

# EFFICACY AND SAFETY IN THE TREATMENT OF RENAL GRAFT ANTIBODY MEDIATED REJECTION

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## OBJECTIVES

To conduct comparative assessment of therapeutic plasma exchange (TPE) and double filtration plasmapheresis (DFPP): to evaluate the efficacy of reduction of the concentrations of antibodies, the influence on biochemical parameters, hemostasis and blood concentrations of tacrolimus.

## METHODS

### PATIENTS

Prospective randomized study in 58 recipients with renal graft antibody mediated rejection (C4d+) was conducted. 28 recipients received treatment with DFPP method, 32 – with TPE method. All patients underwent 3-4 sessions.

### ANTICOAGULATION

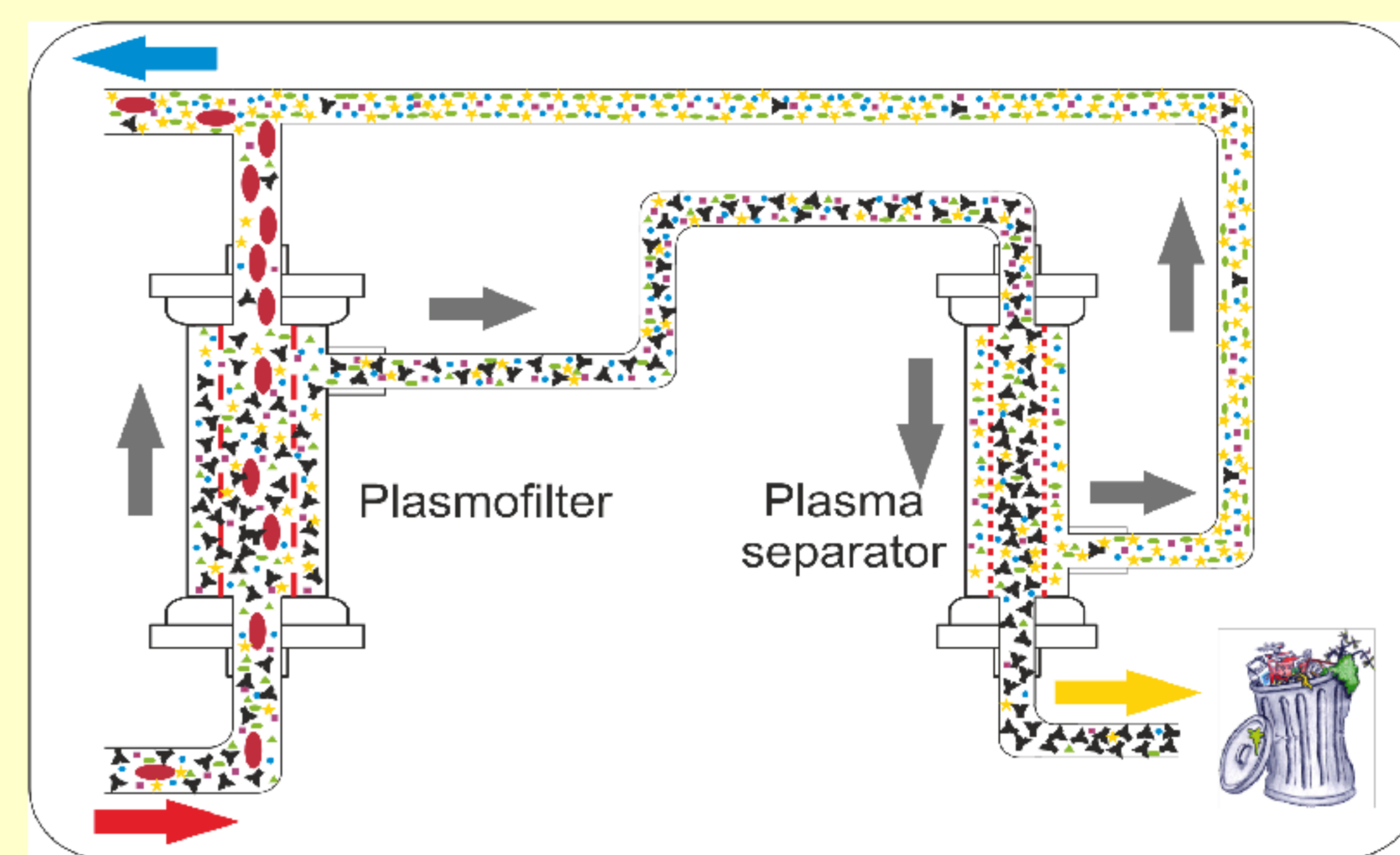
During TPE we used 4% sodium citrate solution in a ratio of 1:16.

During DFPP we used heparin: 20 units/kg bolus prior to beginning the procedure, and then 1000 units per hour via infusion pump.

### PROCEDURES

TPE was performed on plasmofilter with maximum pore size of 0.3 microns. During one session of TPE, 2.5±0.6 L of plasma were removed.

When conducting DFPP (fig. 1), the similar plasmofilter was used and the separator of plasma components was consistently included in extracorporeal circuit: maximum pore size of 0.03 nm; effective surface area of 2 m<sup>2</sup>. During single session of DFPP, 2,8±0,8 L of plasma was treated within the framework of “one way” regime or recycling (regime of thermofiltration).



When conducting DFPP, the plasma replacement was not performed, while during TPE abundant plasma replacement “drop for drop” or more was necessary – tab. 1. In addition, after TPE and DFPP was administered intravenous immunoglobulin G: 100 mg/kg

Table 1

Removed plasma volume	Fresh frozen plasma, ml	Albumin 10% solution, ml	Crystalloids, ml
<50% circulating plasma volume (CPV)	600-1000	100	400
50-70% CPV	1000-1500	200	400
70-90% CPV	1500-2000	300	800
90-110% CPV	1500-2000	400	800

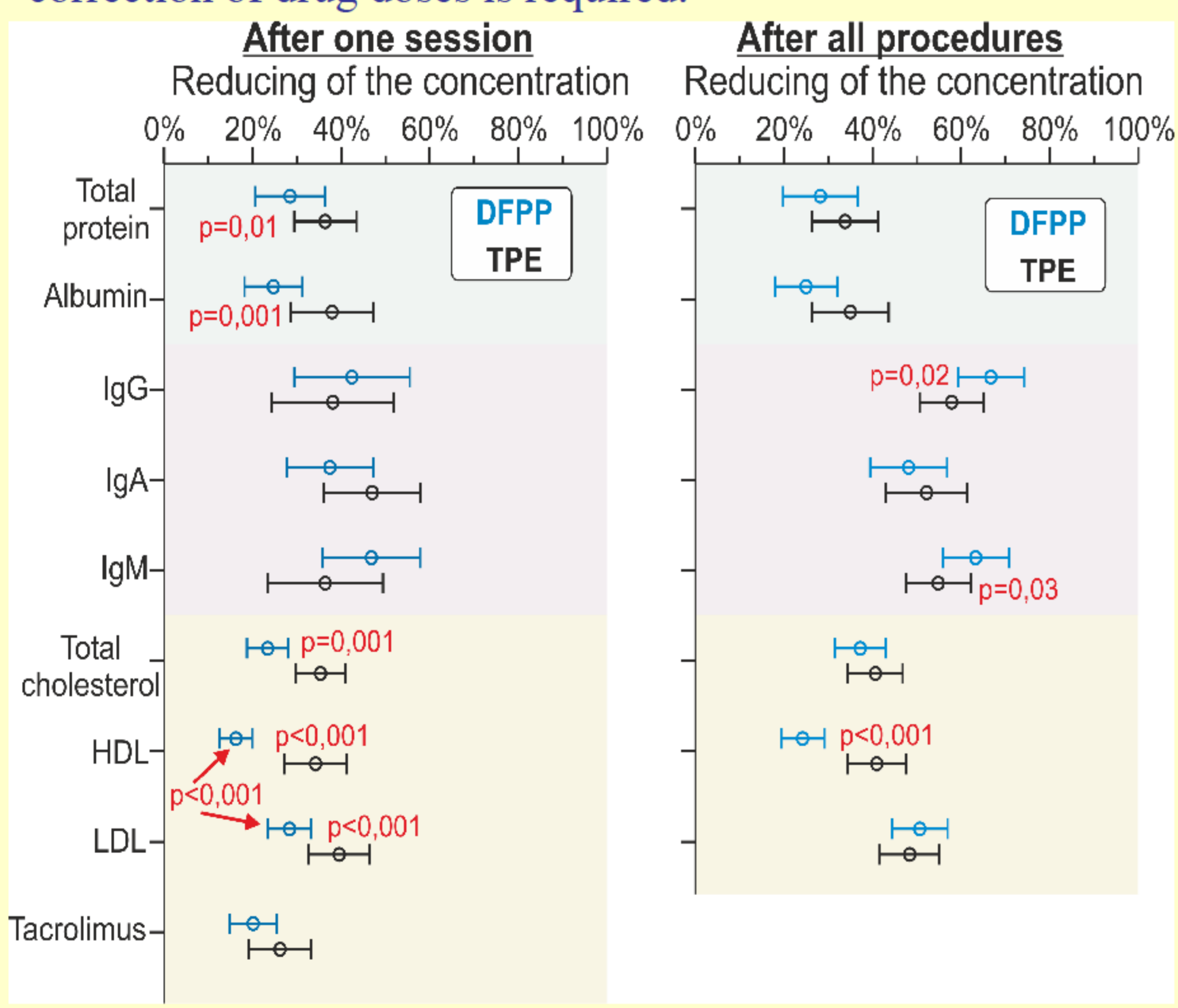
## RESULTS

The decrease in concentrations of IgG and IgM was significantly greater when using DFPP. Thus, the preferential removal of IgM could be of the great value in acute rejection treatment.

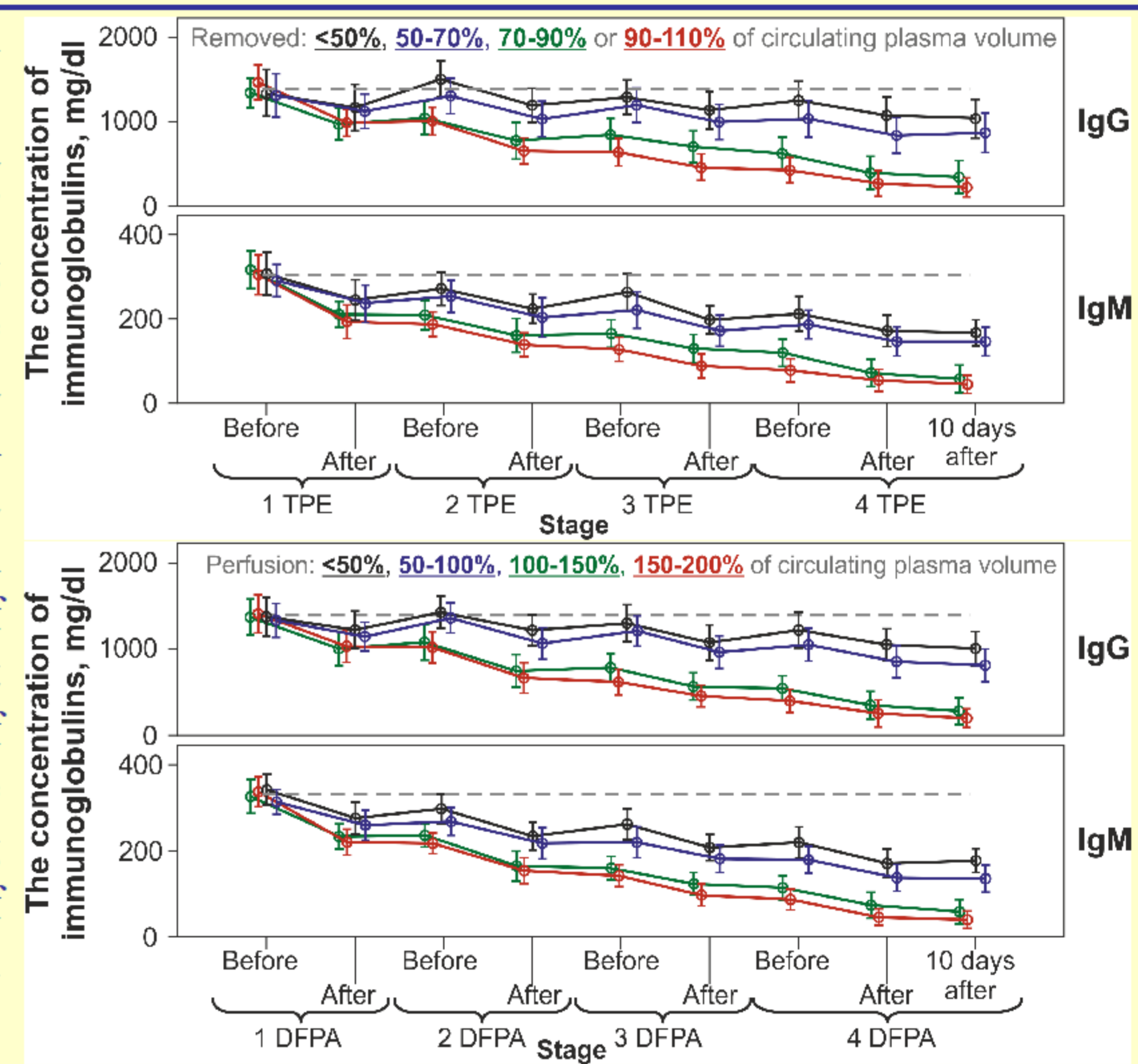
When conducting DFPP, the loss of albumin was significantly lower (p=0.01). This can be important if it is necessary to conduct the procedures for the patients with baseline hypoalbuminemia and hypotension.

TPE leads to equivalent reduction of HDL and LDL. DFPP primarily reduces the concentration of LDL and thereby significantly improves the atherogenic potential of plasma.

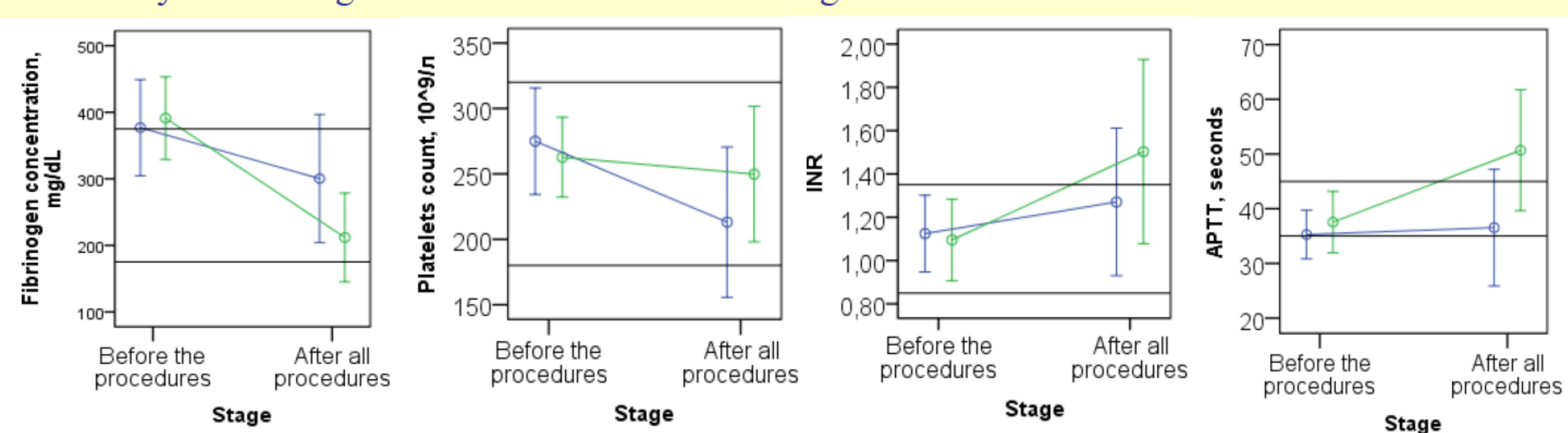
Both TPE and DFPP contribute to the decrease in C0 of tacrolimus in blood of about 15-20%. In this regard, the correction of drug doses is required.



Some patients had the increase in concentrations of IgG and IgM in 1-2 days after the first and second procedures. This effect of “rebound” was observed when conducting DFPP, if less than 100% of volume of circulating plasma was processed during one procedure, and less than 70% of volume of circulating plasma were removed during conventional TPE. In this case, the effectiveness of even the whole course of treatment was low. During the procedure of perfusion of increasing doses, the efficiency was good – the strong decrease in concentrations of antibodies and good clinical dynamics were achieved.



As a result of abundant plasma replacement when using TPE, the platelet count, INR (international normalized ratio), APTT (activated partial thromboplastin time), fibrinogen remained within the normal range. At the same time, DFPP statistically significantly reduced the levels of fibrinogen concentration (p=0.01). Consequently, the patients with baseline deficiency of fibrinogen had the increase in bleeding risk.



## CONCLUSIONS

- DFPP, as well as TPE are effective methods of the treatment of humoral rejection of renal graft only in case of sufficient dose of the procedure.
- Due to various influence on the biochemical parameters and hemostasis, indications for TPE and DFPP can vary considerably.
- In the case of high volume procedures it is necessary to monitor the parameters of hemostasis and the tacrolimus blood concentration.

