

RISK FACTORS OF CHRONIC RENAL
FAILURE :
A single-center preliminary study

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***Objective:* to setup rheopheresis (DFPP) to treat patients with refractory peripheral arteriopathy (early 2015)**

Multidisciplinary approach

- Refractory peripheral arteriopathy : how to manage the very severe patients?
- Multidisciplinary meetings on a monthly basis:
 - Vascular surgeon
 - Vascular physician
 - Nephrologist
 - Diabetologist/diabetic foot physician

- To discuss the medical files of patients with refractory peripheral arteriopathy:
 - Local prostacyclin infusion?
 - Hyperbaric oxygen therapy?
 - Amputation?
 - Is there any other option?
 - **Double-filtration plasmapheresis (DFPP)?**

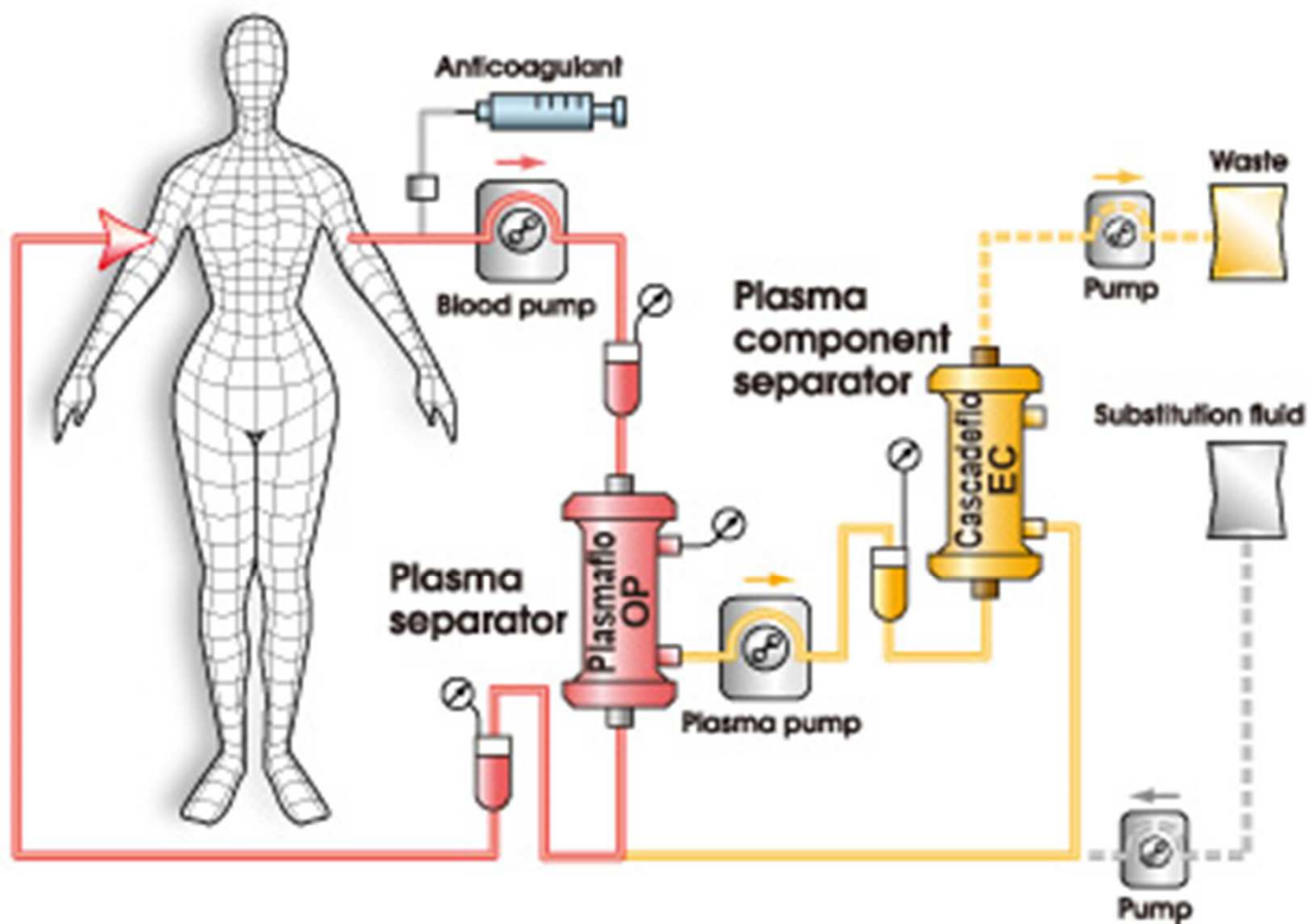
When do we use DFPP in our unit?

- Desensitization protocols for ABOi and/or HLAi kidney-transplant recipients
- Antibody-mediated rejection
- Refractory hypercholesterolemia
- Diabetic foot with severe ischemic lesions
- Stage IV distal arteriopathy in end-stage renal-disease patients
- Age-related macula degeneration

Techniques and Disposables

- Extracorporeal circuit: central venous catheter or arteriovenous fistula
- 1st filter: plasma separation: plasma filtered with Plasmaflo OP-05W
- 2nd filter ER 4000: plasma treatment
- PLASAUTO monitoring: management of the blood circuit and the plasma circuit
- Citrate anticoagulation (on an aspiration line) and CaCl_2 compensation on the return venous line
- ~1.5 plasmatic volumes
- Substitution: 20 g of albumin
- No compensation for coagulation factors
- Monitoring of clinical and biological parameters, including tPCO_2

Circuit diagram



Lipoprotein apheresis (LA) in patients with peripheral artery disease and hyperlipoproteinemia (a).

Poller WC, Dreger H, Morgera S, Berger A, Flessenkämper I, Enke-Melzer K.

Atheroscler Suppl. 2015 May;18:187-93.

Abstract

OBJECTIVE:

Hyperlipoproteinemia(a) [Lp(a)-HLP] is a major risk factor for severe atherosclerosis. The present investigation sought to assess the effect of lipoprotein apheresis (LA) in patients with peripheral artery disease (PAD) and Lp(a)-HLP.

CONCLUSION:

LA improves circulation, oxygen supply, level of pain and walking distance in patients with severe PAD and Lp(a)-HLP. The frequency of revascularization procedures is strongly reduced under LA treatment.

Objectives of rheopheresis

- Means:
 - To improve blood flow at the microcirculation level
 - To improve viscosity
 - To reduce high molecular-weight molecules
- Results
 - Improvement in tissue oxygenation
 - To accelerate wound healing
 - To reduce the need for amputation

Molecules that are removed

- Fibrinogen
- Alpha-2 macroglobulin
- Cholesterol/triglycerides
- LDL, Lp(a)
- Fibronectin
- IgM
- Orosomucoid
-

Patients

- 6 patients with severe distal arteriopathy: of these
 - One chronic hemodialysis patient aged 67 with toes and fingers necrosis
 - One chronic hemodialysis patient aged 54 with ischemic toes on one foot
 - One type I diabetic hemodialysis patient aged 49 with ischemic toes on 1 foot plus ischemic ulcer on Achille's heel on the other foot
 - One diabetic hemodialysis patient aged 48 with bilateral necrosis on the feet
 - One diabetic non-dialyzed (eGFR = 40 mL/min) patient aged 65 with distal necrotic lesions on both feet
 - One kidney transplant patient aged 52 with chronic kidney disease (eGFR= 30 mL/min) and a single necrotic toe

Implementation of rheopheresis in our unit

- Support from HemaT with an onsite very efficient trainer for 3 weeks
- 100% of our nursing staff are now trained
- The nursing staff are very motivated (innovative techniques)
- Very close collaboration between nurses and physicians
- No rheopheresis conducted at weekends

=> scheduling is modulated

1st patient: Mr Delv....

- Age: 66 years
- Chronic hemodialysis since 1991; HCV (+)/ RNA (+)
- 1993 : 1st kidney transplantation
- 2003 :
 - End-stage renal disease (chronic rejection)
 - Calciphylaxis (toes): daily hemodialysis, hyperbaric oxygen therapy: good outcome
 - Parathyroidectomy
- January 2006 :
 - 2nd kidney transplantation
 - Hyperparathyroidism recurrence (Cinacalcet)
- June 2014: arterio-venous fistula setup
- August 2014: return to hemodialysis
- Nov. 2014: ligation of arterio-venous fistula because of downstream finger necrosis

Vascular history

- Right arm:
 - Nov. 2014: necrosis of fingers; ligation of humero-cephalic artereo-venous fistula; amputation of some fingers.

- Left lower leg:
 - Diffuse mediocalcosis; numerous lesions; dry necrosis of toes; trans-tibial amputation with delayed wound healing; pain +++++

- Right lower leg:
 - Necrotic cutaneous lesions of four toes, plus the above disorders.
 - May 2015: rapid onset of osteoarthritis of the 1st metatarsal; ineffective antibiotherapy;
 - At this point we started DFPP sessions

Finger necrosis, downstream of arterio-venous Steal syndrome



Rheopheresis protocol

- 2.5--3 L of plasma
- 9.5--11.5 L of treated blood
- Blood flow: 60--100 mL/min
- ACDA: 1/60, then decreasing to 1/80
- ClCa: 4 cm³/h, then 2 cm³/h
- Substitution: 20 g of albumin during the session
- Tandem procedure with hemodialysis

DFPP program

- 1st week: 2 sessions = 2
- 2nd and 3rd weeks: 3 sessions = 6
- 4th and 5th weeks: 2 sessions = 4
- 6th to 23rd week: 1 session = 16

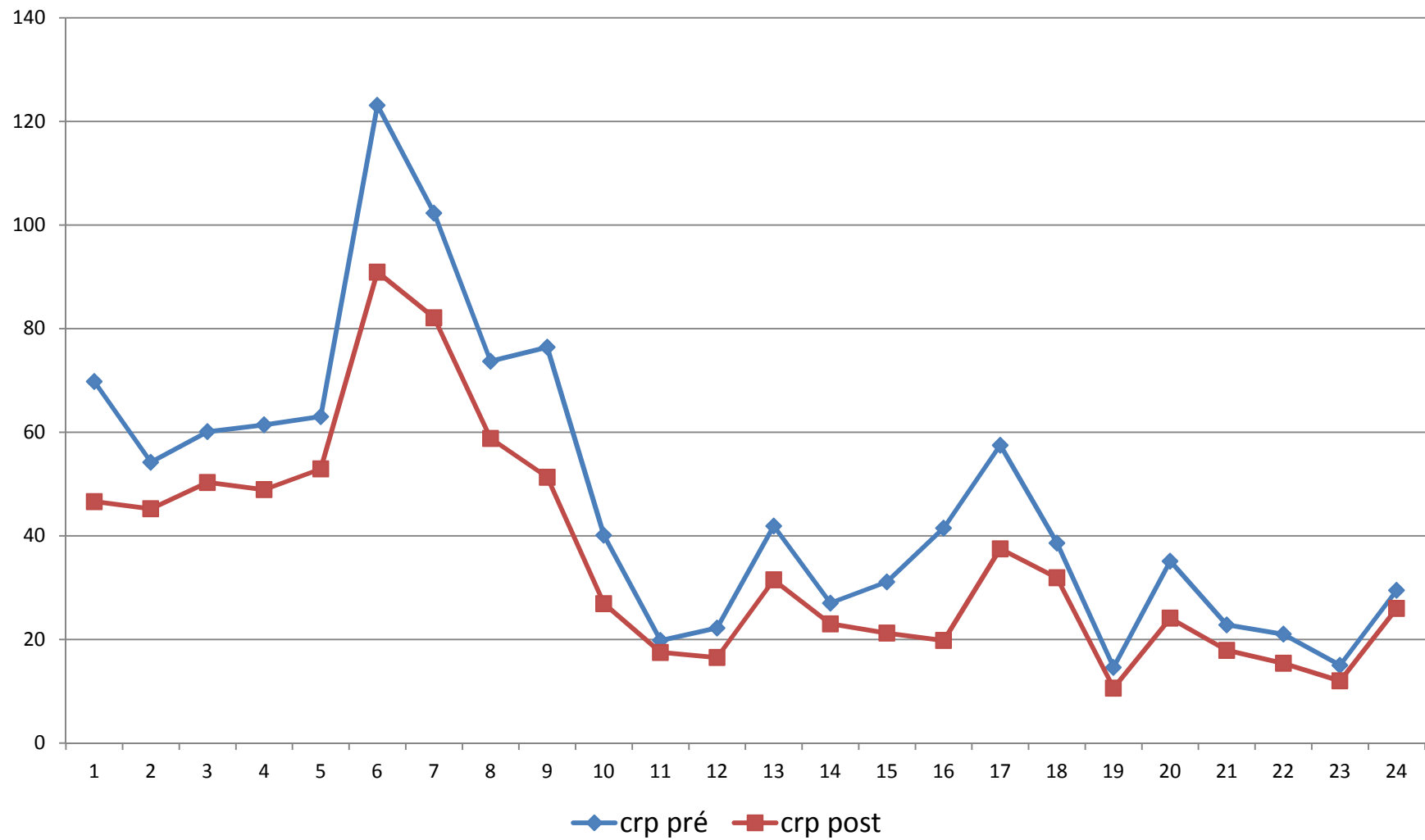
(1 week w/o DFPP)

- At the moment: 1 session every 2 weeks
- Total : **29 sessions in 6 months**

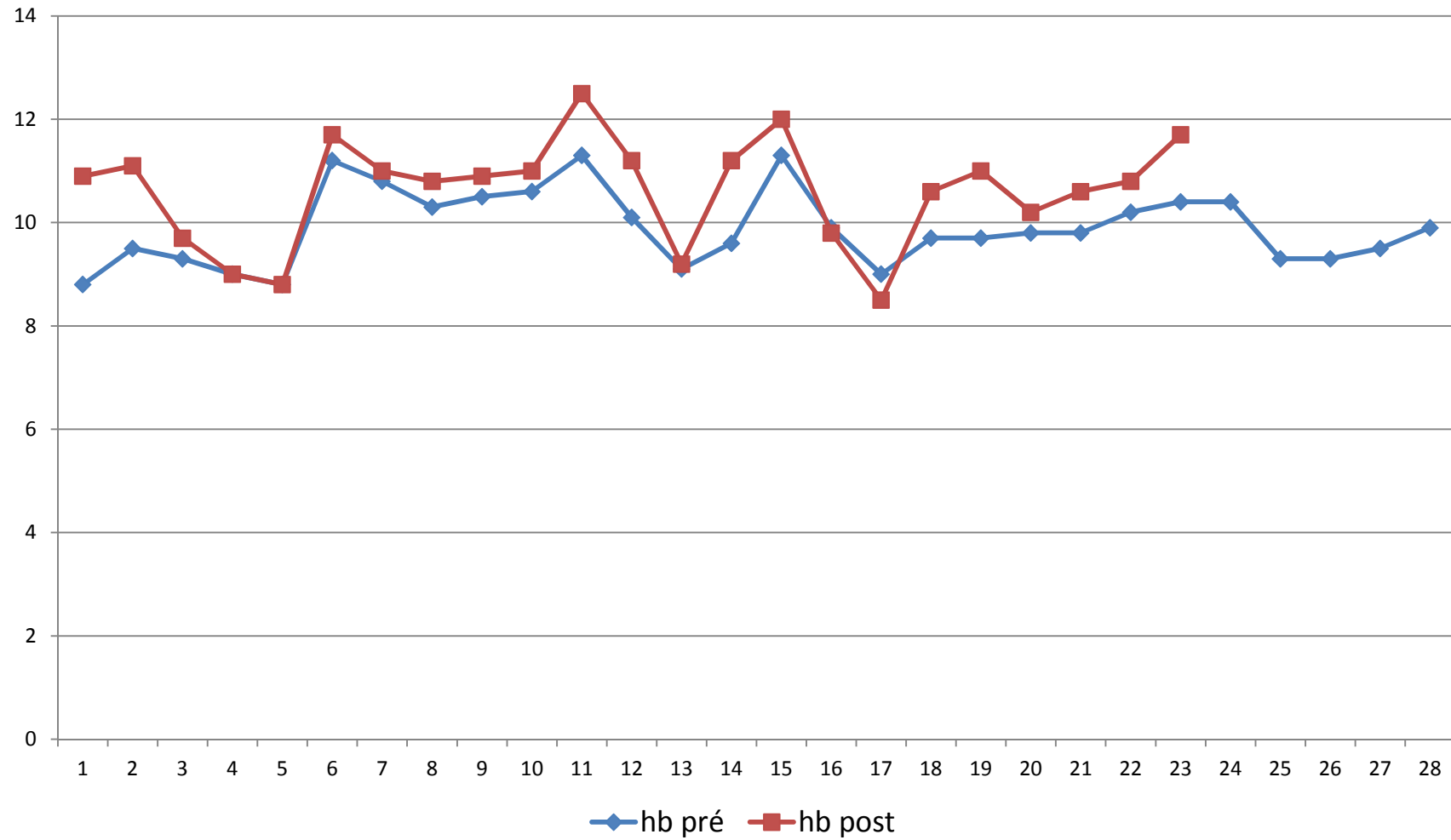
Pain, general status

- Reduction of major analgesics
 - First 2 weeks: 1 vial paracetamol/d + 1 vial of nefopam chlorhydrate/d + oxycodone chlorhydrate 5 mg/d
 - 3rd week: 1 vial of nefopam chlorhydrate/d + oxycodone chlorhydrate 5 mg/d
 - 4th & 5th week: 1 nefopam chlorhydrate on demand +/- paracetamol +/- oxycodone for cutaneous care (10 dfpp)
 - 6th week: analgesics are very rarely taken (13 dfpp)
 - At present NO analgesic, 29 dfpp
- Steady increase in dry weight; improvement of general status.

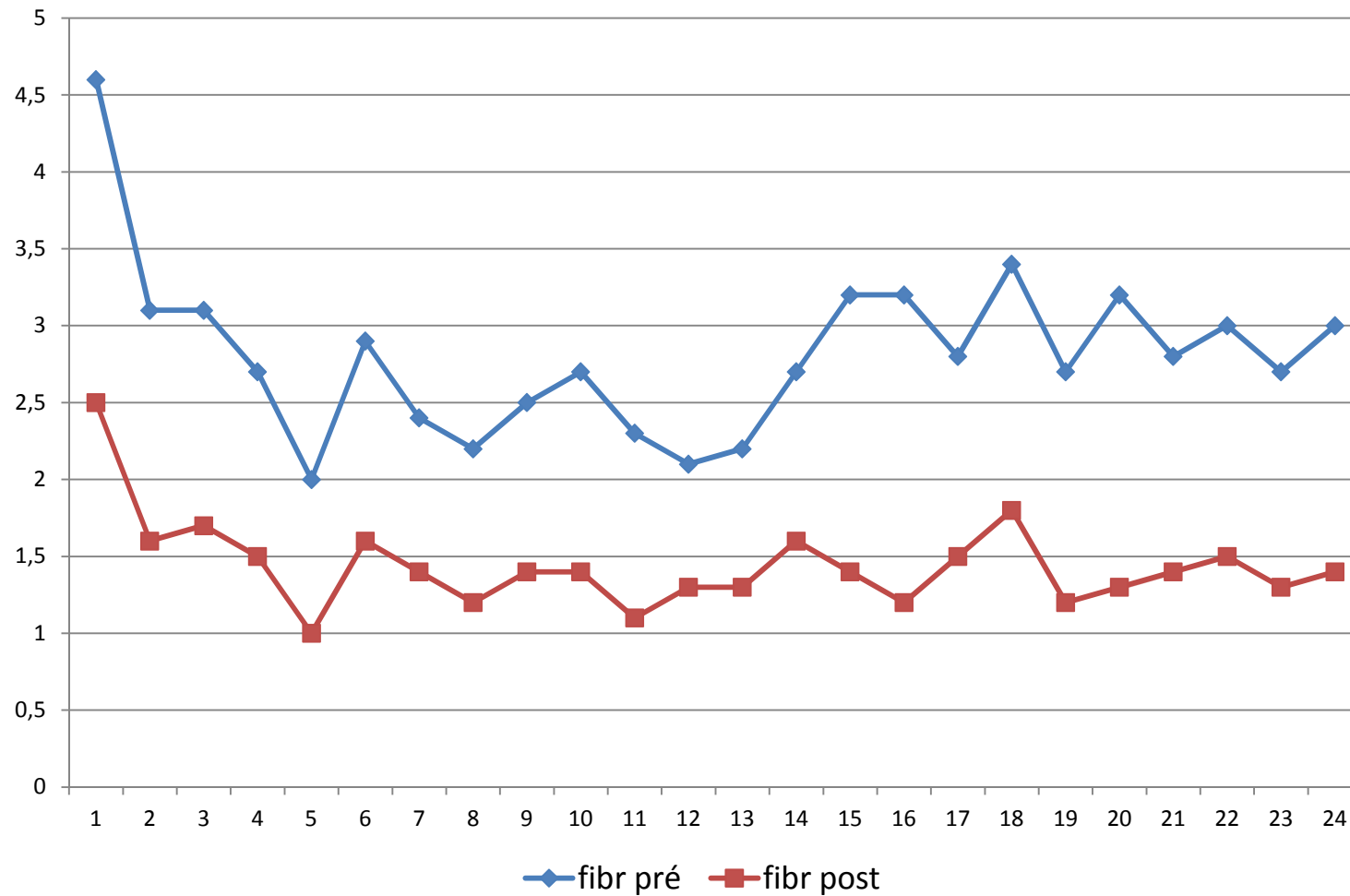
CRP at pre- and post-DFPP



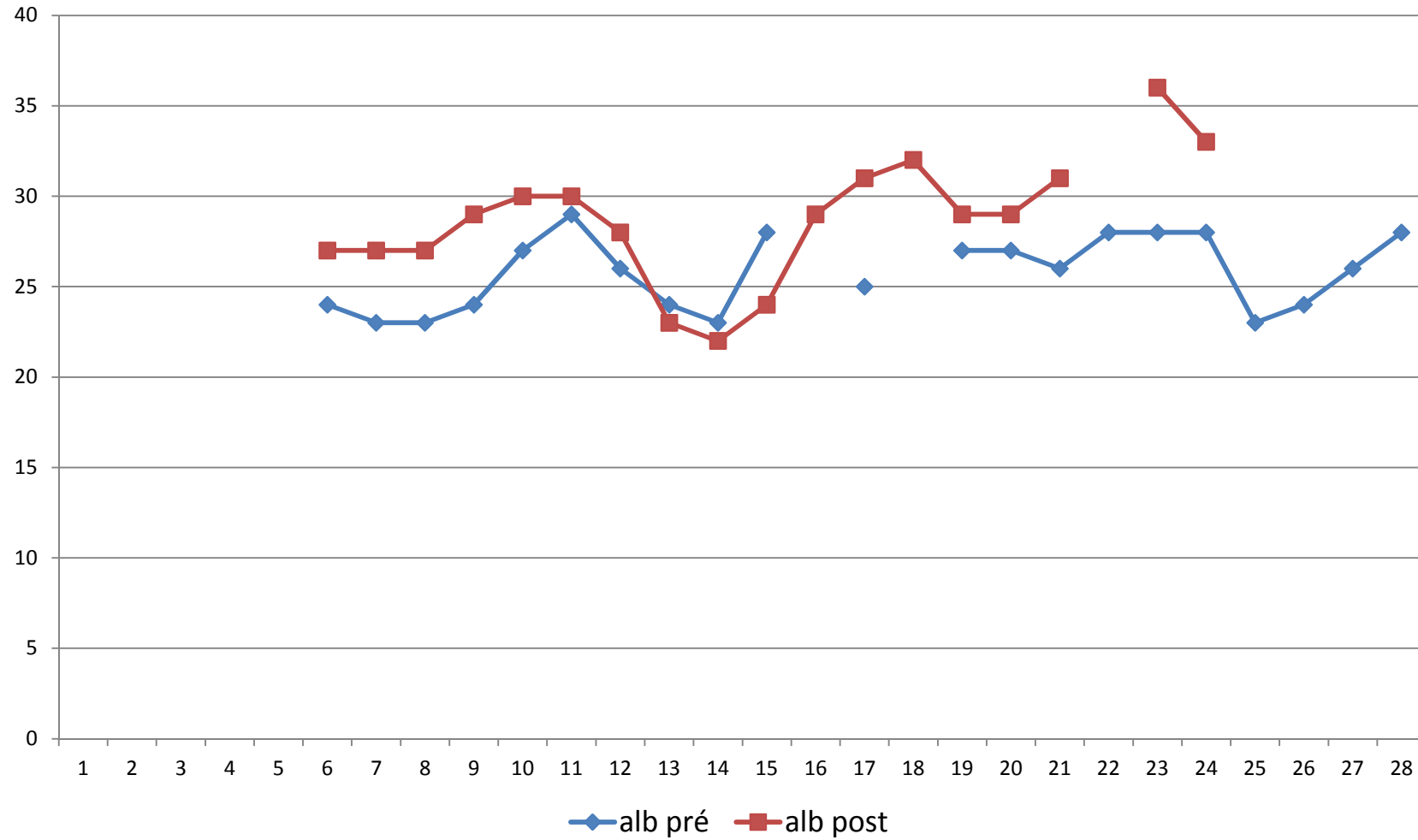
Hb at pre- and post-DFPP



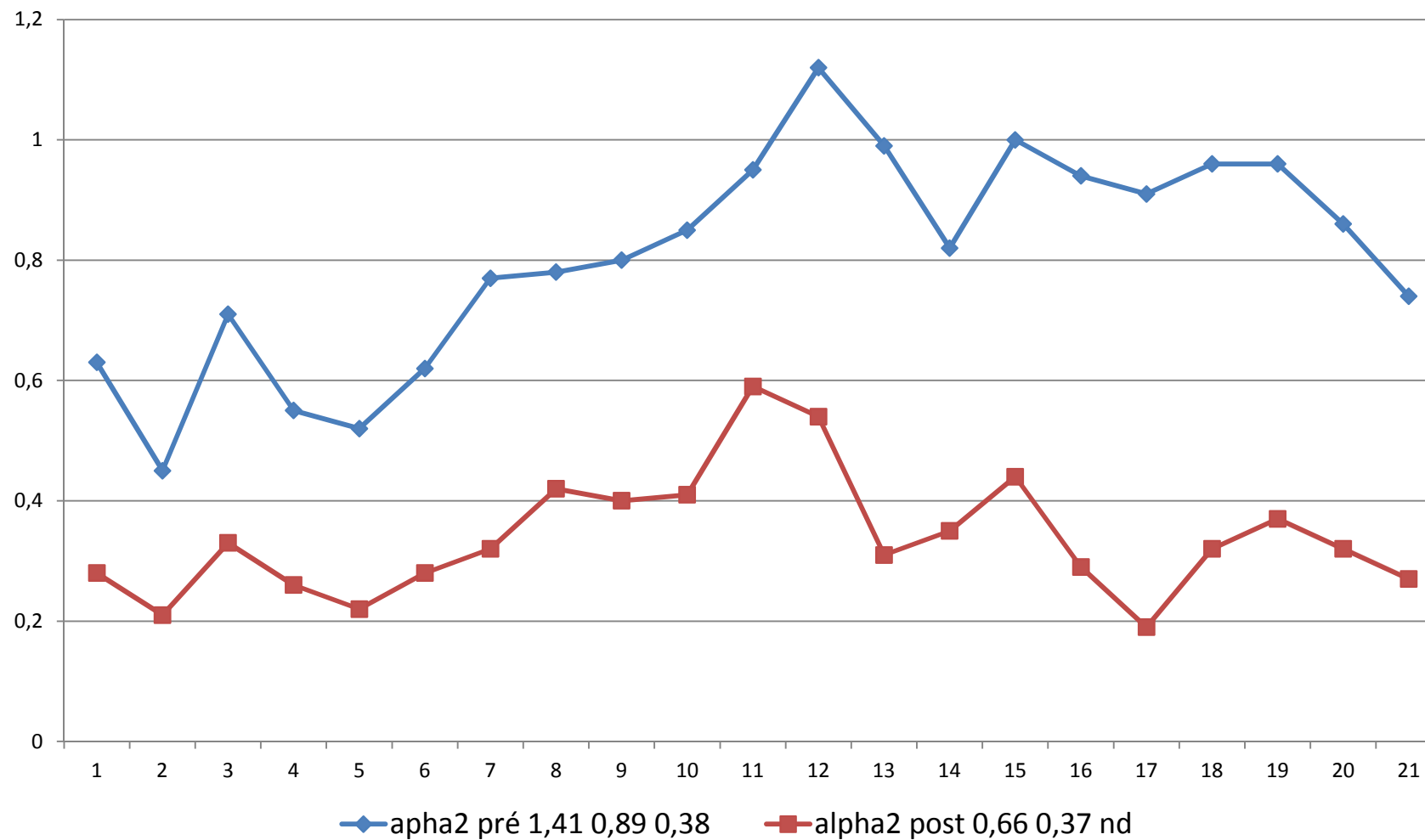
Fibrinogen at pre- and post-DFPP



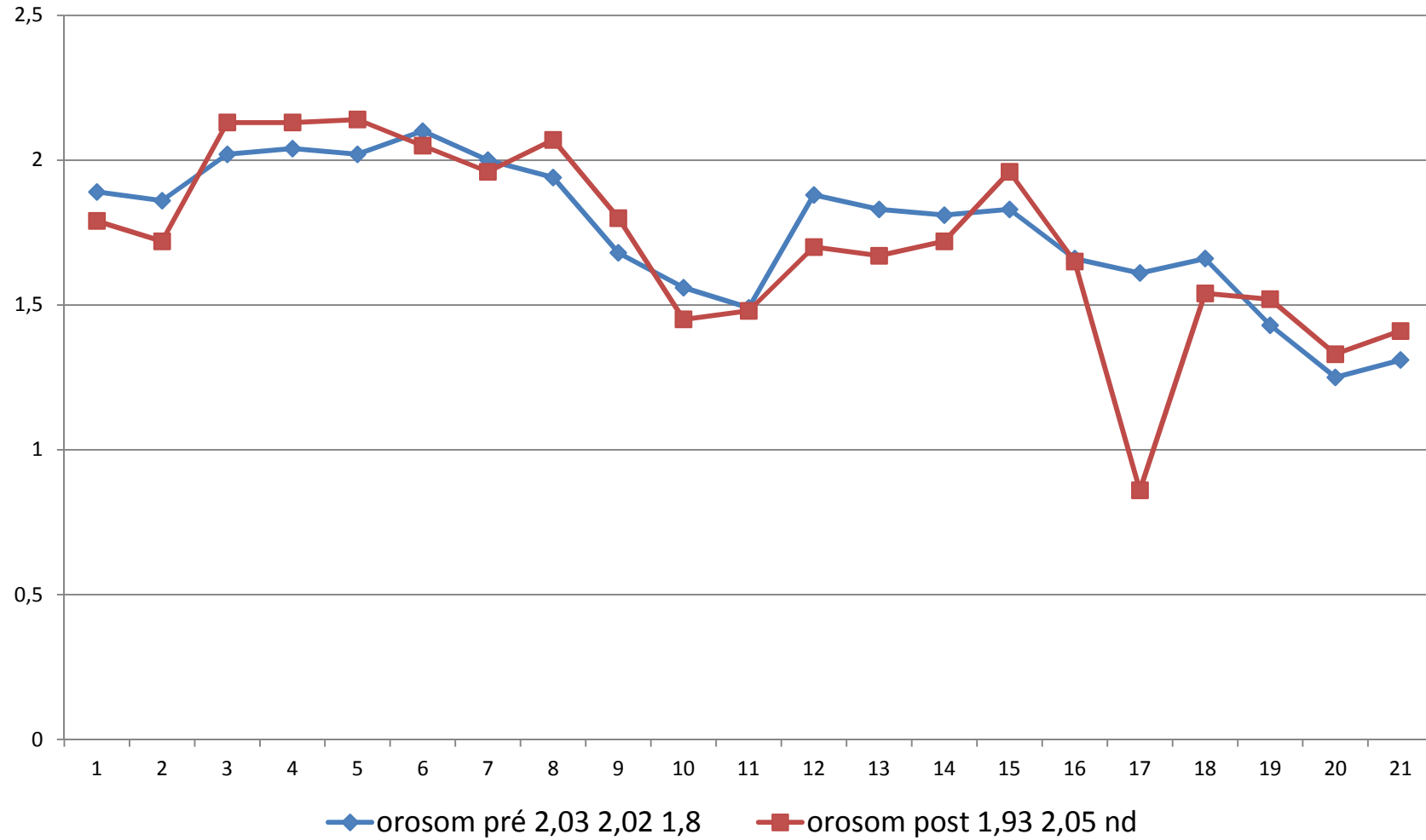
Albumin at pre- and post-DFPP



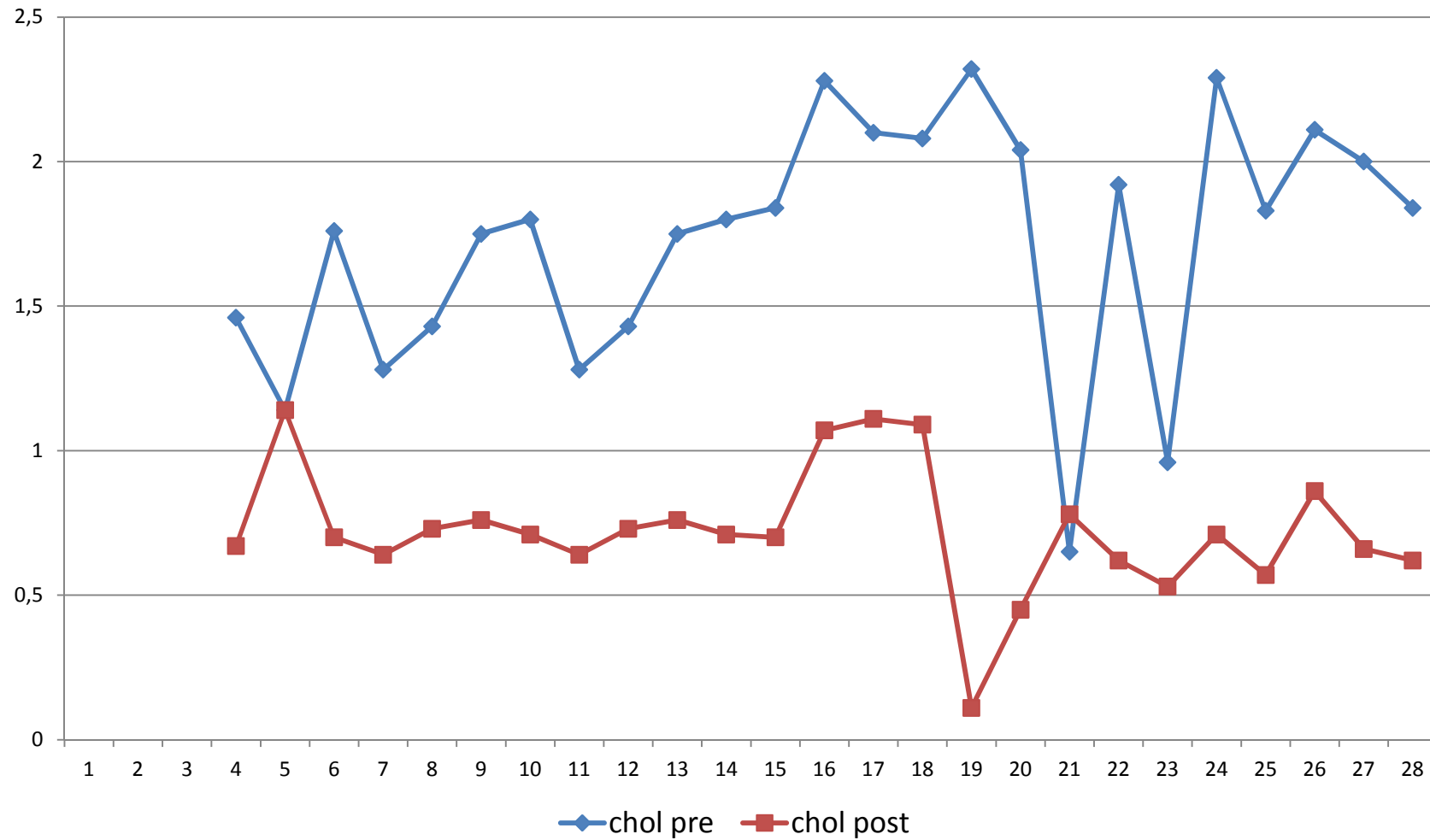
Alpha 2 macrog at pre- and post



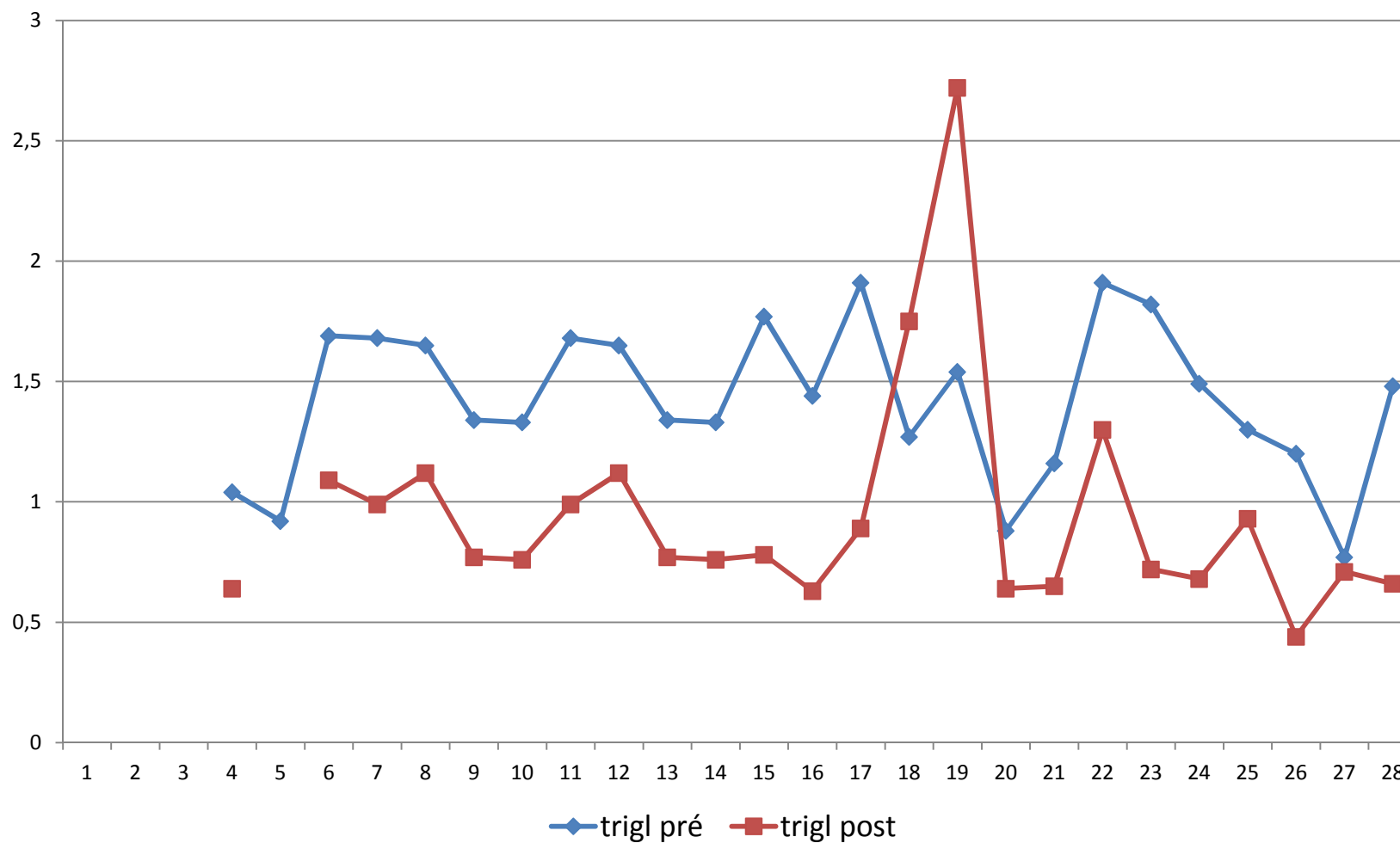
Orosomucoïd at pre- and post-DFPP



Total cholesterol at pre- and post-DFPP



Triglycerides at pre- and post-DFPP



22nd May 2015 after 10 DFPP sessions



Before DFPP



June 16th 2015, 14 DFPP sessions



tCPO₂ outcomes

	06/02/2015	Before DFPP	18/05/15	9 DFPP
	right	left	right	left
Foot	5	53	71	Amputated
1/3 distal leg	41	26	45	Amputated
1/3 proximal leg	43	45	57	ND
1/3 distal thigh	44	82	ND	ND

Surgery

- Because of these improvements, surgery could be limited:
 - Trans-metatarsal amputation
 - Left hand finger amputation

26/8/15, 24 DFPP sessions



26/09/15, 28 DFPP sessions



29 DFPP sessions

5/10/15



10/10/15



As of 23/10/15, DFPP
every 2 weeks

01/16 / healing

23/10/15 DFPP TOUS LES 15 JOURS



April 2016

DEL....AVRIL 2016



2nd patient

- Mr Len... aged 64 years
- Type II insulin-dependent diabetes
- Hypertension
- Ischemic cardiopathy (multiple stents)
- Renal artery stents
- Aorto-bifemoral bypass
- Distal arteriopathy (stage IV) with 3 months of hospitalization and vascular surgery

Patient 2 (cont'd)

- January 2015: emergency arterial femoro-popliteal bypass due to toe necrosis (right foot)
- May 2015: thrombosis and an arterial femoro-popliteal bypass, delayed wound healing, major pain, super infections.
- May 2015: last-chance treatment: DFPP, using a central venous catheter
- July 2015: had to stop DFPP because of infection around the central venous catheter. Skin lesions were partially improved, but the patient had to undergo toe amputations on both feet

Patient 2 (cont'd)

- 19 May until 21 July: 16 DFPP sessions (3 L of plasma were treated each time)
 - 3 times/week for 2 weeks
 - 2 times/week for 2 weeks
 - 1 time/week for 5 weeks
- July: DFPP was stopped due to catheter tunnelitis
- End of July: toe amputation
- September 2015: the patient was doing well

3rd patient

- Mrs Gran....., aged 48 years
- Type 1 diabetes
- Chronic hemodialysis for 11 months
- Distal arteriopathy (stage IV); very low tPCO₂ in both legs
- May 2015: right arterial femoro-popliteal bypass + right iliac artery stenting
 - However, huge pain. Thus, we decided to implement DFPP
- June 2015: rheopheresis: 7 DFPP sessions,
 - 3 times/week for 1 week
 - 2 times/week for 2 weeks

Patient 3 (cont'd)

- July 2015: Severe sepsis + endocarditis + distal critical ischemia of the left lower limb: transfemoral amputation
- September 2015: necrosis of the right large toe; result: a favorable outcome
- October 2015: good general health; no skin lesions

3RD PATIENT



So far....

- We treated 6 patients
 - Pt 1 : 29 sessions: alleviation of pain; limitation of amputation
 - Pt 2: 16 sessions: alleviation of pain; limitation of amputation (stop because of catheter tunnelitis)
 - Pt 3: 7 sessions : alleviation of pain; limitation of amputation (stop because of sepsis)
 - Pt 4 : 9 sessions: alleviation of pain; limitation of amputation
 - Pt 5: 19 sessions; still ongoing; no amputation; alleviation of pain
 - Pt 6: 28 sessions; still ongoing; no⁴² amputation; alleviation of pain

Conclusion

- DFPP is well tolerated
- Problem with vascular access in non-dialysis patients
- Spectacular results with regards to pain (soon after 5 DFPP sessions)
- Multidisciplinary approach with the major aim of avoiding/reducing amputation
- tPCO₂ monitoring
- Earlier DFPP treatment could be valuable
- DFPP treatment could limit the extent of amputation: thus, help rehabilitation after amputation.