

(Alternative) Anticoagulation - HIT-

ELSO SWAC 2016 Abu Dhabi, UAE

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Conflict of interest

- **Mitsubishi Tanabe Pharma Europe Ltd.**



Anticoagulation guideline



UNFH is an antithrombotic agent and is the **most widely used systemic anticoagulant** during the provision of ECLS

Recommended aPTT 1,5-2,5 times normal value: **55-92 sec**

Complications of ECMO

Event	Rate %
Directly related to the ECMO circuit	
Oxygenator failure	17.5
Blood clots	
Oxygenator	12.2
Other circuit	17.8
Cannula-related problems	8.4
Other mechanical complications	7.9
Not directly related to the ECMO circuit†	
Bleeding	
Surgical-site bleeding	19.0
Cannulation-site bleeding	17.1
Pulmonary hemorrhage	8.1
Gastrointestinal hemorrhage	5.1
Intracranial hemorrhage	3.8
Hemolysis	6.9
Disseminated intravascular coagulation	3.7
Culture-confirmed infection at any site (related or unrelated to ECMO)‡	21.3

ECMO patients are difficult to anticoagulate
 or
 Heparin is an unreliable anticoagulant

„Newer“ data

Outcomes	No. (%) (N = 38)
Survival to	
Intensive care unit discharge	28 (73.7)
Hospital discharge	28 (73.7)
Renal replacement therapy	12 (31.6)
Hemodialysis at hospital discharge	3 (7.9)
Bleeding—all sites	10 (26.3)
Cannula site	4 (10.5)
Pulmonary	4 (10.5)
Tracheostomy site	2 (5.3)
Nasal or oropharyngeal	2 (5.3)
Hematuria	1 (2.6)
Cannula-related deep venous thrombosis	8 (23.5) ^a
Occlusive	4 (11.8) ^a
Partially occlusive	4 (11.8) ^a

„low dose anticoagulation“
 aPTT 46,5 s (40,8-50,8)



^a Values are for 34 patients screened for deep venous thrombosis.

Anticoagulation guideline



Heparin induced thrombocytopenia (HIT) is a disorder characterized by thrombocytopenia and, paradoxically, an increased risk of thrombosis. It is frequently suspected due to the ubiquitous use of heparin and the high incidence of thrombocytopenia in critically-ill patients but the **true incidence of HIT in ICU patients is estimated to be only 0,3-0.6%**

HIT Incidence

„ICU patients“

- Prospective study, surgical patients
- 2046 patients
- 210 HIT-testings:

Do not use heparin for flushing the pressure dome

- 0,9% of all admissions
- But in 9% of all testings (HIT suspected)

**Cave: 12 of 19 patients (63%) had no heparin at all!!
But in flushings of the pressure dome!!**

HIT-incidence in cardiac pts.

- In 101 (1,7%) out of 6000 pts. HIT was suspected (decrease in platelet count by 50%, **persistent low platelet count**)
- Performing polyspecific PF4-Test (IgM, IgA, IgG)
- Functional test (HIPA or SRA) positive in **28 (≈0,5%)**
- Thrombembolic events: 64% HIT pos. vs. 20% HIT neg. ($p < 0,001$)
- **Remarkable: Missing increase in platelet count by switching from heparin to alternative anticoagulation**

HIT – Incidence in cardiac pts.

- Only 28 out of 6000 cardiac pts. (0,5%)
- **But!!** HIT was suspected in 101 pts. only
- Therefore in patients with persistent thrombocytopenia HIT incidence was **27%**

ALiCia-Trial

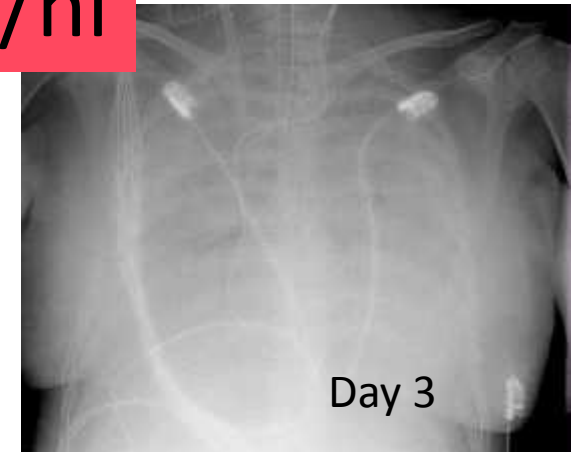
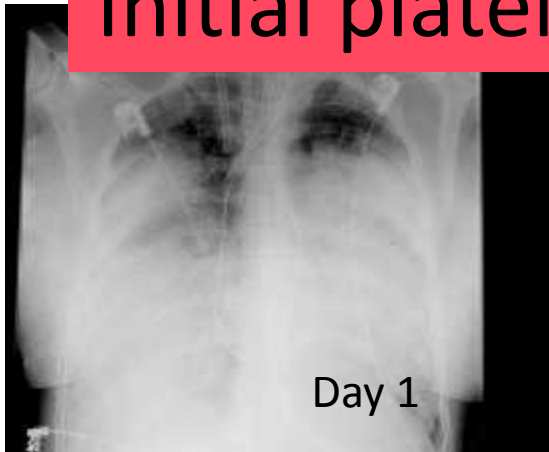
- Screening 5285 ICU patients for **persisting thrombocytopenia** after surgery
- 70 pts. with HIT suspect randomized for argatroban or lepirudin
- 15 patients HIT positive
- Allover HIT-incidence 0,3%
- **But!!** HIT-incidence in critically ill, **thrombocytopenic** patients (**23%**)

ECMO ?



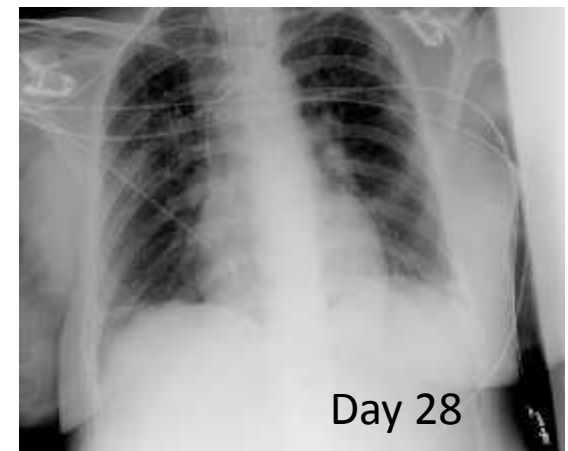
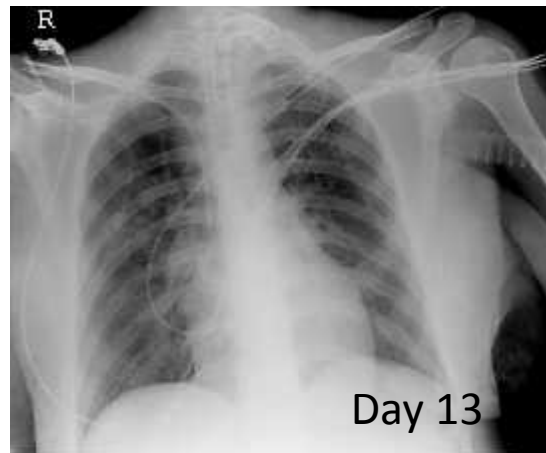
Severe CAP/ARDS on vvECMO

Initial platelet count: 67.000/nl



On day 6: Oxygenator clotting! aPTT 65s, Thr. 47.000/nl, HIT pos.

Schwere CAP/ARDS und ECMO



n = 9	Age	SAPS II	P/F	PEEP	CRRT	ECMO-days	survived	
Mean ± SD	41 ± 13	46 ± 7	54 ± 9	19 ± 2	89%	10,5 ± 8	66%	

HIT-Incidence on ECMO

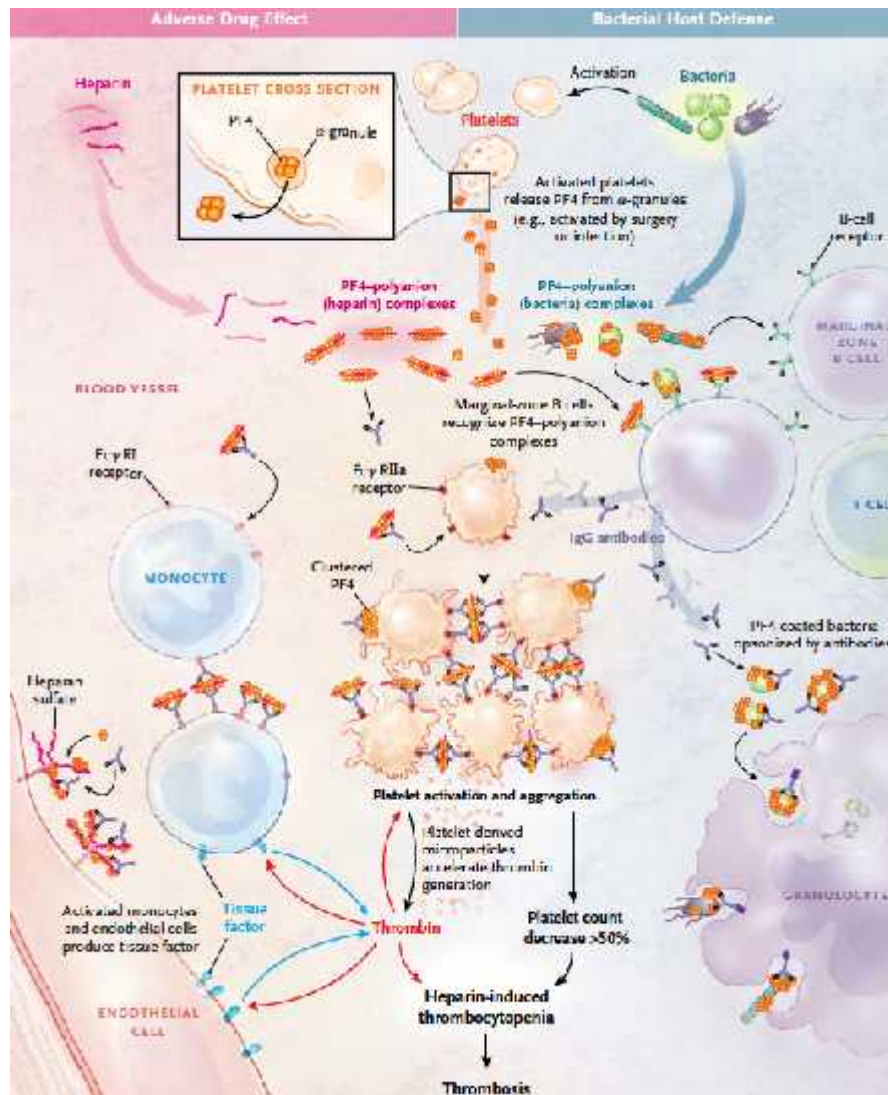
Meeting „Anticoagulation of critically-ill patients with and without ECMO“ June 2015

- University clinic Würzburg (Vv & Va ECMO) **8%**
- University clinic Vienna (Va ECMO) **7,1%**
- MHO (Vv ECMO) **7%**
- **10 – 15% in LVAD** Warkentin, Ann Thorac Surg 2009; 87: 1633
- Koster, Ann Thorac Surg 2007; 83: 72

Summary

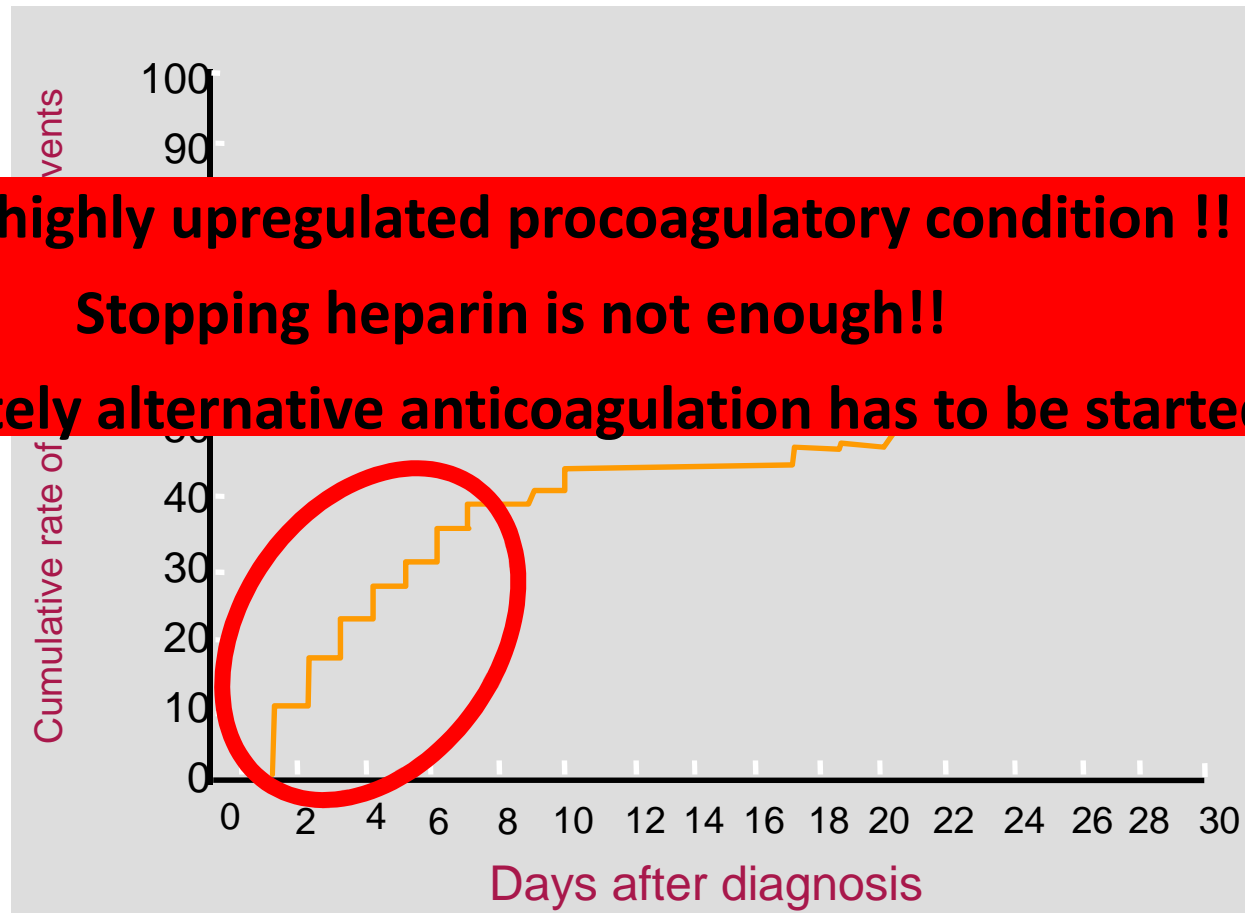
- Incidence of HIT is low (0,5%) in general
- However, incidence of HIT in patients with persistent low platelet count due to critical illness is high (up to 30%)
- **Therefore HIT is an omnipresent daily problem facing the intensivist**
- **„Tarragona strategy for HIT“: Look at your patient and the platelets**

„The sicker the patient the higher the incidence“

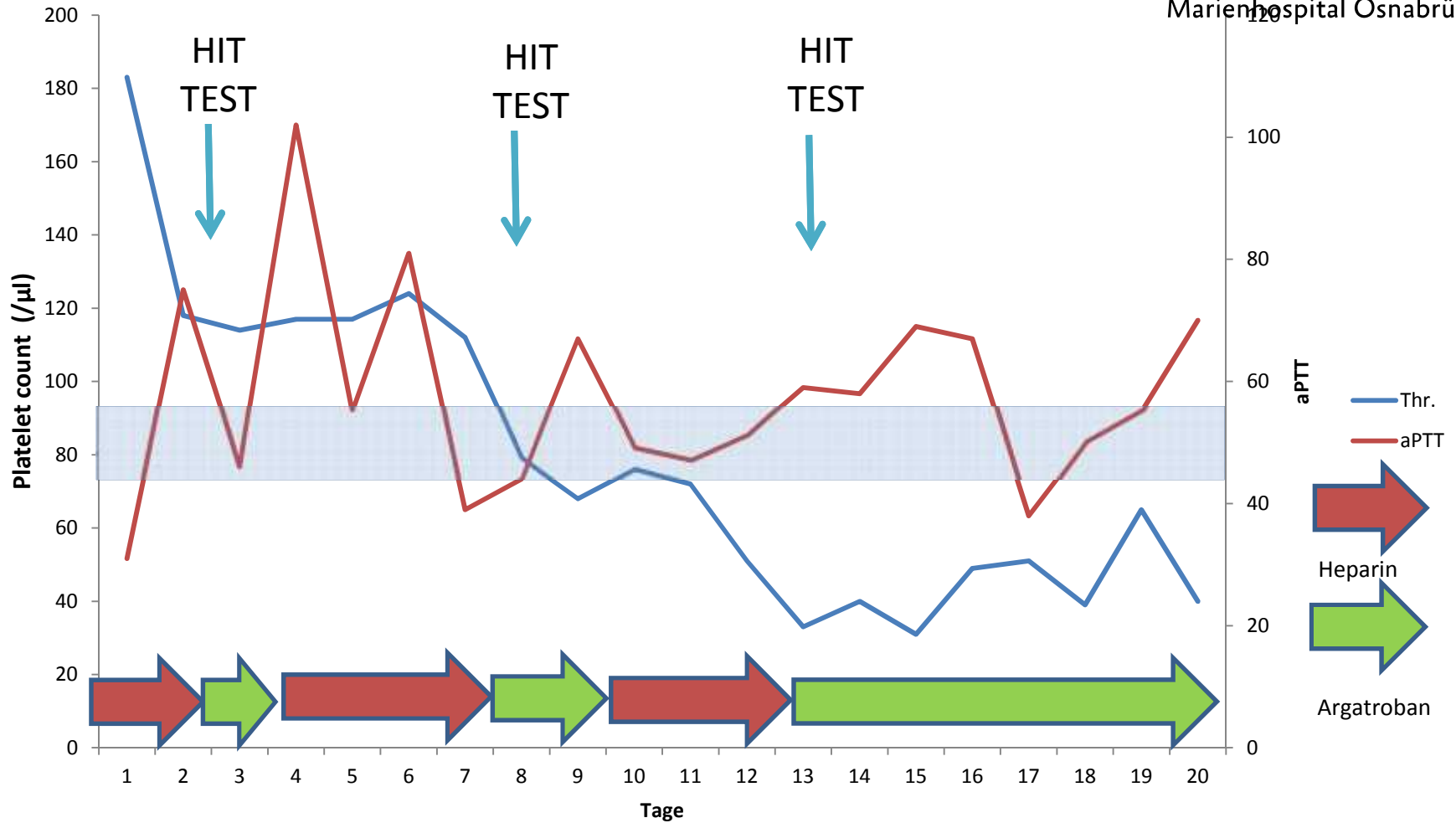


Thrombembolic events

HIT is a highly upregulated procoagulatory condition !!
Stopping heparin is not enough!!
Immediately alternative anticoagulation has to be started

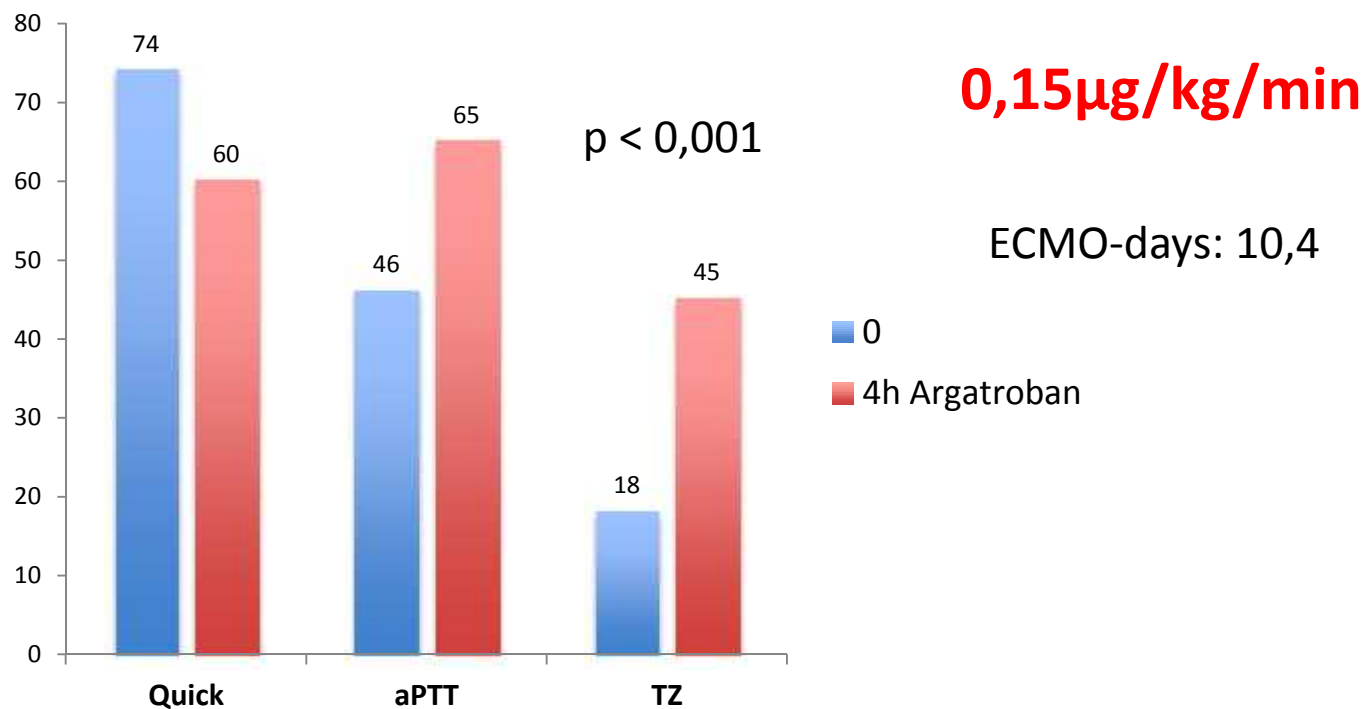


Anticoagulation & HIT suspect



Argatroban & vv ECMO

- n = 9, **target-aPTT (55-65 s)**
- Bilirubin $2,3 \pm 3$ mg/dl (0,5-9,8)
- ICG-PDR 15 ± 5 %/min (9-21)



Argatroban & vv ECMO

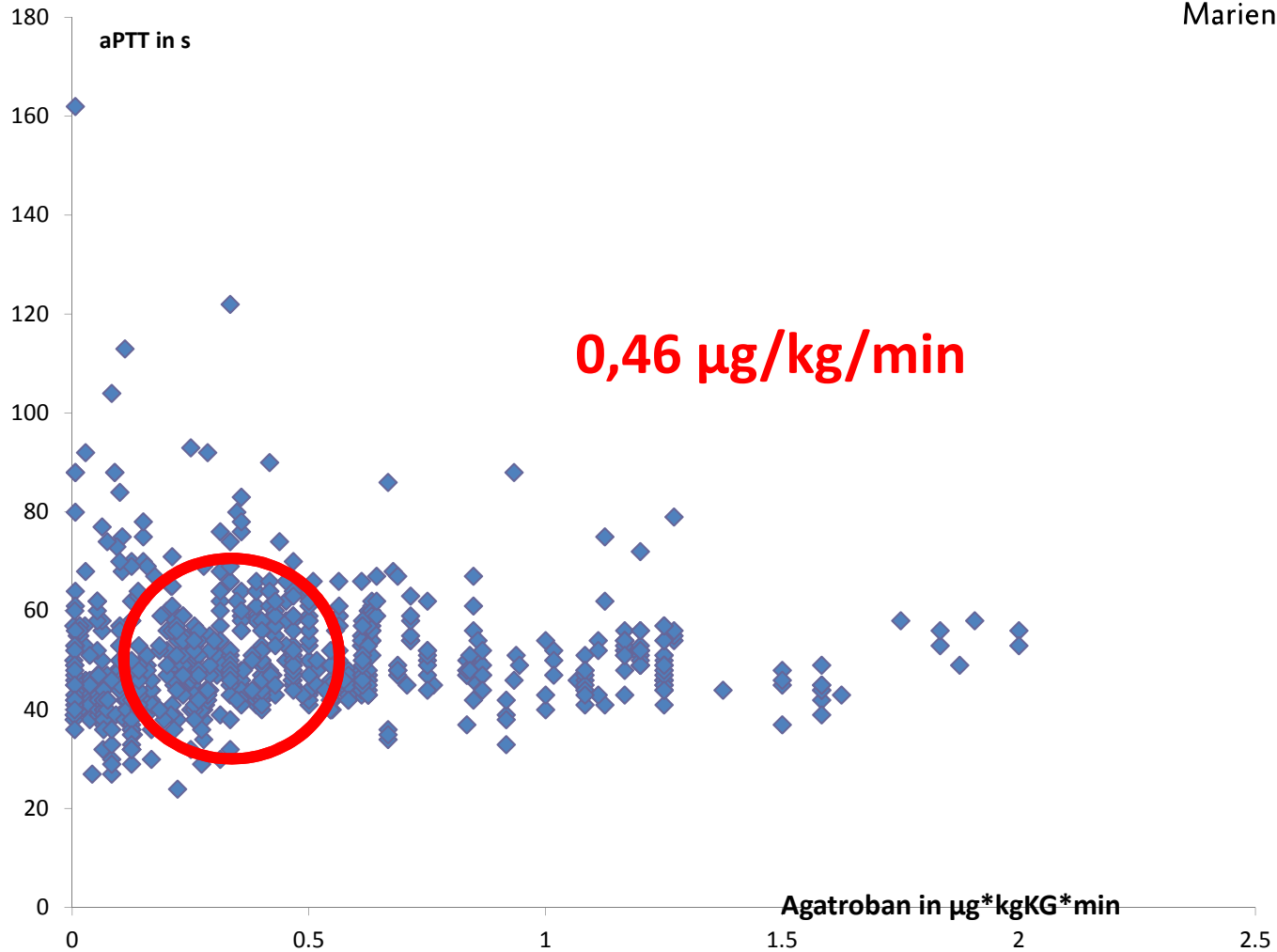
- Retrospektive analysis n= 63 pts.
anticoagulated with argatroban

Age	SAPS	SOFA	P/F	pCO ₂	PEEP	Compl	pH	Lac	Crea	Bili	Surv
			mmHg	mmHg	mbar	mbar/ml		mmol/l	mg/dl	mg/dl	
51,9	44,6	12,9	103	83,7	16	35,3	7,1	3,6	1,3	1,5	35
±	±	±	±	±	±	±	±	±	±	±	
15	10,4	2,4	68	23	4,4	12,9	0,2	2,9	0,9	0,9	55,5%

Anticoagulation management with argatroban

- After cannula insertion bolus heparin (≈ 25 U/kg)
- Start continuous infusion with argatroban (0,2 $\mu\text{g}/\text{kg}/\text{min}$)
- Perform aPTT testing and dose adjustment every 2-4 hours (target aPTT: 45-55 sec)
- Once in steady state (after 18 hours) perform aPTT tests 6 hourly
- Changes in argatroban dose correlate with severity of illness indirectly

Argatroban in vv ECMO



Take home message

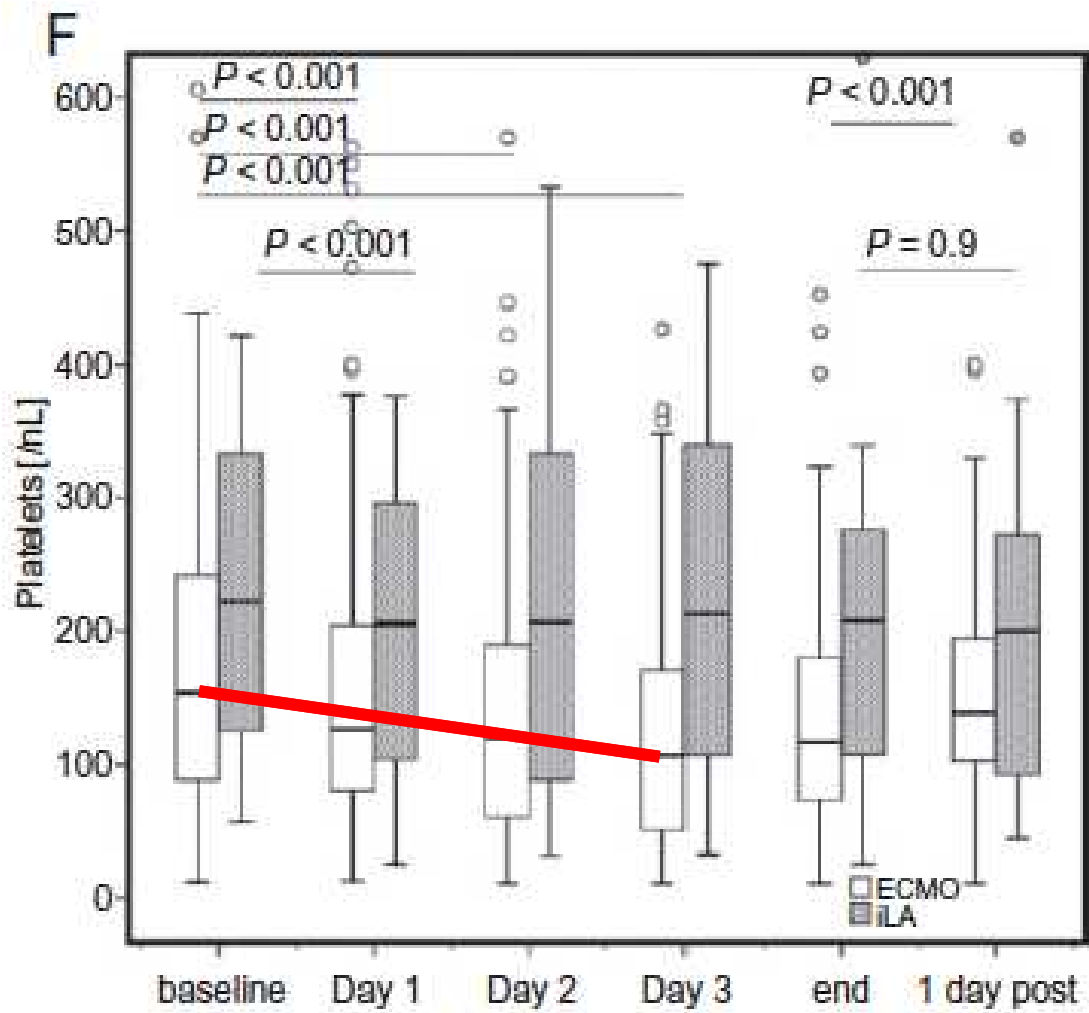
- Anticoagulation with heparin remains unsatisfactorily (balance between coagulation and anticoagulation)
- Additionally: Heparin may cause thrombembolic (arterial and venous) complications: **Be aware of HIT**
- Argatroban is a safe and efficient anticoagulant for vv ECMO
- If it's superior to heparin remains speculative

Thank you very much

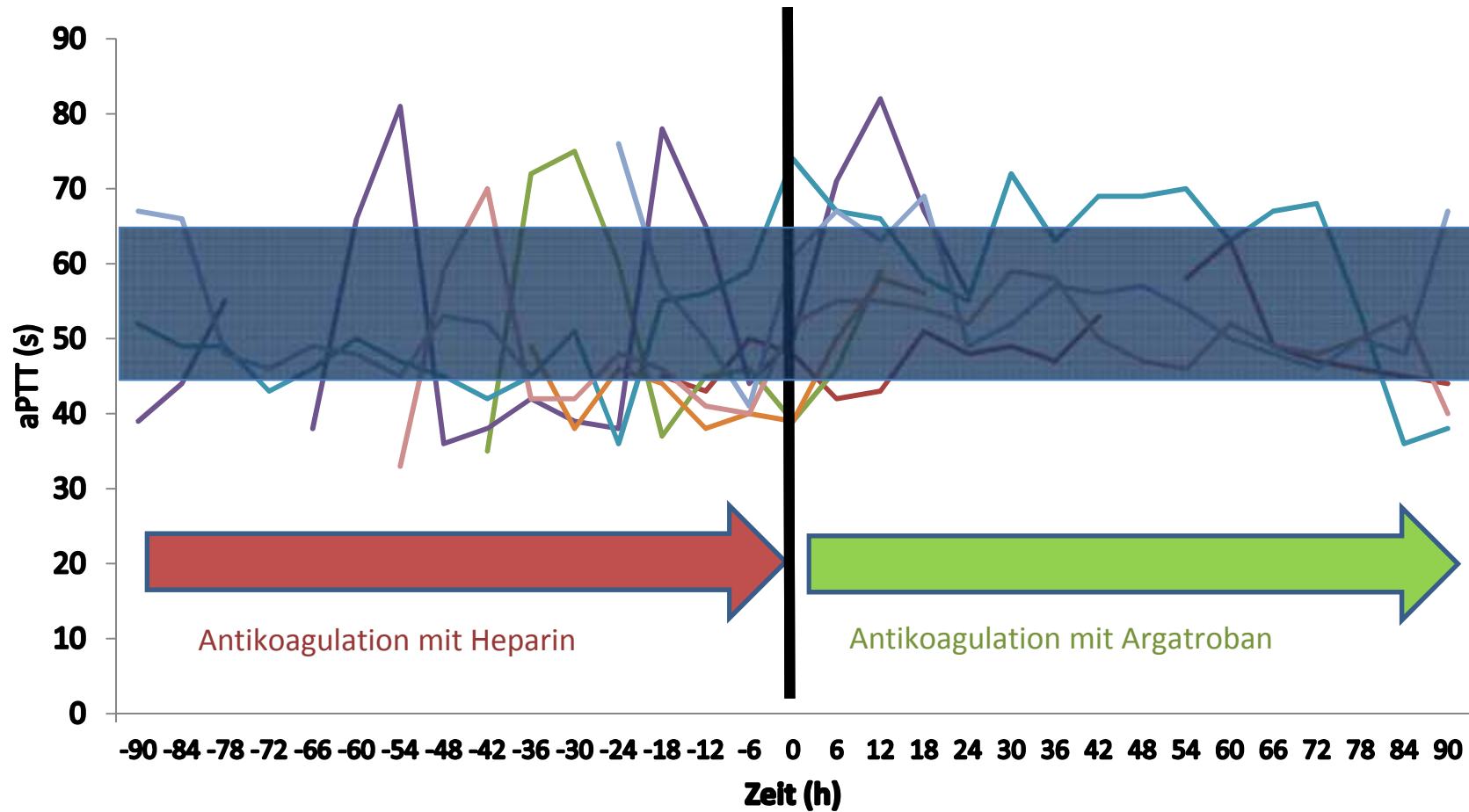
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Absence of
Evidence
IS
Evidence
of Absence



Argatroban und vv ECMO



Bleeding roller vs. centrifugal

