45° Convegno Nazionale di Studi di Medicina Trasfusionale

Rimini | 29-31 maggio 2024

SIMTI

Aggiornamenti sulle linee guida ASFA 2023

Dott.ssa Monica Castelli

UOC Medicina Trasfusionale

Ospedale San Bortolo, ULSS8 Berica, Vicenza

La sottoscritta, in qualità di Relatrice
dichiara che

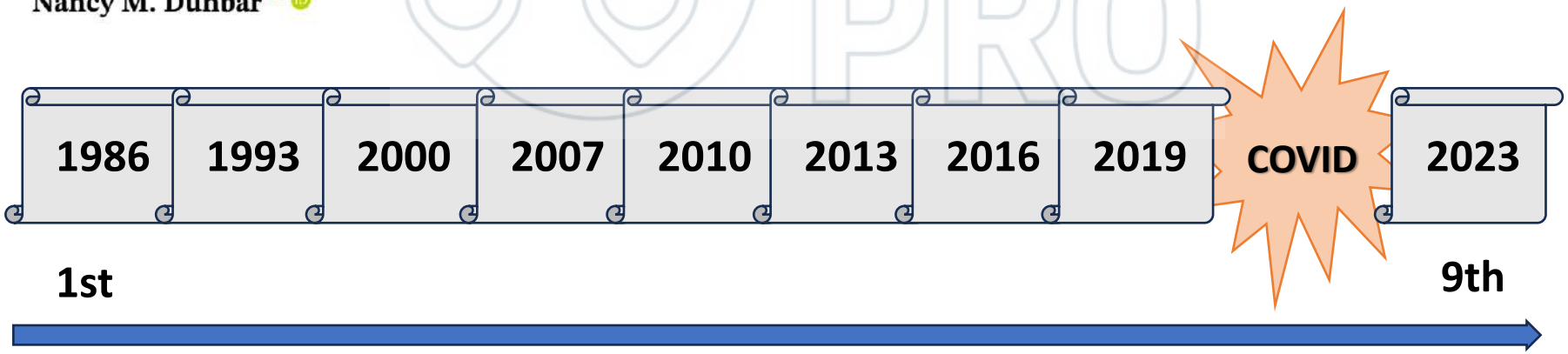
nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatrice di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le sue funzioni al fine di trarne vantaggio.

Received: 29 November 2022 | Revised: 25 January 2023 | Accepted: 27 January 2023
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]



THE 9TH SPECIAL ISSUE

11 MEMBRI REVISORI

Selezionati da 42 esperti, rappresentativi di diverse provenienze geografiche, età professionale e pertinenza clinica

- **Revisione stringente della letteratura aggiornata**
- Analisi della qualità delle evidenze
- Analisi della forza della raccomandazione

Approccio basato sulle evidenze:

- **Uniformare le categorie ASFA assegnate**
- **Definire la forza della raccomandazione con uno schema definito**
- **Fornire informazioni sintetiche e comprensibili utili alla pratica clinica aferetica**

ASFA categories

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.

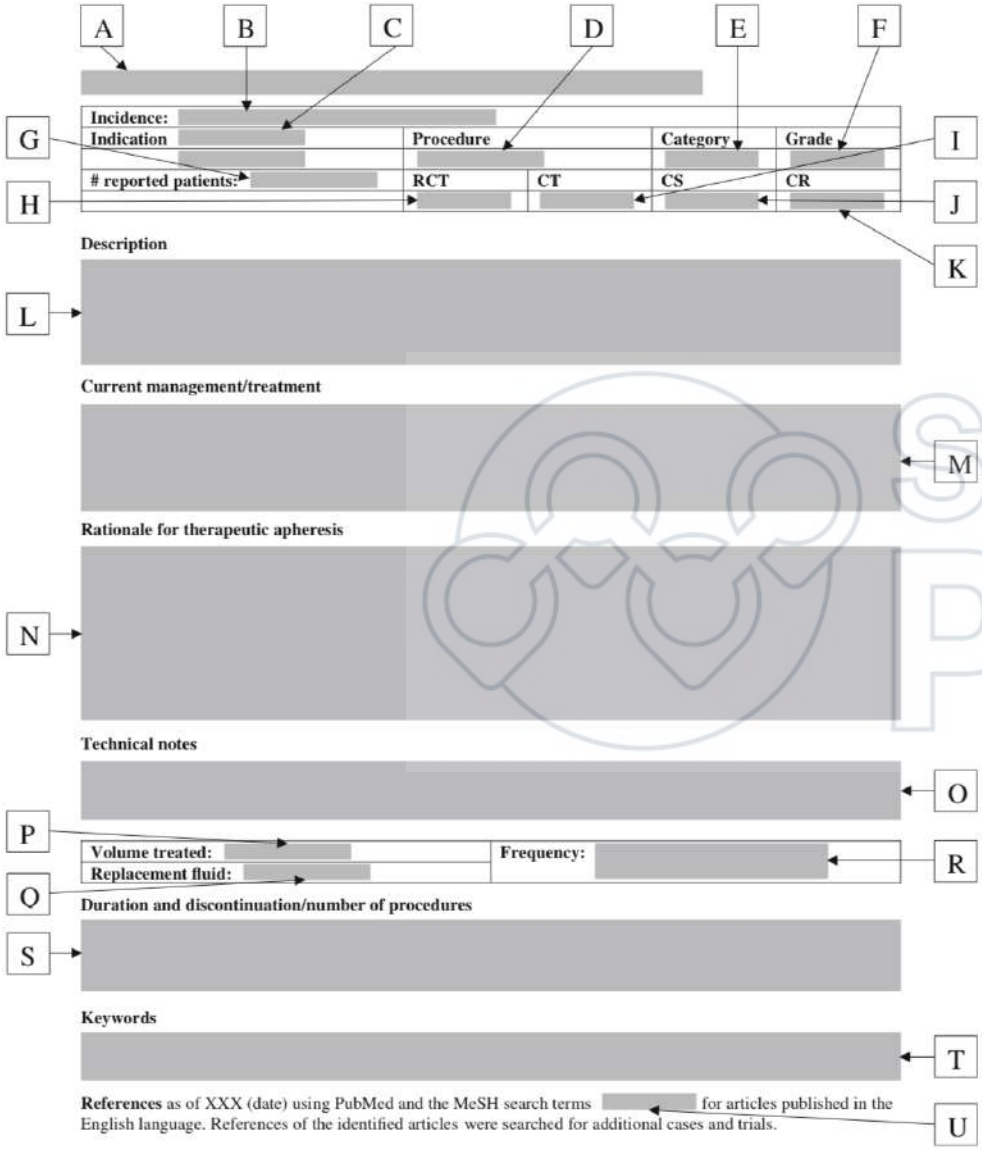
Abbreviation: IRB, Institutional Review Board.

GRADE SYSTEM

Grading Recommendations, strenght and quality of evidence

Recommendation	Description	Methodological quality of supporting evidence	Implications
Grade 1A	Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
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
Grade 1C	Strong recommendation, low-quality or very low-quality evidence	Observational studies or case series	Strong recommendation but may change when higher-quality evidence becomes available
Grade 2A	Weak recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2B	Weak recommendation, moderate-quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2C	Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

FACT SHEETS FOR 91 DISEASES/CONDITIONS



- **Stesso format della precedente edizione**
- Anche più indicazioni e procedure per la stessa patologia
- Invertite le posizioni di categoria e grado
- Testo limitato **(quick reference)**
- 25 voci bibliografiche

DEVELOPING NEW AND AMENDING OLD FACT SHEETS

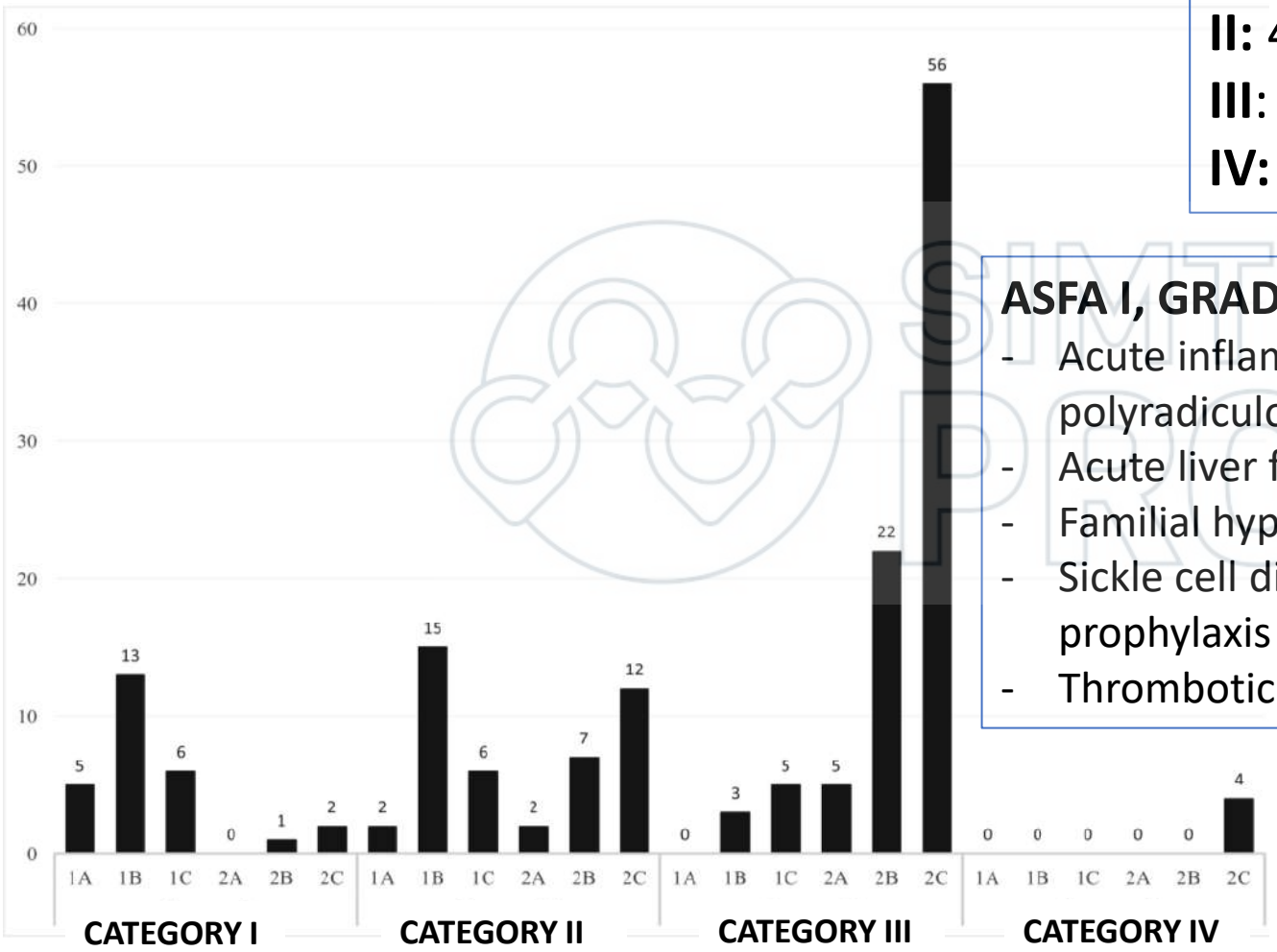
- **OLD FACT SHEET:** l'autore revisiona ogni nuovo sviluppo sulla conoscenza e il trattamento della patologia rispetto all'ultima revisione.
- **NEW FACT SHEET:** l'autore revisiona gli ultimi 10 anni di letteratura inerente, considerando solo lavori in inglese, *peer-reviewed,* indicizzati *PubMed.*

Fino a 10 «fact sheets» per autore

JCA Special Issue 2023
(9th edition)

Significant expansion in the number of indications (91 fact sheets, 166 indications)

ASFA:
I: 27
II: 44
III: 91 (56 grade 2C)
IV: 4 (grade 2C)



ASFA I, GRADE 1-A

- Acute inflammatory demyelinating polyradiculoneuropathy
- Acute liver failure
- Familial hypercholesterolemia (homoz)
- Sickle cell disease, non acute, stroke prophylaxis
- Thrombotic thrombocytopenic purpura

Retired category IV recommendations for TA

Disease/condition	Procedure	Full fact sheet in JCA special edition
Amyloidosis, causes other than dialysis	TPE	2019
Amyotrophic lateral sclerosis	TPE	2013
Dermatomysitis/ polymyositis	TPE, ECP	2016
HELLP syndrome, antepartum	TPE	2019
Idiopathic polyarteritis nodosa	TPE	2019
Inclusion body myositis	TPE, leukocytapheresis	2013
Multifocal motor neuropathy	TPE	2019
POEMS syndrome	TPE	2013
Rheumatoid arthritis	TPE	2010
Schizophrenia	TPE	2013

Several naming and wording changes

Name changes to reflect the current state of the role of TA in the disease/condition

NINTH EDITION	EIGHT EDITION
Amyloidosis, systemic, dialysis related	Amyloidosis, systemic
Red blood cell alloimmunization, pregnancy complications	Red cell alloimmunization, prevention and treatment
Coagulation factor deficiency and inhibitors	Coagulation factor inhibitors

Journal of Clinical Apheresis ASFA

ACUTE INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

Eponyms were removed from the title

Incidence: 1 to 2/100,000/year

Indication	Procedure	Category	Grade
Primary treatment	TPE	I	1A
	IA	I	1B

Treatment:

- Supportive care
- TPE **and/or** IVIG (0,4 g/kg for 5 consecutive days)

«Zipper Method» (Kesici 2019):
TPE+IVIG (24 h), 5 procedures in 7 days (1,5 TPV and then 1 TPV), 5% albumin and fresh frozen plasma from the third procedure.

«Modified Zipper Method» (Nikolaus 2022)»
TPE+IVIG (48 h), 7-10 procedures (1,5 TPV). Fresh frozen plasma.

Low mortality, short mechanical ventilation time, short hospital stay in children with severe GBS or ADEM

16 Diseases/conditions considered for new fact sheets

Incorporated as new fact sheets
Alzheimer's disease
Autoimmune dysautonomia
Idiopathic inflammatory myopathies
Immune checkpoint inhibitors, immune-related adverse events
Paraneoplastic autoimmune retinopathies
Transplantation, intestine
Vaccine-induced immune thrombotic thrombocytopenia
Incorporated into existing fact sheets
Mechanical hemolysis incorporated into acute toxins, venoms and poisons
Methemoglobinemia incorporated into acute toxins, venoms and poisons
Bone marrow necrosis/fat embolism syndrome incorporated into sickle cell disease, acute
Insufficient evidence at time of review
Autoimmune myofasciitis
Autoimmune recurrent pregnancy failure
Hyperbilirubinemia, kidney failure/bile cast nephropathy
Pancreatic transplantation
Platelet refractoriness due to human leukocyte antigen (HLA) antibodies
Transplantation, composite tissue

- Not sufficient published evidence
- Too few cases to meet the criteria

COVID-19

La pandemia da SARS-CoV-2 ha avuto un impatto globale sul sistema sanitario ma anche nel mondo aferetico

Nuovo fact-sheet

VACCINE-INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA

Incidence: ChAdOx1 (1st dose) 1:26,500 to 127,300 doses; Ad26.COV.S 1:263,000 doses

Indication	Procedure		Category	Grade
Refractory*	TPE		III	2C
# reported patients: <100	**RCT**	**CT**	**CS**	**CR**
	0	0	3 (26)	9 (11)

*Severe thrombocytopenia (<30 × 10^9/L) or cerebral venous sinus thrombosis, unresponsive to first-line management

Ma anche **nuove indicazioni e commenti** su una possibile associazione con il COVID-19 **in diversi altri «fact-sheets»**

COVID-19 and…

- ACUTE DISSEMINATED ENCEFALOMYELITIS
- ACUTE INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY
- ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE
- MYASTENIA GRAVIS
- AUTOIMMUNE DYSAUTONOMIA
- IMMUNE THROMBOCYTOPENIA
- N-METHYL-D-ASPARTATE RECEPTOR ANTIBODY ENCEPHALITIS
- SEPSIS WITH MULTIORGAN FAILURE
- THROMBOTIC MICROANGIOPATHY, THROMBOTIC THROMBOCYTOPENIC PURPURA
- TOXIC EPIDERMAL NECROLYSIS
- VASCULITIS, OTHER

«CHOOSING WISELY»

GENERAL	DESCRIPTION
Rationale	Rationale for the procedure and patient specific risks from the procedure
Impact	The effect of TA on co-morbidities and medications
Therapeutic plan	Total number and frequency of TA procedures
Clinical and/or laboratory end-points	Parameters to monitor effectiveness of the treatment
Timing and location	The accetable timing of initiation (emergent, urgent, routine) and location (or transfer of the patient)
Technical issues	Type of anticoagulant, replacement solution, vascular access, volume of whole blood processed

TIMING OF INITIATION OF TA

- **EMERGENT**
- **URGENT**
- **ROUTINE**

« ***NOT ADDRESSED DIRECTLY*** *IN THE FACT SHEETS GIVEN THE* ***HETEROGENEITY OF PATIENT DISEASE PRESENTATION*** *AND* ***VARIABILITY IN THE AVAILABILITY OF APHERESIS****.»*

« THE PATIENT'S CLINICAL CONDITION AND DIAGNOSIS, AS WELL AS AVAILABILITY OF ALTERNATIVE THERAPIES, SHOULD BE CAREFULLY EVALUATED WHEN DETERMINING THE OPTIMAL TIMING OF TA».

THROMBOTIC MICROANGIOPATHY, THROMBOTIC THROMBOCYTOPENIC PURPURA

Incidence: <1/100,000/year				
Procedure	**Category**		**Grade**	
TPE	I		1A	
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
	7 (301)	5 (270)	NA	NA

…..**To initiate treatment for presumed TTP <u>within 4 to 8 hours of diagnosis suspicion</u>**, after other causes of systemic TMA have been considered unlikely….

TPE has decreased overall mortality...

<u>TPE should be initiated emergently</u> once the diagnosis is suspected. <u>If TPE is not immediately available, **large dose plasma infusions**</u> (25-30 ml/kg) should be given.

Corticosteroids should be used as an adjunt…

Caplacizumab has been approved for the treatment of immune TTP together TPE…

Rituximab … is now often added as adjuntive agent with initial TPE and corticosteroids.

The 9° edition of the JCA Special Issue seeks to continue to serve a key resource to guide the utilization of TA

3 McLeod Criteria to assess indication for TA in rare diseases/conditions

1. **PLAUSIBLE PATHOGENESIS:** the understanding of the disease process suggests a clear rational for TA;
2. **BETTER BLOOD:** evidence suggesting that the abnormality that makes apheresis plausible is meaningfully corrected by TA;
3. **PERKIER PATIENTS:** evidence that TA confers benefit that is clinically worthwhile.

GRAZIE PER L'ATTENZIONE

TEAM AFERESI VICENZA:
Dott.ssa Manuela Rigno
Dott.ssa Gabriella Errigo
Dott. Giacomo Sartori

Barbara Sartori
Carla Zampieri
Giulia Vezzaro
Keti Anzolin

Nicola Leonetti
Ilaria Di Camillo
Debora Ferrando