PLATELET INHIBITION
Assessment
Individualization

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Platelet Function

(„Born“)-Aggregation

PFA-100®

Accumetrics®

Plateletworks®

Chrono-log®
Aggregometry

Multiplate®
Aggregometry

Flowcytometry
ADP Receptor Antagonists and Aspirin
Main Mechanisms

- Hemostasis during operation, trauma, menstruation, after injuries
- Stent thrombosis
- Myocardial infarction
- Ischemic stroke
- Other ischemic events

- Formation of Thromboxane A2 via COX
- Positive feedback

- Release of ADP

- Aggregation via GpIIbIIIa (fibrinogen receptor)
Follow up of platelet function after Clopidogrel stop
Price et al (AJC 2006)
Siemens PFA-100 / 200

- High shear rate >5000 /s

- Capillary 200µm

- Epinephrine or ADP

- Membrane with collagen coating

- Only routine analyzer on the market that measures a haemostasis parameter under conditions of flow (high shear)

- Citrated blood is aspirated through a small aperture in a collagen-coated membrane

- Platelets adhere to the collagen surface and lead to a cessation of blood flow

- Parameter = Closure Time (CT)

- 3 cartridges:
  - EPI: costimulation by: shear stress, collagen, epinephrin
  - ADP: costimulation by: shear stress, collagen, ADP
  - P2Y: costimulation by: shear stress, ADP, PGE1 and Ca²⁺
Verifynow – Test principle
Verifynow (Werfen)

3 tests available:
- IIbIIIa test: stimulated by the thrombin receptor
- Aspirin test: stimulated with arachidonic acid
- P2Y12 test: stimulated by ADP + PGE1

+ very easy to use
+ cartridges for Aspirin, ADP receptor antagonists, IIbIIIa antagonists

- limited data on bleeding and surgery
- strong correlation of results to hematocrit

- 3 negative intervention trials in cardiology :
  - ARCTIC (NEJM 2012: Management of anti-platelet therapy in PCI patients n=2440)
  - TRIGGER PCI (J Am Coll Cardiol. 2012 Jun 12;59(24):2159-64.)
  - GRAVITAS (JAMA 2011: Management of anti-platelet therapy in PCI patients n=2214)
Multiplate

- platelets aggregate on metal sensors and increase electrical resistance
- platelet function analysis on surfaces
- twin sensor

- 5 channels for parallel tests
- electronic pipetting
- windows-based user interface

adhered platelets increase the electrical resistance between the metal sensors
Distribution of measurement

(Patients on Clopidogrel)

Median = 213 AUC
75 % Percentile = 341 AUC
90 % Percentile = 544 AUC
95 % Percentile = 699 AUC

n=1043 patients

(DHZ D. Sibbing)
Multiplate

Tests:

• TRAPtest: stimulated by the thrombin receptor
• ASPItest: stimulated with arachidonic acid
• ADPtest: stimulated by ADP

+ high sensitivity for Aspirin, ADP receptor antagonists
+ positive experiences in perioperative use

- Limited sensitivity for VWF
- Recently users reported problems with support
HIGH RESPONDERS may experience bleeding

Cardiac Surgery - Bleeding Clopidogrel
Ranucci et al, Annals of Thoracic Surgery

→ High responders (< 31 U)
High bleeding risk

Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial

Randomized, prospective study
35 centers
2610 patients

Lancet. 2017 Oct 14;390(10104):1747-17
De-escalation of P2Y12 inhibitor treatment (e.g., with a switch from prasugrel or ticagrelor to clopidogrel) guided by platelet function testing may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for 12-month potent platelet inhibition.\textsuperscript{717}
RESULTS: CLINICAL OUTCOMES & HPR

CVD, MI, ST or Stroke

Event rate (%)

Time (days)

Numbers at risk:
Control group, HPR: 188 186 185 182 178 176 173 173
Control group, no HPR: 1073 1055 1050 1043 1034 1030 1020
Guided group, HPR: 511 505 504 501 494 492 491
Guided group, no HPR: 755 749 744 737 732 730 721

Control group: HPR on prasugrel
Guided group: no HPR on clopidogrel
Guided group: no HPR on prasugrel
Guided group: HPR on clopidogrel, switch to prasugrel

HR: 0.99 (0.78-1.25) p=0.91
Platelet Function Testing

Identify medical need

Identify suitable test system

Standardize local process
(normal/therapeutic range, preanalytics, quality assessment)