Results of histopathological thrombus evaluation in patients presenting with stent thrombosis across Europe: a report of the PRESTIGE Consortium

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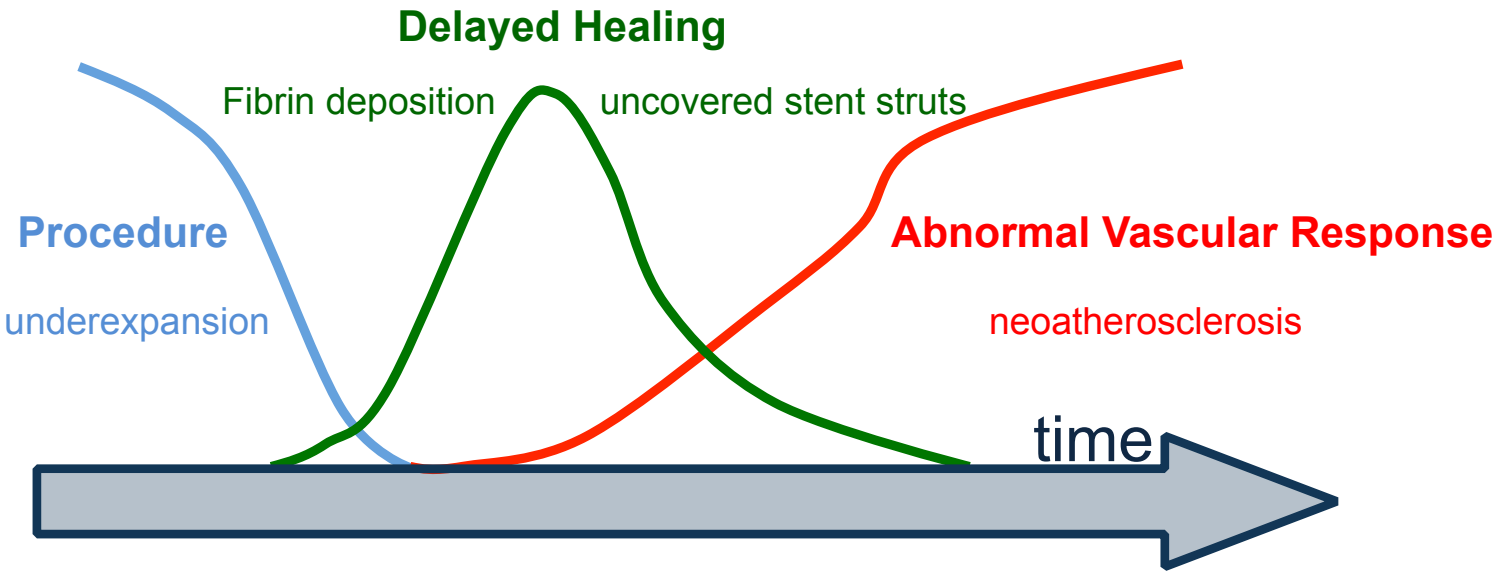
Conflicts of interest: none

Stent thrombosis – mechanisms and triggers differ with time after PCI

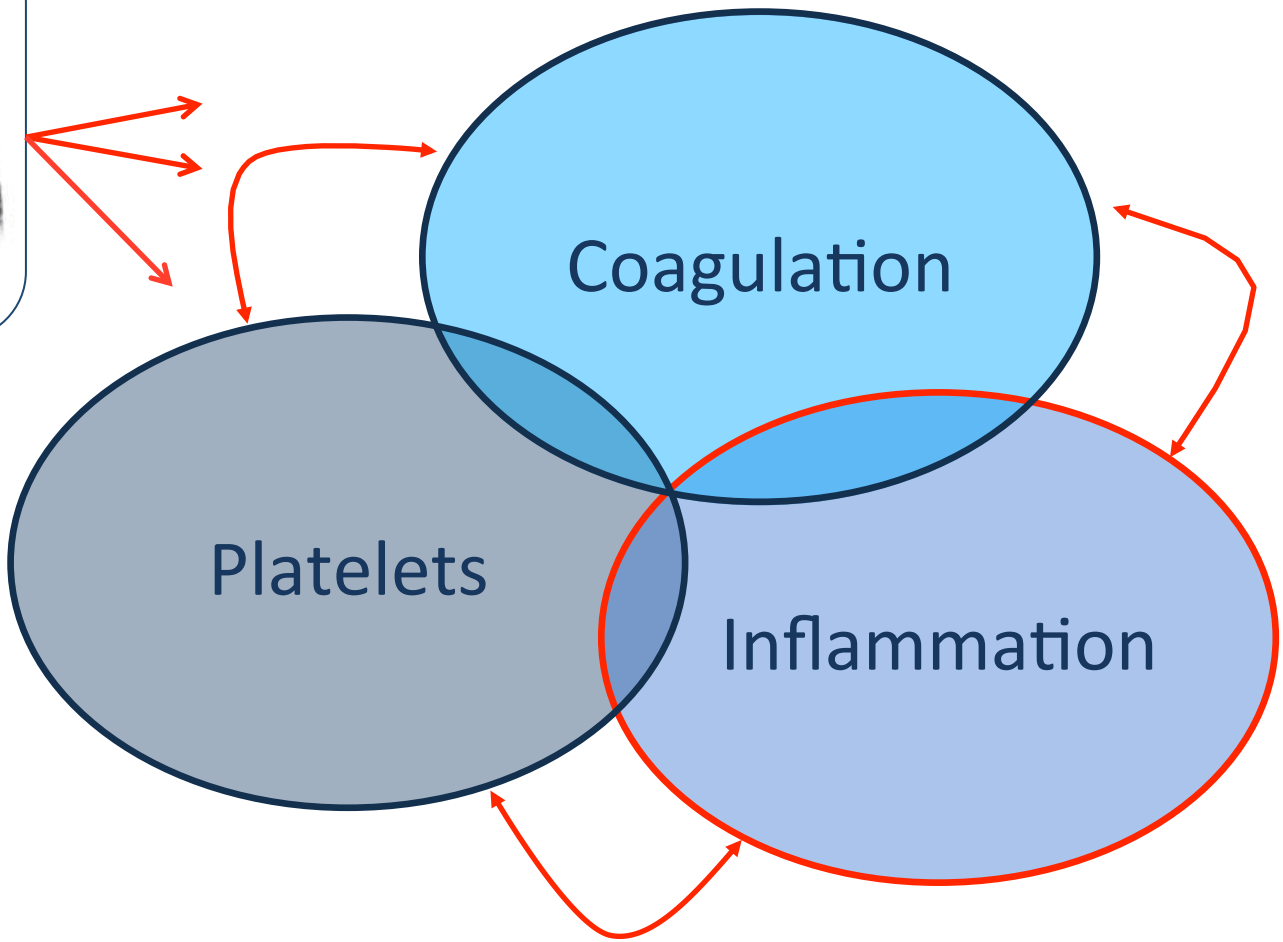


Nakazawa, J. Cardiol. 2011

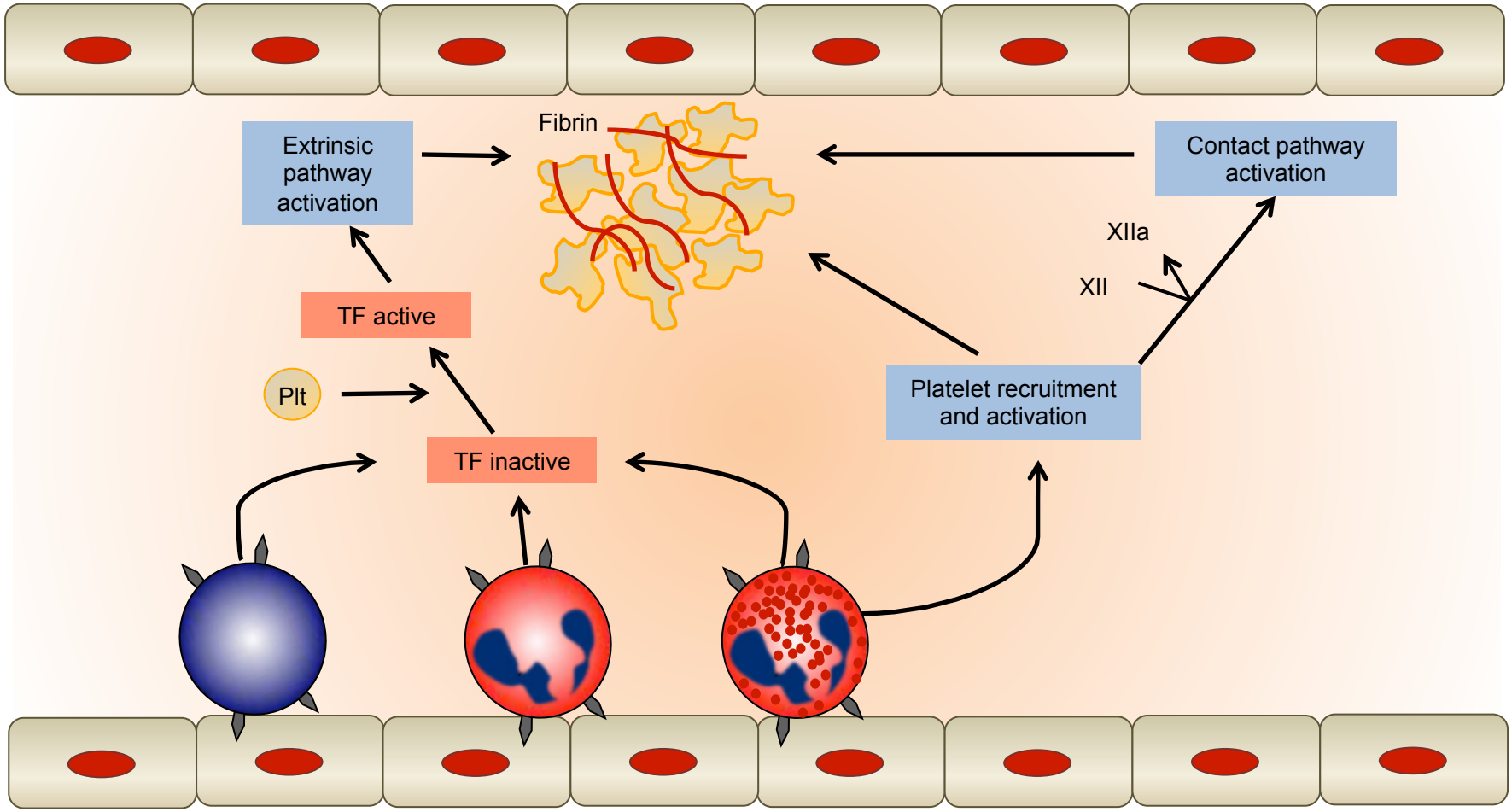
Stent thrombosis – moderated and implemented by a fatal triad ?

Cellular mechanisms ?

Therapeutic target ?



Stent thrombosis – relevance of inflammatory cells ?



Engelmann & Massberg, Nat. Rev. Immunol. 2013; Schulz et al., J Thromb Haemost. 2013; Massberg et al., Nat. Med. 2010;

PRESTIGE – Register (**PRE**vention of **S**tent **T**hrombosis by an **I**nterdisciplinary **G**lobal **E**uropean effort)

UK
- A. Gershlick, A. Goodall, N. Malik, University of Leicester

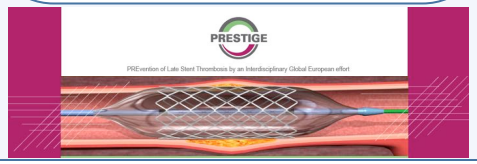
Poland
- D. Dudek, R. Wojdyla, Jagiellonian University Medical College, Krakow

Italy
- G. Guagliumi, Azienda Ospedaliera Papa Giovanni XXIII, Bergamo

France
- L. Feldman, P. Steg, INSERM, Paris

Germany
- R.Byrne, M.Joner, A.Kastrati, DHZ, Munich
- S.Massberg, C.Schulz, LMU Munich
- F.-J. Neumann, D. Trenk, C. Valina, HZF. Bad Krozingen

COOPERATION



Spain
- F. Alfonso, Hospital Universitario de la Princesa, Madrid

Netherlands
- J. ten Berg, T. Godschalk, D. Jhagroe, St. Antonius Hospital, Nieuwegein

Belgium
- T. Adriaenssens, W. Desmet, P. Sinnaeve, Katholieke Universiteit Leuven

Lithuania
- G. Kerch, Rigas Tehniska Universitate

Project Funding

PRESTIGE – a multi-disciplinary European approach

PRESTIGE Stent thrombosis cohort

Suspicion of stent thrombosis

↓

Angiographic confirmation of stent thrombosis

↓

Blood sampling

↓

Thrombus aspiration (when indicated) → Fix aspirated thrombus for analysis

↓

IVUS and/or OCT of the target vessel (if possible/when available)

↓

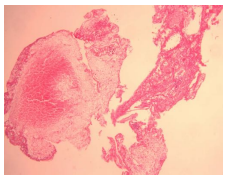
PCI

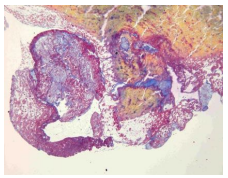
↓

Angiography + IVUS and/or OCT post-emergent PCI

Histological sub study

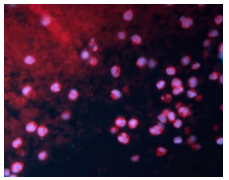
Standard histological stainings

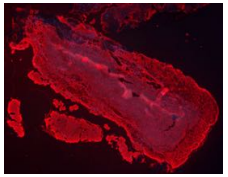




→ ST n=253
Spont. MI n = 104

Immunofluorescence stainings





Baseline characteristics

	Early (<30d) n=79	Late (>30d) n=174	p-Value
Age	66 [57,74]	62 [54,72]	0.94
Sex			
Male	68.4%	82.2%	0.014
Coronary artery disease			
1-vessel	48.0%	59.1%	0.24
2-vessel	33.3%	28.0%	
3-vessel	18.7%	12.9%	
Multivessel disease	52.0%	40.9%	0.11
History of coronary bypass	6.4%	9.2%	0.46
Ejection fraction < 30%	2.7%	2.4%	>0.99

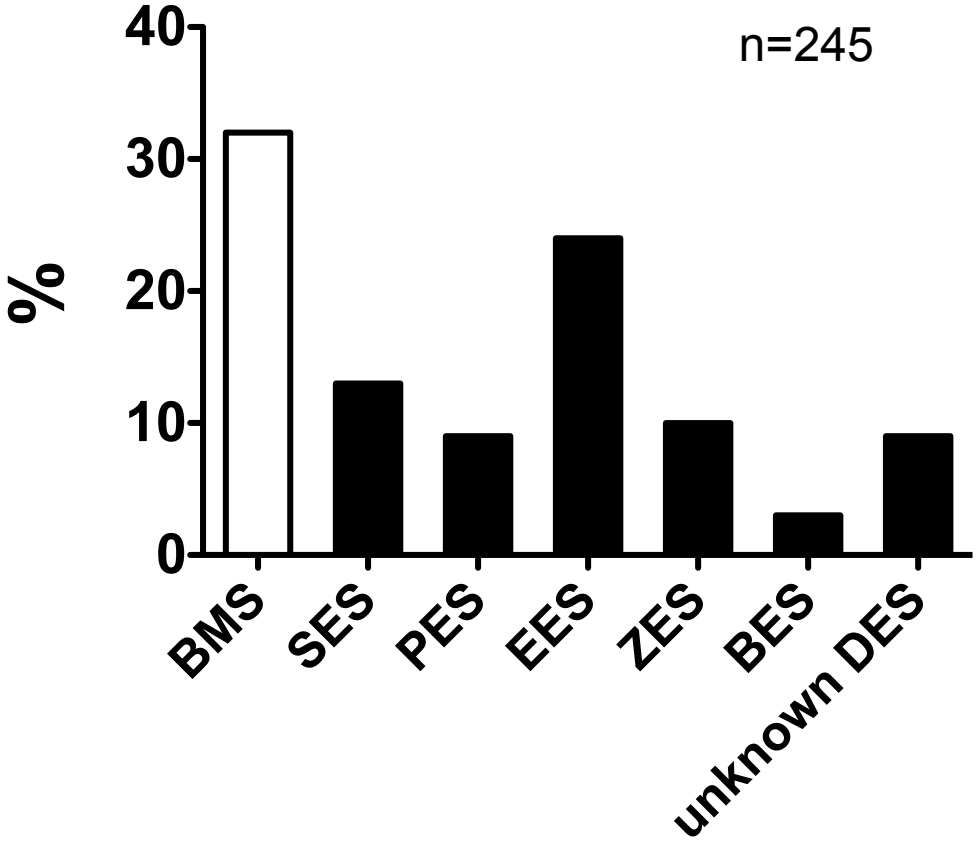
Baseline characteristics

	Early (<30d) n=79	Late (>30d) n=174	p-value
Risk factors			
Diabetes	38.5%	20.2%	0.002
Hypertension	55.3%	41.3%	0.043
Ex-/smoker	65.4%	72.3%	0.22
Hypercholesterolaemia	83.5%	90.2%	0.13
Clinical presentation			
Unstable angina pectoris	3.8%	3.5%	0.629
Non-ST-elevation MI	11.5%	16.2%	
ST-elevation MI	84.6%	80.3%	

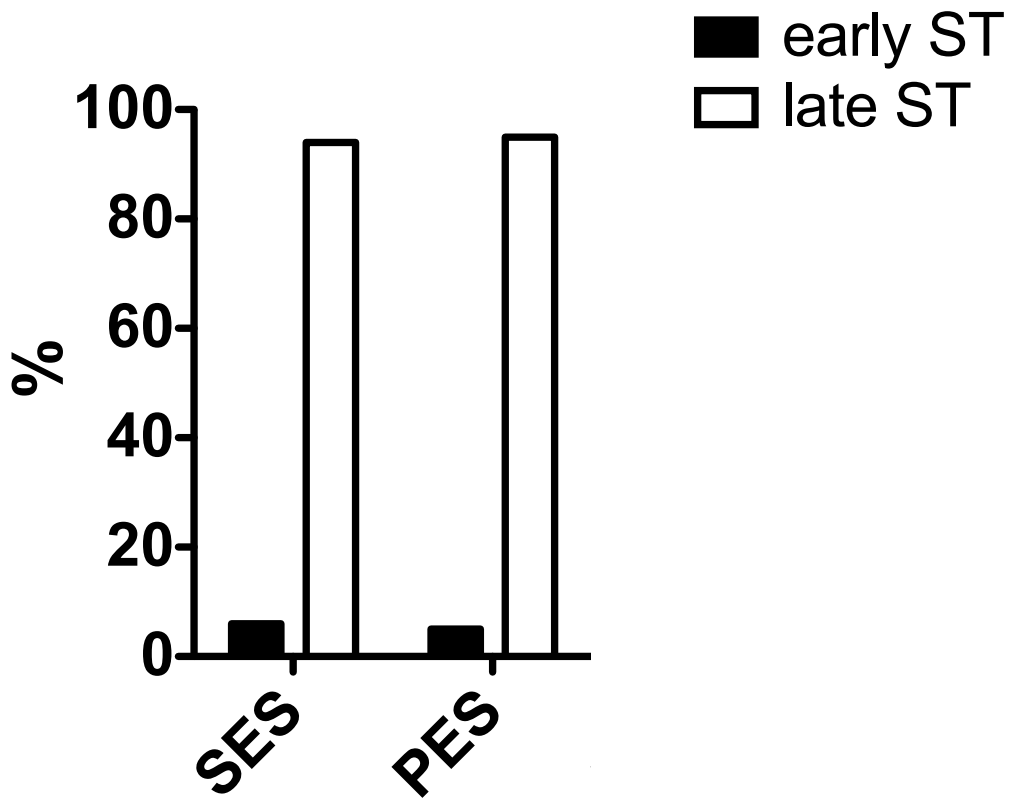
Baseline characteristics

	Early (<30d) n=79	Late (>30d) n=174	p-value
Antiplatelet Therapy			
Aspirin	87.3%	80.7%	0.20
ADP-receptor antagonist	82.3%	25.0%	<0.001
Clopidogrel	66.2%	60.5%	
Prasugrel	10.8%	25.6%	
Ticagrelor	23.1%	14%	
Dual antiplatelet therapy	75.9%	20.9%	<0.001
Coexisting conditions			
Renal failure (GFR<30ml/min)	7.8%	5.8%	0.580
Dialysis	1.3%	1.1%	>0.99
Stroke	7.7%	5.2%	0.57
Autoimmune disease	1.4%	2.9%	0.67
Active malignancy	3.9%	3.0%	0.71

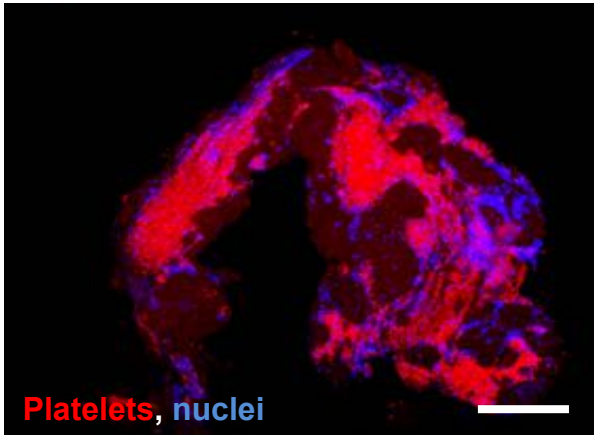
Results: Frequency of stent types

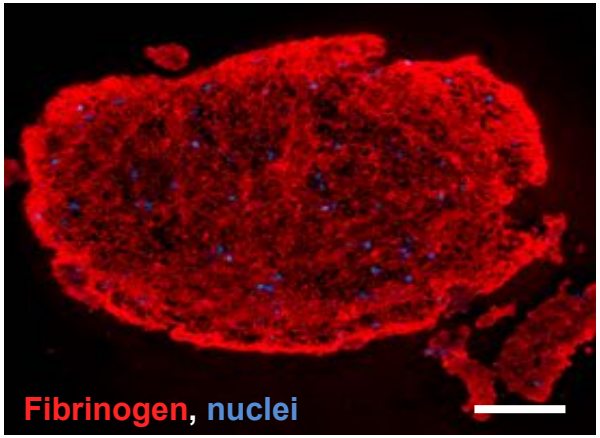


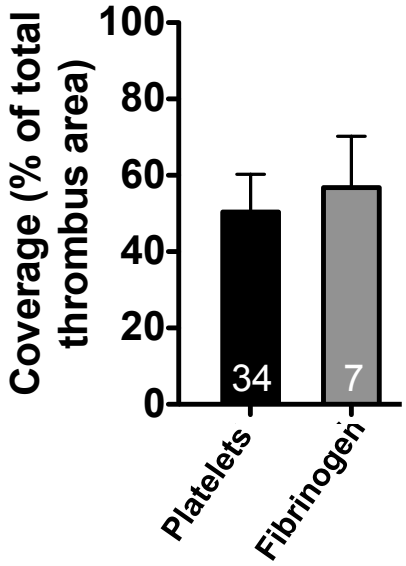
Results: Timing of ST depending on stent type



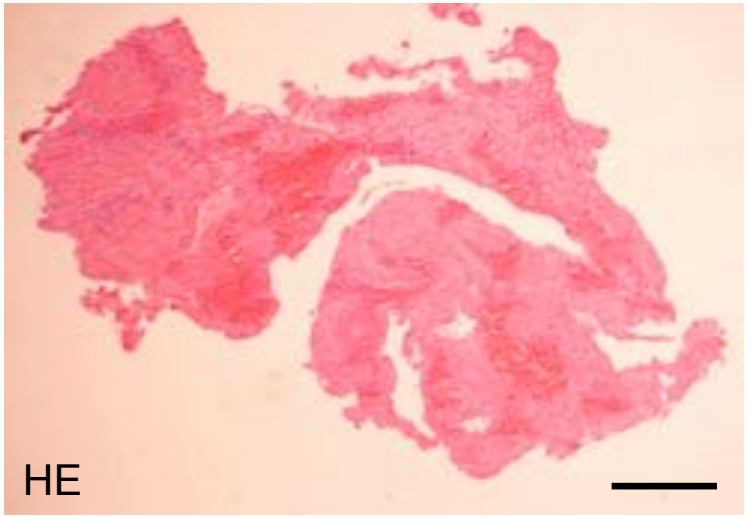
Results: Platelets and coagulation – key players in ST

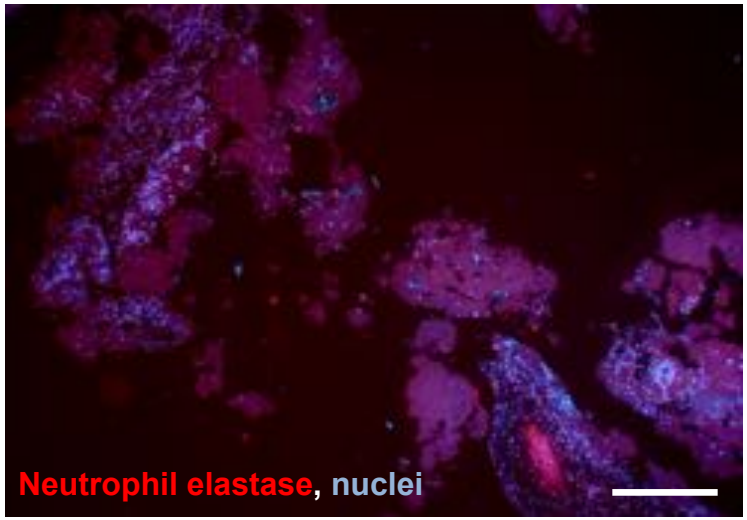


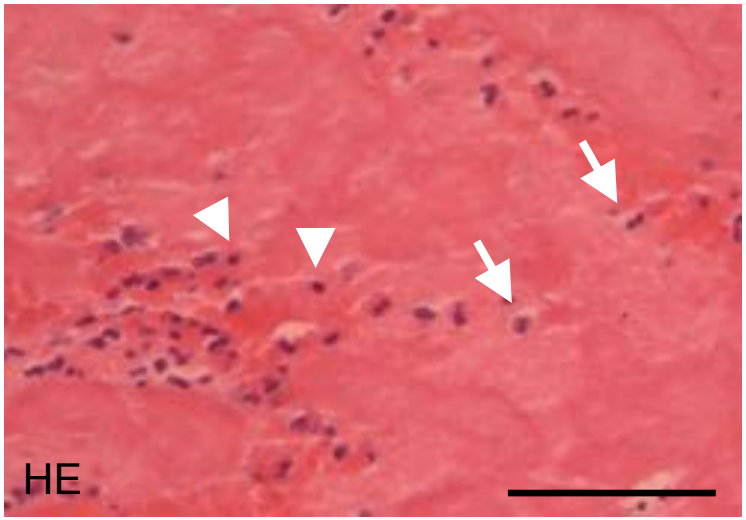


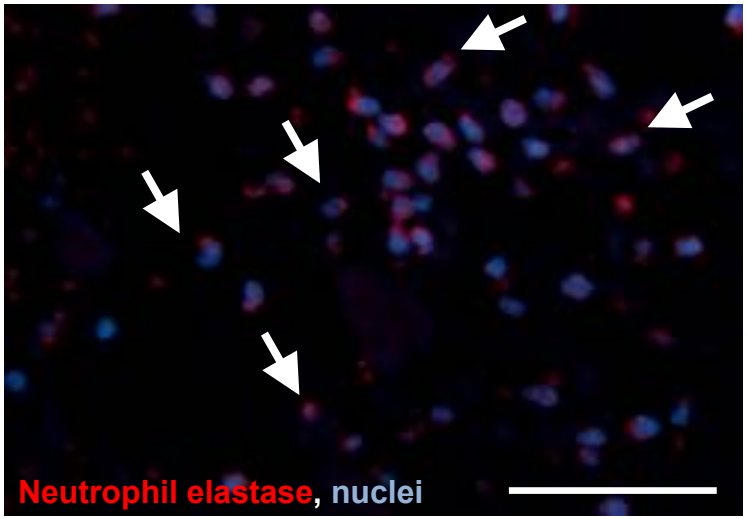


Results: Recruitment of leukocytes

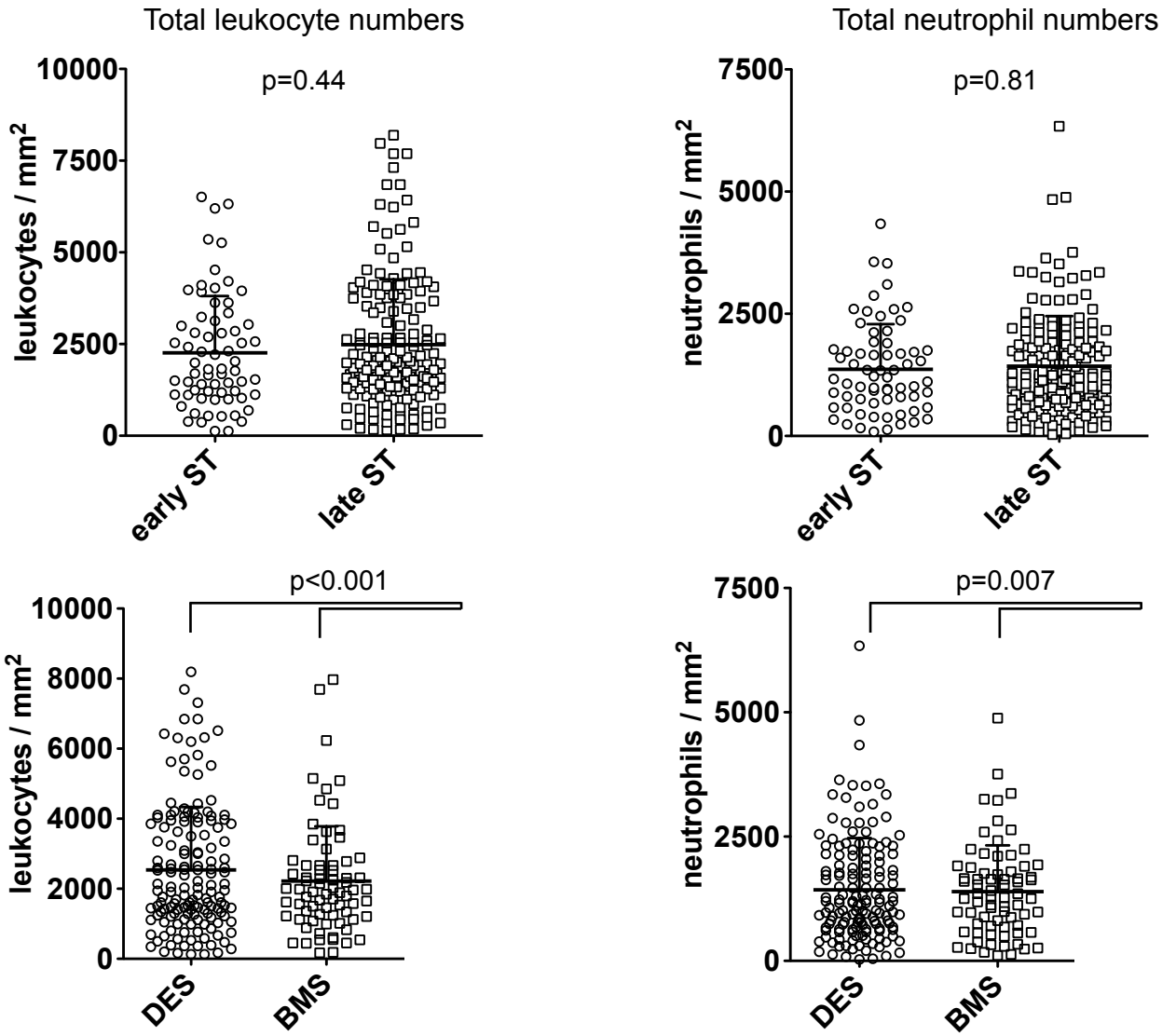




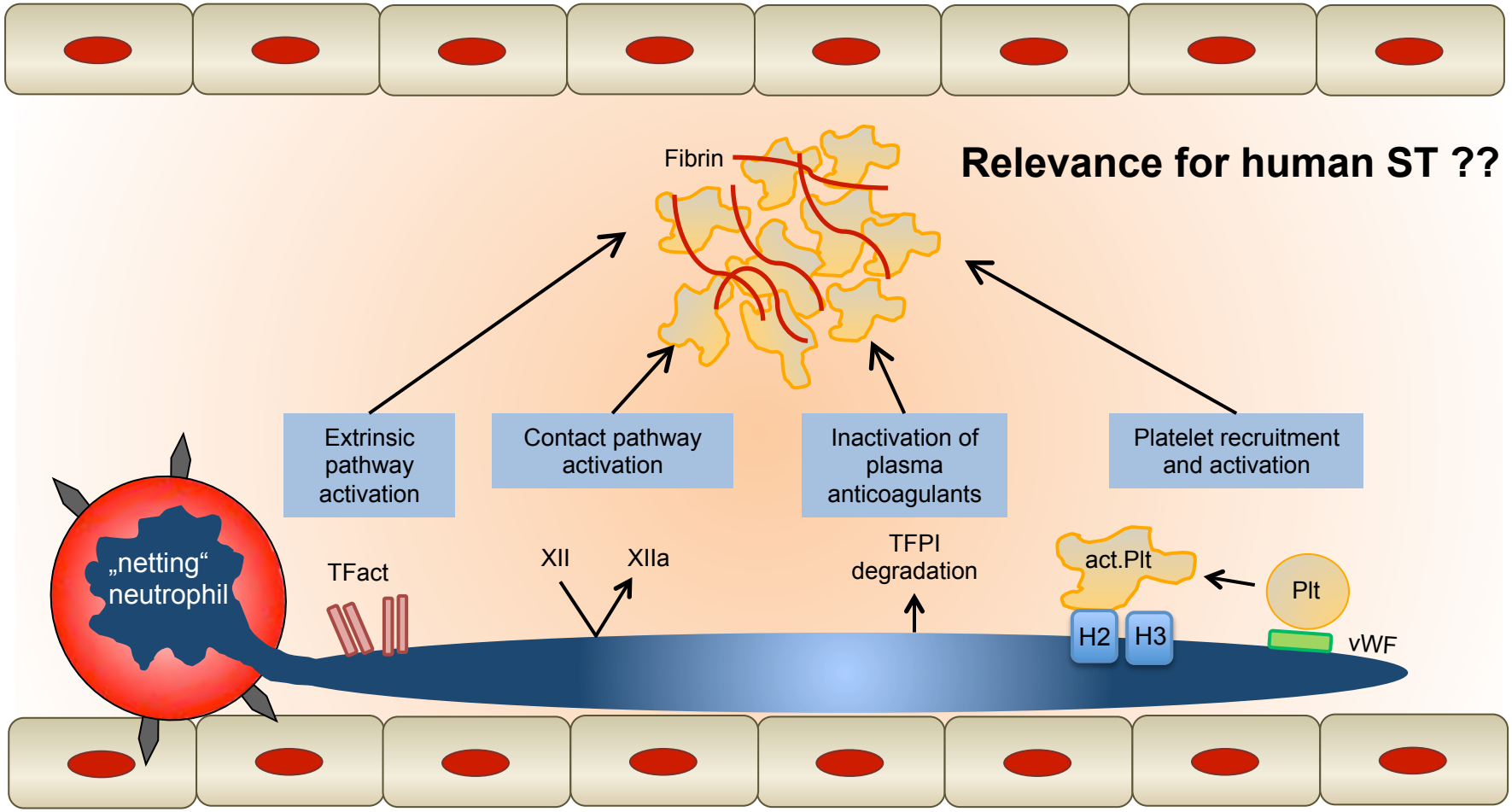




Results: Recruitment of leukocytes – impact of timing & stent type

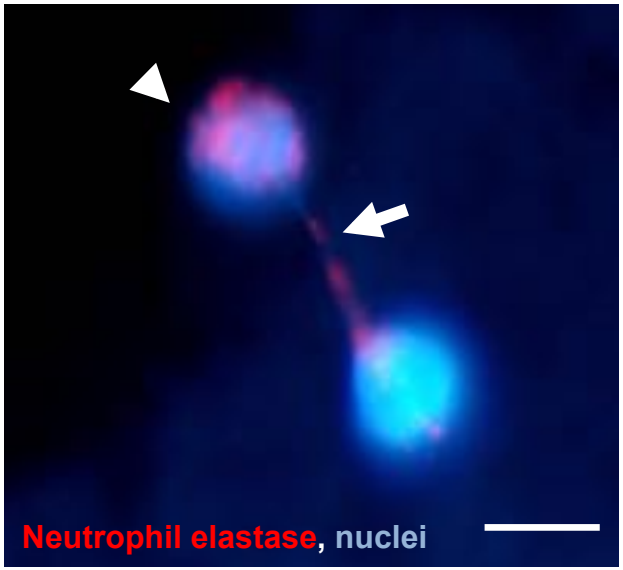


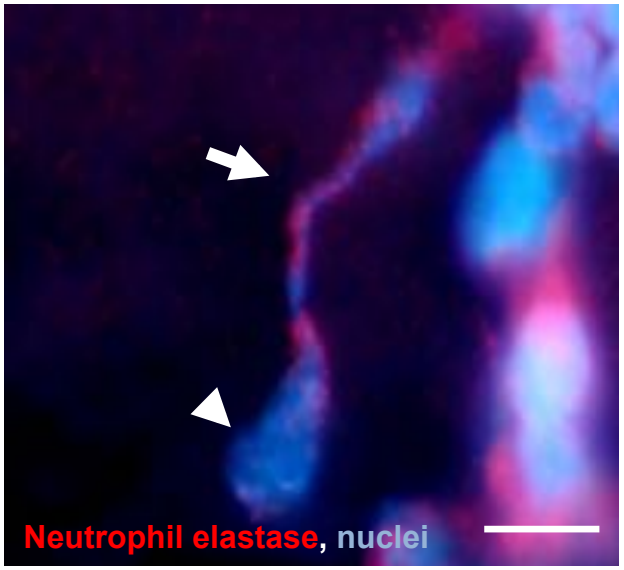
Arterial thrombosis – an inflammatory process called “Immunothrombosis”

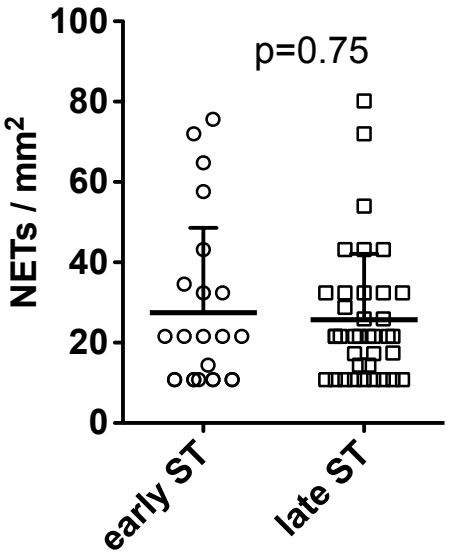


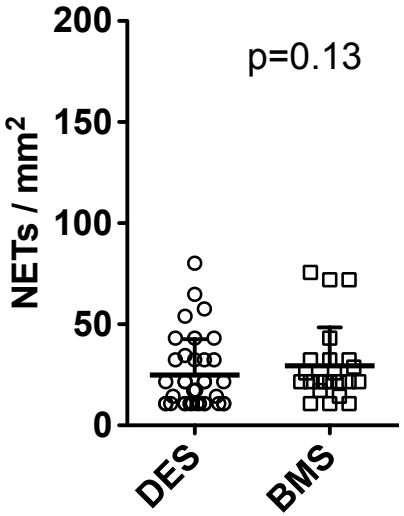
Engelmann & Massberg, Nat. Rev. Immunol. 2013; Schulz et al., J Thromb Haemost. 2013; Massberg et al., Nat. Med. 2010;

Results: NET formation in human ST

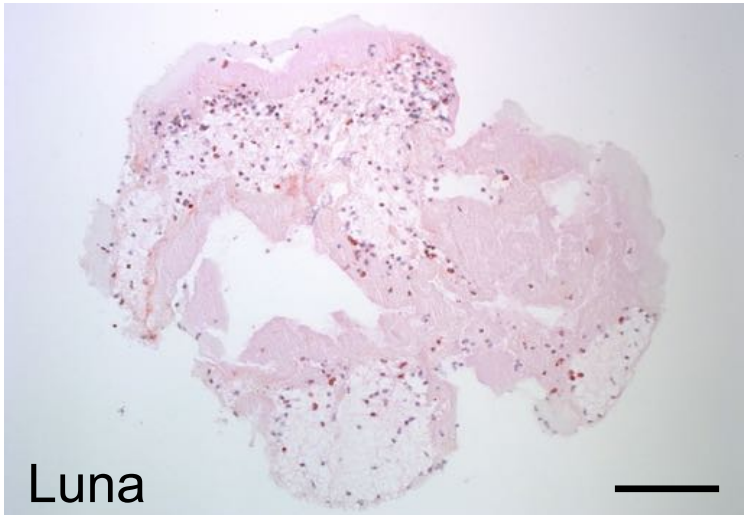


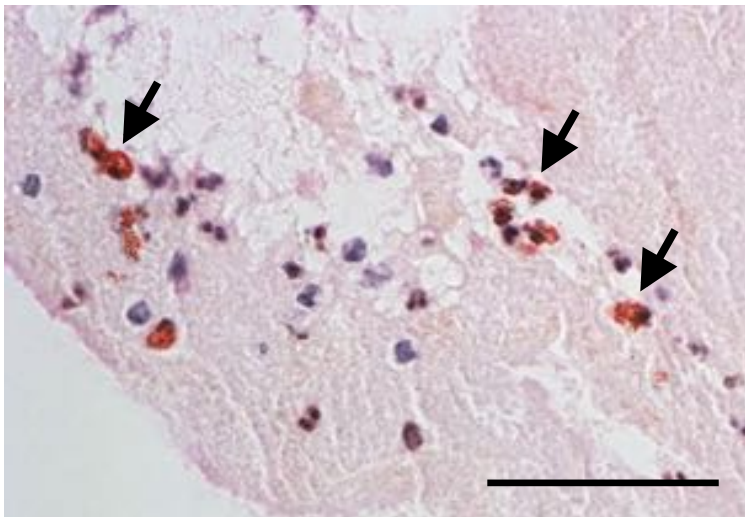


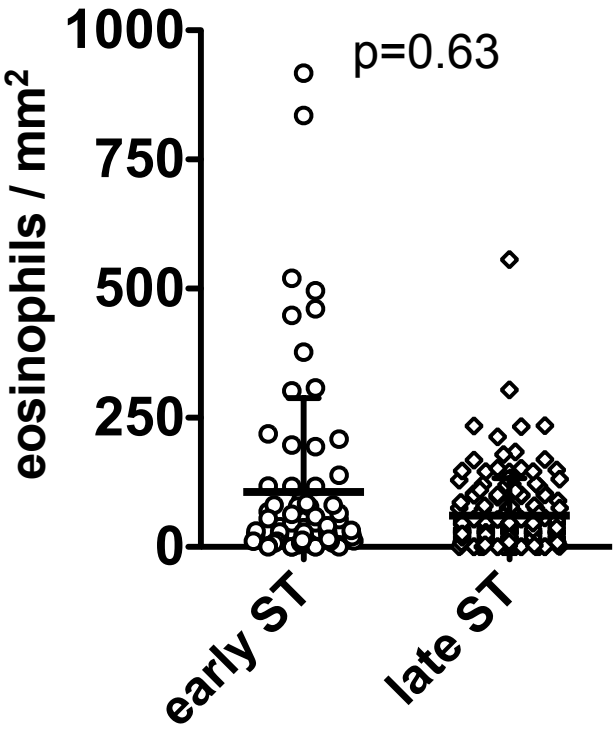




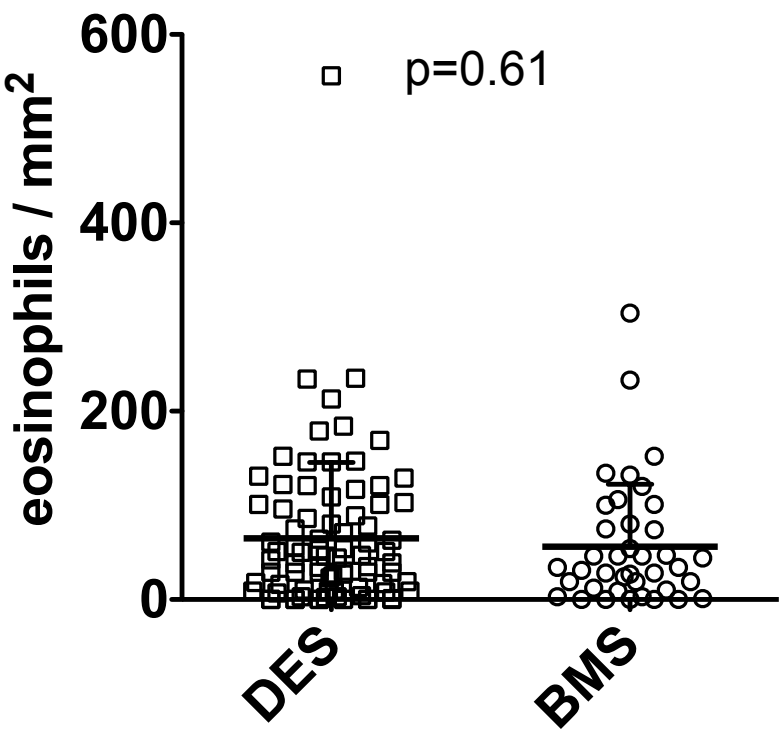
Results: Evidence of eosinophils in ST – impact of timing

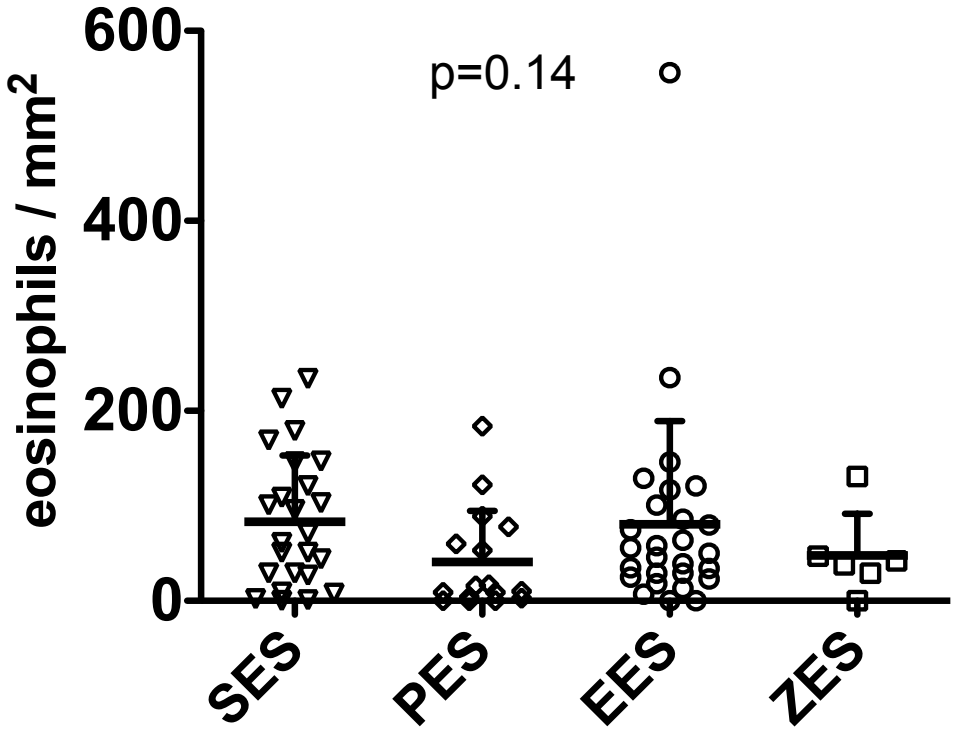






Results: Evidence of eosinophils in very late ST – impact of stent type





Conclusions

- PRESTIGE: largest ST registry
- Inflammation is a hallmark in ST with higher numbers of leukocytes in ST compared to spontaneous MI
- NETs, central effectors of immunothrombosis, were detected in 23% of human ST
- Eosinophils were observed with higher numbers in very late ST in SES and EES
- Pharmacological targeting of immunothrombosis may represent a realistic target for novel therapies

Thank you to all investigators!

Tom Adriaenssens	Peter Sinnaeve	Elena Guerra	Amir Rosenthal	Giulio Guagliumi	Dariusz Dudek	Anthony Gershlick
Emanuele Barbato	Ota Hlinomaz	Michael Joner	Alexander Rzany	Kenichi Komukai	Łukasz Rzeszutko	Alison H. Goodall
Ann Belmans	Helene Abergel	Adnan Kastrati	Christian Schulz	Vasile Sirbu	Roman Wojdyla	Simon Hetherington
Ian Buysschaert	Laurent Feldman	Elisabeth Kennerknecht	Kristin Steigerwald	Garry Kerch	Wojciech Zasada	Jonathan Hill
Mickaël Chausson	Martine Jandrot-Perrus	Ildiko Konrad	Tomohisa Tada	Giovanni Amoroso	Fernando Alfonso	Damian Kelly
Dries De Cock	Didier Letourneur	Tobias Koppara	Anna Titova	Jurriën ten Berg	Javier Cuesta	Nikesh Malik
Jo Dens	Pierre Mangin	Steffen Massberg	Dietmar Trenk	Willem J.M. Dewilde	Miguel Medina	Keith Oldroyd
Walter Desmet	Véronique Olivier	Franz-Josef Neumann	Christian Valina	Thea C. Godschalk	Colin Berry	Helen Routledge
Sandrine Gautier	Caroline Roques	Vasilis Ntziachristos	Andreas Vogelsang	Antonius Heestermans	James Cotton	Joanne Shannon
Nick Hiltrop	Robert A. Byrne	Sheryl Opinaldo	Erion Xhepa	Darshni A. Jhagroe	Nick Curzen	Venkatesan Suresh
Katleen Vandenberghe	Sue Chandraratne	Vanessa Philippi	Chiara Bernelli	Joanne J. Wykrzykowska	Margaret McEntegart	Azfar Zahman
Paul Vermeersch	Matthias Gratz	Julia Riegger	Micol Coccato	Mark H.M. Winkens	Robert Gerber	

Simultaneous publication: Eur Heart J doi:10.1093/eurheartj/ehv419