

Heparin-induzierte Thrombozytopenie

Ingrid Pabinger

Clinical Division of Haematology and Haemostaseology, Department of Medicine I Medical University Vienna

MEDICAL UNIVERSITY OF VIENNA

Immune-mediated heparin-induced thrombocytopenia (HIT type II)

HIT

clino-pathological syndrome
(clinical + antibodies)

MEDICAL UNIVERSITY OF VIENNA

Platelet count decrease > 50% and/or new thrombotic complications

between day 5-14

platelet count ($10^9/l$)

day

trauma surgery

T

By courtesy of A. Greinacher

General features of HIT diagnosis and treatment - Literature

The NEW ENGLAND JOURNAL OF MEDICINE

CLINICAL PRACTICE

Gene C. Samama, M.D., Editor
Heparin-Induced Thrombocytopenia
Andreas Greinacher, M.D.

N Engl J Med 2015 Jul 16; 373 (3): 252-61.

CLINICAL GUIDELINES

● blood advances

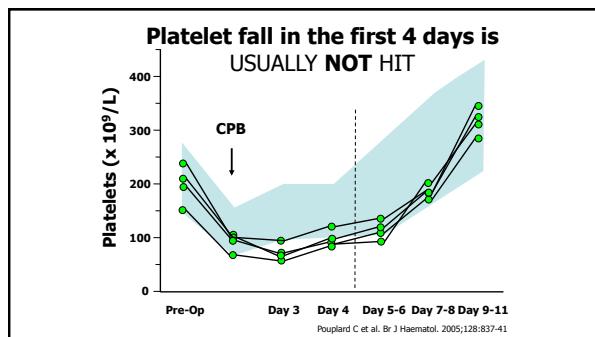
American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia

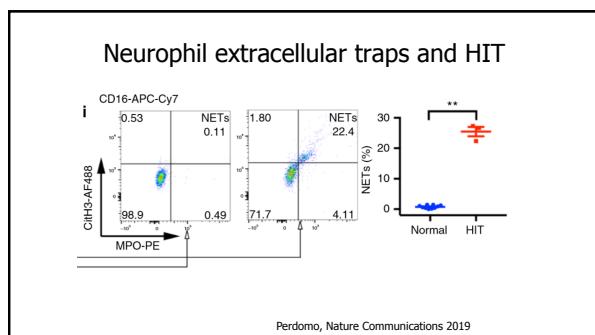
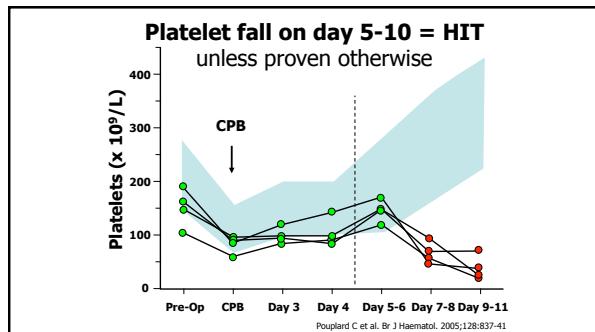
Adam Coler,^{1,2} Goutham M. Arppally,³ Beng H. Chong,⁴ Douglas B. Cines,^{1,2} Andreas Greinacher,⁵ Yves Goulet,⁶ Lon A. Linkins,⁷ Stephen B. Roselli,⁸ Svenn Seleng,⁹ Theodore E. Wakefield,^{1,10} Asleigh Wex,¹¹ Reen A. Mustafa,^{1,12} Rebecca L. Morgan,¹² and Nancy Sempleton¹¹

Open access

Acute HIT

Clinical symptoms of HIT present:
thrombocytopenia, acute thrombosis, HIT antibodies





Diagnosis - Pretest Probability: the 4 T's

Scoring points:	2	1	0
A Thrombocytopenia	>50% nadir ≥ 20 G/L	30-50% nadir 10-19 G/L	<30% nadir ≤ 10 G/L
B Timing (onset)	day 5-10 (\pm recent heparin)	> day 10, or unclear	before day 4
C Thrombosis	new thrombosis	progressive thrombosis	None
D Other cause for thrombocytopenia	no other cause	possible	definite

0-3 low score 4-6 medium score 6-8 high score

Lo et al. J Thromb Haemost 2006;4:759-65

<http://www.medizin.uni-greifswald.de/transfus>

Diagnosis - Pretest Probability

Interpretation of 4 T's score

Score 0 - 3:

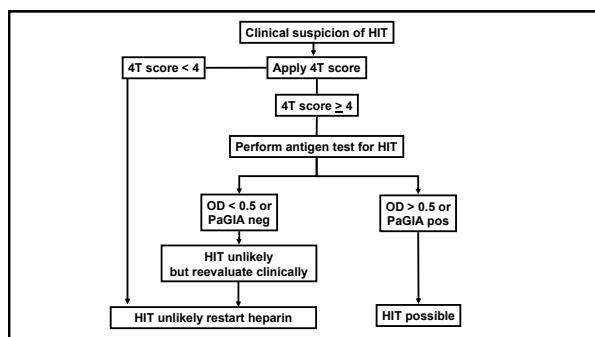
very unlikely to be HIT (<5%)

Lo et al. J Thromb Haemost 2006;4:759-65

+

negative antigen test

**if the 4T score can be obtained reliably
rules out HIT**



Acute HIT very likely or confirmed

Alternative Anticoagulants in HIT

	Half life	Renal insufficiency	Liver insufficiency	s.c./i.v./oral
Danaparoid	aXa 25h; aIIa 8h	+ (+) ~30%	0	s.c./i.v.
Argatroban	50 min	0	+++	i.v.
Fondaparinux	18h	+++	0	s.c.
Bivalirudin	25 min	++	+ (+)	i.v.
Dabigatran	8-9 h	+++	0	oral
Rivaroxaban	7-8 h	++	0	oral
Apixaban	7-8 h	++	0	oral

Acute HIT – DOACs?

Regular Article



CLINICAL TRIALS AND OBSERVATIONS

Direct oral anticoagulants for treatment of HIT: update of Hamilton experience and literature review

Theodore E. Warkentin,^{1,4} Menaka Pai,^{1,4} and Lori-Ann Linkins^{2,4} *Blood*. 2017;130(9):1104-1113

Fondaparinux for HIT Studies with ≥ 5 Patients and +EIA

	N (% with HIT-thrombosis)	New Thrombosis	Major Bleeding
Kuo & Kovacs. <i>Thromb Haemost</i> 2005	N=5 (100%)	0/5 (0%)	0/5 (0%)
Lobo et al. <i>Thromb Haemost</i> 2007	N=7 (86%)	0/7 (0%)	0/7 (0%)
Grouzi et al. <i>Clin Appl Thromb Haemost</i> 2009	N=24 (58%)	0/24 (0%)	0/24 (0%)
Warkentin. <i>J Thromb Haemost</i> 2011	N=16 (56%)	0/16 (0%)	1/16 (0%)
Goldfarb & Blostein. <i>J Thromb Haemost</i> 2011	N=8 (75%)	0/8 (0%)	0/8 (0%)
Pooled data	N=60 (67%)	0/60 (0%)	1/60 (2%)

Use of Fondaparinux Off-Label or Approved Anticoagulants for Management of Heparin-Induced Thrombocytopenia.

Schwarz S, Koenigstorfer A, Schilling S, Dommen M, Brachmann J, Madlener K, Pötsch B, Klamroth R, Hankowitz J, Bank N, Eberle S, Müller MM, Kroft S, Lindhoff-Last E. J Am Coll Cardiol. 2017 Nov 28;70(21):2636-2648

- Fondaparinux is effective and safe in suspected acute HIT
- Lepirudin was recalled from the market
- Danaparoid access has been limited
- Argatroban is contraindicated in patients with impaired liver function, and activated partial thromboplastin time confounding may interfere with monitoring

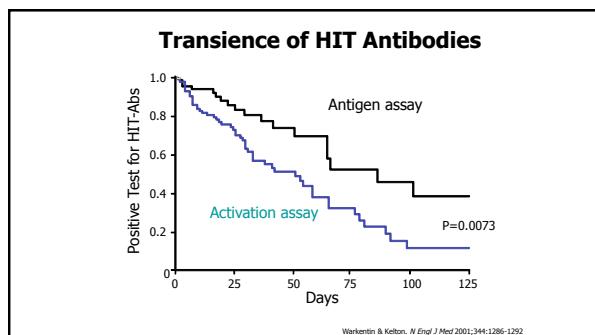
From the retrospective Registry of Patients With Acute Heparin-induced Thrombocytopenia Type II

Acute HIT and Interventions

- Acute prothrombotic state
- Interruption of anticoagulation: high risk for thrombotic complications
- Vascular interventions: high risk for thrombotic complications
- Only limb or life saving interventions (cardiac surgery: bivalirudin)

Subacute HIT

Platelet counts normalized but HIT antibodies still present



Early Onset of HIT

Relevant in patients who did receive heparin within the last
30 days
((100 days))

Subacute HIT
therapeutic dose anticoagulation required

	Danaparoid	Argatroban	Fondaparinux	Bivalirudin	DOACs
Recent HIT Plt count normalized, HIT antibodies present	++ S.C. (or i.v.)	+	+++ S.C.	+	+++ oral

Subacute HIT and Interventions

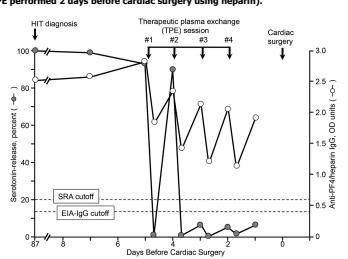
- Acute prothrombotic state has normalized
- Interruption of anticoagulation possible
- HIT-antibodies present -> NO HEPARIN
- Perisurgical thrombosis prophylaxis: danaparoid, fondaparinux, (DOACs)

Subacute HIT and Interventions

- Therapeutic dose anticoagulation:
 - cardiac surgery (bivalirudin)
 - complex vascular surgery
- Reexposure to heparin?

Therapeutic plasma exchange

(last TPE performed 2 days before cardiac surgery using heparin).

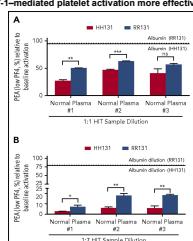


©2015 by American Society of Hematology

Theodore E. Warkentin et al. Blood 2015;125:195-198

HIT and Plasmapheresis

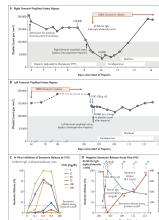
Normal plasma inhibits HIT-1-mediated platelet activation more effectively than 5% albumin.



©2018 by American Society of Hematology

Curtis G. Jones et al. Blood 2018;131:703-706

Intravenous Immune Globulin to Prevent Heparin-Induced Thrombocytopenia

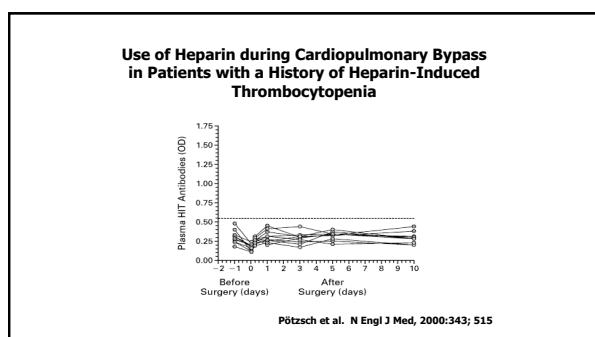


Warkentin TE et al. N Engl J Med 2018; 378:1845-1848

History of HIT

Platelet counts normalized,
no HIT antibodies

	Danaparoid	Argatroban	Fondaparinux	Bivalirudin	DOACs
History of HIT no HIT antibodies present					
prophylactic dose	+++	-	+++	-	(+)
therapeutic dose	+++	+++	+++	+++	++



Readministration of Heparin in Dialysis Patients with a History of HIT

- 15 dialysis patients with HIT: alternative anticoagulation.
- Readministration of heparin >100 days after the PF4/H EIA became negative.
- 14 patients tolerated heparin dialysis
- 1 patient recurrent HIT

Wanaka K et al ISTH 2013 Abstract

Summary HIT 2018 Management of Interventions

- Acute HIT: no interventions, no interruption of anticoagulation
- Subacute HIT (HIPA pos): no heparin
- Subacute HIT (HIPA neg): short term heparin
- History of HIT: short term heparin

Summary HIT 2018 Management of Interventions

- Alternative Anticoagulants
 - Danaparoid
 - Argatroban
 - Bivalirudin
 - Fondaparinux
 - DOACs
- Additional options
 - Plasmaexchange
 - ivIgG

Danksagung

- Prof A. Greinacher für die Überlassung von Folien
