Anticoagulation in STEMI patients
insight from the ATLANTIC study

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*For the **ACTION** Group*

COI and Presentation on www.action-cœur.org

COI

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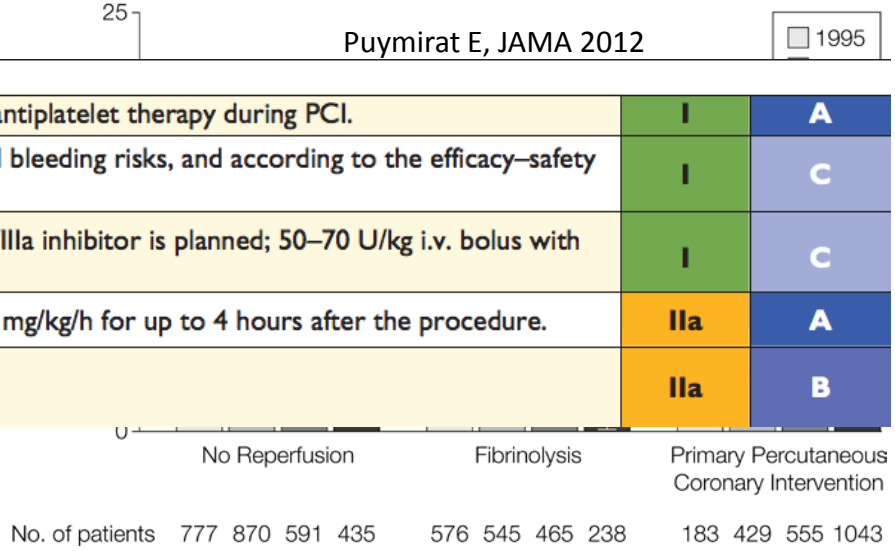
Background

- Progress made in the treatment of STEMI patients undergoing PPCI has resulted in a reduction of mortality over the past 20 years

Anticoagulants		
Anticoagulation is recommended for all patients in addition to antiplatelet therapy during PCI.	I	A
The anticoagulation is selected according to both ischaemic and bleeding risks, and according to the efficacy–safety profile of the chosen agent.	I	C
Unfractionated heparin: 70–100 U/kg i.v. bolus when no GP IIb/IIIa inhibitor is planned; 50–70 U/kg i.v. bolus with GP IIb/IIIa inhibitor.	I	C
Bivalirudin 0.75 mg/kg i.v. bolus followed by i.v. infusion of 1.75 mg/kg/h for up to 4 hours after the procedure.	IIa	A
Enoxaparin i.v. 0.5 mg/kg with or without GP IIb/IIIa inhibitor.	IIa	B



Puymirat E, JAMA 2012

Background

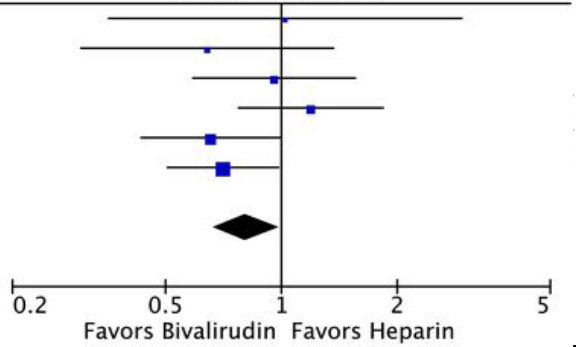
- UFH remains the most widely used anticoagulant drug for primary PCI although bivalirudin and enoxaparin have shown advantages over UFH in several trials

C All-cause mortality at 30 days

Study or Subgroup	Bivalirudin Events	Bivalirudin Total	Heparin Events	Heparin Total	Weight	Odds Ratio M-H, Fixed, 95% CI	ochran Q for eterogeneity
BRAVE 4	7	269	7	275	2.9%	1.02 [0.35, 2.96]	
BRIGHT	9	655	27	1270	7.8%	0.64 [0.30, 1.37]	
EUROMAX	32	1089	34	1109	14.2%	0.96 [0.59, 1.56]	0.53
HEAT-PPCI	46	905	39	907	16.0%	1.19 [0.77, 1.84]	0.50
HORIZONS-AMI	37	1800	56	1802	23.7%	0.65 [0.43, 1.00]	0.80
MATRIX	59	3610	83	3603	35.4%	0.70 [0.50, 0.99]	0.69
Total (95% CI)		**8328**		**8966**	**100.0%**	**0.81 [0.67, 0.98]**	0.56
Total events	190		246				

Heterogeneity: $Chi^2 = 5.64$, $df = 5$ ($P = 0.34$); $I^2 = 11\%$

Test for overall effect: $Z = 2.13$ ($P = 0.03$)



IJ 2012

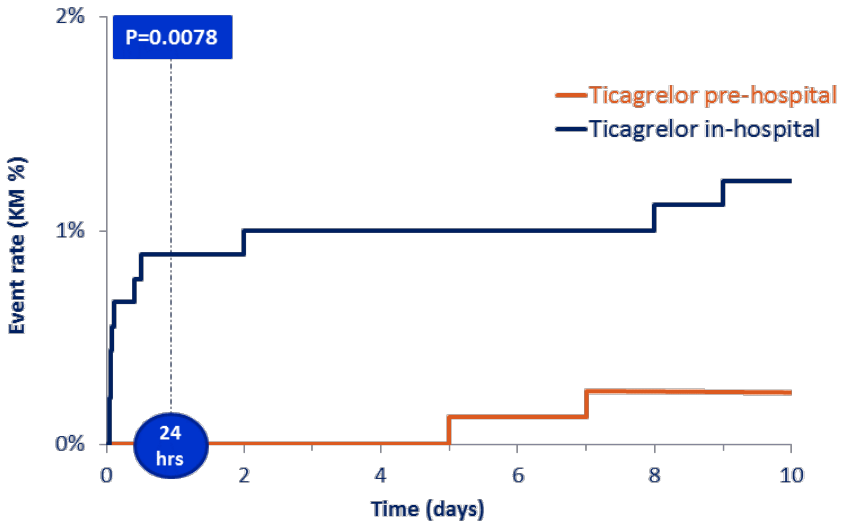
Gregor Fahrni et al. J Am Heart Assoc 2016;5:e003515

Objectives

- No randomized study has compared enoxaparin to bivalirudin or all three agents in the same trial.
- No study has compared these drugs when patients received new P2Y12 antagonists

AIM = To evaluate the association between the use of i.v. **UFH**, i.v. **enoxaparin**, **combination of both** or, i.v. **bivalirudin** **during the first 24 hours** with the occurrence of clinical events in the PPCI **ATLANTIC Population**

The ALANTIC Trial



Montalescot G, NEJM, 2014

Endpoints - post hoc analysis

- **Primary endpoint = net clinical benefit at 30 days**
  - occurrence of death, myocardial infarction, stroke, urgent revascularization, stent thrombosis or non-CABG TIMI major bleeding.

- **Secondary endpoints = individual ischemic endpoints and TIMI/STEEPLE major bleedings**

Statistics

The association was assessed by two analyzes using the randomization group as co-variable and a propensity score weighted logistic regression model with all co-variables forced into the model:

-age (<75, >=75)
-sex
-BMI (<30 kg/m², >=30 kg/m²)
-hypertension
-arterial access
-DES, BMS
-Thromboaspiration
-GPI use.

1862 STEMI patients randomized in the ATLANTIC Trial

1630 patients treated with PPCI

181 patients excluded :
13 patients : fondaparinux only
168 patients : no anticoagulant received or recorded

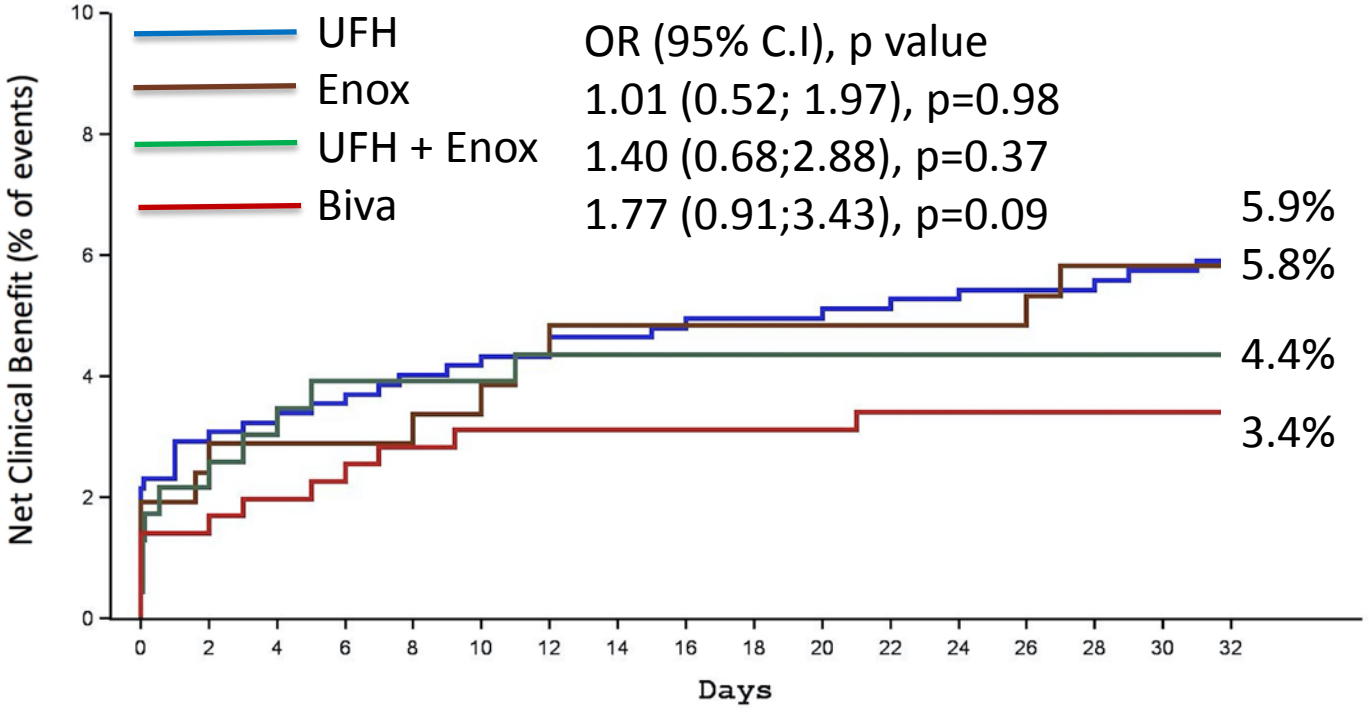
1449 PPCI patients with anticoagulation

i.v UFH	i.V enoxaparin	i.V bivalirudin	i.V UFH and enoxaparin
N = 653	N = 208	N = 356	N = 232

Results

	UFH N=653	Enoxaparin N=208	Enoxaparin and UFH N=232	Bivalirudin N=356	Overall N=1449	P value
Age >=75, n (%)	96 (14.7%)	22 (10.6%)	30 (12.9%)	69 (19.4%)	217 (15.0%)	0.0245
Women, n (%)	116 (17.8%)	28 (13.5%)	37 (15.9%)	80 (22.5%)	261 (18.0%)	0.0383
BMI >=30, n (%)	139 (21.3%)	28 (13.5%)	41 (17.7%)	77 (21.6%)	285 (19.7%)	0.0549
Hypertension, n (%)	300 (45.9%)	77 (37.0%)	88 (37.9%)	140 (39.3%)	605 (41.8%)	0.0309
Radial, n (%)	368 (56.9%)	176 (84.6%)	177 (76.3%)	255 (71.8%)	976 (67.7%)	<.0001
ThromboAsp., n (%)	340 (52.1%)	137 (65.9%)	152 (65.5%)	208 (58.4%)	837 (57.8%)	0.0002
BM Stent — no. (%)	267 (40.9%)	89 (42.8%)	106 (45.7%)	98 (27.5%)	560 (38.6%)	<.0001
GPI before PCI — no.(%)	287 (44.0%)	87 (41.8%)	97 (41.8%)	4 (1.1%)	475 (32.8%)	<.0001

Net clinical benefit



When adjusted…

	Multivariate Logistic Model Propensity score weighted[£] N=1441	
	Odds-ratio (95% CI)	P-value
UFH vs. LMWH	0.96 (0.46;1.97)	0.9036
UFH vs. LMWH and UFH	1.25 (0.60;2.60)	0.5495
UFH vs. Bivalirudin	2.31 (1.06;5.01)	0.0345

Ischemic and Bleeding endpoints

	UFH N=653	Enoxaparin N=208	Enox and UFH N=232	Bivalirudin N=356	Overall N=1449	P value
Any death	16 (2.5%)	5 (2.4%)	2 (0.9%)	9 (2.5%)	32 (2.2%)	0.4800
Myocardial Infarction	11 (1.7%)	1 (0.5%)	2 (0.9%)	2 (0.6%)	16 (1.1%)	0.3871
Stroke	3 (0.5%)	1 (0.5%)	0 (0.0%)	1 (0.3%)	5 (0.3%)	0.8587
Urg. revascularization	8 (1.2%)	1 (0.5%)	1 (0.4%)	1 (0.3%)	11 (0.8%)	0.4121
Stent thrombosis	3 (0.5%)	1 (0.5%)	5 (2.2%)	2 (0.6%)	11 (0.8%)	0.0966
TIMI Major Bleeding	9 (1.4%)	4 (1.9%)	4 (1.7%)	1 (0.3%)	18 (1.2%)	0.1749
STEEPLEMajor Bleeding	27 (4.1%)	10 (4.8%)	10 (4.3%)	8 (2.2%)	55 (3.8%)	0.3476

Bleeding endpoints

	Multivariate Logistic Model Propensity score weighted[£] N=1441	
TIMI MAJOR BLEEDING	Odds-ratio (95% CI)	P-value
UFH vs. LMWH	0.88 (0.28;2.83)	0.8356
UFH vs. LMWH and UFH	1.14 (0.31;4.20)	0.8474
UFH vs. Bivalirudin	3.84 (0.66;22.36)	0.1342
STEEPLE MAJOR BLEEDING	Odds-ratio (95% CI)	P-value
UFH vs. LMWH	0.80 (0.38;1.68)	0.5509
UFH vs. LMWH and UFH	1.07 (0.44;2.59)	0.8809
UFH vs. Bivalirudin	2.27 (0.93;5.53)	0.0713

Limits

- Small number of events and post-hoc nature of this analysis.
- Geographic differences in use of the anticoagulant strategies
- Absence of control of the dose regimens of these anticoagulant strategies
- Lack of control of the timing of administration of the anticoagulants (prehospital or not)

Take Home Messages

1/ when left to the physician's choice, the type of anticoagulant strategy has little impact on clinical outcomes

2/ the propensity score weighted logistic regression model suggests superiority of bivalirudin over UFH in our STEMI patients on the net clinical benefit

3/ However, these results must be considered with caution as they are driven by a reduction of major bleeding in the bivalirudin group that did not receive GPIs

Thank You !

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