

Immunoabsorption plasmapheresis with tryptophan adsorbents in dilated cardiomyopathy

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Introduction:

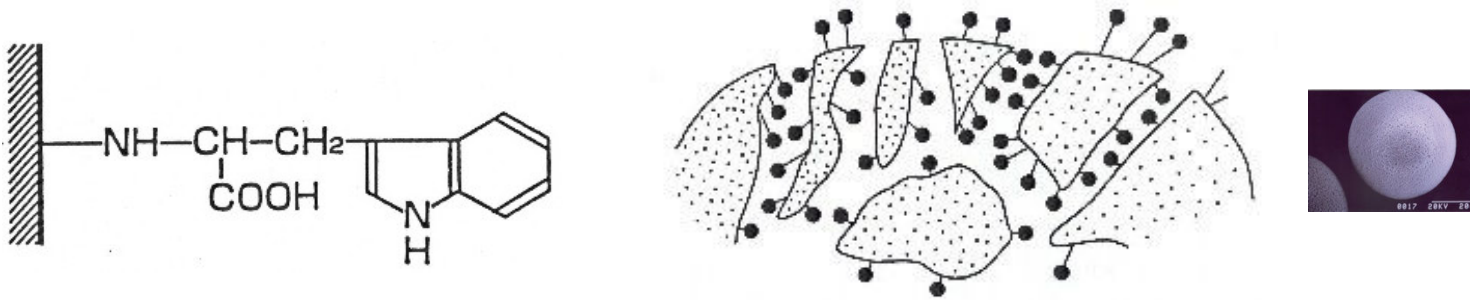
Removal of cardiodepressant autoantibodies has been reported to induce early haemodynamic improvement in patients with dilated cardiomyopathy (DCM). Immusorba TR-350 (Asahikasei-Kuraray Medical Co., Ltd., Japan) (TR) is a tryptophan-immobilised column for immunoadsorption plasmapheresis (IAPP) and is currently used for the treatment in patients with Myasthenia gravis or Guillain-Barré syndrome. This column has a property to have high affinity to immunoglobulin G (IgG) subclass 3. With this property, IG substitution is not usually required after the IAPP treatment. Since cardiodepressant antibodies belong to IgG subclass 3, we investigated the effect of IAPP using this column on circulating levels of cardiodepressant autoanyibodies and cardiac function in patients with DCM.

Patients:

- 18 cases; male 9: female 9
- average age: 53 ± 4
- diagnosed as dilated cardiomyopathy (DCM) for 82 ± 15 months
left ventricular ejection fraction $<30\%$
- NYHA functional class at the entry of the study: 3.1 ± 0.1
- treated medically with:
digitalis, diuretics,
angiotensin converting enzyme inhibitor (ACEI),
angiotensin II receptor blocker (ARB),
carvedilol, amiodarone

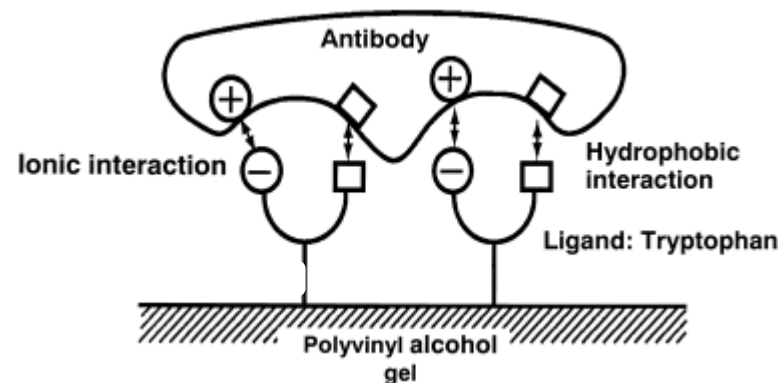
The column (TR):

Tryptophan is immobilised on the carrier material of polyvinylalcohol gel .

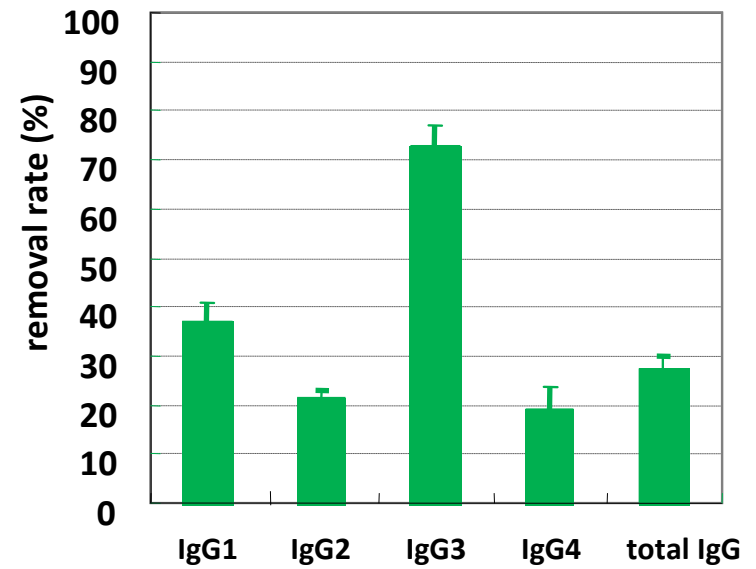
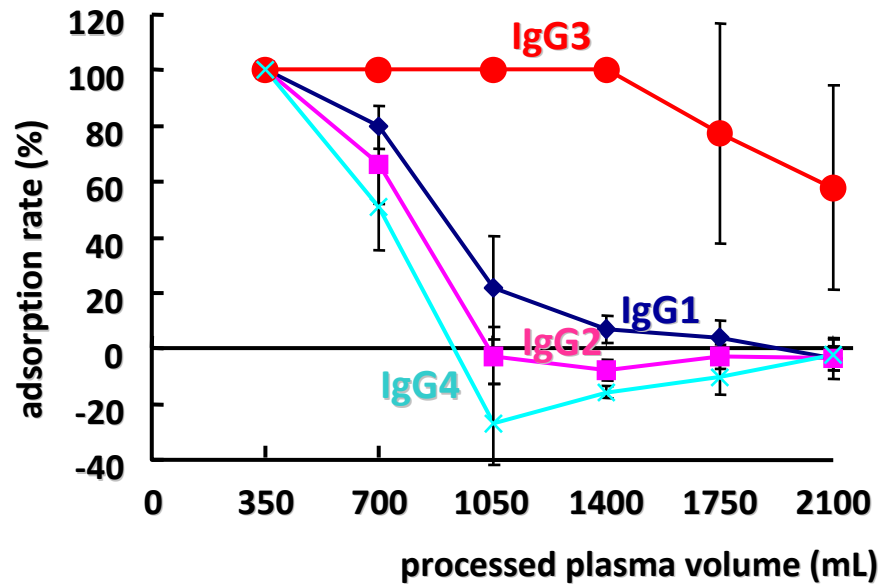


particle size, 100 μm ; pore size, 0.05 μm

The adsorption is mainly by the hydrophobic interaction and partially by the ionic interaction based on carboxylic group.

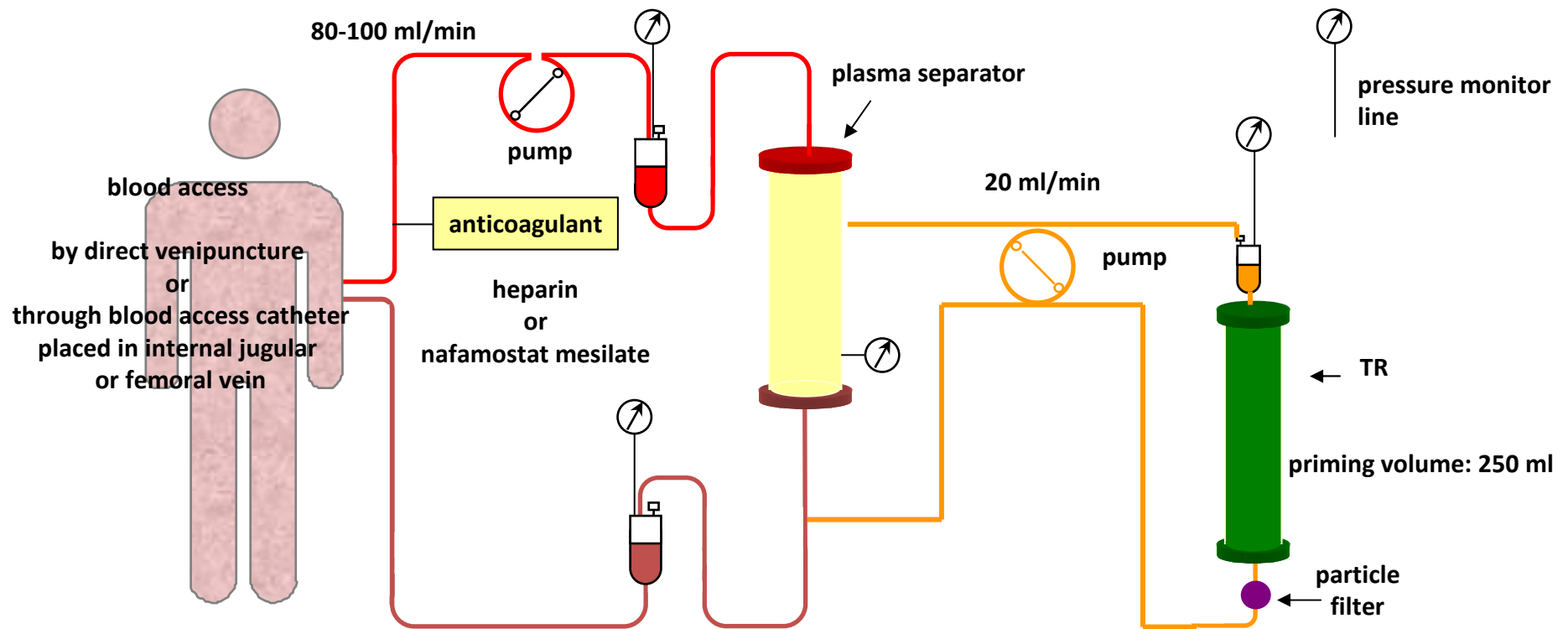


affinity to IgG subclasses



The TR column has high affinity to IgG3 subclass.

The circuit of the immunoadsorption plasmapheresis (IAPP) therapy:



1. A total of 1500-2000 ml of plasma was processed per one session of the IAPP treatment.
2. The IAPP was conducted every other or 2 days up to 3-5 sessions for each patient.

Measurement of cardiodepressant autoantibodies:

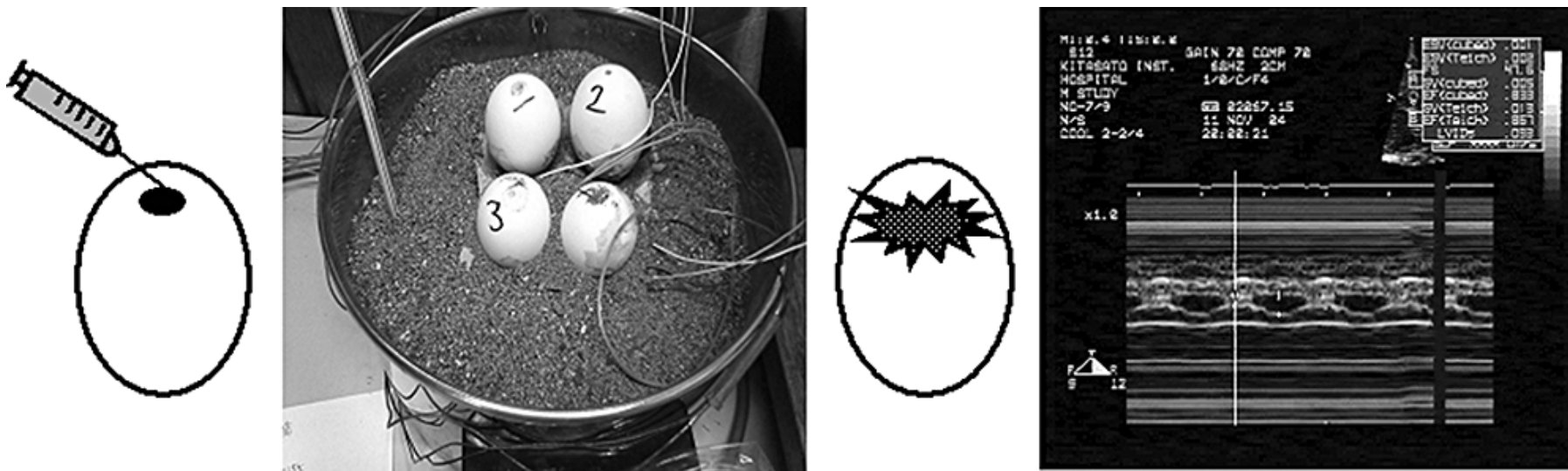
1. In vitro assay

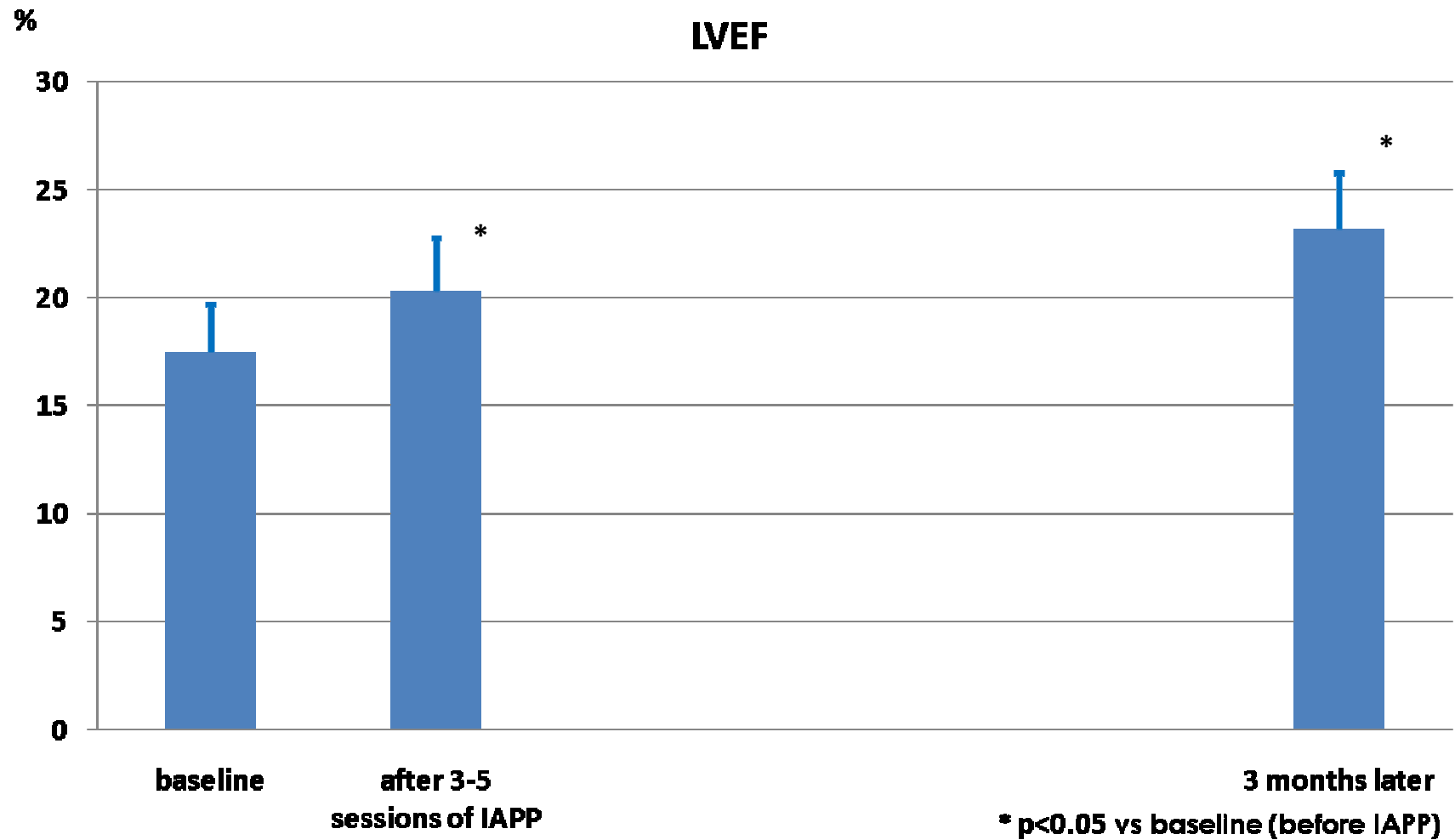
β -1-adrenoreceptor antibody and muscarinic M₂-acetylcholine receptor antibody
by enzyme-linked immunosorbent assay (ELISA)

2. ex vivo assay

The cardiodepressant autoantibody was assayed *ex vivo*. Briefly, normal saline (served as a control) or immunoglobulin G from the patients with dilated cardiomyopathy was applied to an egg and the ejection fraction (EF) of the chick embryo heart was measured by a B-mode echocardiogram. The cardiodepressant autoantibody was expressed as the difference;

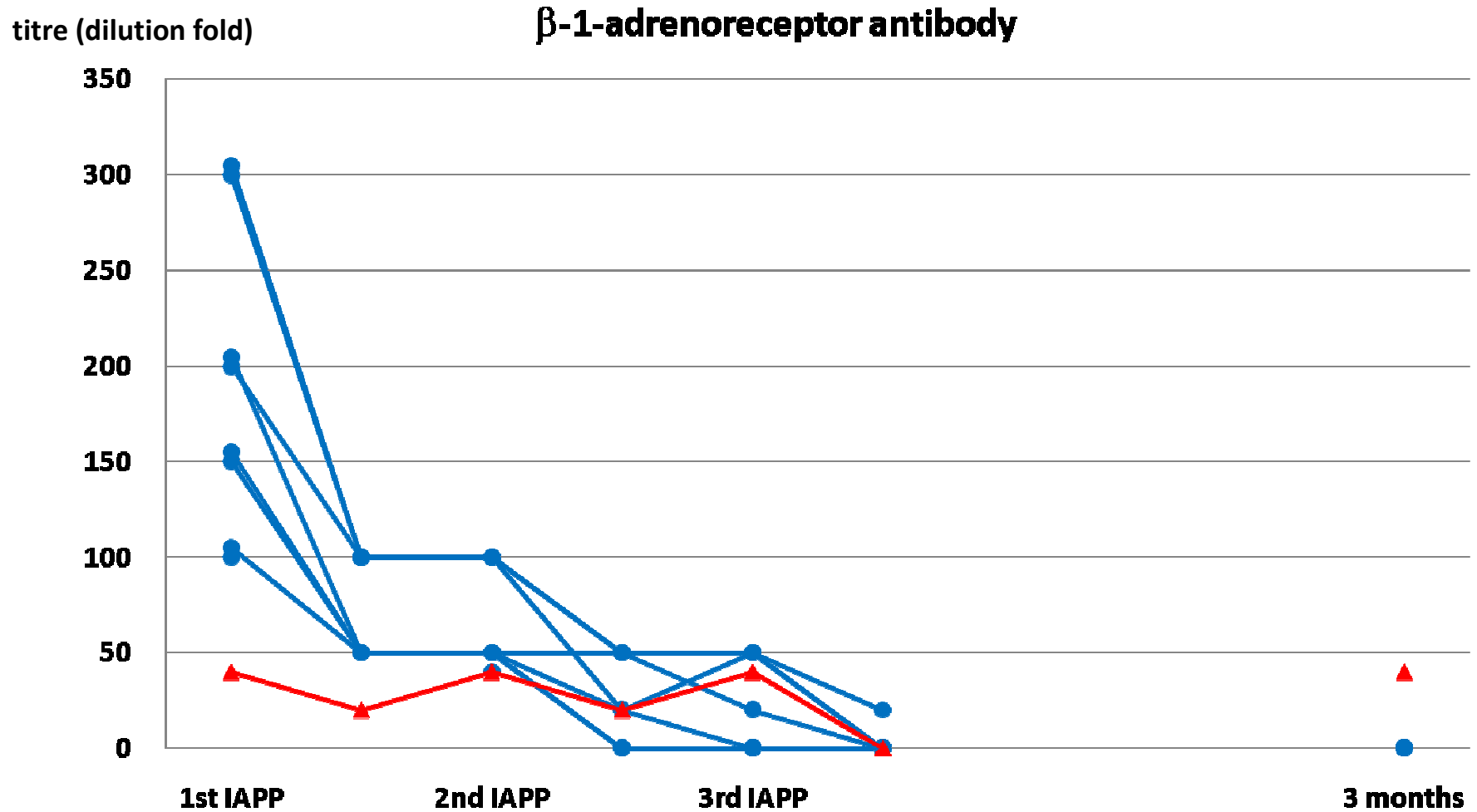
$$\text{EF (saline-applied)} - \text{EF (IgG-applied)} \quad (\%)$$





The left ventricular ejection fraction (LVEF) was determined by gated-single photon emission computed tomography (gated-SPECT).

It significantly increased after the 3-5 sessions of the immunoabsorption treatment. Three months later, it still kept increased.

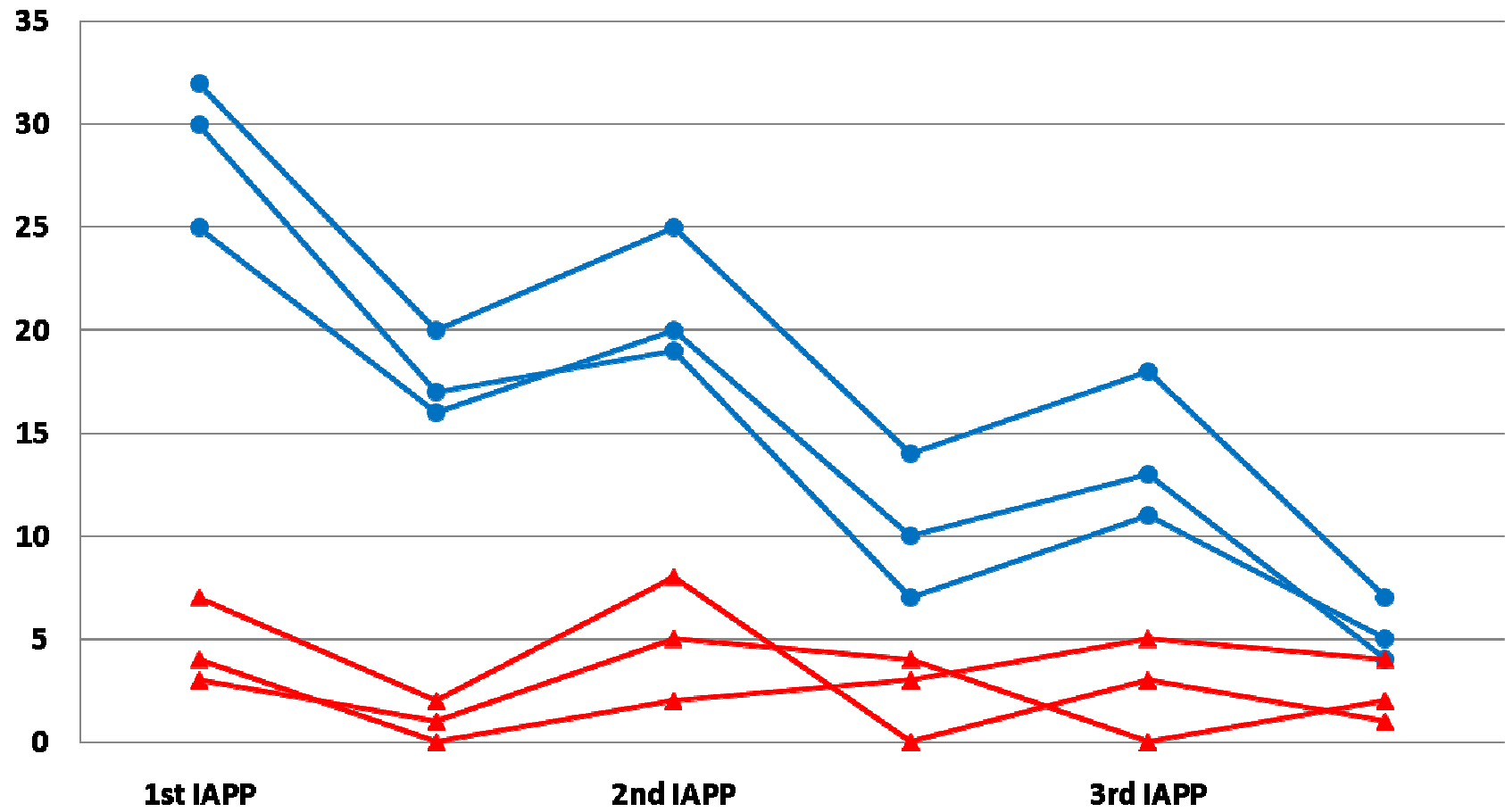


β-1-adrenoreceptor antibody, determined by an enzyme-linked immunoassay, was almost cleared from the circulation by the 3rd session of the immunoadsorption plasmapheresis (IAPP) therapy. It was not detected 3 months after the treatment, except one case. The muscarinic M₂-acetylcholine receptor antibodies showed the same tendency.

● — ● a case having a high titre initially
 ▲ — ▲ a case showing a low titre initially

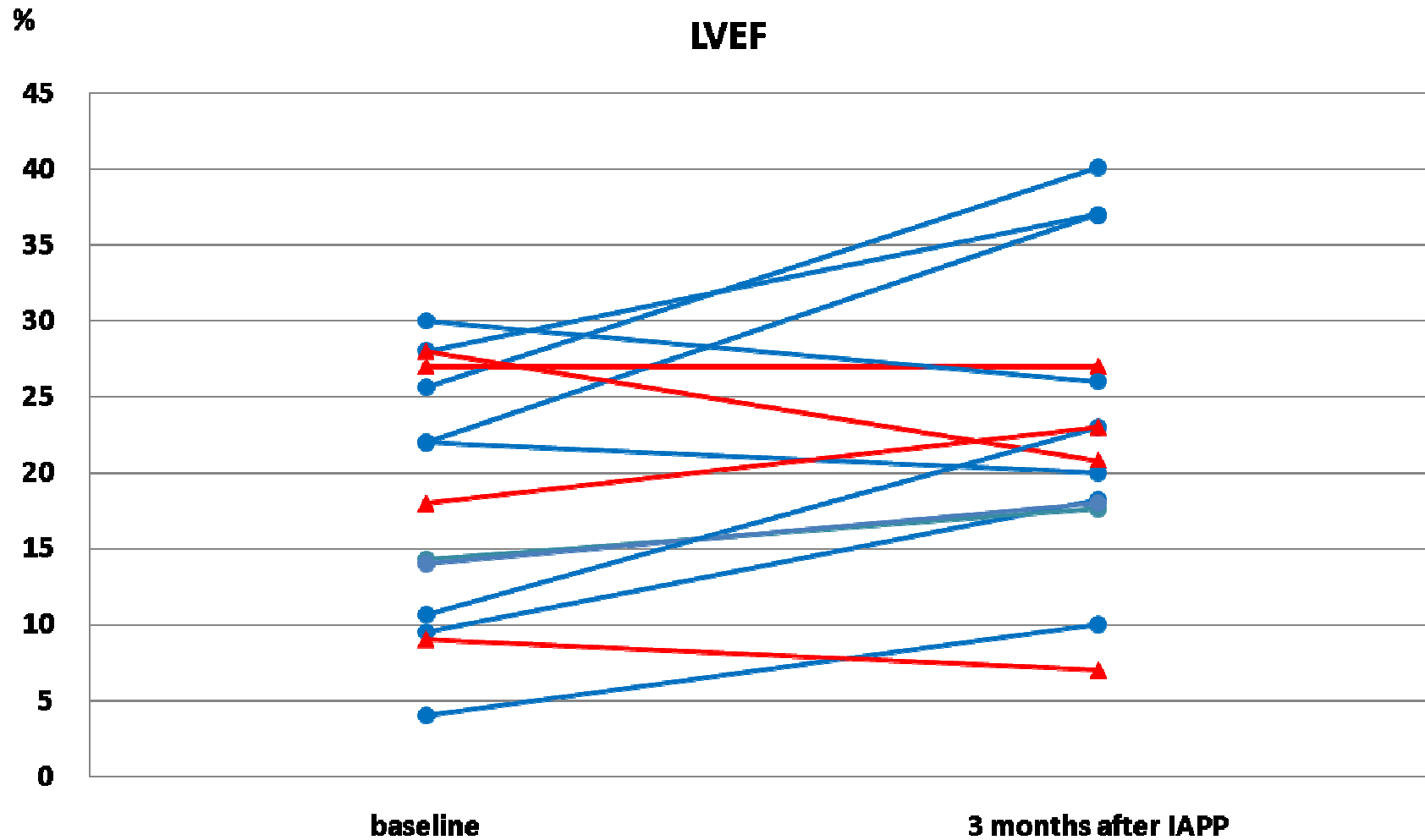
decrement of inhibition of EF (%)

cardiodepressant autoantibody



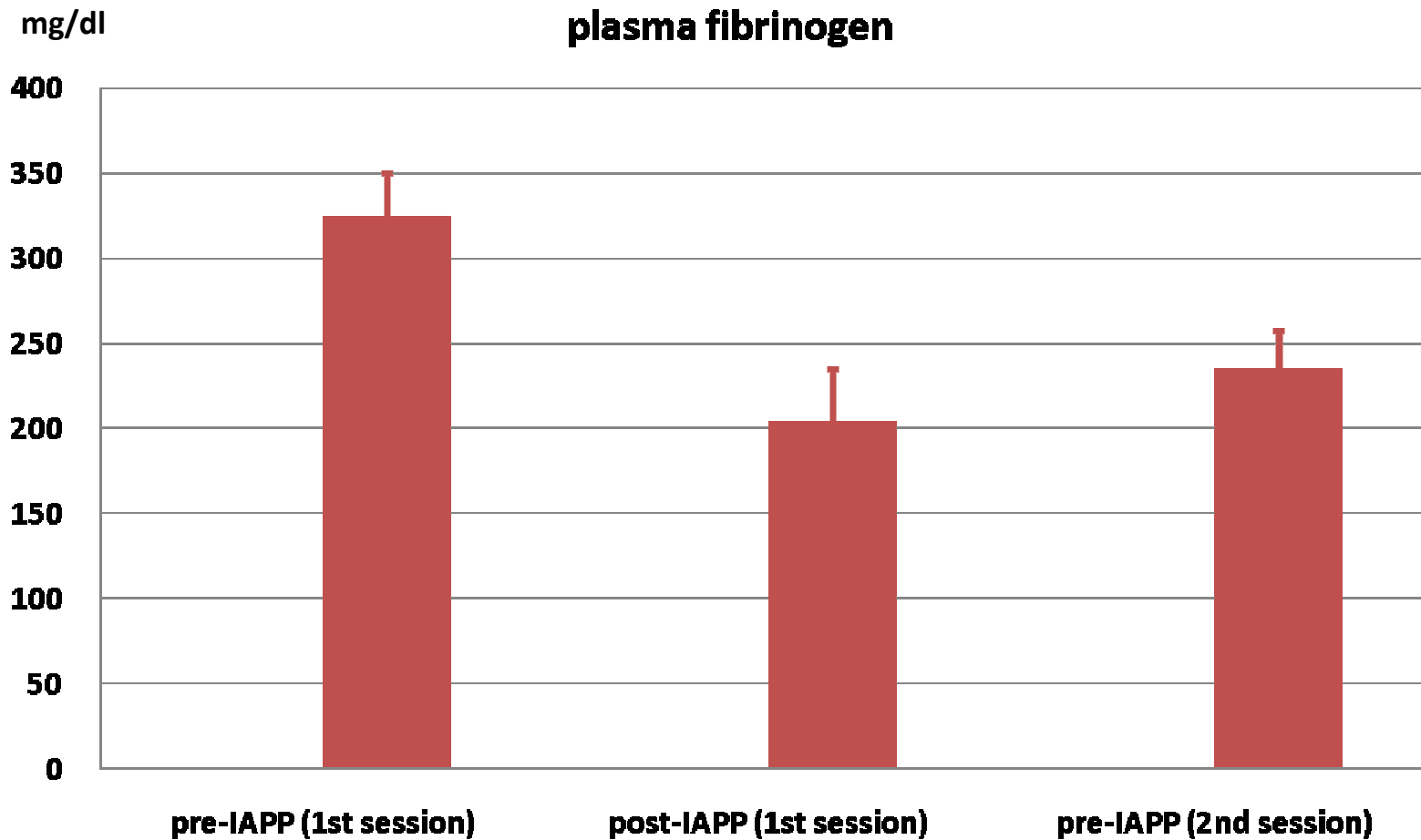
The cardiodepressant autoantibody, determined by the *ex vivo* assay, decreased by the 3rd session of the immunoadsorption plasmapheresis (IAPP) therapy.

● — ● a case having a high titre initially
▲ — ▲ a case showing a low titre initially

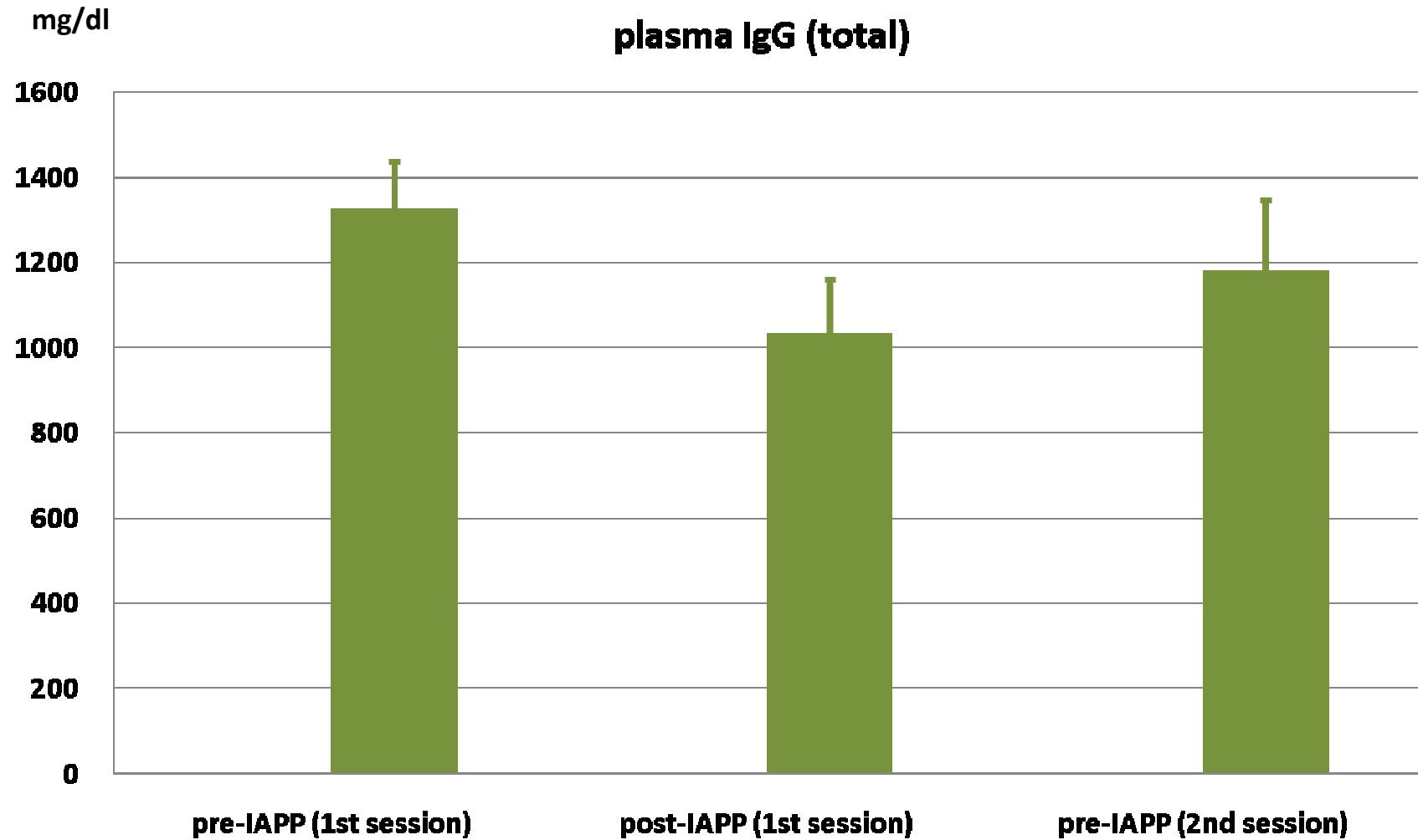


The change in the left ventricular ejection fraction 3 months after the immunoadsorption plasmapheresis (IAPP) therapy.
 The increase was higher in the cases who had high titre of cardiac autoantobody before the treatment (blue circle) . Red triangle denote the cases whose antibody titres were low.

● — ● a case having a high titre initially
 ▲ — ▲ a case showing a low titre initially



The plasma level of fibrinogen decreased by 39 ± 5 % after the immunoadsorption plasmapheresis (IAPP) therapy. However, It recovered up to 70% of the baseline level before the start of the next session.



The plasma level of total immunoglobulin G decreased by $23 \pm 4\%$ after the immunoadsorption plasmapheresis (IAPP) therapy. However, it recovered up to 90% of the baseline level before the start of the next session.

Clinical outcome:

All patients tolerated IAPP without any haemodynamic, haematological or infectious complication. Any cardiac event or mortality did not take place over the period of 3 months.

Conclusions:

The IAPP with TR demonstrated a simple and safe procedure in reducing circulating cardiodepressant autoantibodies and it may bring benefit in cardiac function in patients with DCM. However, further long-term follow-up as well as an accumulation of patients' population are required before assessing its efficacy.