The Role Of Mural Thrombus In The Development Of Late Type II Endoleaks: How Best To Prevent Them And Treat Them

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VEITH SYMPOSIUM
Connecting The Vascular Community

Disclosures

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Article

Endovascular Treatment of Abdominal Aortic Aneurysm: Impact of Diabetes on Endoleaks and Reintervention

Charlotte Praca [1], Natzi Sakalihasan [1,2], Jean-Olivier Defraigne [1], Nicos Labropoulos [3], Adelin Albert [4], Laurence Seidel [4] and Lucia Musumeci [1,2,*]

Time of Endoleaks Occurrence

From the Eastern Vascular Society

Late type II endoleaks after endovascular aneurysm repair require intervention more frequently than early type II endoleaks

Danielle M. Pineda, MD, Keith D. Calligaro, MD, Sam Tyagi, MD, Douglas A. Troutman, DO, and Matthew J. Dougherty, MD, Philadelphia, Pa

- **Take Home Message:** Type II endoleaks (T2ELs) occurred in 21% of 462 patients who underwent endovascular aortic aneurysm repair. Late T2ELs resolved less frequently than early T2ELs (29% vs 75%) and required more frequent interventions (55% vs 8%).

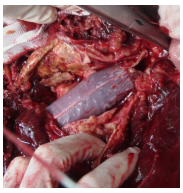
)leaks)

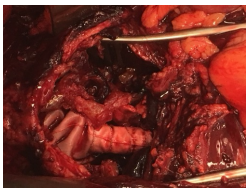
th	12 - 24 month *n (%)*	24 m- 36 month *n (%)*	≥ 36 month *n (%)*
	7 (6,5%)	5 (4,6%)	11 (10,2%)
	6 (7,4%)	4 (4,9%)	8 (9,9%)
	1 (3,7%)	1 (3,7%)	3 (11,1%)

21,3% Late Type 2 EL

Prognosis of the AAA after EVAR

Despite decreasing parietal pressure, rupture occures in some AAA after EVAR. Which one?





Potential issues of endovascular aneurysm repair

Sakalihasan N, Limet R, Defawe O. Abdominal aortic aneurysms, Lancet 2005

Activated forms of MMP2 and MMP9 in abdominal aortic aneurysms

MMPs activities in normal and aneurysmal aortic wall evaluated by "soluble assay »

	serum		Tissues samples			
	control	AAA	AAA			normal
			thrombus			
			luminal	parietal	Aortic wall	Aortic wall
	n = 6	n = 10	n = 10	n = 10	n = 10	n = 6
72 kDa	1.6 ± 0.4	1.6 ± 0.3	8.0 ± 6.7	3.2 ± 1.7	3.6 ± 1.1	3.6 ± 0.3
72 kDa Act.	0	0	0	1.2 ± 1.0	1.9 ± 0.7	0.7 ± 0.2
92kDa	1.3 ± 0.4	1.1 ± 0.3	39.9 ± 6.7	8.0 ± 2.1	4.5 ± 1.2	1.6 ± 0.4
92kDa Act.	0	0.1 ± 0.2	0	0.8 ± 0.9	1.2 ± 0.9*	0

* p < 0.05

ELSEVIER

Sakalihasan et al, J.Vasc.Surg 1996

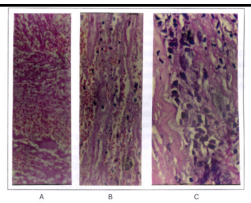


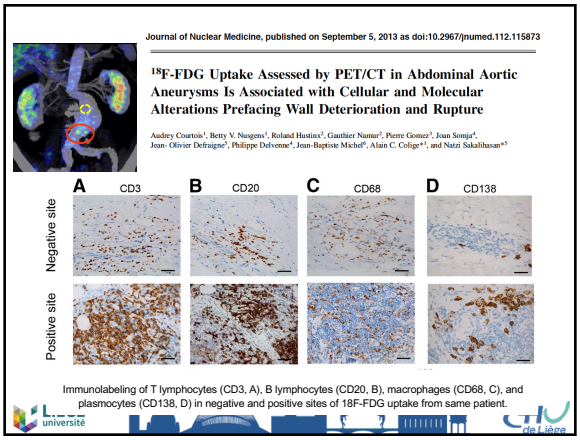
Figure V-2. Hematoxylin and eosin stained sections of internal thrombus (A), adherent thrombus (B) and aortic wall (C). The thrombi consisted essentially of a fibrinous material infiltrated by degenerated red cells and rare leucocytes (A and B). The aortic wall specimen showed a medial and intimal fibrosis associated with a mononuclear cell infiltrate predominating in the adventicia and media (C).

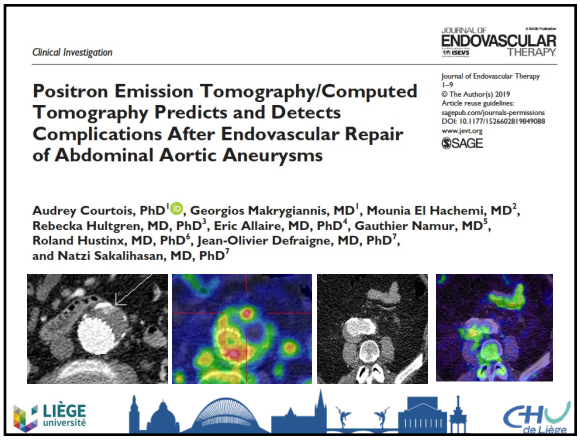
Table V-V. Relationship between inflammatory cell infiltrate and activation of 72 kDa gelatinase.

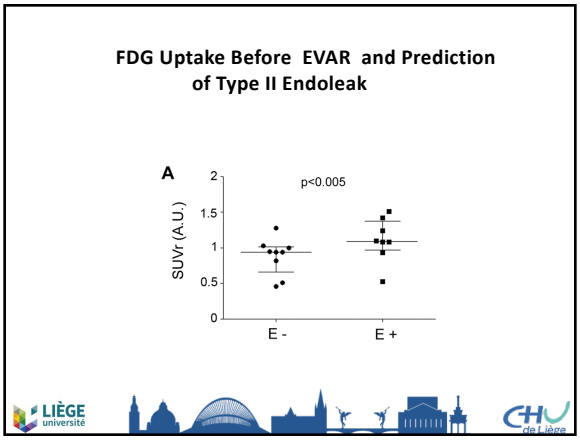
Score	n	72 kDa active form (cpm/mg) Mean	Min – Max
3	2	264	135 – 393
5	5	404	175 – 785
6	2	657	334 – 981

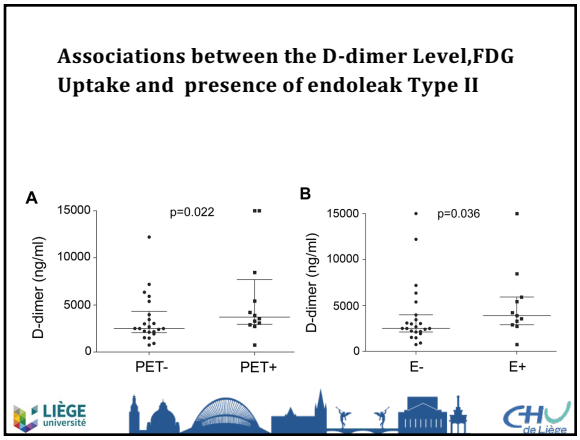
Positive linear correlation between the inflammatory cell infiltrate and the individual values of 72 kDa gelatinase active forms.
($y = 117 + 129x$; $r = 0.46$)

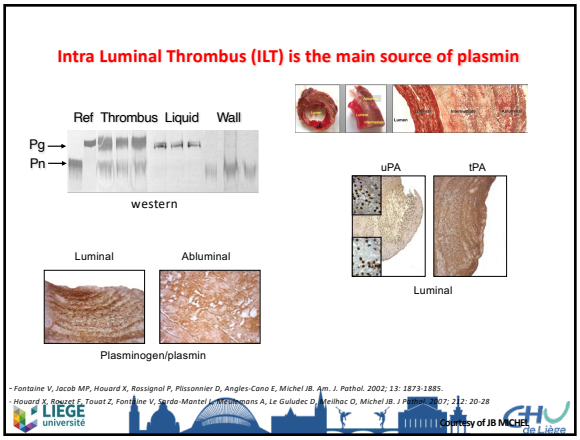
"Involvement of MMP2 and MMP9 in the developement of abdominal aortic aneurysms".
N SAKALIHASAN, P DELVENNE, B NUSGENS, R LIMET, CH LAPIERE.
Cell Biol Intern, 1995, 19 : 250-251

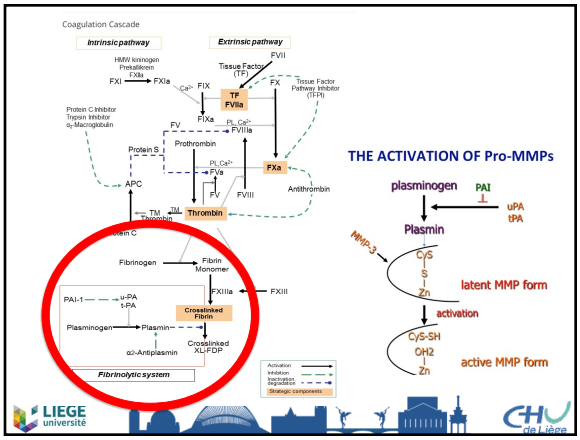

Journal of Nuclear Medicine, published on September 5, 2013 as doi:10.2967/jnumed.112.115873
18F-FDG Uptake Assessed by PET/CT in Abdominal Aortic Aneurysms Is Associated with Cellular and Molecular Alterations Prefacing Wall Deterioration and Rupture
Audrey Courtois[1], Betty V. Nusgens[1], Roland Hustinx[2], Gauthier Namur[2], Pierre Gomez[2], Joan Somja[4], Jean- Olivier Defraigne[3], Philippe Delvenne[4], Jean-Baptiste Michel[6], Alain C. Colige*[1], and Natzi Sakalihasan*[2]
A CD3
B CD20
C CD68
D CD138
Negative site
Positive site
Immunolabeling of T lymphocytes (CD3, A), B lymphocytes (CD20, B), macrophages (CD68, C), and plasmocytes (CD138, D) in negative and positive sites of 18F-FDG uptake from same patient.


Clinical Investigation
Journal of Endovascular Therapy
Positron Emission Tomography/Computed Tomography Predicts and Detects Complications After Endovascular Repair of Abdominal Aortic Aneurysms
Audrey Courtois, PhD[1], Georgios Makrygiannis, MD[1], Mounia El Hachemi, MD[2], Rebecka Hultgren, MD, PhD[3], Eric Allaire, MD, PhD[4], Gauthier Namur, MD[5], Roland Hustinx, MD, PhD[6], Jean-Olivier Defraigne, MD, PhD[7], and Natzi Sakalihasan, MD, PhD[7]

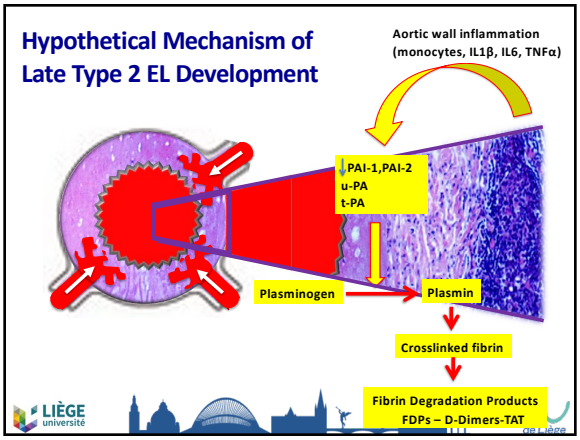

FDG Uptake Before EVAR and Prediction of Type II Endoleak
A
p<0.005
SUVr (A.U.)
2
1.5
1
0.5
0
E -
E +


Associations between the D-dimer Level,FDG Uptake and presence of endoleak Type II
A
p=0.022
D-dimer (ng/ml)
15000
10000
5000
0
PET-
PET+
B
p=0.036
D-dimer (ng/ml)
15000
10000
5000
0
E-
E+


Intra Luminal Thrombus (ILT) is the main source of plasmin
Ref Thrombus Liquid Wall
Pg
Pn
western
Luminal
Abluminal
Plasminogen/plasmin
uPA
tPA
Luminal
- Fontaine V, Jacob MP, Houard X, Rossignol P, Plissonnier D, Angles-Cano E, Michel JB. Am. J. Pathol. 2002; 13: 1873-1885.
- Houard X, Rouzet F, Touat Z, Fontaine V, Sirodo-Mantel V, Meilhac O, Michel JB. J Pathol. 2007; 212: 20-28
Courtesy of JB MICHEL

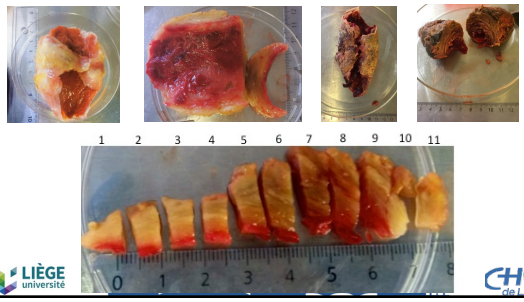

Coagulation Cascade
Intrinsic pathway
Extrinsic pathway
Fibrinolytic system
THE ACTIVATION OF Pro-MMPs
plasminogen
PAI
uPA
tPA
Plasmin
MMP-3
latent MMP form
activation
active MMP form

Hypothetical Mechanism of Late Type 2 EL Development

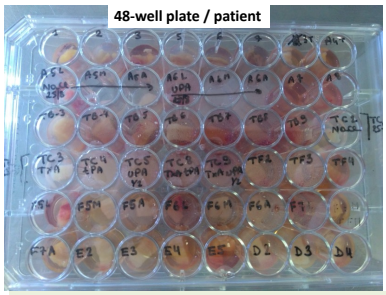


PILOT STUDY
Materials & Methods

Parietal Thrombus collection (N:8)



PILOT STUDY
Materials & Methods
STEP I



Incubate at 37°C in 600ul NaCl 0,9% at 37°C in 48-well plate

PILOT STUDY
Materials & Methods
(Enzymes & inhibitors)

Physiological solution NaCl 0,9%

Plasminogen Activator Inhibitor 1 **(PAI-1)**

Plasminogen Activato rInhibitor 2 **(PAI-2)**

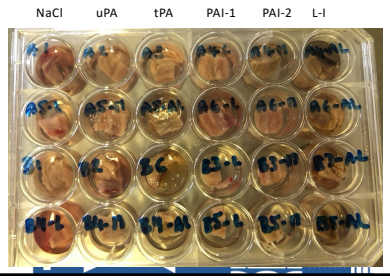
urokinase Plasminogen Activator **(uPA)**

tissue Plasminogen Activator **(tPA)**

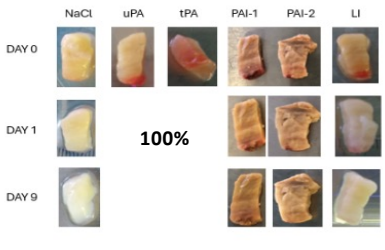
Liege Plasminogen inhibitor **(L-I)**

PILOT STUDY
Materials & Methods
STEP II

Incubation with Solutions



PILOT STUDY
Results
Thrombus reduction



Conclusion

- Importance to perform PET/CT before EVAR to predict EL2 risk
- Close follow up using circulatory fibrinolytic markers (D-dimers, TAT, PAP)
- Based on preliminary results of our pilot study a medical treatment (systemic or local) with inhibitors of plasminogen could avoid symptomatic late EL2