Βασικά στοιχεία της συμβουλευτικής για απόφαση Θεραπευτικής Αφαίρεσης στη ΜΕΘ ενός τριτοβάθμιου νοσοκομείου

Παναγάκου Στέλλα
Νεφρολόγος
Νεφρολογική Κλινική 424 ΓΣΝΕ

Τι είναι Αιμαφαίρεση?

- “Διαδικασία κατά την οποία το αίμα ενός ασθενούς ή δότη διέρχεται μέσω εξωτερικής συσκευής, η οποία το διαχωρίζει σε διαφορετικά συστατικά. Εν συνεχεία μπορεί να αφαιρέσει ένα ή περισσότερα συστατικά και να επιστρέψει τα υπόλοιπα, με ή χωρίς αντικατάσταση του διαχωριζόμενου συστατικού”
- Θεραπεία επιλογής για πλήθος αιματολογικών, νευρολογικών και νεφρολογικών παθήσεων.

Kaplan AA. J Clin Apher. 2013; 28: 3-10

Guidelines

DOI: 10.1002/jca.22043

Journal of Clinical Apheresis ... ASFA WILEY

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

Laura Connelly-Smith[1] | Caroline R. Alquist[2] | Nicole A. Aqui[3] | Jan C. Hofmann[4] | Reinhard Klingel[5,6] | Oluwatoyosi A. Onwuemene[7] | Christopher J. Patriquin[8] | Huy P. Pham[9] | Amber P. Sanchez[10] | Jennifer Schneiderman[11] | Volker Witt[12] | Nicole D. Zantek[13] | Nancy M. Dunbar[14]

Ταξινόμηση Ενδείξεων (ASFA 2023)

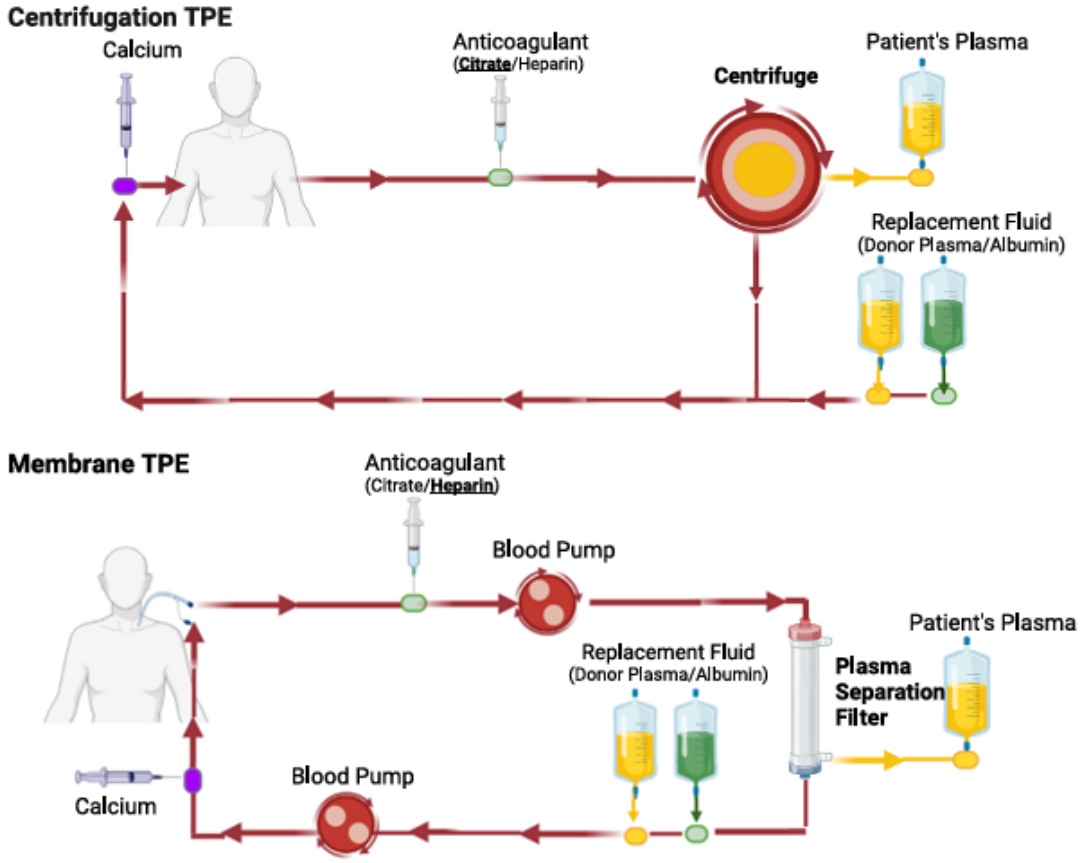
TABLE 2 Category definitions for therapeutic apheresis

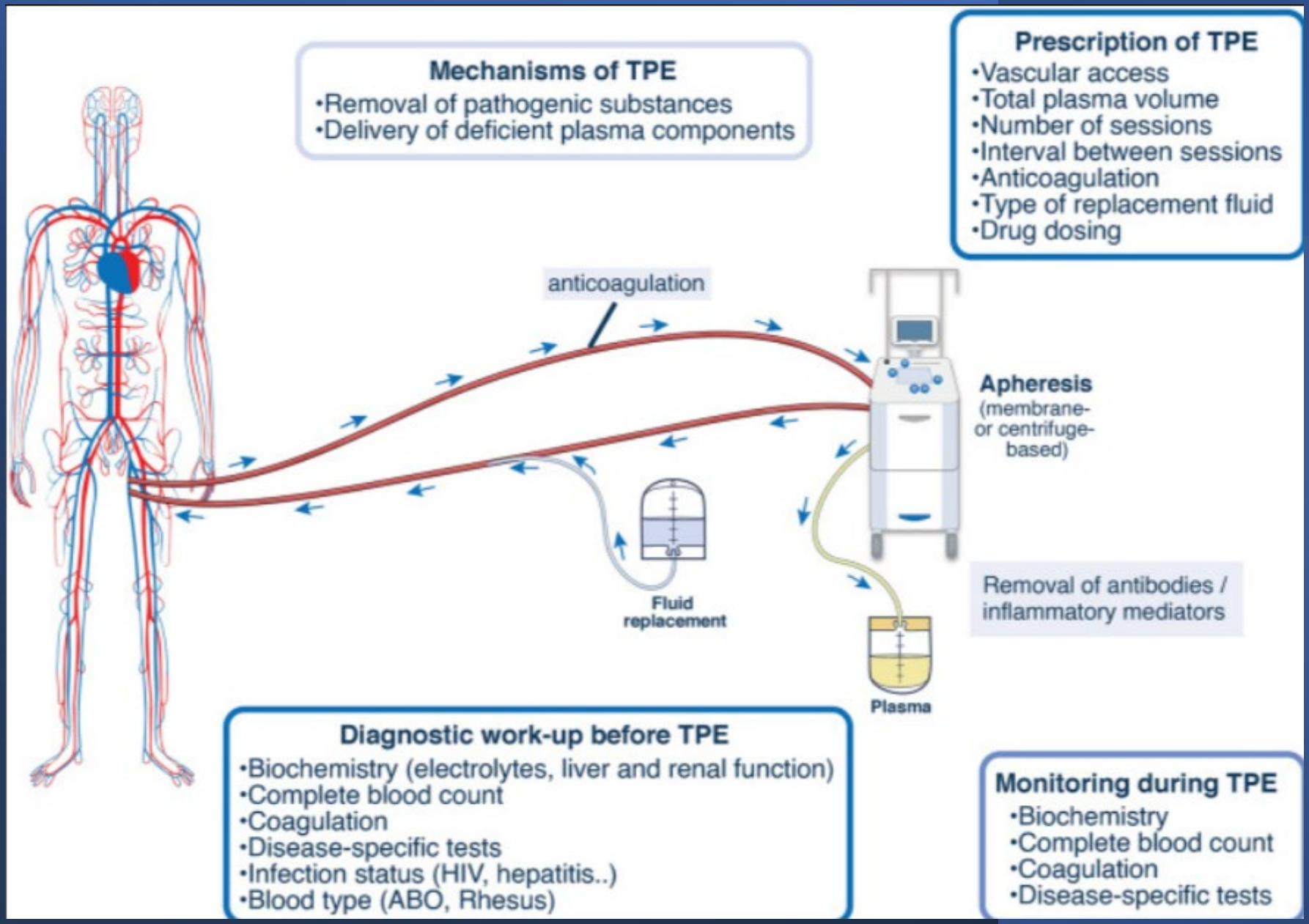
Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision-making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB/Ethics Committee approval is desirable if apheresis treatment is undertaken in these circumstances.

Abbreviation: IRB, Institutional Review Board.

Τεχνικές αιμαφαίρεσης

- ✓Φυγοκέντρηση
- ✓Διήθηση μέσω μεμβράνης
- ✓Προσρόφηση ουσιών από ολικό περιφερικό αίμα ή από πλάσμα που έχει ήδη διαχωριστεί


Centrifugation TPE
Calcium
Anticoagulant
(Citrate/Heparin)
Centrifuge
Patient's Plasma
Replacement Fluid
(Donor Plasma/Albumin)
Membrane TPE
Anticoagulant
(Citrate/Heparin)
Blood Pump
Patient's Plasma
Replacement Fluid
(Donor Plasma/Albumin)
Plasma
Separation
Filter
Blood Pump
Calcium


Mechanisms of TPE
•Removal of pathogenic substances
•Delivery of deficient plasma components
Prescription of TPE
•Vascular access
•Total plasma volume
•Number of sessions
•Interval between sessions
•Anticoagulation
•Type of replacement fluid
•Drug dosing
anticoagulation
Apheresis
(membrane- or centrifuge-based)
Fluid replacement
Plasma
Removal of antibodies / inflammatory mediators
Diagnostic work-up before TPE
•Biochemistry (electrolytes, liver and renal function)
•Complete blood count
•Coagulation
•Disease-specific tests
•Infection status (HIV, hepatitis..)
•Blood type (ABO, Rhesus)
Monitoring during TPE
•Biochemistry
•Complete blood count
•Coagulation
•Disease-specific tests

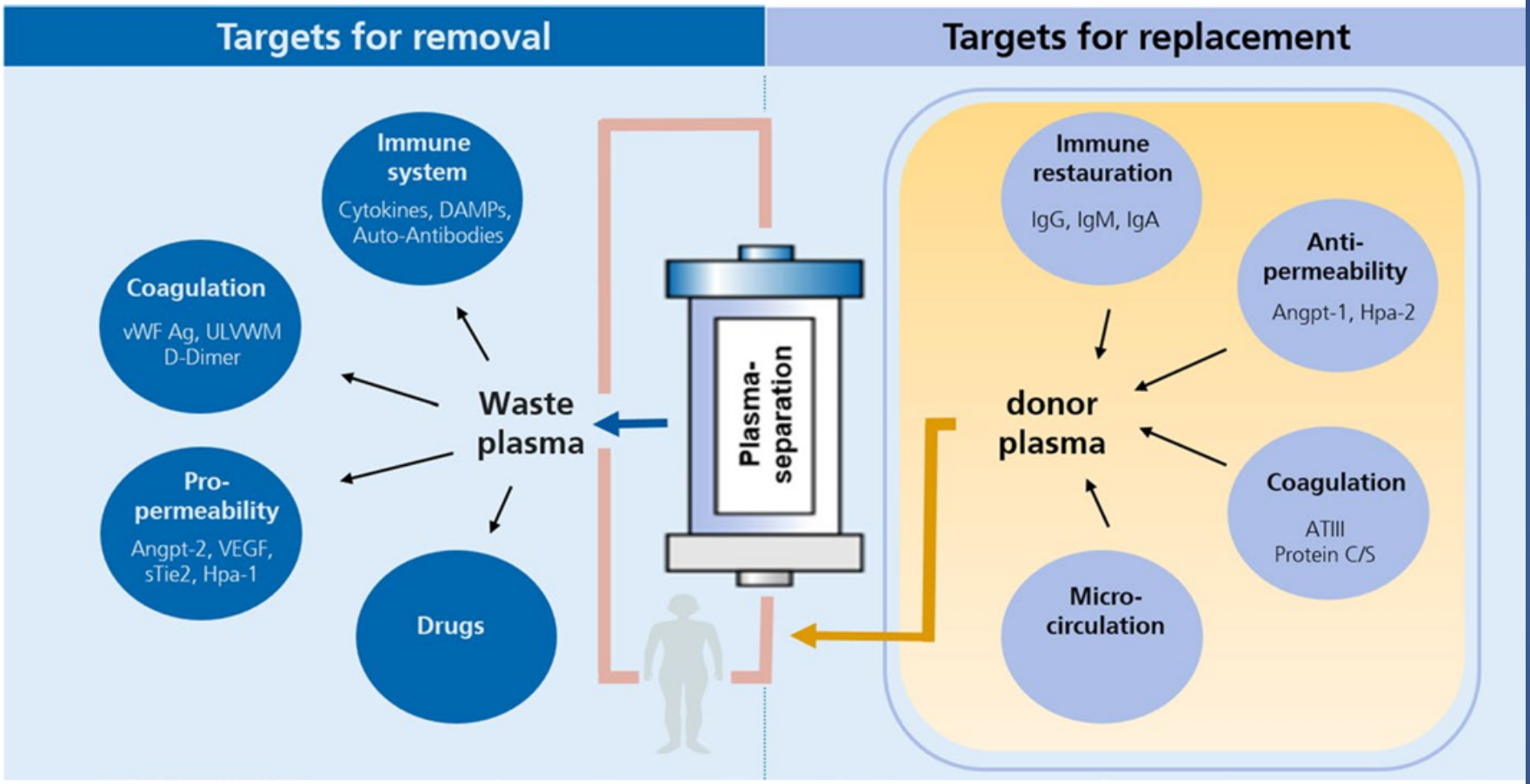


Fig. 2 Schematic illustration of potential (explorative) targets for replacement and removal by plasma exchange (adjusted from [99]). *DAMPs* damage associated molecular patterns, *VWF* von Willebrand factor, *ULVWM* ultralarge von Willebrand multimers, *Angpt-1/-2* angiopoietin, *VEGF* vascular endothelial growth factor, *Hpa-1/-2* heparanase, *ATIII* antithrombin III, *ADAMTS13* A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13

Table 2 Circulating factors that might be modulated by therapeutic plasma exchange

Removal			
Potential target	**Role**	**Disease**	**Available data**
Cytokines	Inflammation	Sepsis, SIRS	Experimental
Autoantibodies (e.g. ANCA)	Autoimmune	vasculitis, Goodpasture's syndrome	SOC
Donor-specific antibodies	Rejection	Transplantation	SOC, expert opinion
Immunoglobulins	Hyperviscosity	Hyperviscosity syndrome	SOC
Angiopoietin-2	Permeability	ARDS, sepsis	OBS
vWF antigen	Coagulopathy	Sepsis, DIC	OBS
Heparanase-1	Glycocalyx shedding	Systemic inflammation, Covid-19	OBS
Active viral particles (HSV, EBV)	infectious diseases	Virus-induced acute liver failure	CR
Heparin/PF4 antibody	Coagulation	Heparin-induced thrombocytopenia	CS
Replacement			
Potential target	**Role**	**Disease**	**Available data**
ADAMTS13	vWF cleaving protease	TTP	RCT, SOC
Heparanase-2	Glycocalyx stabilisation	Systemic inflammation, Covid-19	OBS
Immunoglobulins	Ig deficiencies	Infection	OBS
Angiopoietin-1	Anti-permeability	Sepsis, systemic inflammation	OBS
Protein C	Coagulation, microcirculation	Sepsis, purpura fulminans	OBS
Coagulation factors	Coagulopathy/DIC	Investigated in acute liver failure	RCT

Table 1. Indications for therapeutic plasma exchange (TPE) (adapted from ASFA 2023 guidelines).

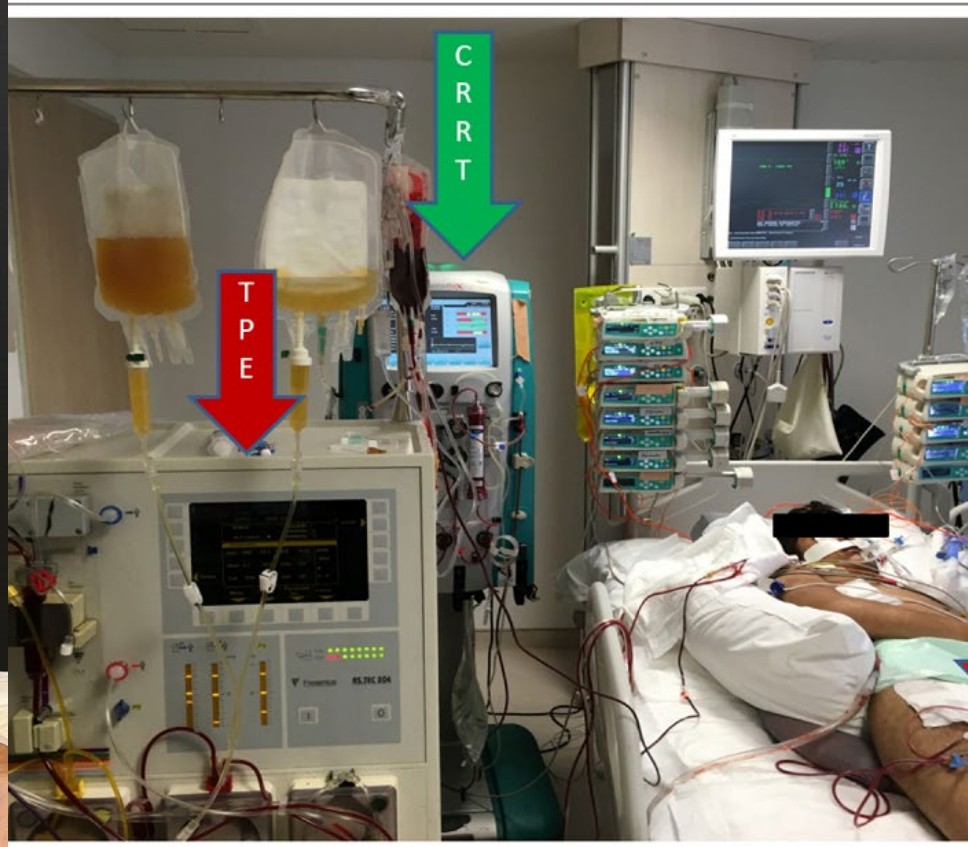
System	Lines	Diagnosis	Specific Condition
Neurological disorders	First-line	Acute inflammatory demyelinating polyneuropathy	
		Chronic acquired demyelinating polyneuropathies, IgG/IgA/IgM-related	
		Chronic inflammatory demyelinating polyradiculoneuropathy	
		Myasthenia gravis	Acute, short-term treatment
		N-methyl-D-aspartate receptor antibody encephalitis	
	Second-line	Lambert–Eaton myasthenic syndrome	
		Multiple sclerosis	Acute attack/relapse; long-term treatment
		Neuromyelitis optical spectrum disorder	Acute attack/relapse
		Pediatric autoimmune neuropsychiatric disorders	PANDAS/PANS, exacerbation
		Steroid-responsive encephalopathy associated with autoimmune thyroiditis	
Hematological disorders	First-line	Catastrophic antiphospholipid syndrome	
		Hyperviscosity in hypergammaglobulinemia	Prophylaxis for rituximab; symptomatic hyperviscosity syndrome
		Thrombotic microangiopathy, complement-mediated	Factor H autoantibody-related only
		Thrombotic microangiopathy, drug-induced	Ticlopidine-related only
		Thrombotic microangiopathy, thrombotic thrombocytopenic purpura	
	Second-line	Lambert–Eaton myasthenic syndrome	
		Multiple sclerosis	Acute attack/relapse; long-term treatment
		Neuromyelitis optical spectrum disorder	Acute attack/relapse
		Pediatric autoimmune neuropsychiatric disorders	PANDAS/PANS, exacerbation
		Steroid-responsive encephalopathy associated with autoimmune thyroiditis	
Transplantation-associated complications	First-line	Transplantation, kidney, ABO-compatible	Antibody-mediated rejection; Desensitization/prophylaxis, living donor
		Transplantation, kidney, ABO-incompatible	Desensitization, living donor
		Transplantation, liver	Desensitization, ABOi, living donor
	Second-line	Transplantation, heart	Desensitization; rejection prophylaxis
		Transplantation, hematopoietic stem cell, ABO-incompatible	Major ABO incompatible: HPC(M); HPC(A)
		Transplantation, kidney, ABO-incompatible	Antibody-mediated rejection
Renal disorders	First-line	Antiglomerular basement membrane disease	Diffuse alveolar hemorrhage; dialysis-independent disease
		Focal segmental glomerulosclerosis	Recurrent in kidney transplant
Hepatic disorders	First-line	Acute liver failure (TPE-HV preferred over regular TPE)	Other than acute fatty liver of pregnancy
		Wilson disease, fulminant	

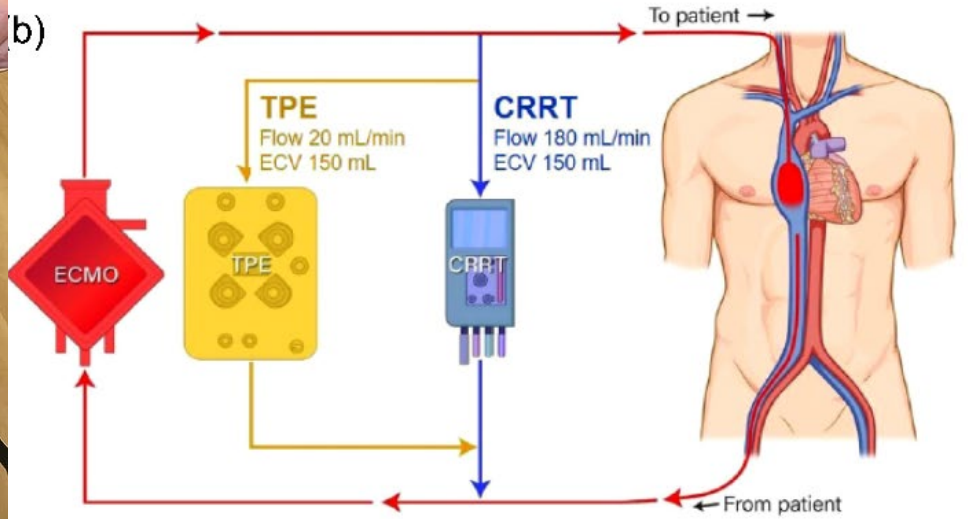
Συχνές Ενδείξεις στη ΜΕΘ

Others

Systemic lupus erythematosus
Thyroid storm
Familial hypercholesterolemia
Phytanic acid storage disease
Hepatitis B related polyarteritis nodosa vasculitis
Voltage-gated potassium channel antibody-related diseases
Mushroom poisoning

Medicina **2023**, *59*, 2152





mbination of therapeutic plasma exchange (TPE), continuous renal replacem

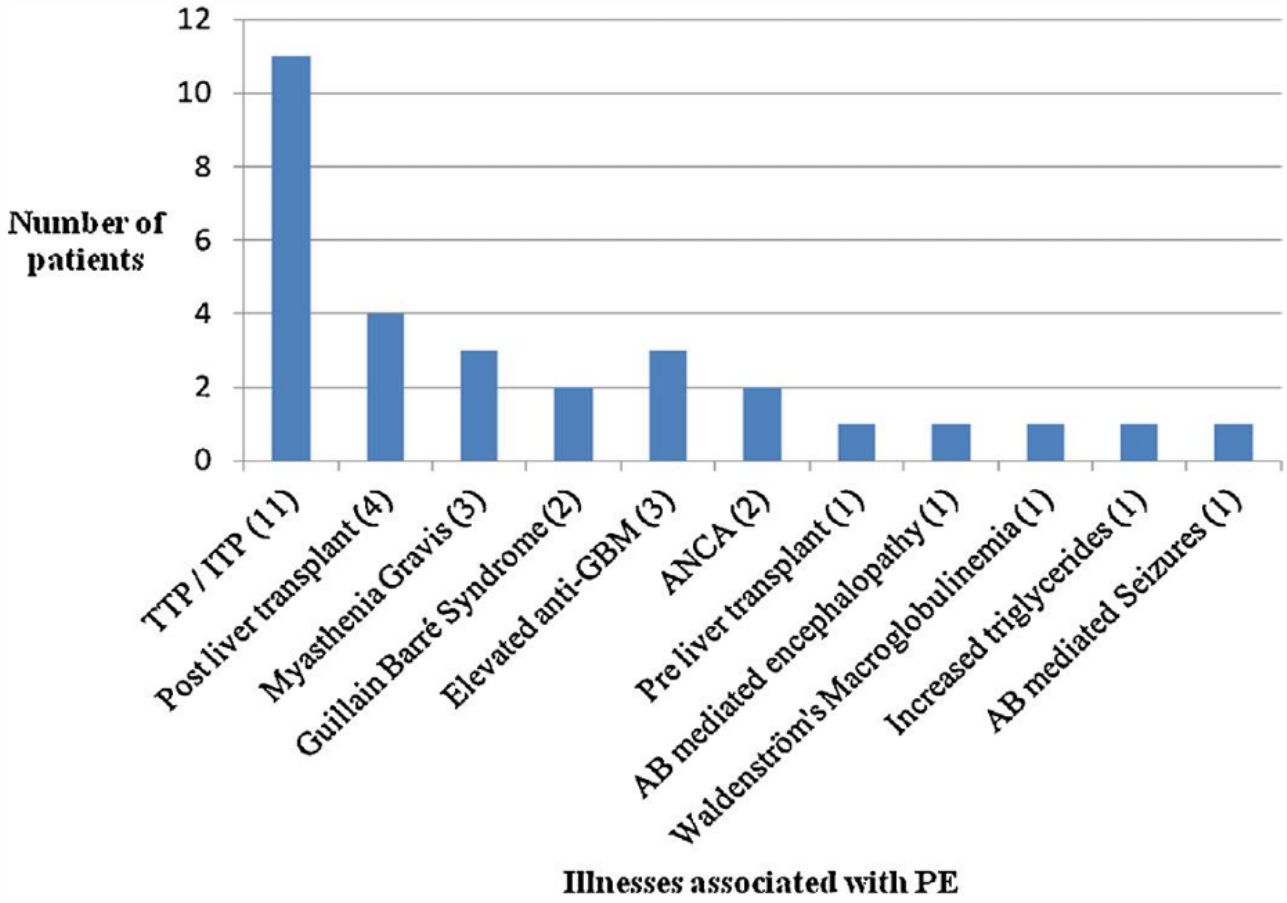
Contents lists available at ScienceDirect

Australian Critical Care

journal homepage: www.elsevier.com/locate/aucc

Plasma exchange in the intensive care unit: A 10 year retrospective audit

Emily Paton RN, Grad. Dip (Crit Care Nurs), ACCCN *,
Ian C. Baldwin RN, PhD, (ICU Cert), ACCCN [1]



Paton & Baldwin. Aus Crit Care 2023

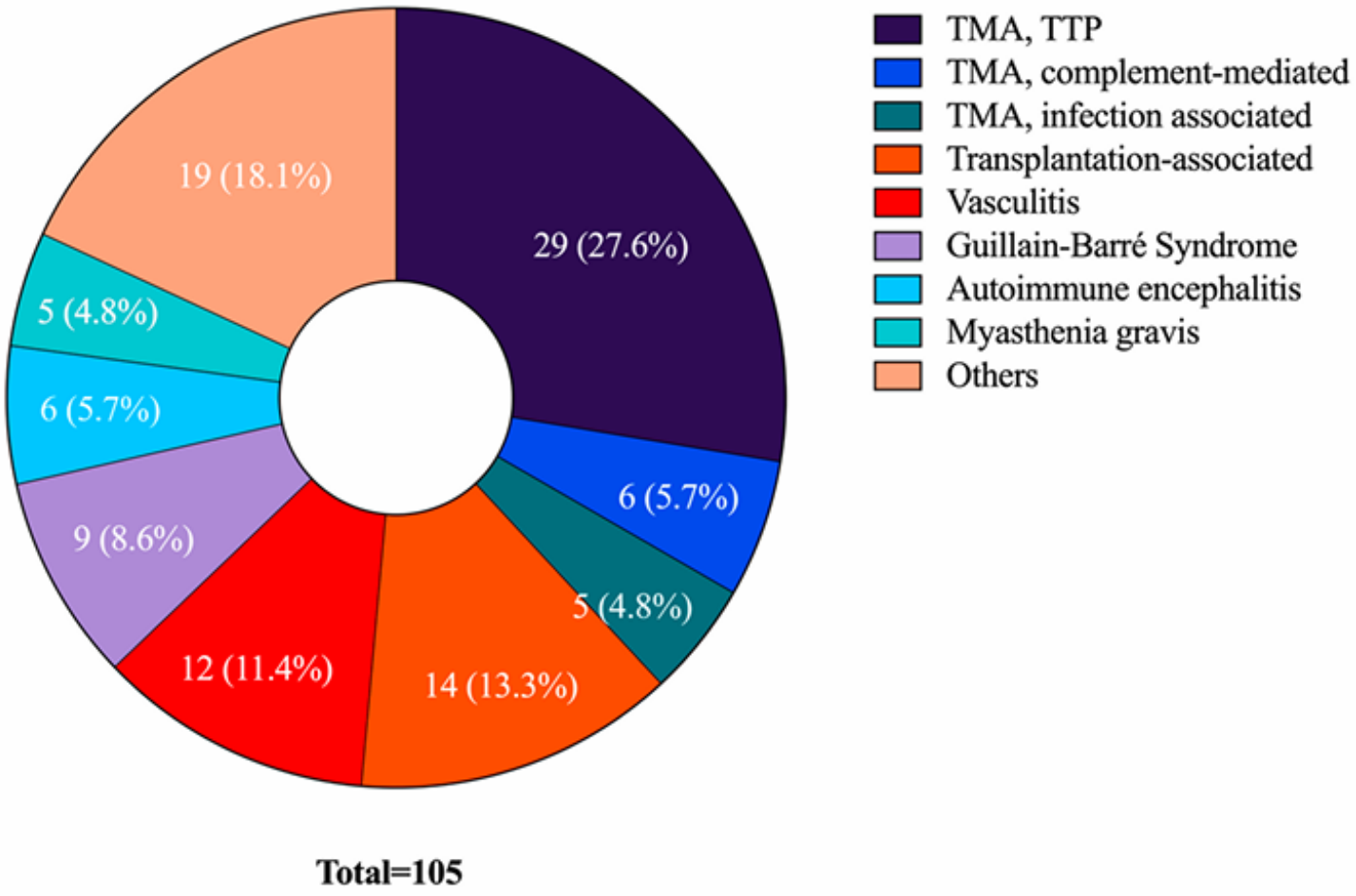
Indications and Outcomes of Patients Receiving Therapeutic Plasma Exchange under Critical Care Conditions: A Retrospective Eleven-Year Single-Center Study at a Tertiary Care Center

Alexander Ring [1,2,†], Wolfgang Alexander Sieber [1,†], Jan-Dirk Studt [2], Reto A. Schuepbach [1], Christoph Camille Ganter [1], Markus Gabriel Manz [2], Antonia Maria Susanne Müller [2,*,‡] and Sascha David [1,*]

- n = 105 patients
- n = 408 TPEs
- The most common was thrombotic microangiopathies (TMA) (38%), transplant-associated complications (16.3%) and vasculitis (14%). One-third of indications (35.2%) could not be classified according to ASFA.
- Anaphylaxis was the most common TPE-related complication (6.7%), while bleeding complications were rare (1%).
- The median duration of ICU stay was 8- 14 days. Ventilator support, renal replacement therapy or vasopressors were required in 59 (56.2%), 26 (24.8%), and 35 (33.3%) patients, respectively, and 6 (5.7%) patients required extracorporeal membrane oxygenation.
- The overall hospital survival rate was 88.6%.

J. Clin. Med. **2023**, *12*, 2876

Indication	Number of Patients n (%)	Median TPE Sessions (IQR)	ASFA Category	ASFA Grade
All	105 (100)	3 (4)	variable	variable
TMA, all	40 (38)	2 (3.25)	variable	variable
TMA, TTP	29 (27.6)	2 (4)	I	1A
TMA, complement-mediated	6 (5.7)	2 (1.5)	I or III	variable
TMA, infection associated	5 (4.9)	2 (1)	III	2C
Transplantation-associated	14 (13.3)	1.5 (2.75)	variable	variable
Vasculitis	12 (11.4)	5 (3)	variable	variable
Guillain-Barré Syndrome	9 (8.6)	5 (1)	I	1A
Acute liver failure	2 (1.9)	1.5 (0.5)	III	2B
Macrophage-activation Syndrome	1 (0.95)	1	III	2C
Progressive bulbar palsy	1 (0.95)	5	III	2C
Hypertriglyceridemia, idiopathic	1 (0.95)	1	III	1C or 2C
Coagulopathy after polytrauma	1 (0.95)	1	unclear	unclear
Anti-IgLON5-associated encephalopathy	1 (0.95)	2	unclear	unclear
Systemic sclerosis	1 (0.95)	4	I	1A
Chronic inflammatory demyelinating neuropathy	1 (0.95)	1	I	1B
Postpartum microangiopathy	1 (0.95)	7	I or III	1A or 2C
Miller-Fisher Syndrome	1 (0.95)	1	I	1A
Polyradiculoneuritis	1 (0.95)	1	unclear	unclear
Paraneoplastic neurological syndrome	1 (0.95)	8	III	2C
Catastrophic antiphospholipid syndrome	1 (0.95)	4	I	2C
acute demyelinating neuropathy	1 (0.95)	1	unclear	unclear
Hyperviscosity in hypergammaglobulinemia	1 (0.95)	2	I	1B



J. Clin. Med. **2023**, *12*, 2876

Διεπιστημονική Συνεργασία

- Εντατικολόγος
- Αιματολόγος-Αιμοδοσία
- Νεφρολόγος
- Νοσηλευτής ΜΕΘ
- Λοιπές ειδικότητες

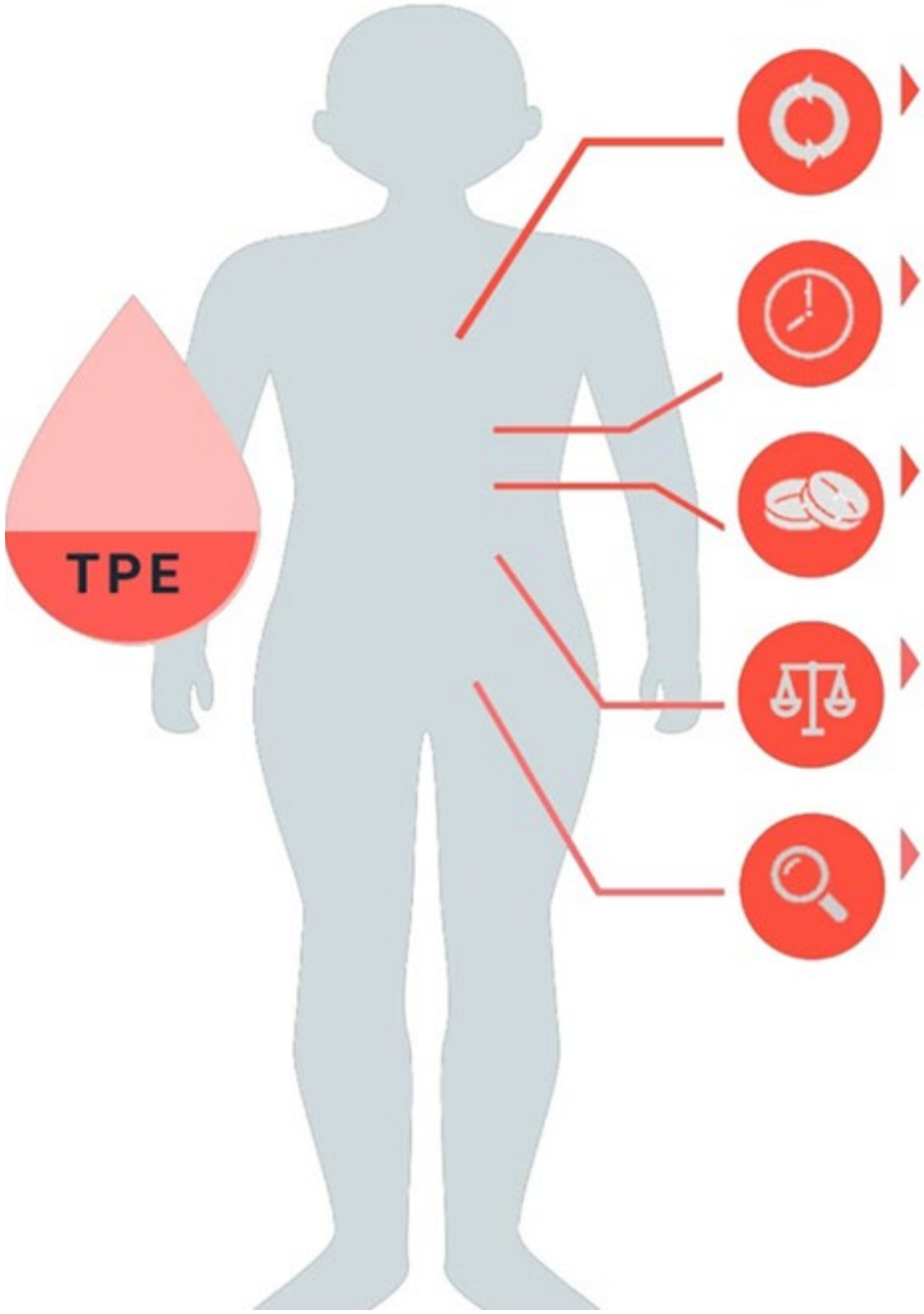
Κλινική αξιολόγηση και στόχοι

Η συμβουλευτική ομάδα οφείλει να καθορίσει:

- **Τον θεραπευτικό στόχο** (π.χ. απομάκρυνση παθολογικών αντισωμάτων ή τοξινών)
- **Το προσδοκώμενο όφελος** έναντι των κινδύνων
- **Το χρονοδιάγραμμα** (αριθμός συνεδριών, συχνότητα)
- **Εναλλακτικές θεραπείες**

Κριτήρια Απόφασης

- Τεκμηριωμένη ένδειξη (ASFA I–II)
- Αναστρέψιμη κατάσταση / δυνητικό όφελος
- Αποδοχή κινδύνων – ενημέρωση-συναίνεση
- Διαθεσιμότητα εξειδικευμένου προσωπικού και εξοπλισμού



Removal and Replacement

What is the pathophysiological role of removal and replacement in critical illness?

Timing

What is the optimal timing of TPE in respect to other critical treatments?

Dosing and Regimen

What is the optimal dose and regimen of TPE in critical illness?

Risk - Benefit

How to identify critically ill patients at risk and avoid complications?

Explorative indications

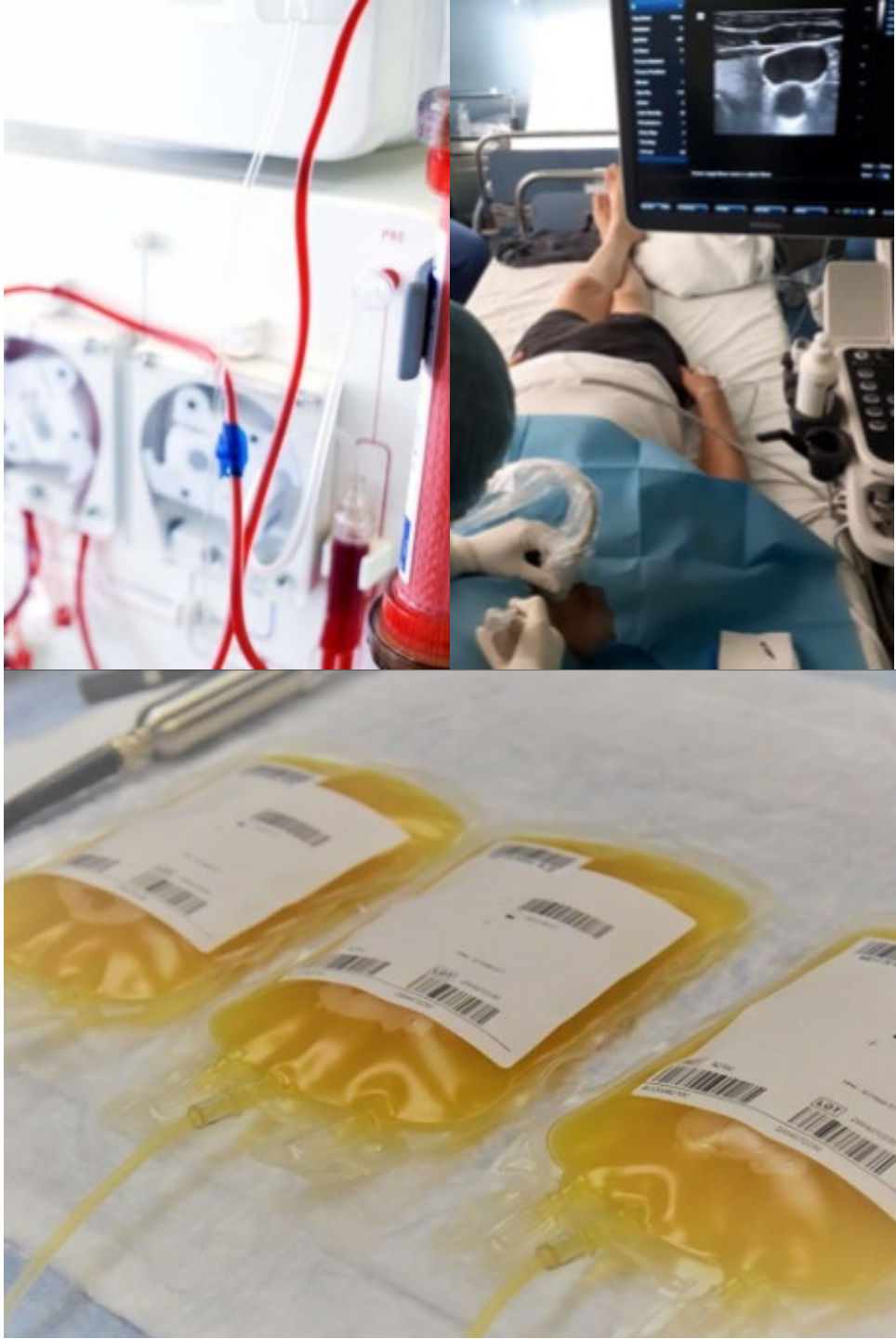
What are explorative indications for critically ill patients?

Διαδικασία Εφαρμογής

- Αίτημα από ΜΕΘ
- Επιβεβαίωση ένδειξης (ASFA)
- Ενημέρωση- συναίνεση
- Προγραμματισμός συνεδριών
- Παρακολούθηση αποτελεσμάτων

Τεχνικές Παράμετροι

- **Αντικαθιστώμενος όγκος**: 1–1,5 × πλάσμα
- **Υποκατάστατα**: 5% λευκωματίνη ± FFP
- **Συχνότητα**: Καθημερινά ή ανά 48 ώρες
- **Φλεβική προσπέλαση**: Κεντρικός φλεβικός καθετήρας ή περιφερική φλέβα
- **Αντιπηκτικό**: Κιτρικά ή ηπαρίνη



Αντενδείξεις

- Μη αντιρροπούμενη αιμοδυναμική αστάθεια
- Σοβαρή αιμορραγική διάθεση
- Υποπρωτεϊναιμία
- Μη ελεγχόμενη σήψη
- Αλλεργία σε υποκατάστατα πλάσματος

ICU, apheresis or nephrology nurses providing TPE: planning and clinical considerations associated with TPE in ICU

Timing of commencement	We recommend the treatment be delivered during day time hours with the preferred avoidance of shift change overlap where possible
Nursing allocation	TPE requires an experienced critical care nurse with advanced understanding of the fundamentals of CRRT and the management of an EC for potential troubleshooting
Drug removal	Due to removal of larger molecules and proteins, drugs are cleared readily. This may require administration of these drugs post completion of TPE, for example, rituximab is a key agent often used to suppress antibodies[15], [36]
Electrolyte management	The monitoring and potential need for electrolyte replacement such as Ca, K+, and $MgSO_4$ [18]
Hemodynamic instability	As with any EC therapy, hemodynamic[36] instability due to fluid shifts and exposure to foreign plasma replacement fluids may require vasopressor support as required[1]
Acid base disturbances	Critically ill patients who also require CRRT for an AKI will lose this treatment time when TPE is implemented. This needs to be considered in daily care planning and promotes the concurrent use of TPE and CRRT[18] from one vascular access (see below).

J Clin Apher. 2022 Apr 6;37(4):397–404. doi: 10.1002/jca.21984

Παρακολούθηση Αποτελεσματικότητας

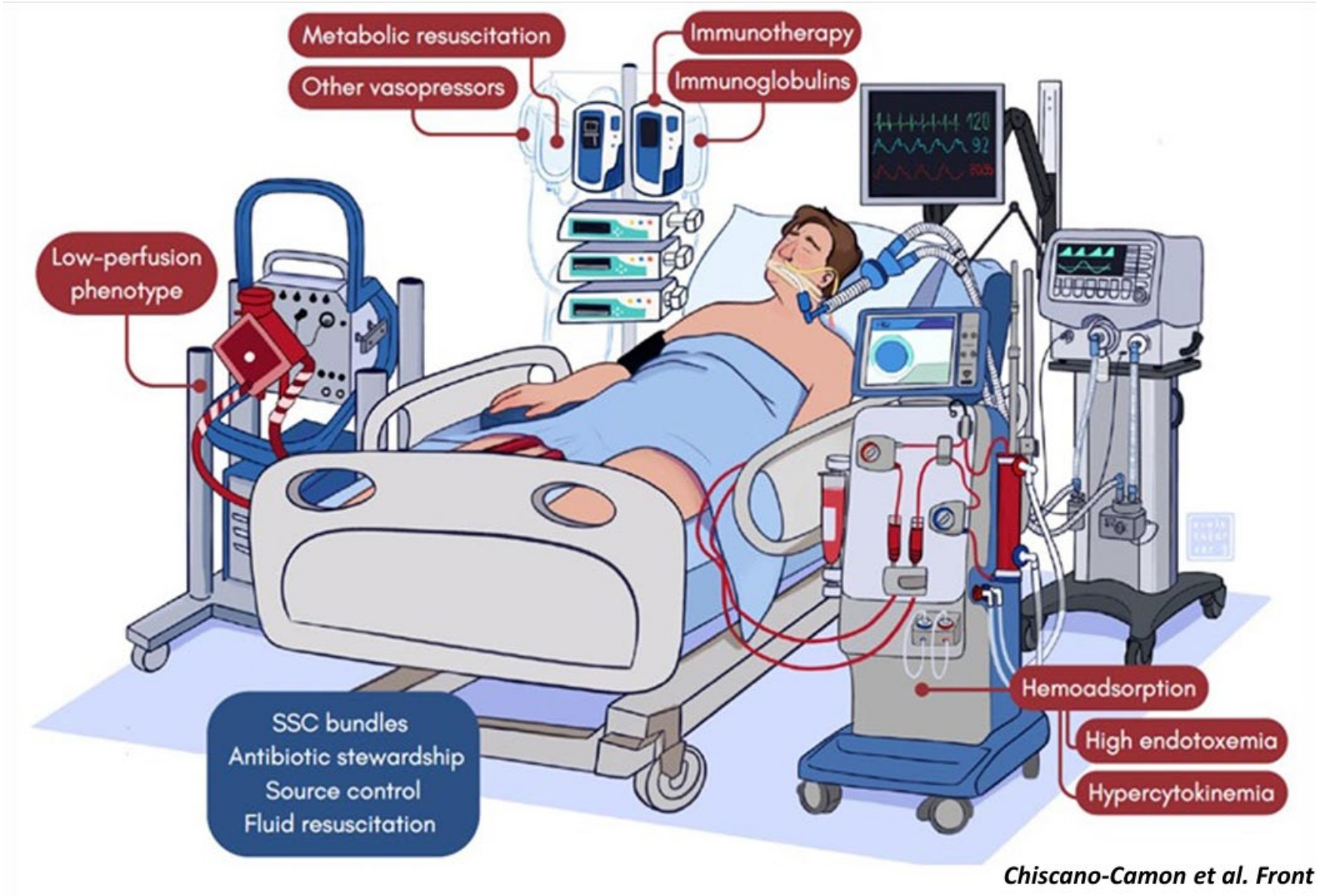
- Κλινική βελτίωση
- LDH, PLT, Cr, αντισώματα
- Καταγραφή ανεπιθύμητων ενεργειών
- Επανεκτίμηση ανάγκης συνέχισης

Παράδειγμα Πρωτοκόλλου (TTP)

- Καθημερινή TPE × 5–7 ημέρες
- Αντικατάσταση με FFP
- Παρακολούθηση PLT, LDH, αιμοδυναμικής κατάστασης
- Συνδυασμός με άλλη θεραπευτική αγωγή: κορτικοστεροειδή ± rituximab

Συμπεράσματα

- Η πλασμαφαίρεση είναι ζωτικής σημασίας σε επιλεγμένες κρίσιμες καταστάσεις
- Απαιτεί τεκμηριωμένη ένδειξη και πολυεπιστημονική συνεργασία
- Ασφαλής εφαρμογή → σωστή επιλογή, τεχνική και παρακολούθηση



Chiscano-Camon et al. Front

Ευχαριστώ για την προσοχή σας!