation, platelet activation, and inflammation by elimination of cardiotomy suction in patients undergoing coronary artery bypass grafting treated with heparin-bonded circuits. J Thorac Cardiovasc Surg 2002;123(4):742-55.

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6. Traitements de surfaces

Biopassive coatings

Commercial
- Albumin
- Polyethylene glycol
- Phosphorylcholine
- Poly(2-methoxyethyl acrylate)

Underdeveloped
- Zwitterionic polymers
- Non-ionic polymers
- Tethered liquid perfluorocarbon

Bioactive coatings

Commercial
- Heparin

Underdeveloped
- Heparin-based coatings (e.g. different ways of bonding)
- Nitric oxide releasing
- Nitric oxide + other bioactives (e.g. argatroban)
- Complement inhibitor

Combination

Commercial
- Heparin + albumin
- Poly(ethylene oxide)/sulfate/sulfonate
- Poly(ethylene oxide)/sulfate/sulfonate/ heparin

Underdeveloped
- Not available

Figure 1. Overview of currently commercial and underdeveloped anti-thrombogenic surface coatings for ECMO. These coatings can be categorized as bioactive coatings, biopassive coatings, and their combination.

Zhang, M. *et al.* Anti-thrombogenic Surface Coatings for Extracorporeal Membrane Oxygenation: A Narrative Review. *ACS Biomater. Sci. Eng.* 7, 4402-4419 (2021).

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6. Traitements de surfaces

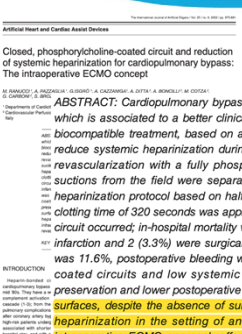
Alternatives aux heparin-coatings

Reduced systemic heparin dose with phosphorylcholine coated closed circuit in coronary operations

An ex vivo evaluation of blood coagulation and thromboresistance of two extracorporeal circuit coatings with reduced and full heparin dose

53 03/03/2025

Biopassif vs Bioactif



Closed, phosphorylcholine-coated circuit and reduction of systemic heparinization for cardiopulmonary bypass: The intraoperative ECMO concept

- **Duraflo II** vs **Phisio**
- 100 UI/Kg vs 150 UI/Kg
- ACT @ 300s vs ACT @ 320s

ABSTRACT: Cardiopulmonary bypass with heparin-bonded circuits reduces systemic heparinization which is associated to a better clinical outcome in cardiac operations. In the present study, a novel biocompatible treatment, based on a phosphorylcholine coating without heparin, has been used to reduce systemic heparinization during cardiopulmonary bypass. Sixty patients underwent coronary revascularization with a fully phosphorylcholine-coated circuit. The circuit was entirely closed; suctions from the field were separated during the cardiopulmonary bypass time. A low systemic heparinization protocol based on half the loading dose of heparin (150 IU/kg) and a target activated clotting time of 320 seconds was applied. No thrombus formation inside the extracorporeal circulation circuit occurred; in-hospital mortality was absent. One patient (1.6%) had a postoperative myocardial infarction and 2 (3.3%) were surgically revised due to bleeding. Homologous blood transfusion rate was 11.6%, postoperative bleeding was 310 ± 136 ml. If compared to patients treated with heparin-coated circuits and low systemic heparinization, these patients have better platelet count preservation and lower postoperative bleeding. The low thrombogenicity of phosphorylcholine-treated surfaces, despite the absence of surface-immobilized heparin, allows a safe reduction of systemic heparinization in the setting of an ECMO-like intraoperative cardiopulmonary - bypass. This intraoperative ECMO approach offers promising results in terms of clinical outcome after coronary revascularization operations. (Int J Artif Organs 2002; 25: 875-81)

7. Lutte contre hémodilution

- Provoque une augmentation de l'ACT non liée à l'héparinisation
- Contribue aux déperditions sanguines et au risque transfusionnel
- Majore le risque d'AVC *(Karkouti K et al Ann Thorac Surg 2005;80(4):1381-7)*
- Majore le risque d'IRA *(Karkouti K et al J Thorac Cardiovasc Surg 2005;129(2):391-400)*
- Attention au remplissage excessif préopératoire

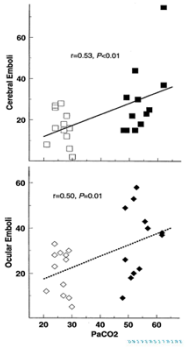
Recourir aux techniques de priming rétrograde autologue pour éliminer autant que possible le volume d'amorçage de la CEC

Recommendations	Class[a]	Level[b]
Implementation of institutional measures to reduce haemodilution by fluid infusion and CPB during cardiac surgery to reduce the risk of bleeding and the need for transfusions is recommended.	I	C

Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA), Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):88-120.

8. Limiter l'utilisation du CO2

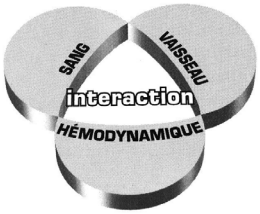
- Utilisé lors des purges cavitaires pour diminuer les embolies gazeuses
- **MAIS:**
  - → Induit une acidose
  - → Diminue les propriétés anticoagulantes de l'héparine
  - ➢ **Augmente le risque thrombotique**
  - → Provoque une vasodilatation cérébrale
  - ➢ **Augmente le risque embolique cérébral**



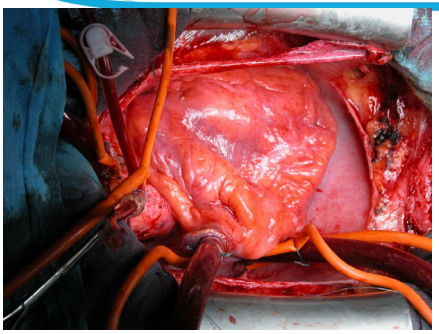
Cook DJ et al. Effect of temperature and PaCO2 on cerebral embolization during cardiopulmonary bypass in swine.. Ann Thorac Surg 2000;69(2):415-20.

9. Eviter la stagnation sanguine

Triade de Virchow



10. Hémostase chirurgicale rigoureuse



03/03/2025

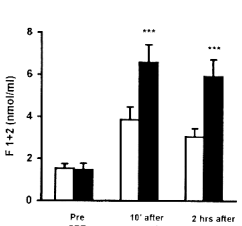
Complications?

Existe-t-il un risque de morbidité lié à la réduction de l'héparine ou de l'anticoagulation ?

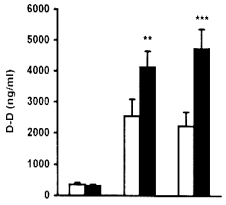
Réduction de l'anticoagulation sans gestion des aspirations

Réintroduction du sang activé dans la CEC !

Thrombin generation



Fibrinolytic activity



white bars: uncoated + full heparinization

black bars: coated + low heparinization

Kuitunen AH et al. Cardiopulmonary bypass with heparin-coated circuits and reduced systemic anticoagulation. Ann Thorac Surg 1997;63(2):438-44.

Surtout ne pas croire qu'un ACT très élevé protège de l'activation de la coagulation

Off-Pump Coronary Artery Bypass Operation Does Not Increase Procoagulant and Fibrinolytic Activity: Preliminary Results

Lars Englberger, MD, Franz F. Immer, MD, Friedrich S. Eckstein, MD, Pascal A. Berdat, MD, Andre Haeberli, PhD, and Thierry P. Carrel, MD

1. ACT 250 s in off-pump
2. ACT 480 s in uncoated CPB (32° C) with cardiotomy suction return: ACT at 692 s after heparin and >1000s during CPB

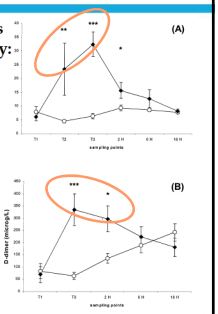


Fig 3. (A) Thrombin–antithrombin complex (TAT [ANOVA $p < 0.01$]). (B) D-dimer (ANOVA $p < 0.0001$). Values shown not corrected for hemodilution. Data are presented as mean ± SEM. Significant intergroup differences (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$). Circles = off-pump group; diamonds = on-pump group. (ANOVA = analysis of variance; H = hours postoperative; T1 = baseline; T2 = during operation; T3 = end of operation.)

Augmenter l'ACT ne protège **pas en l'absence de gestion des aspirations** de l'augmentation de la thrombine circulante

Quelle est la place du ''moins d'héparine'' dans les suites ?

Ou est-ce juste l'approche multifactorielle qui rend cette stratégie efficace ?

Simple réduction de l'héparine Repenser ses pratiques

Patients receiving lower dose of heparin has lower postoperative blood loss. The added benefit of significant drop in postoperative blood loss is evident.

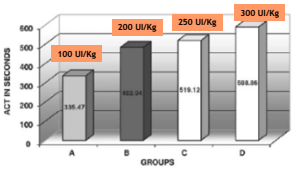


Fig. 2. Mean ACT after the initial dose of heparin in different groups.

- 20% p=0.0039

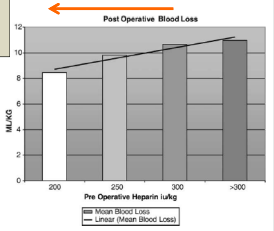


Fig. 3. Mean postoperative blood loss in millilitre per kilogram of patients receiving different preCPB heparin doses.

Shuhaibar MN, et al. How much heparin do we really need to go on pump? A rethink of current practices. Eur J Cardiothorac Surg. 2004;26(5):947-50.

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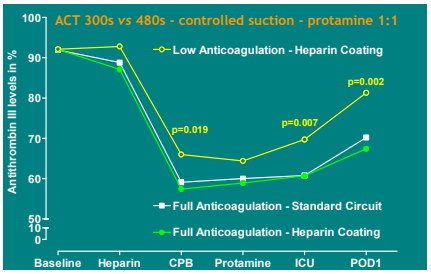
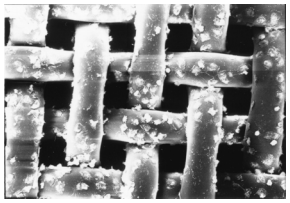
Préservation des concentrations d'antithrombine après CEC en réduction d'anticoagulation

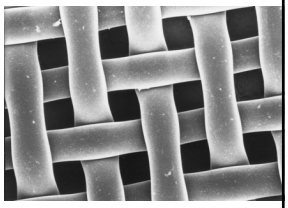


Ranucci M, et al. The Antithrombin III-Saving Effect of Reduced Systemic Heparinization and Coated Circuits. J Cardiothorac Vasc Anesth 2002;16(3):316-20.

Réduction d'anticoagulation et dépôts cellulaires sur les surfaces artificielles

Microscopie électronique à balayage x350





Heparin-coated ECC
Full heparinization
300 IU/Kg ACT > 400 s.

Heparin-coated ECC
Reduced heparinization
200 IU/Kg ACT > 300 s.

Nakajima T, et al. Reduction of heparin dose is not beneficial to platelet function. Ann Thorac Surg 2000;70(1):186-90.

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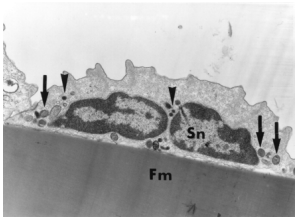
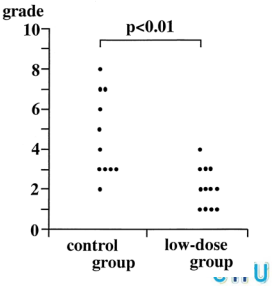
Réduction d'anticoagulation et dépôts cellulaires sur les surfaces artificielles

Microscopie électronique à transmission x 7500



Adhésion leucocytaire



Nakajima T, et al. Reduction of heparin dose is not beneficial to platelet function. Ann Thorac Surg 2000;70(1):186-90.

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Impact de l'héparine sur l'activation endothéliale en chirurgie à cœur ouvert

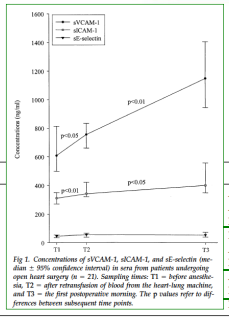

Fig 1. Concentrations of sVCAM-1, sICAM-1, and sE-selectin (median ± 95% confidence interval) in sera from patients undergoing open heart surgery (n = 21). Sampling times: T1 = before anesthesia, T2 = after retransfusion of blood from the heart-lung machine, and T3 = the first postoperative morning. The p values refer to differences between subsequent time points.

The higher heparin dose, the higher endothelial activation

Variable	Significant Variables	*p* Value	Coefficient
sICAM-1 at T2	Age	0.012	−6.174
sICAM-1 at T3	Age	0.034	−0.329
sVCAM-1 at T2	Heparin dose	0.005	0.003
...	Protamine dose	0.007	−0.002
sVCAM-1 at T3	Aortic cross-clamping time	0.037	0.009
sE-selectin at T2	Heparin dose	0.002	0.179
sE-selectin at T3	Age	0.005	−2.072
...	Heparin dose	0.003	0.185
...	Protamine dose	0.060	0.164

Elkemo H, Sellevold OFM, Videm V. Markers for endothelial activation during open heart surgery. Ann Thorac Surg. 2004;77(1):214-9.

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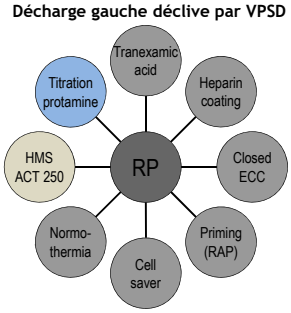
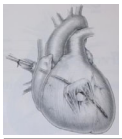
Cette approche est elle également fiable et réalisable en chirurgie à cœur ouvert ?

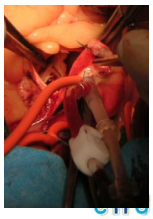
Principes en chirurgie à cœur fermé

Décharge gauche déclive par VPSD





A cœur fermé:
- Déclivité
- Sang toujours en contact de surface hémocompatible



La décharge gauche par déclivité disparaît quand on ouvre les cavités cardiaques

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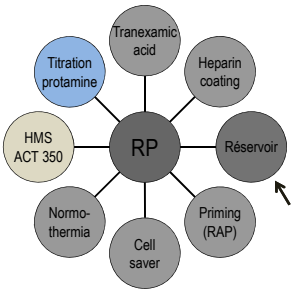
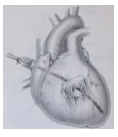
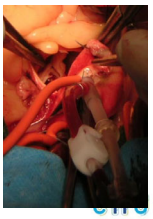
Adaptations en chirurgie à cœur ouvert

Décharge gauche déclive par VPSD





A cœur ouvert (valve)
- Sang toujours en contact de surface hémocompatible



La décharge gauche par déclivité disparaît quand on ouvre les cavités cardiaques

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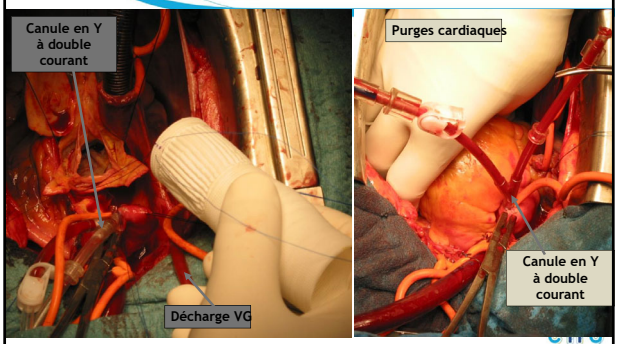
Intervention de Tirone David avec ACT 350 s

Décharge ventriculaire gauche et purges des cavités cardiaques



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Optimisation de la CEC
Guidelines OpECC - MiECC - ERAS (RAAC)

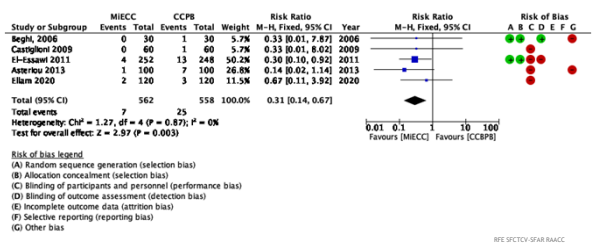
2021 MiECTiS focused update on the 2016 position paper for the use of minimal invasive extracorporeal circulation in cardiac surgery

Perfusion

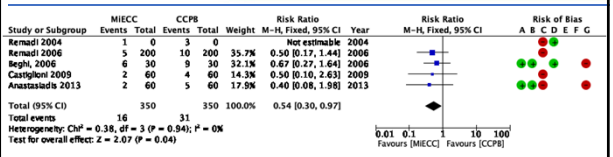
Anaesthesia Critical Care & Pain Medicine

Guidelines on enhanced recovery after cardiac surgery under cardiopulmonary bypass or off-pump

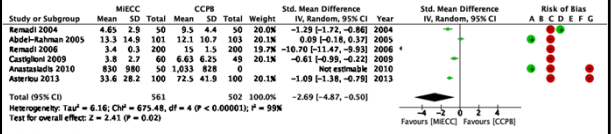
Méta-analyse comparant CEC conventionnelle et optimisée
Infarctus myocardique postopératoire



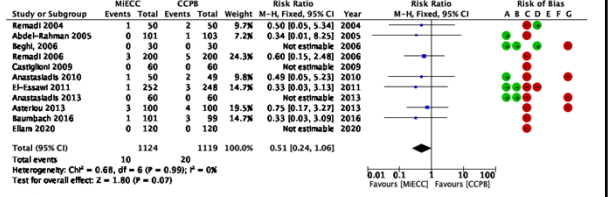
Méta-analyse comparant CEC conventionnelle et optimisée
Bas débit cardiaque



Libération enzymatique
Souffrance cellulaire myocardique

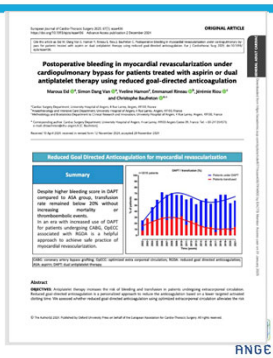


Méta-analyse comparant CEC conventionnelle et optimisée
Mortalité postopératoire



Les résultats dans notre pratique quotidienne

Impact de la réduction ciblée d'anticoagulation sous CEC optimisée chez les patients avec double antiaggrégation plaquettaire


ORIGINAL ARTICLE

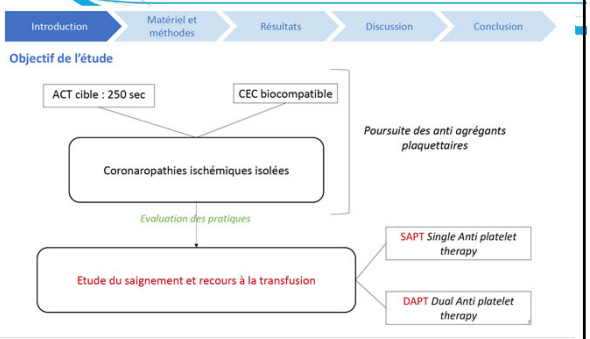
Postoperative bleeding in myocardial revascularization under cardiopulmonary bypass for patients treated with aspirin or dual antiplatelet therapy using reduced goal-directed anticoagulation

Reduced Goal Directed Anticoagulation for myocardial revascularization

Summary

Abstract

Les résultats dans notre pratique quotidienne

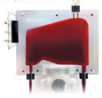


Les résultats dans notre pratique quotidienne

Introduction | Matériel et méthodes | Résultats | Discussion | Conclusion

Gestion per et post opératoire immédiate du patient

- CEC biocompatible
  - Circuit biocompatible/clos
  - Limitation de l'hémodiluton
  - Normothermie
  - Gestion des aspirations

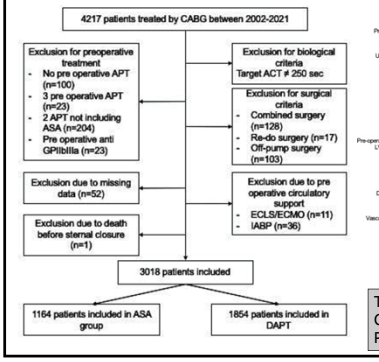


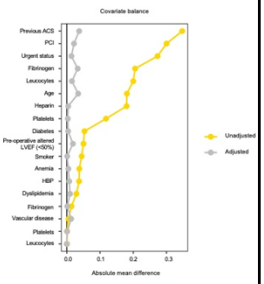
- Suivi de l'anticoagulation per CEC : Hepcon-HMS PLUS® (MEDTRONIC)
  - ACT cible 250 secondes
  - Protaminothérapie adaptée à chaque patient

- Réanimation
  - Cut-off transfusionnels définis
  - Reprise précoce pour hémostase

Baufreton, C. *et al. Perfusion.* (2002)

Les résultats dans notre pratique quotidienne
Flowchart et score de propension



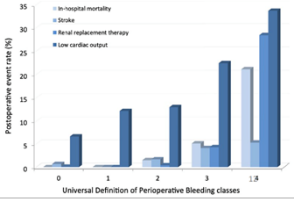


Ticagrelor < 3 j
Clopidogrel < 5 j
Prasugrel < 7 j

Les résultats dans notre pratique quotidienne
Scores UDPB et E-CABG

Bleeding definition	Sternal closure delayed	Postoperative chest tube blood loss within 12 hours (mL)	PRBC (units)	FFP (units)	PLT (units)	Cryoprecipitate	PCCs	rFVIIa	Reexploration/ tamponade
Class 0 (insignificant)	No	<600	0*	0	0	No	No	No	No
Class 1 (mild)	No	601-800	1	0	0	No	No	No	No
Class 2 (moderate)	No	801-1000	2-4	2-4	Yes	Yes	Yes	No	No
Class 3 (severe)	Yes	1001-2000	5-10	5-10	N/A	N/A	N/A	No	Yes
Class 4 (massive)	N/A	>2000	>10	>10	N/A	N/A	N/A	Yes	N/A

Dyke C, Aronson S, Dietrich W, Hofmann A, Karkouti K, Levi M, et al. Universal definition of perioperative bleeding in adult cardiac surgery. The Journal of Thoracic and Cardiovascular Surgery. 2014 May;147(5):1458-1463.e1.



Kinnunen EM et al. The Journal of Thoracic and Cardiovascular Surgery. 2014 Oct;148(4):1640-1646.e2.

- E-CABG

Grades	Intervention for treatment of bleeding	Additive score
Grade 0	No transfusion of blood products with the exception of 1 unit of RBCs	0
Grade 1	Transfusion of platelets	2
	Transfusion of fresh frozen plasma or Octaplas	3
	Transfusion of 2-4 units of RBC	3
Grade 2	Transfusion of 5–10 units of RBC	5
	Reoperation for bleeding	5
Grade 3	Transfusion of > 10 units of RBC	7

Biancari, F. *et al. J. Cardiothorac. Surg.* (2015)

Les résultats dans notre pratique quotidienne
Score BARC-4
Bleeding Academic Research Consortium

Special Report

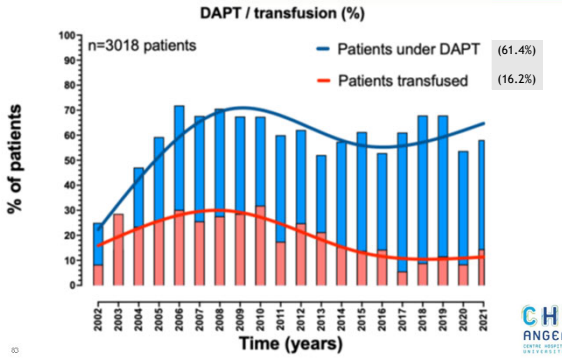
Standardized Bleeding Definitions for Cardiovascular Clinical Trials

A Consensus Report From the Bleeding Academic Research Consortium

Type 4: CABG-related bleeding

- Perioperative intracranial bleeding within 48h
- Re-operation after closure of sternotomy for the purpose of controlling bleeding
- Transfusion of ≥ 5 U whole blood or packed red blood cells within a 48-h period
- Chest tube output ≥2L within a 24-h period

Les résultats dans notre pratique quotidienne
Population globale (n=3018)



Les résultats dans notre pratique quotidienne

Variable	Propensity-score matched population			
	Overall	ASA	DAPT	p-value
	n=2275	n=1164	n=1111	
Arterial grafts				
LIMA, n (%)	2259 (99.3)	1156 (99.3)	1103 (99.3)	0.984
BIMA, n (%)	1298 (57)	694 (59.6)	604 (54.3)	0.019
Aortic cross clamp time (min), mean (SD)	63.1 (24)	62.7 (24.5)	63.6 (23.4)	0.408
CPB time (min), mean (SD)	89.8 (30.9)	88.9 (31.4)	90.7 (30.3)	0.213
Total heparin dose delivered (IU), mean (SD)	13960 (5070)	14470 (5190)	13430 (4880)	<0.0001
Total protamine dose delivered (mg), mean (SD)	67.5 (26.6)	69.6 (26.5)	65.3 (26.4)	0.0004
Baseline ACT before CPB (s), mean (SD)	137.6 (12.4)	137.2 (12.3)	137.9 (12.5)	0.222
Maximum ACT (s) on pump, mean (SD)	322.3 (45.7)	318.7 (43.7)	326.0 (47.4)	0.0006
Minimum ACT (s) on pump, mean (SD)	240.9 (30.1)	239.5 (29.1)	242.4 (31.1)	0.0404
Post-protamine ACT (s), mean (SD)	137.6 (14.1)	136.6 (13.9)	138.7 (14.1)	0.0011

Les résultats dans notre pratique quotidienne

Variable	Propensity-score matched population			
	Overall	ASA	DAPT	p-value
	n=2275	n=1164	n=1111	
E-CABG score ≥2, n (%)	94 (4.11)	34 (2.92)	59 (5.31)	0.0065
UDPB score ≥3, n (%)	61 (2.68)	21 (1.8)	40 (3.57)	0.0162
BARC 4, n (%)	96 (4.2)	40 (3.44)	57 (5.09)	0.0624
Reoperation for bleeding, n (%)	75 (3.33)	29 (2.49)	46 (4.18)	0.03
Pleural effusion, n (%)	84 (3.70)	32 (2.75)	51 (4.62)	0.033
Units of RBC transfused, mean (SD)	0.402 (1.3)	0.248 (1.1)	0.56 (1.5)	<0.0001
Units of FFP transfused, mean (SD)	0.071 (0.5)	0.045 (0.5)	0.098 (0.5)	0.021
Units of PLT transfused, mean (SD)	0.016 (0.18)	0.009 (0.18)	0.023 (0.17)	0.08
Overall transfusion, n (%)	349 (15.3)	109 (9.5)	239 (21.5)	<0.0001
Chest tube blood loss volume at 12H (mL), mean (SD)	224 (161.9)	192 (136.4)	258 (178.8)	<0.0001
Chest tube blood loss volume at 24H (mL), mean (SD)	322 (211.3)	284 (187.8)	361 (226.9)	<0.0001
Overall chest tube blood loss volume (mL), mean (SD)	386 (296)	338 (274.8)	435 (309)	<0.0001

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Les résultats dans notre pratique quotidienne

Variable	Propensity-score matched population			
	Overall	ASA	DAPT	p-value
	n=2275	n=1164	n=1111	
30-days mortality, n (%)	25 (1.09)	11 (0.94)	14 (1.24)	0.497
Death of cardiac cause, n (%)	10 (0.44)	3 (0.26)	7 (0.64)	0.278
Postoperative myocardial infarction, n (%)	6 (0.26)	2 (0.17)	4 (0.34)	0.415
Stroke, n (%)	15 (0.67)	5 (0.43)	10 (0.91)	0.217
TIA, n (%)	9 (0.38)	2 (0.17)	7 (0.6)	0.185
AKI, n (%)	189 (8.3)	75 (6.44)	113 (10.17)	0.0025
Wound infection, n (%)	44 (1.94)	13 (1.11)	31 (2.8)	0.010
Ventilation time >24H, n (%)	71 (3.12)	24 (2.06)	47 (4.2)	0.0061
ICU time (hours), mean (SD)	88.8 (101.1)	86.4 (90.3)	91.3 (111.4)	0.301
Total hospitalization time (days), mean (SD)	10.3 (6.6)	9.8 (5.1)	10.8 (7.8)	0.0069

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Impact du niveau d'ACT (cohorte totale de 3078 patients)

- Analyses multivariées
- Régression logistique des transfusions (tous types)
  - → Maximum ACT on pump: *p*-value < 0.001
- Régression linéaire du saignement à H12 postopératoire
  - → Maximum ACT on pump: *p*-value < 0.001

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DAPT et saignement/recours à la transfusion Comparaison au registre E-CABG

	ANGERS (PS matched) (n=2275)	Registre E-CABG* (n=7118)	
DAPT	48,9%	11,6%	(3% à 25%)
Grade E-CABG ≥ 2	5,31%	6,5%	
Grade UDPB ≥ 3	3,57%	8,4%	
Reprise pour saignement	4,18%	2,6%	
Transfusion	21,5%	40,9%	(24,1% à 71,3%)

* Biancari F, Mariscalco G, Gherli R, Reichart D, Onorati F, Faggian G, et al. Variation in preoperative antithrombotic strategy, severe bleeding, and use of blood products in coronary artery bypass grafting: results from the multicentre E-CABG registry. European Hear J - Qual Care Clin Outcomes 2018;4:246–57.

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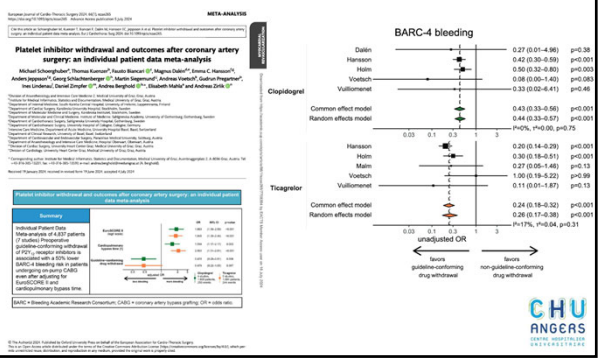
Comparaison avec EBM Impact de la RGDA



Comparaison avec EBM Impact de la RGDA

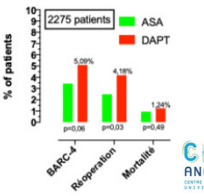
Table 2: Outcome variables according to type of $P2Y_{12}$ receptor inhibitor and drug-specific withdrawal time

Characteristic	Clopidogrel		Ticagrelor		Prasugrel
	<5 days (N = 1391)	≥5 days (N = 1007)	<3 days (N = 644)	≥3 days (N = 1656)	N = 139
BARC-4 bleeding	460 (33%)	99 (9.9%)	214 (33%)	135 (8.2%)	58 (42%)
RBC ≥5 units in 48 h	307 (22%)	77 (7.7%)	166 (27%)	83 (5.1%)	40 (29%)
24-h Chest tube drainage ≥2000 ml	118 (8.6%)	16 (1.6%)	43 (7.1%)	32 (2.0%)	21 (15%)
Reoperation	125 (9.0%)	45 (4.5%)	62 (9.6%)	68 (4.1%)	10 (7.2%)
Intracranial bleeding	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
30-day mortality	41 (4.0%)	11 (1.1%)	33 (6.5%)	18 (1.1%)	6 (7.9%)
Postoperative ischaemic events	93 (8.7%)	28 (2.8%)	53 (9.1%)	46 (2.8%)	10 (9.2%)

BARC-4: Bleeding Academic Research Consortium type 4.

Type 4: CABG-related bleeding

- Perioperative intracranial bleeding within 48 h
- Reoperation after closure of sternotomy for the purpose of controlling bleeding
- Transfusion of ≥5 U whole blood or packed red blood cells within a 48-h period†
- Chest tube output ≥2L within a 24-h period



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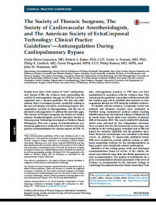
Shore-Lesserson L, et al. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines—Anticoagulation During Cardiopulmonary Bypass. Ann Thorac Surg. 2018 Feb;105(2):650–62.

Un homme intelligent
résout le problème.
Un homme sage l'évite.
Un homme stupide
le crée....
et si le monde est plein
de problèmes, c'est qu'il
doit y avoir une raison.

- Albert Einstein -



2018

It is reasonable to maintain activated clotting time above 480 seconds during CPB. However, this minimum threshold value is an approximation and may vary based on the bias of the instrument being used (Level of Evidence C)

To maintain a margin of safety above 400 seconds, the minimum acceptable ACT value of approximately 480 seconds became a "standard of care" that was used in numerous future studies and in clinical practice, but was ***based on limited evidence***

Options for calculating the initial heparin bolus include a fixed, weight-based dose, (eg, 300 IU/kg), or use of point-of-care tests that measure the whole blood sensitivity to heparin using an associated dose response.

EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery.

2019

Recommendations for periprocedural anticoagulation management

Recommendations	Class[a]	Level[b]	Ref[c]
Heparin management			
ACT above 480 s during CPB should be considered in CPB with uncoated equipment and cardiotomy suction. The required target ACT is dependent on the type of equipment used.	IIa	C	
Individualized heparin and protamine management should be considered to reduce postoperative coagulation abnormalities and bleeding complications in cardiac surgery with CPB.	IIa	B	[165, 166, 169]
In the absence of individual heparin dosing tools, it is recommended that ACT tests be performed at regular intervals based on institutional protocols, and heparin doses have to be given accordingly.	I	C	

2024

Recommendation Table 37. Recommendations for heparin administration

Recommendations	Class[a]	Level[b]	Ref[c]
Individualized heparin and protamine management should be considered to reduce postoperative coagulation abnormalities and bleeding complications in cardiac surgery with CPB.	IIa	B	[479, 480]
It is recommended that ACT checks be performed at regular intervals based on institutional protocols and that heparin doses be administrated accordingly, especially in the absence of individual heparin dosing services.	I	C	-

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
ACT: activated clotting time; CPB: cardiopulmonary bypass.

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Conclusion

Rôle essentiel du chirurgien par la qualité et la pertinence de ses pratiques

Major Bleeding, Transfusions, and Anemia: The Deadly Triad of Cardiac Surgery

Marco Ranucci, MD, FESC, Ekaterina Baryshnikova, BD, Serenella Castelvecchio, MD, FESC, and Gabriele Pelissero, MD, PhD; for the Surgical and Clinical Outcome Research (SCORE) Group

EDITORIAL

Editorials represent the opinions of the authors and *JAMA* and not those of the American Medical Association.

Blood Transfusion as a Quality Indicator in Cardiac Surgery

Aryeh S. Shander, MD
Lawrence T. Goodnough, MD

In the other study, Bennett-Guerrero et al[3] analyzed data from more than 100 000 patients undergoing coronary artery bypass graft surgery with cardiopulmonary bypass in