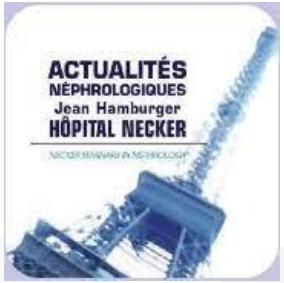


Rheopheresis, a targeted Intervention in Microvascular Pathologies ?

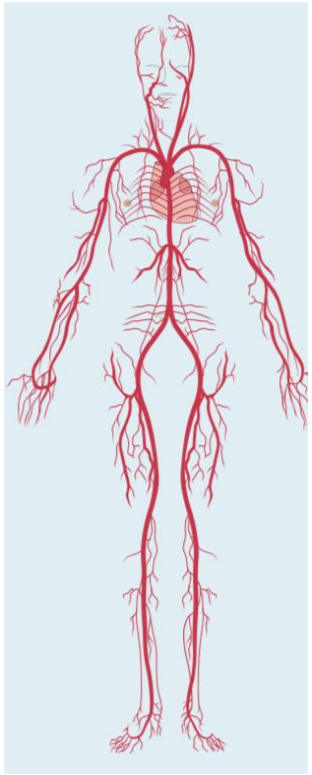
Thomas Robert
Centre de Néphrologie et Transplantation Rénale
Hôpital de la Conception
UMR 1251 - MMG
Aix-Marseille Université

Interest conflict

Grants/Research Support : HEMA.T medical Pollet Medical Group

Speaker's fees: ASAHI

Circulation basis



Blood circulation:

Arteries 11,5%
Vein 14,5%

Macrocirculation function

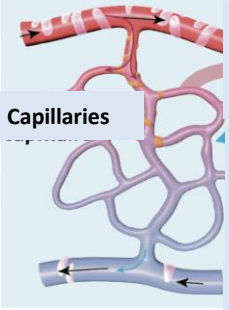
blood delivery
continuous
blood flow

Capillaries 74%

Diameter < 0,1 mm

Microcirculation function

Regulation and exchange function



Arteriola

Nutrient and oxygen supply

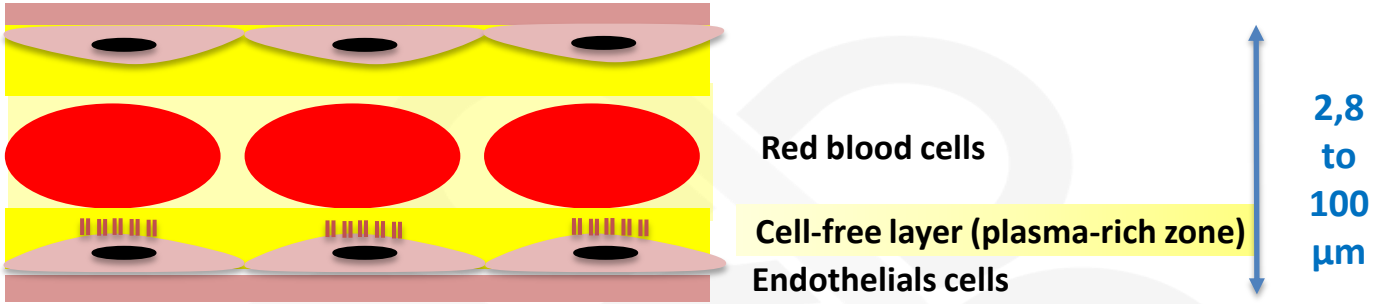
Capillaries

extraction of residual substances (i.e carbon dioxide)

Veinula

Vessel	Cross-Sectional Area (cm^2)
Aorta	2.5
Small arteries	20
Arterioles	40
Capillaries	2500
Venules	250
Small veins	80
Venae cavae	8

Microcirculation rheology



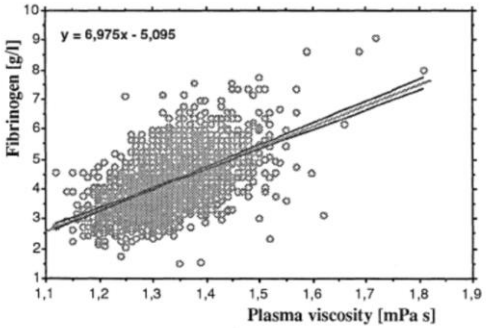
1. Plasma: main interface between the vascular endothelium and the blood
2. Shear stress applied to the endothelium modify its functions through the endothelial glycocalyx
3. The plasma viscosity is one of the determinants of the shear stress.

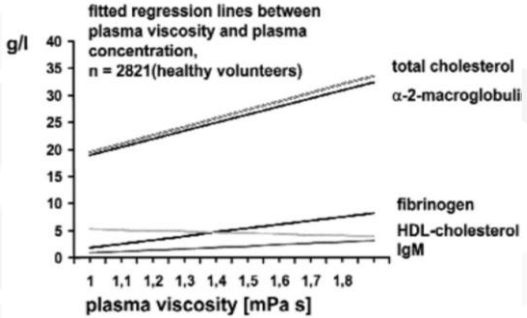
Plasma viscosity is a determinant of endothelial function.

Plasma viscosity and fibrinogen

AACHEN study : 2821 volunteers from 1984 to 1985

Measurement of plasma viscosity by capillary tube viscometer





Estimated plasma viscosity = 1,04 + 0,55* fb + 0,18 * Chol + 0,15*IgM + 0,01* Tg + 0,09* α2MacroG –0,08*HDLc

Normal plasma viscosity values : 1.24 ± 0.10 mPa/s

Fibrinogen and vascular disease

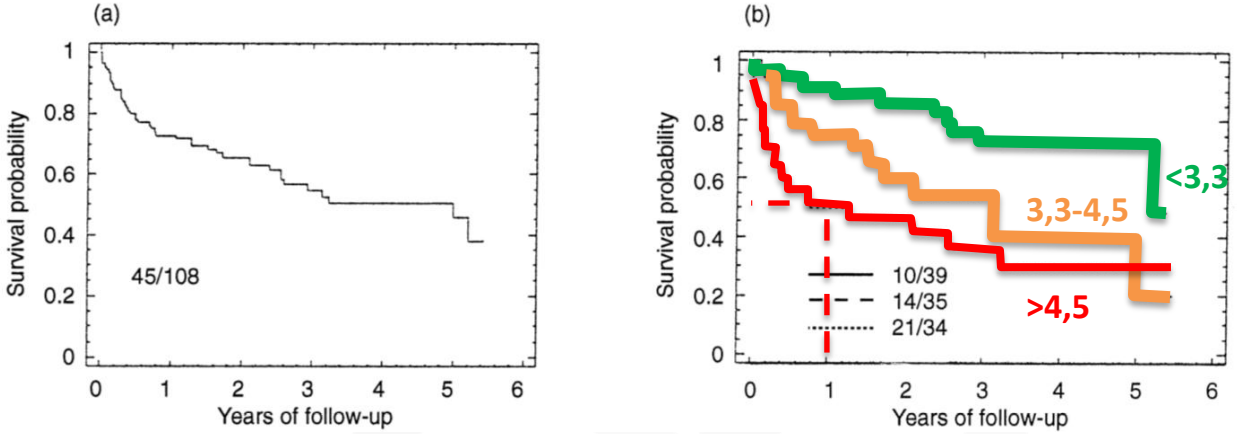
Table 2. Values of parameters analyzed in the study group within the subgroups of patients with intermittent claudication (IC) and critical limb ischemia (CLI) against the control group.

Parameter and Unit	Value	Study Group (PAD, *n* = 80)		Control Group (C, *n* = 30)	*p*
		IC (*n* = 65) *a*	CLI (*n* = 15) *b*	*c*	
fibrinogen (g/L)	Me (Q25;Q75)	4.19 (3.5;4.99)	**5.33** (4.64;6.16)	3.36 (2.8;3.7)	*a vs b* = 0.026 *a vs c* < 0.001 *b vs c* < 0.001

Fibrinogène	
↗ Intermittent Claudication	↗↗↗↗ Critical limb ischemia

Radosław Wieczór, J Clin Med, 2020

Fibrinogen and critical limb ischemia



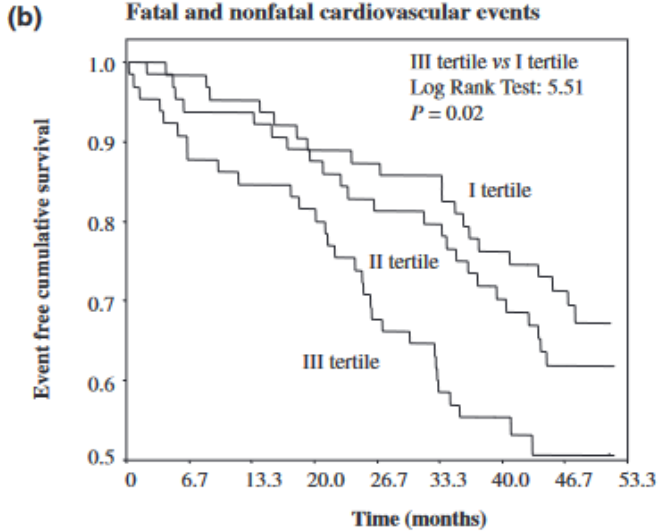
Fibrinogen > 4,5 g/l = 50 % one year survival

Pedrinelli, Journal of Internal Medicine 1999
Doweik, Eur J Vasc Endovasc, 2003

Fibrinogen and hemodialysis patients

Journal of Internal Medicine 2003; **254**: 132–139

Fibrinogen, mortality and incident cardiovascular complications in end-stage renal failure



I tertile: <3.09 g/L
II tertile: 3.09–4.69 g/L
III tertile: >4.69 g/L

CVD is the primary cause of death in up to 40% in dialysis patients.

Zoccali, Journal of internal medicine, 2003

Fibrinogen and MACE

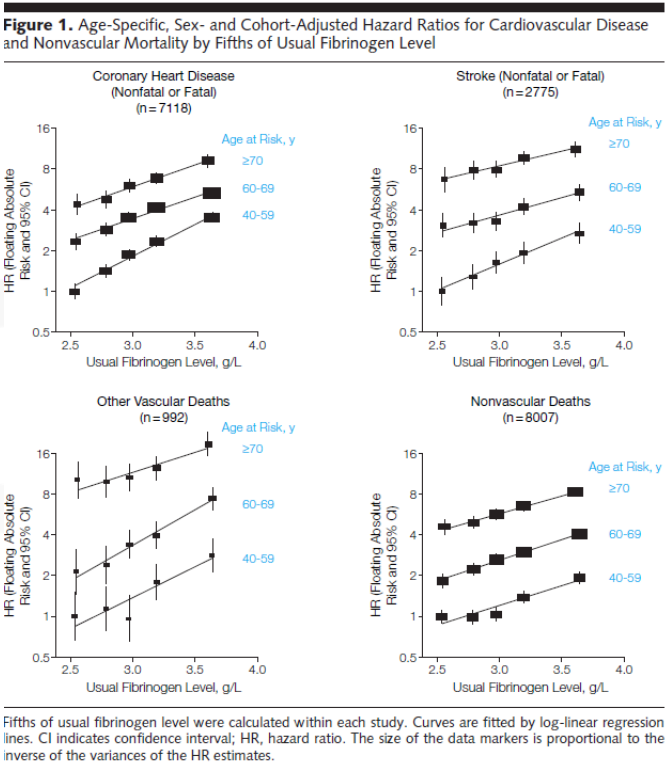


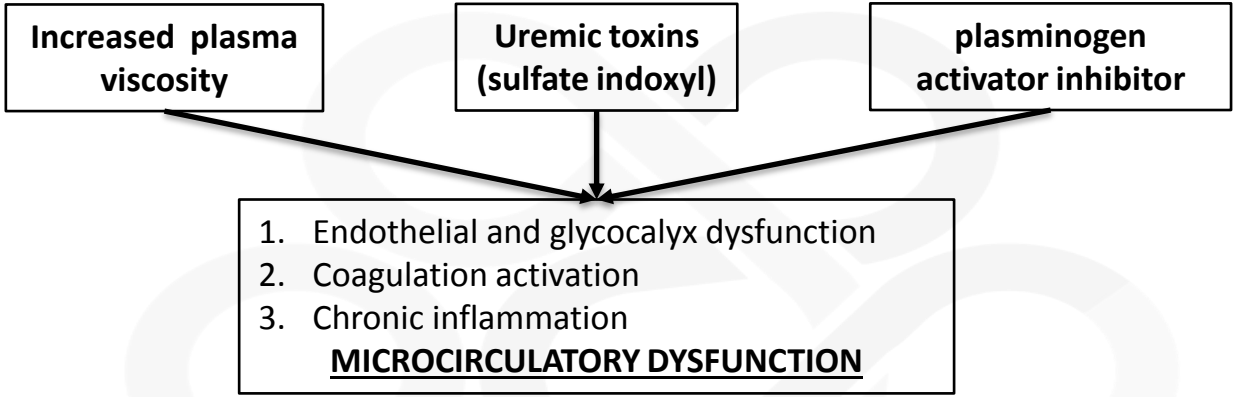
Figure 1. Age-Specific, Sex- and Cohort-Adjusted Hazard Ratios for Cardiovascular Disease and Nonvascular Mortality by Fifths of Usual Fibrinogen Level

Fifths of usual fibrinogen level were calculated within each study. Curves are fitted by log-linear regression lines. CI indicates confidence interval; HR, hazard ratio. The size of the data markers is proportional to the inverse of the variances of the HR estimates.

Increased fibrinogen level is associated with all major cardiovascular event

Fibrinogen Studies Collaboration, JAMA, 2005

Hemodialysis Patients

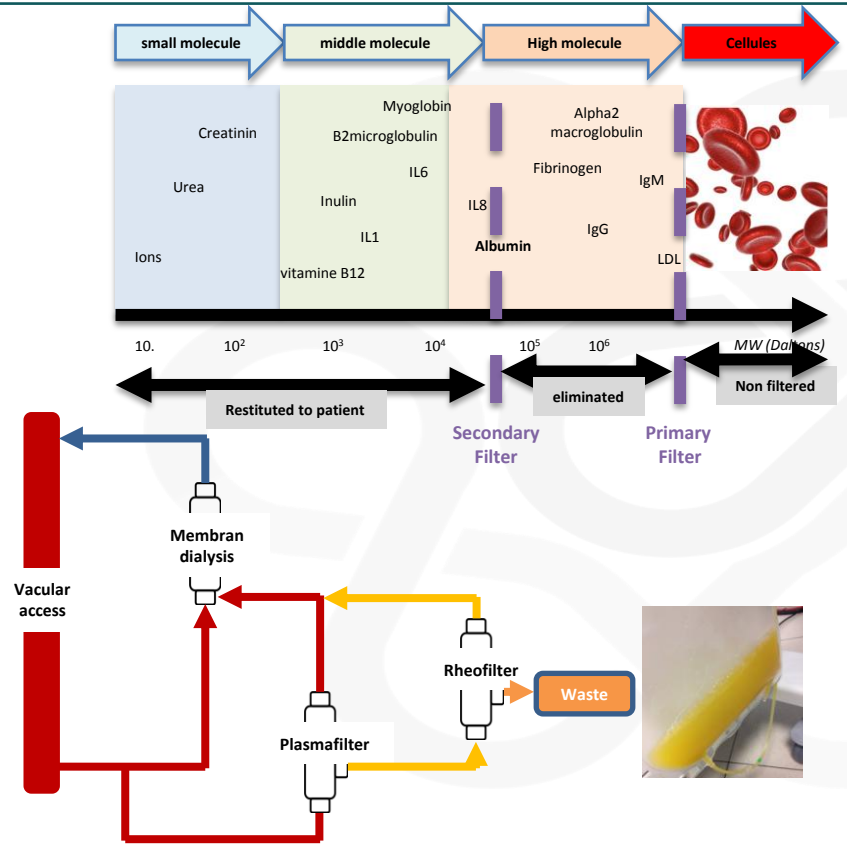


2 frequents disease with microcirculation dysfunction in HD patients:

- Critical limb ischemia
- Calciphylaxis

Dubin R, BMC nephrol, 2011
Kirmizis D, Med Sci Monit, 2006
Gondouin B, Kidney Int, 2013
Anne-Clémence Vion, JCB, 2018
Vlahu, JASN, 2014

Rheopheresis principle



REDUCTION OF PLASMA VISCOSITY

Rheopheresis in critical limb ischemia

Critical limb ischemia (N= 28)

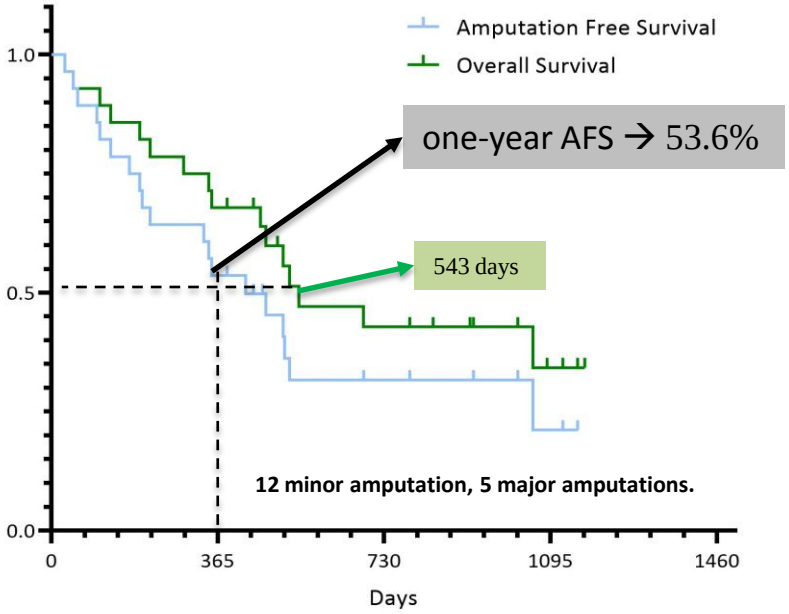
Follow-up from
February 2017 to April 2019

	Hospital of la Conception, Marseille	Phocean Nephrology Institute, Marseille	AURA Dialysis Center, Paris
Number of patients	12	10	6
Blood flow (ml/min)	130	200	180-200
Plasma extraction (% of blood flow)	30	20	25
Target plasma to be treated	40 ml/kg two times a week over 2 weeks then 60 ml/kg once a week	40 ml/kg two times a week over 2 weeks then 50 or 60 ml/kg once a week	50 ml/kg
Waste (% of plasma extraction)	5	10	5
Replacement (% of plasma extraction)	No replacement	5	5
Nature of replacement solution	No replacement	Albumin 20 g	Saline infusion
Anticoagulation	Citrate	Heparin	Citrate

Main clinical characteristics	
Age (years)	75.5 ± 14.5
Male gender	22 (78.6%)
Duration of hemodialysis (years)	2.5 ± 3.8
BMI (kg/m^2)	24.9 ± 9
Diabetes	22 (78.6%)
Hypertension	26 (92.9%)
Statin therapy	20 (71.4%)
Left ventricular ejection fraction (%)	56 ± 23
Coronary disease	15 (53.6%)
Smoking history	11 (39.3%)
Serum albumin (g/L)	35 ± 5.3
Serum fibrinogen (g/L)	5.4 ± 1.6
CRP (mg/L)	33.8 (20.1;76.7)
LDLc (mmol/L)	2.1 ± 0.7
Triglycerides (mmol/L)	1.7 ± 0.9
Characteristics of CLTI	
Chronic ulceration	18 (64.3%)
Minor tissue loss (Rutherford 5)	10 (35.7%)
Major tissue loss (Rutherford 6)	8 (28.6%)
Minor amputation with delayed healing	10 (35.7%)
Endovascular treatment within the 2 previous months	12 (42.9%)
Bypass surgery within the 2 previous months	3 (10.7%)

Solignac J, Journal of clinical apheresis, *2021*

Clinical effects of rheopheresis in critical limb ischemia



	Days	30	60	100	180	365	730
Number at risk	AFS	28	26	25	22	16	7
	OS	28	27	27	25	20	11

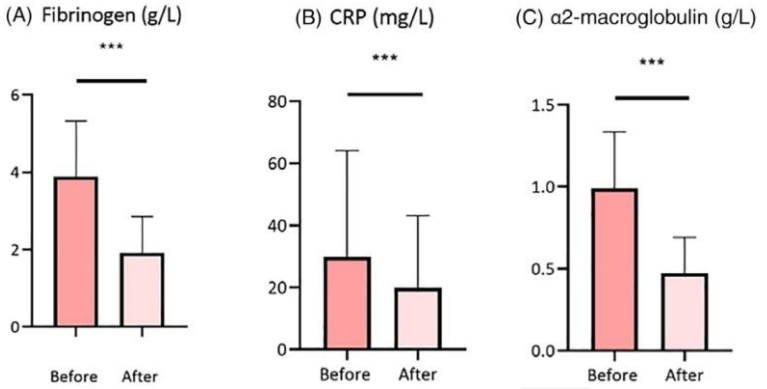
Fallon and al. reported a one-year AFS rate at 40% in a large cohort of 394 HD patients

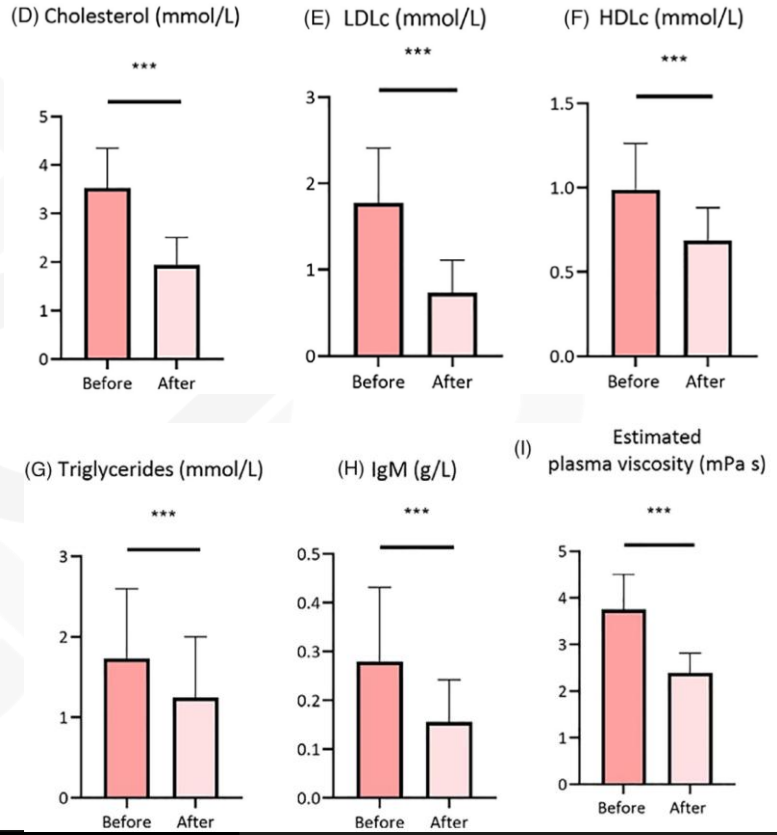
Fallon JM, J Vasc Surg. 2015

TABLE 3 Causes of death during follow-up

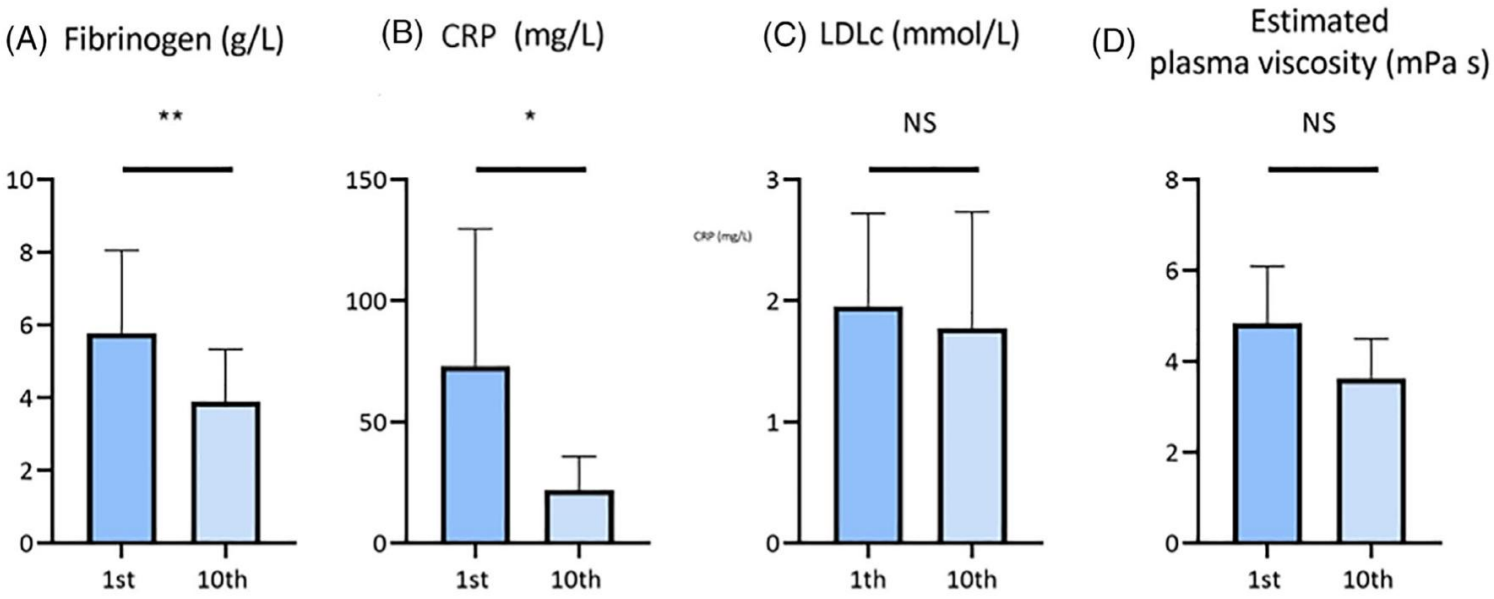
Total	**16**
Hospice palliative care	6
Septic shock	5
Unexplained sudden cardiac arrest	2
Major bleeding resulting from accidental falls	2
Terminal cardiac failure	1

ON-OFF rheopheresis effects





Long term rheopheresis effects



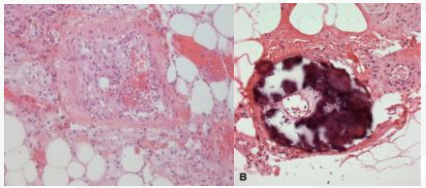
All the limitations of a small retrospective study

No comparator group
No adequate Pain assessment (Brief pain questionary)
No Vascu**Qol** assessment
No WIFI score
No TCpO2 assessment

Calciphylaxis in hemodialysis Patients

1. Endothelial and glycocalyx dysfunction
2. Coagulation activation
3. Chronic inflammation

MICROCIRCULATORY DYSFUNCTION



thrombosis

hypercoagulability
inflammation

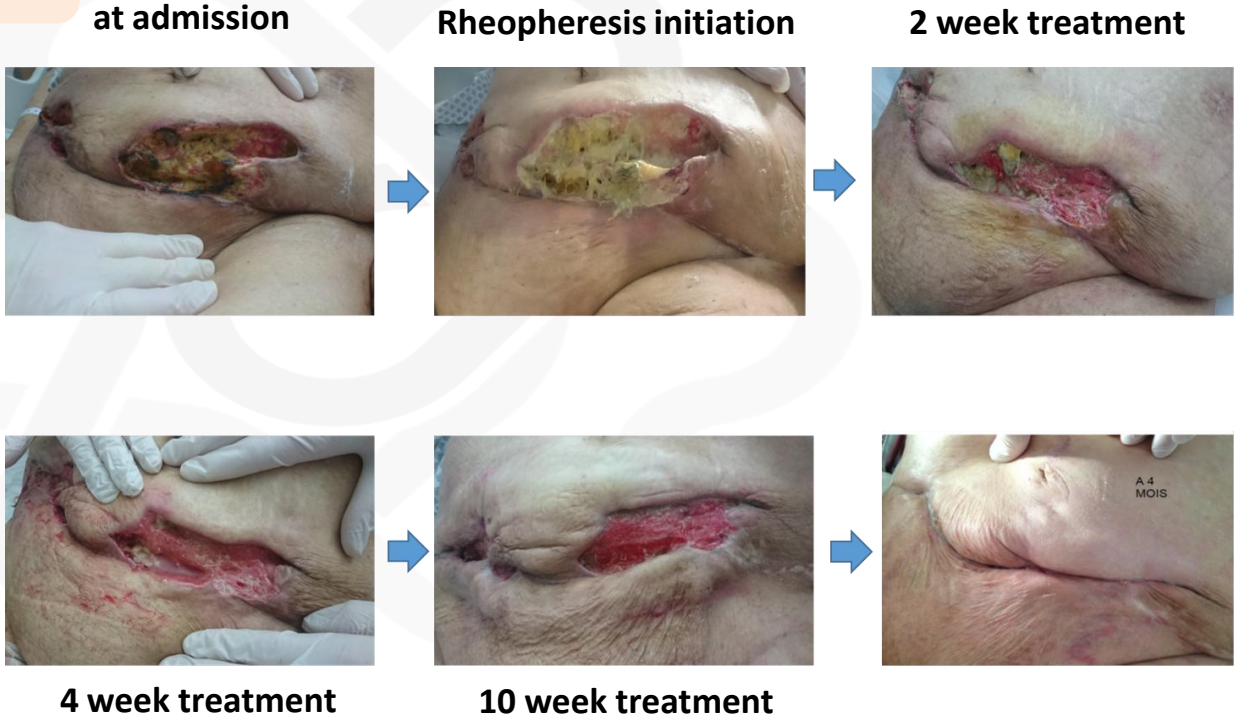
necrosis

Rheopheresis in Calciphylaxis

Rheopheresis for Adjuvant Treatment in Resistant Calciphylaxis

Bouderlique E, Ther Apher Dial, *2018*

- **Hemodialysis intensity > 20h weekly**
- **Lowering circulating P×Ca product, Nutritional support,**
- **intravenous sodium thiosulfate (25 g three times a week)**
- **Vitamin K implementation**
- **Local wound care.**



Courtesy to Arnaud lionet

Rheopheresis in Calciphylaxis

ORIGINAL ARTICLE

NEPHROLOGY WILEY

Robert T, Nephrology, 2019

Rheopheresis: A new therapeutic approach in severe calciphylaxis

Thomas Robert[1] | Arnaud Lionet[2] | Stanislas Bataille[3,4] | Guillaume Seret[5]

- **Median age 69 y**
- **75% diabetes**
- **Obesity 7/8**
- **VKA in 5/8**

	Age	Sex	BMI	Diabetes mellitus	Malnutrition	Anuria	HD/HDF	Kt/V <1.2	VKA	Secondary hyperparathyroidism	Dialysis vintage (months)
Patient 1	70	M	42	Yes	No	Yes	HD	Yes	Yes	No	91
Patient 2	55	M	28	Yes	No	No	HD	Yes	Yes	No	37
Patient 3	73	F	38	Yes	Yes	No	HD	Yes	No	Yes	1
Patient 4	73	F	33	No	No	Yes	HDF	No	Yes	Yes	48
Patient 5	66	F	43	Yes	Yes	Yes	HD	No	Yes	Yes	5
Patient 6	68	F	40	Yes	Yes	Yes	HDF	No	No	Yes	40
Patient 7	91	F	35	No	No	No	HD	No	Yes	Yes	34
Patient 8	58	M	67	Yes	Yes	Yes	HD	Yes	No	Yes	1

4/8 biopsy-proven calciphylaxis

Rheopheresis in Calciphylaxis

Robert T, Nephrology, 2019

TABLE 3 Evolution of clinical and biological parameters before and after 12 sessions of rheopheresis

	Rheopheresis start, median (interquartile range)	After 12 sessions, median (interquartile range)	*p*-Value
Wound length	20.5 (10.3–24)	12.3 (6.5–16.9)	.29
Wound width	11.5 (5.5–15)	4.5 (3.3–8)	.58
C-reactive protein	49.6 [35.9–63.5)	17.5 (12.3–34)	.07
Fibrinogenemia	5.8 (4.8–7.2)	3.7 (3.1–4.2)	.007
Albuminemia	31 (25–37)	29 (22–36)	.8
Triglycerides	1.7 (1.1–2.3)	1.5 (1.2–1.6)	.09

Rheopheresis in Calciphylaxis

- **100% sodium thiosulfate (≥75mg weekly)**
- **HD intensification (50% daily HD)**
- **50% VKA discontinuation**
- **38% (3/8) surgical debridement**
- **Nutritionnal support**

Robert T, Nephrology, 2019

	CUA diagnosis, median (SD)	Rheopheresis initiation, median (SD)	*p*-Value
Parathyroid hormone (pg/mL)	244 (164–402)	161 (92–290)	.03
Ca (mmol/L)	2.3 (2.2–2.4)	2.3 (2.2–2.4)	.8
P (mmol/L)	2.4 (2.0–2.6)	1.2 (0.6–1.9)	.14
25-hydroxyvitamin D (ng/mL)	33 (30–56)	33 (29–52)	.1
Albuminemia (g/L)	32 (30.8–33.8)	31.4 (28.5–33.8)	.1
C-reactive protein (mg/L)	17.2 (9.6–45.6)	49.6 (35.9–63.5)	.3
Haemoglobin (g/dL)	11.4 (10.6–12.5)	10.9 (8.4–12)	.036
Kt/V	1.19 (1.1–1.5)	1.4 (1.2–1.6)	.34
Weekly dialysis time (h)	12.0 (12–12.8)	16 (15–22)	.035

Rheopheresis in Calciphylaxis

Robert T, Nephrology, 2019

TABLE 4 Duration of treatment and results obtained with rheopheresis in patients treated for calciphylaxis

	Delay before rheopheresis start (days)	Number of rheopheresis sessions	Rheopheresis treatment (days)	Complete remission	Death	Relapse	Total follow up (months)
Patient 1	1	15	84	Yes	No	No	2.8
Patient 2	1	19	114	Yes	No	Yes	3.8
Patient 3	77	25	119	Yes	No	No	6.5
Patient 4	39	27	128	No	Yes	No	5.6
Patient 5	13	10	59	No	Yes	No	2.4
Patient 6	65	55	196	Yes	No	Yes	8.7
Patient 7	158	39	274	Yes	No	No	14.4
Patient 8	4	8	25	No	Yes	No	1.0
Median (interquartile range)	26.0 (3.2–68)	22.0 (13.8–30)	116.5 (77.8–145)				4.7 (2.7–7)

- **5 (60%) complete remission**
- **2 (25%) relapse,**
- **3 (38%) death**

- **Close to 1 month of delay from diagnosis**

Journal of Clinical Medicine 2023

MDPI

Article

Rheopheresis Performed in Hemodialysis Patients Targets Endothelium and Has an Acute Anti-Inflammatory Effect

Justine Solignac [1,2,*], Romaric Lacroix [2,3], Laurent Arnaud [3], Evelyne Abdili [3], Dammar Bouchouareb [1], Stéphane Burtey [1,2], Philippe Brunet [1,2], Françoise Dignat-George [2,3] and Thomas Robert [1,2]

Chronic inflammation and no active vasculopathy

Hemodialysis (N=10)

Critical limb ischemia Calciphylaxis

Hemodialysis + rheopheresis N=13

Pre et post session

Exploration of endothelial dysfunction

- **circulating endothelial adhesion molecules** — *sICAM-1, sVCAM-1, sE-Selectine, sP-Selectine*
- **Cytokines** — *TNF-α, sCD40-L, IL-1ß, IL-6, IL-8, IL-10*
- **angiogenic factors** — *Angiopoietine 2, sEndogline, VEGF-A*
- **Circulating endothelial cells (CEC)**

P value < 0,001 considered statistically significant

Rheopheresis effect

on-off dialysis effects

Chronic inflammation and no active vasculopathy pateints

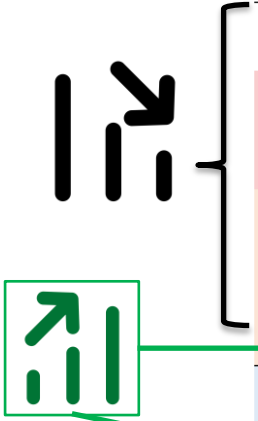
	HD Group without Rheopheresis		
	Pre-Dialysis (N = 10)	Post-Dialysis (N = 10)	*p* Value
ICAM-1 (ng/mL)	222 (146–347)	193 (130–317)	0.04
VCAM-1 (ng/mL)	1146 (801–1556)	1120 (701–1629)	0.49
E-Selectin (ng/mL)	30.3 (26.6–45.6)	30.7 (24.5–45.4)	0.62
P-Selectin (ng/mL)	41.8 (39.8–48.7)	48.0 (46.3–64.2)	0.004
sCD40L (pg/mL)	81.9 (27.8–179)	669 (195–881)	0.002
IL-1β (pg/mL)	1.6 (1.0–4.6)	8.7 (0.9–11.6)	0.027
IL-6 (pg/mL)	1.0 (1.0–1.0)	0.9 (0.8–1.5)	0.57
IL-8 (pg/mL)	9.3 (5.0–17.4)	6.9 (4.2–16.6)	0.08
TNF-α (pg/mL)	57.8 (49.2–67.3)	38.8 (31.3–49.8)	0.009
IL-10 (pg/mL)	2.2 (1.0–7.5)	7.0 (1.7–9.8)	0.19
Angiopoietin (ng/mL)	3.0 (3.0–4.0)	2.68 (2.4–3.2)	0.04
sEndoglin (pg/mL)	1347 (873–1474)	1061 (766–1536)	0.19
VEGF-A (pg/mL)	59.8 (25.0–113)	114 (24.0–250)	0.43
CECs (n/mL)	1 (1.0–4.0)	1 (1.0–2.0)	0.13

Variables are expressed as median [Quartile 1–Quartile 3]. Values after dialysis sessions were corrected according to the hemoconcentration by Van Beaumont equation. Statistical test used was Wilcoxon test. $p < 0.001$ was considered statistically significant. HD: hemodialysis; and CECs: circulating endothelial cells.

No statistically significant modifications

Rheopheresis effect

on-off rheopheresis effects



	HD Group with Rheopheresis			
	Pre-Rheopheresis (N = 37)	Post-Rheopheresis (N = 37)	Percentage Change (%)	*p* Value
Fibrinogen (g/L)	4.72 (3.0–6.0)	1.9(1.4–2.7)	−53.4 [(−59.2)–(−45.4)]	<0.0001
CRP (mg/L)	15.3(5.2–36.9)	9.0 (2.8 –21.5)	−39.5 [(−48.1)–(−34.2)]	0.001
ICAM-1 (ng/mL)	148 (116–182)	132 (102–175)	−10 [(−20.7)–(−3.1)]	0.02
VCAM-1 (ng/mL)	1856 (1257–2707)	1330 (908–1654)	−34.7 [(−45.0)–(−23.2)]	<0.0001
E-Selectin (ng/mL)	21.0 (15.5–30.5)	12.3 (7.3–20.3)	−38.6 [(−54.8)–(−31.8)]	<0.0001
P-Selectin (ng/mL)	44.0 (26.5–53.0)	21.8 (16.1–33.8)	−38.3 [(−48.1)–(−29.1)]	<0.0001
sCD40L (pg/mL)	44.9 (31.3–64.3)	61.6 (34.3–96.1)	38.0 (7.7–104)	0.06
IL-1β (pg/mL)	1.0 (1.0–1.0)	0.9 (0.9–1.07)	−9.1 [(−22.1)–0]	0.04
IL-6 (pg/mL)	1.0 (1.0–11.3)	2.6 (0.9–13.5)	0 [(−12.4)–37.7]	0.93
IL-8 (pg/mL)	10.4 (7.7– 15.6)	9.6 (7.1–15.1)	−19.4 [(−32.1)–(−6.0)]	0.99
TNF-α (pg/mL)	39.1 (30.1–47.0)	25.7 (22.2–30.4)	−32.6 [(−42.2)–(−22.5)]	<0.0001
IL-10 (pg/mL)	5.6 (2.1–10.9)	60.9 (31.3–64.3)	674 (306–1299)	<0.0001
Angiopoietin2 (ng/mL)	3.5 (3.0–6.8)	3.3 (2.8–6.3)	−9.2 [(−14.8)–(−1.6)]	0.37
sEndoglin (pg/mL)	694 (353–1018)	474 (224–697)	−31.5 [(−43.1)–(−17.2)]	<0.0001
VEGF-A (pg/mL)	25.0 (25.0–56.0)	26.1 (23.7–46.0)	0 [(−29.0)–0]	0.6
CECs (n/mL)	13 (3–33)	43 (8–140)	317 (14.6–574)	0.002

Rheopheresis effect

Long-term treatment effects

	HD Group with Rheopheresis		
	Pre-Rheopheresis First Session (N = 13)	Pre-Rheopheresis Last Session (N = 13)	*p* Value
Fibrinogen (g/L)	5.9 (5.2–6.5)	3.7 (2.7–4.6)	0.0007
CRP (mg/L)	36.0 (12.0–49.0)	11.5 (2.3–23.1)	0.12
ICAM-1 (ng/mL)	243 (54.0–189)	213 (54.0–159)	0.04
VCAM-1 (ng/mL)	1735 (1324–2150)	2485 (1172–3337)	0.05
E-Selectin (ng/mL)	25.0 (19.0–35.5)	18.0 (14.5–27.5)	0.009
P-Selectin (ng/mL)	45.0 (27.5–53.0)	44.0 (26.0–53.5)	0.69
sCD40L (pg/mL)	46.3 (33.9–81.1)	43.2 (29.9–75.2)	0.83
IL-1β (pg/mL)	1.0 (1.0–1.5)	1.0 (1.0–1.0)	0.99
IL-6 (pg/mL)	6.2 (1.0–17.3)	1.0 (1.0–5.4)	0.32
IL-8 (pg/mL)	11.9 (8.7– 17.7)	10.4 (6.2–14.4)	0.26
TNF-α (pg/mL)	37.8 (29.0–45.1)	40.4 (32.3–50.4)	0.73
IL-10 (pg/mL)	9.6 (5.1–13.1)	3.4 (1.4–8.2)	0.01
Angiopoietin2 (ng/mL)	4.1 (3.0–6.9)	3.0 (3.0–5.8)	0.71
sEndoglin (pg/mL)	662 (574–971)	740 (202.0–1117)	0.73
VEGF-A (pg/mL)	42.0 (25.0–56.0)	30.0 (25.0–53.5)	0.9
CECs (n/mL)	16 (2–34)	10 (2–27)	0.44

Rheopheresis effect

RHEOPHERESIS BIOLOGICAL EFFECTS : Assay of inflammatory and endothelial markers

Extracorporeal circulation effects ?

Hemodialysis patients not treated by rheopheresis (N=10)

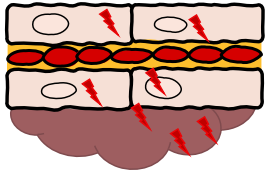
Pre and post dialysis session

⇩

No effect of dialysis sessions

Rheopheresis in tandem with hemodialysis

- Chronic critical limb ischemia (N= 8)
- Calciphylaxis (N=5)



↓ Plasmatic viscosity

Pre and post rheopheresis session

⇩

ANTI-INFLAMMATORY SIGNAL

↓ *Fibrinogen*
↓ *CRP*
↓ *TNF-α*
↓ *VCAM-1*
↓ *sE-Selectin*
↓ *sP-Selectin*

↑↑ *IL-10*

ACUTE EFFECT

PRO-ANGIOGENIC SIGNAL ?

↑↑ *CEC*

↑ *sEndoglin*

THE RHEOPHERESIS TARGETS ENDOTHELIUM AND HAS ACUTE ANTI-INFLAMMATORY EFFECT

Cholesterol embolism and Rheopheresis

68 y Woman, HTA, coronary disease

Disease history:

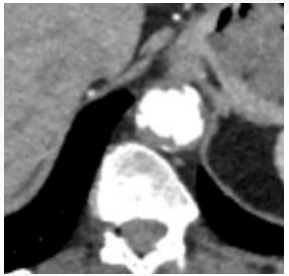
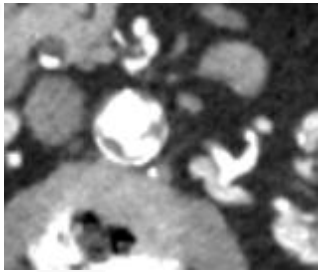
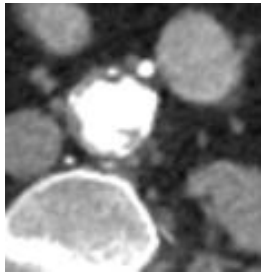
November 2021: First coronarography, femoral access — Creatinin 98 µmol, Double AAP

January 2022: Second coronarography, femoral access — Creatinin 180 µmol, hypereosinophilia, no proteinuria

March 2022: Blue toe syndrom — TCpO2 normal

Creatinin pic 283 µmol and fibrinogen at 5,2 g/L



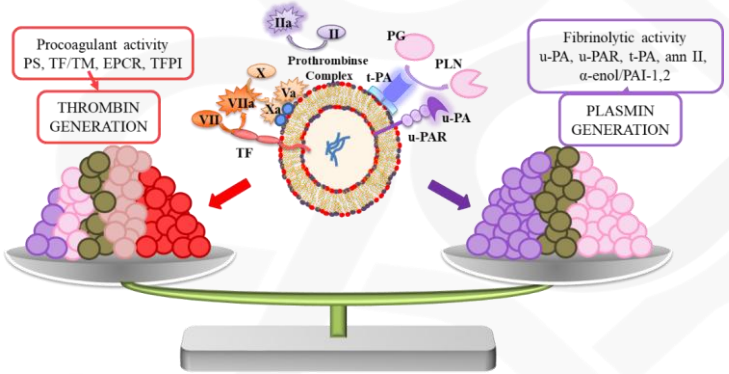
Tunneled catheter and rheopheresis session start after medical optimization for 3 months

One years later : Creatinin 130 µmol/L No blue toe syndrom, no relapse

CLI or calciphylaxis is a prothrombotic condition with defective fibrinolysis

H. Parsson, Eur J Vasc Endovasc Surg, 2004
Radosław Wieczór, J. Clin. Med. 2020

Coagulolytic balance of the microvesicles (MV)



Lacroix et al Thromb Res 2012
Lacroix et al. STH 2013,
Lacroix et al. J Thromb. Haemost 2013
Vallier, Lacroix et al. STH 2017
Berkman, Lacroix et al JEV 2019

MP-TF assay

MP-PGC assay

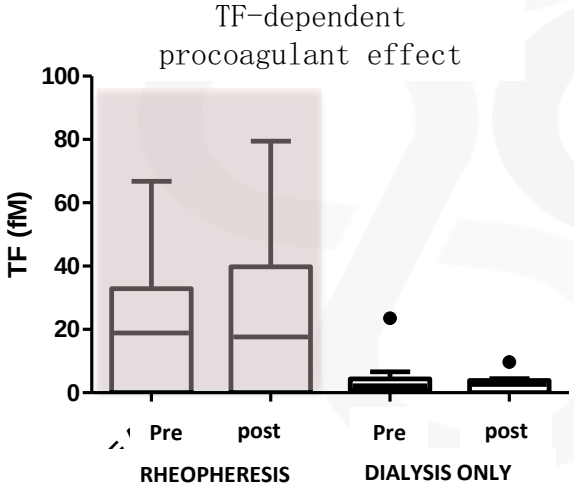
Vallier…et Lacroix Thromb Res 2019
Franco, Lacroix et al. Thromb Res 2020

Cointe …et Lacroix JEV 2018

Microvesicles

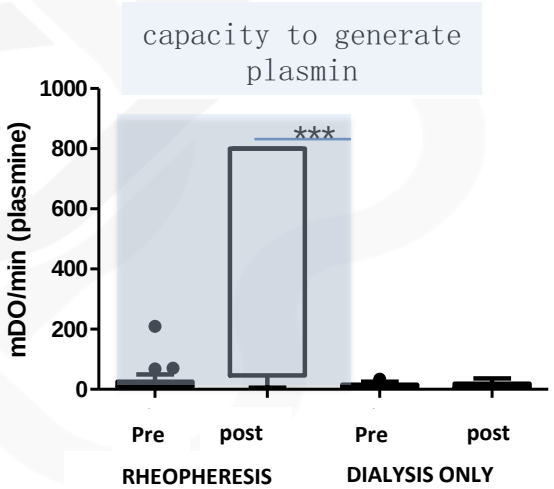
procoagulant activity

Méthod : TF-dependent FXa generation assay
(Vallier et al Thromb Res 2019)



Fibrinolysis activity

Méthod : immunomagnetic separation assay
(Cointe et al JEV 2018)

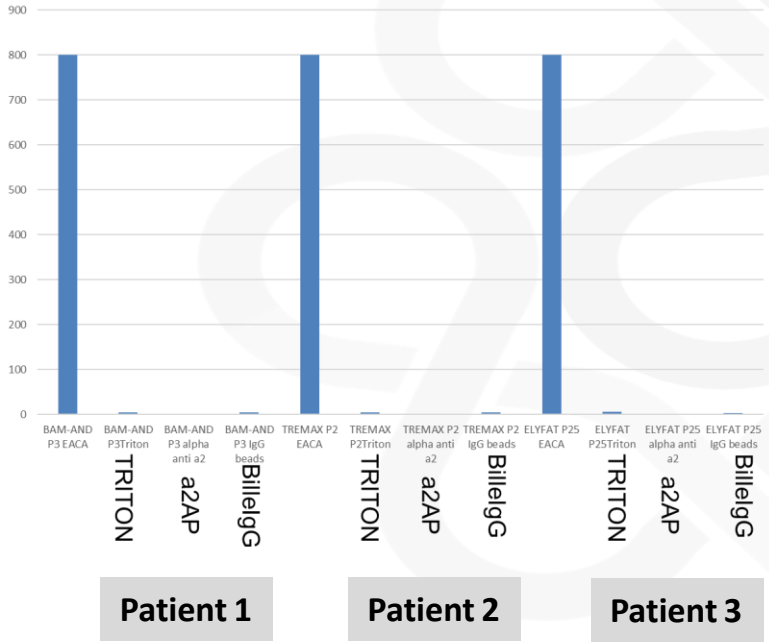


Unpublished data

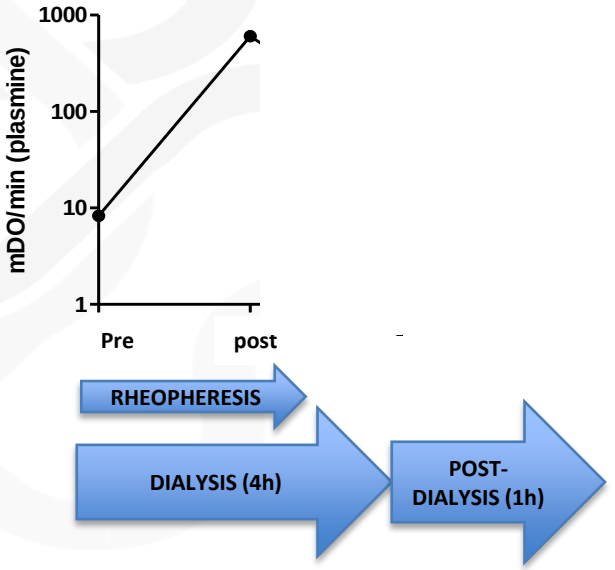
Rheopheresis effect

Microvesicles ***Fibrinolysis activity***

SPECIFICITY



KINETIC



Unpublished data

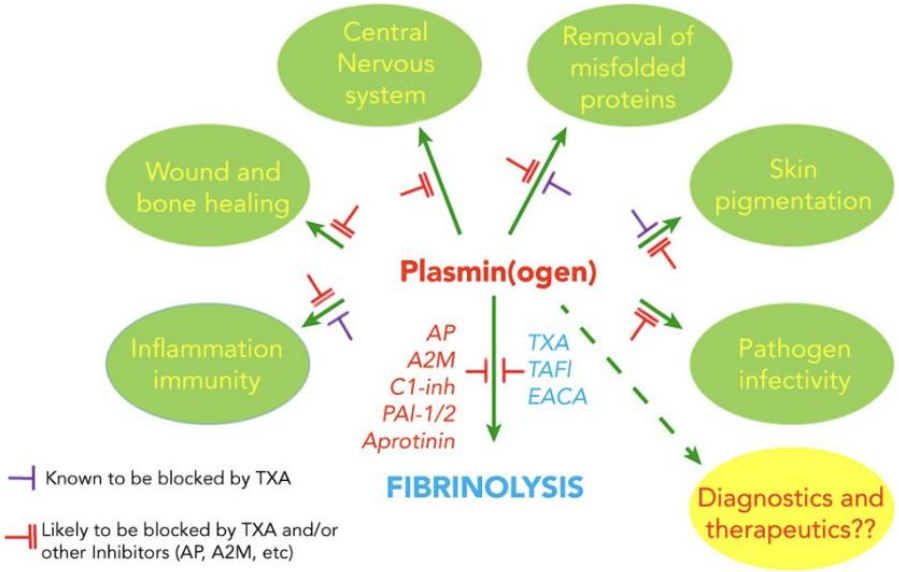
Aix*Marseille université
Initiative d'excellence

Marseille Medical Genetics

Hôpitaux Universitaires de Marseille | ap·hm

Hôpitaux de Provence
Groupement Hospitalier et Universitaire des Bouches-du-Rhône

Rheopheresis effect



Plaminogen span functions in:

- Fibrinolysis,
- Interaction with complement proteins,
- Resolving Inflammation
- Resolution of inflammation
- Wound healing

Rima Sulniute et al. Thrombosis and Haemostasis 2016

Blasi et al. Nature Review 2002

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue **2023**

Journal of Clinical Apheresis ASFA

PERIPHERAL VASCULAR DISEASES

Prevalence: ~5% at 40 to 44 years and ~12% at 70 to 74 years				
Procedure	**Category**		**Grade**	
LA*	II		1B	
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
Acute/short course of treatment**	0	1 (87)	>10 (>200)	NA
Chronic treatment	1 (42)	0	2 (40)	0

*LA in this setting reflects a variety of methods including HELP-apheresis, dextran-sulfate adsorption, DFPP, and others; **includes some patients that transitioned to chronic treatment after an initial short course.

II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.	Grade 1B	Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation

→**La calciphylaxie ne figure toujours pas dans les guidelines**

CONCLUSION

Rheopheresis is a safe modality of therapeutic apheresis to treat microcirculatory disorders

Rheopheresis represent a novel therapeutic approach for critical limb ischemia and calciphylaxis as an adjuvant therapy, a new therapeutic way for cholesterol embolism ?

Rheopheresis mechanisms might be multiples :

- Rheological effect-induced through plasma viscosity (fibrinogen +++)
- Anti-inflammatory effect-induced through IL10 generation
- Thrombolysis and Wound Healing effect-induced through high microvesicul plasmin generation capacity

Remains the infectious risk du to IgG removal which need to be investigated

- What matters most for patients :
  - Quality of life
  - Perception of life

→ We need to investigate soroughly these paramaters

Evidence based fact are lacking and we need trial

NIH U.S. National Library of Medicine
ClinicalTrials.gov

RHEO-PAD
PHRC-N

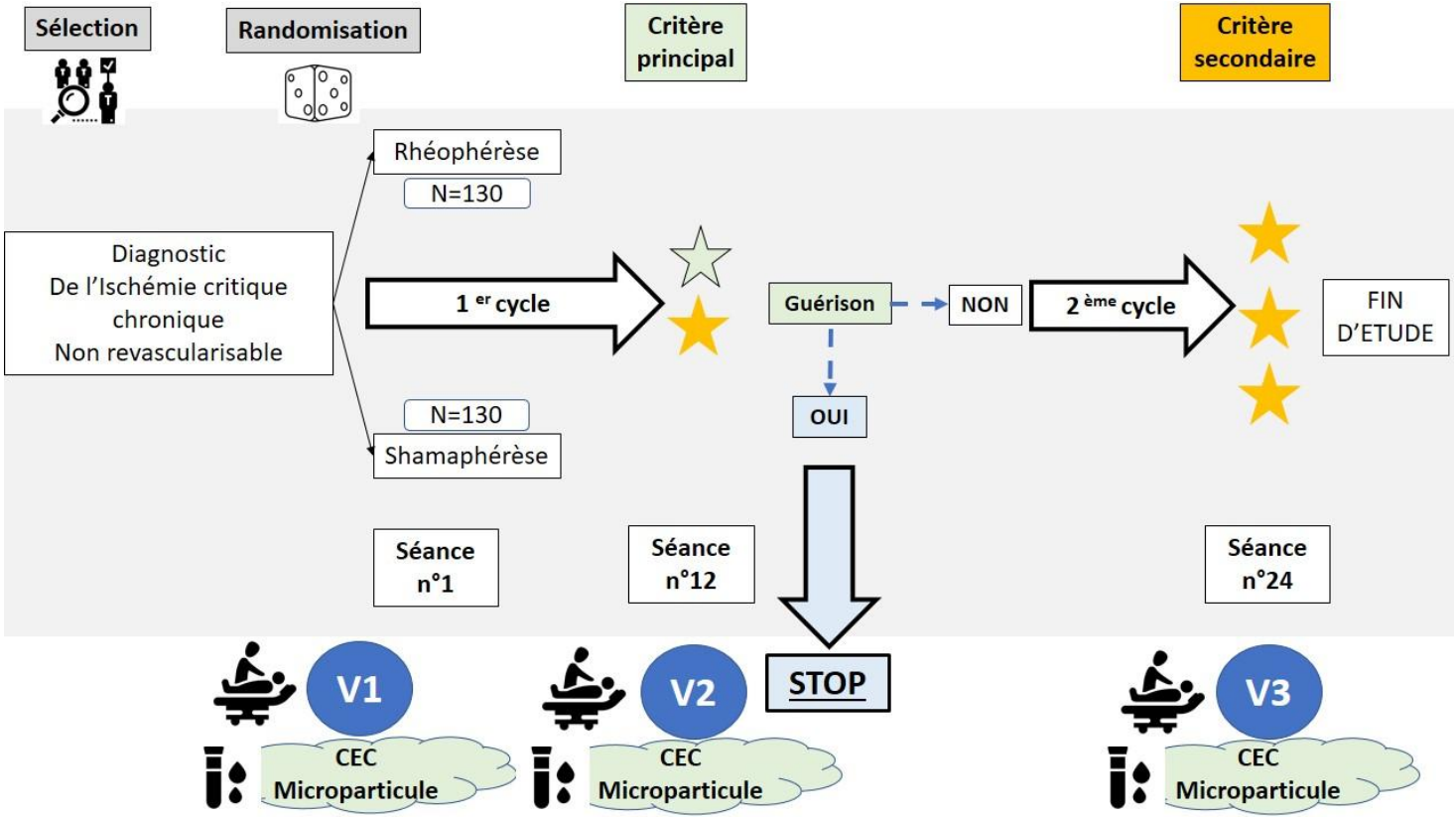
Critical limb ischemia
CHU de Marseille
Dr Thomas Robert

RHEOCAL

Calciphylaxis
CHU de Lille
Dr Arnaud Lionet

MINISTÈRE
DES SOLIDARITÉS
ET DE LA SANTÉ

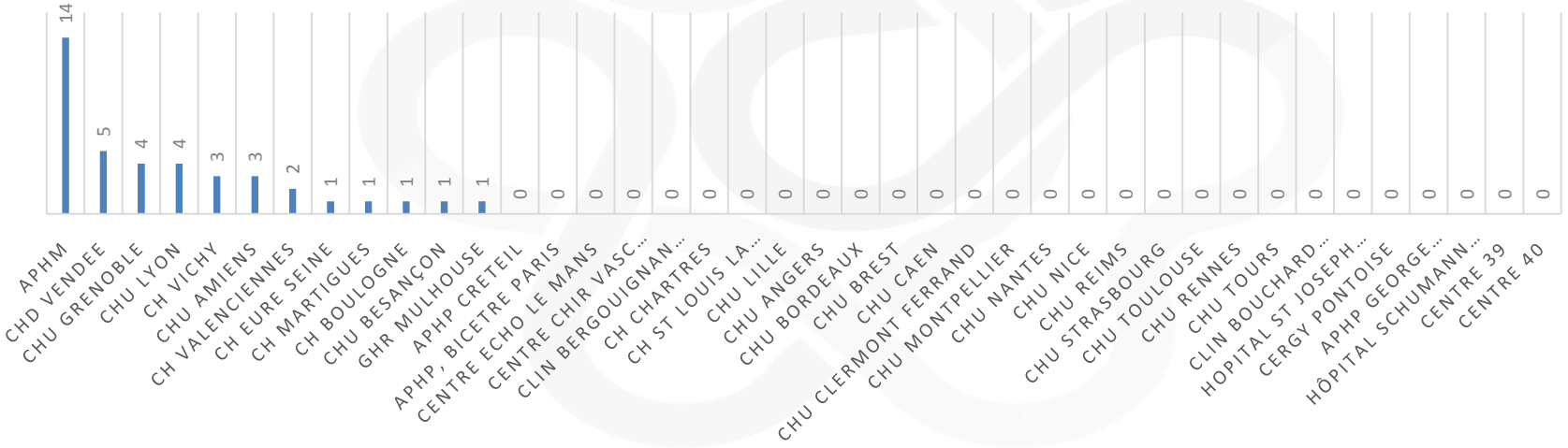
PERSPPECTIVE

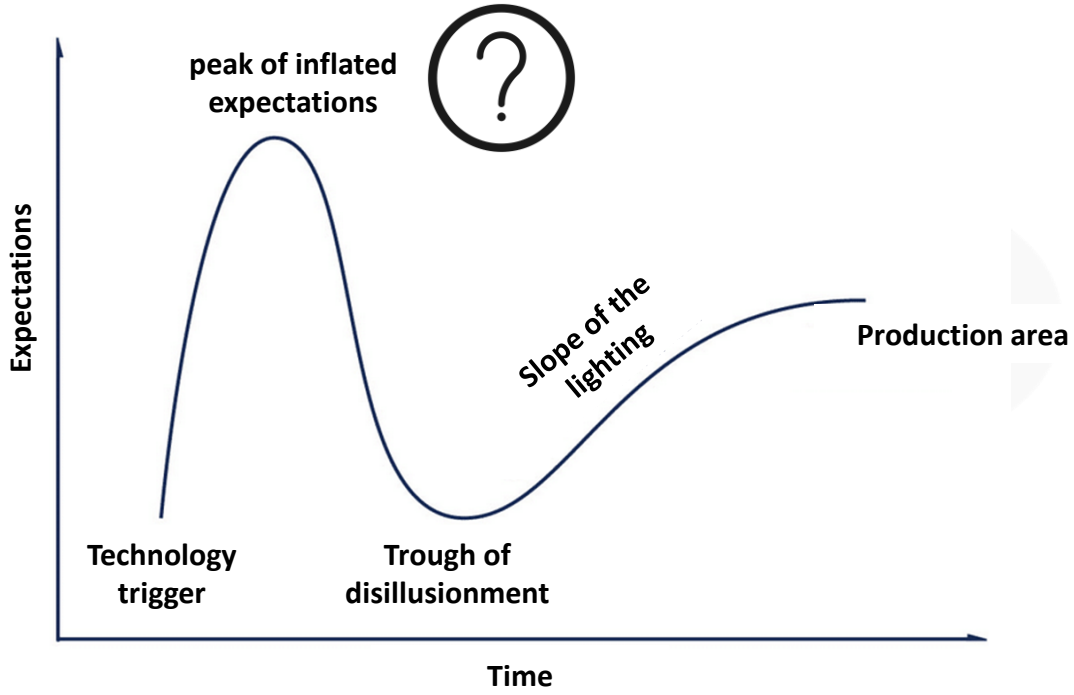


PERSPPECTIVE

RHEO-PAD
PHRC-N

NOMBRE D'INCLUSION




peak of inflated expectations
Expectations
Slope of the lighting
Production area
Technology trigger
Trough of disillusionment
Time

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