Transfusion and Apheresis Science 65 (2026) 104423

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

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

Italian register of therapeutic apheresis: 30 years of activity

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ARTICLE INFO

Keywords:
Transfusion services
Therapeutic apheresis
Italian registry of therapeutic apheresis

ABSTRACT

The Italian Registry of Therapeutic Apheresis (IRTA) collects clinical data on patients undergoing therapeutic apheresis procedures in Italy. In this study, we outline the main changes in IRTA activity from its inception to 2024 in terms of indications, approaches, and outcomes, and provide details on the main areas of development of therapeutic apheresis based on the IRTA data collected. Over the years, there has been a progressive increase in procedures, from about 13,000 in the initial years to approximately 37,000 in 2024. Overall, more than 300,000 procedures have been performed across all centers (median number of procedures per year: 28,673) and have been included in the IRTA. Indications for therapeutic apheresis have evolved in parallel with changes in American Society for Apheresis indications. IRTA data demonstrate the continued use of apheresis treatment in neurological medicine and solid organ, bone marrow, or stem cell transplantation. Starting from 2019, apheresis cell collections were also performed for the manufacture of CAR-T cells. The safety of these procedures has always been very high. Additionally, the transition from discontinuous to continuous-flow cell separators and the subsequent introduction of automated procedures have further improved overall treatment management. The IRTA proves to be an important tool both for monitoring therapeutic apheresis activity nationwide and for identifying its main areas of development. Emerging pathologies not yet covered by guidelines, especially in neurology, new areas of use for cell therapies, such as CAR-T cells, and the advancement of organ and tissue transplantation represent the challenges in the coming years.

1. Introduction

The Italian national apheresis registry was first established in 1997 [1], with fully manual, voluntary data collection and no cross-checking tools for about 20 years.The turning point occurred in 2017, when SIdEM in collaboration with the National Blood Center decided to transfer data collection to the Transfusion Services Information System (SISTRA), the national software used to record data on all the activities of transfusion centers operating in Italy. The first data collection within SISTRA refers to 2019, which was considered a pilot year but was nonetheless indicative of user participation. In 2020, the COVID-19 pandemic significantly affected all healthcare activities, and apheresis therapy was limited to emergency situations or to patients with severe conditions lacking alternative treatment options. Consequently, activity data from 2019 and 2020 were evaluated together [2]. The first reliable data collection refers to 2021, a year still heavily affected by the pandemic but characterized by longer, though not continuous, periods of access to therapy. With the inclusion of IRTA data in SISTRA, pathologies were classified according to the therapeutic apheresis guidelines of the ASFA (American Society for Apheresis), allowing a high level of detail even within the same pathology, depending on clinical presentation and specialist area. Complete data for the years 2019–2024, classified according to the new system, are presented below. The integration of IRTA into the SISTRA information system has also enabled analysis of pathologies that do not fall within the consolidated indications of the ASFA Guidelines. All clinical areas now include an "Other" category, in which these cases are recorded; this category mainly comprises autoimmune neurological diseases such as encephalitis and myelitis [3]. The aim of this study was to analyze therapeutic apheresis activity in Italy over the last three decades, highlight how the

Abbreviations: NBC, the Italian National Blood Center; SIdEM, the Italian Scientific Society of Haemapheresis and Cell Manipulation; SISTRA, the Information System of Transfusion Services; IRTA, the Italian Registry of Therapeutic Apheresis; TA, Therapeutic Apheresis; ASFA, American Society for Apheresis.

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https://doi.org/10.1016/j.transci.2026.104423
Received 12 January 2026; Received in revised form 3 March 2026; Accepted 6 March 2026
Available online 8 March 2026

Table 1
Number of procedures, percentage per transfusion center.

YEAR	1997	2000	2009	2015	2017	2019	2020	2021	2022	2023	2024
Total procedures	**13,439**	**15,202**	**31,909**	**27,633**	**23,515**	**23,715**	**28,673**	**34,734**	**35,205**	**36,868**	**36,631**
N° Procedures /Center	**MANUAL RECORDING**					**SISTRA**					
< 50	54%	44%	(*)	8%	7%	15%	26%	20%	18%	21%	21%
51–100	16%	15%	(*)	12%	7%	15%	14%	17%	18%	17%	15%
101–300	15%	24%	(*)	25%	33%	36%	26%	26%	29%	26%	20%
301–500	7%	11%	(*)	28%	18%	5%	12%	16%	10%	8%	14%
> 500	8%	6%	(*)	27%	35%	29%	22%	21%	25%	28%	30%

(*) data not available

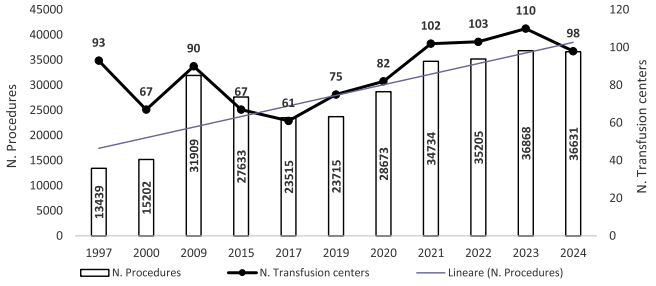

Fig. 1. Number transfusion centers and therapeutic apheresis procedures from 1997 to 2024.

indications and clinical settings of use have changed, monitor the safety aspects of the procedures, and verify the treatment outcomes.

2. Material and methods

Data for the years 1997–2017 were collected through the voluntary completion of forms made available on the SIdEM scientific society website. These forms were printed, completed by individual centers, and subsequently sent to SIdEM. The collected data were entered into an Excel spreadsheet and published. Since 2019, data from the IRTA therapeutic apheresis registry have been entered into SISTRA. Cumulative annual data are submitted to IRTA between January and April of each year following the survey by the designated contact person of each Therapeutic Apheresis (TA) center, who has authorized access to the SISTRA registry via the National Blood Center website. Data are reviewed by the registry manager to identify significant outliers or implausible values. Participation in the data collection has always been voluntary, with annual submissions. From 1997–2017, data collection was conducted using different criteria, and since records were exclusively on paper, data from some years are no longer available in the archive. The 2018 data are also incomplete, as the new data collection system within SISTRA was still under development. Therefore, this study reports data from the most complete years prior to the introduction of SISTRA (1997, 2000, 2009, 2015, and 2017). Additionally, data submitted for the period 2019–2024 have been updated, as centers were allowed to enter or revise data even after the initial submission deadline.

3. Results

Over the years, an increase in the number of procedures has been observed, rising from 13,459 in 1997–36,631 in 2024 (Table 1). In 1997, a total of 93 operational centers were registered, without distinction between those providing both productive and therapeutic apheresis and those offering only one of these services. The primary objective in 1997 was to obtain a comprehensive overview of apheresis activities and supporting resources, including the number and type of cell separators and healthcare personnel dedicated to apheresis. In 1997, 54% of centers performed fewer than 50 procedures. This percentage progressively decreased until 2017, then increased to 21% in 2023 and 2024. In 1997, only 8% of centers performed more than 500 apheresis procedures, whereas in 2024, this proportion increased to 30% (Table 1).

We observed that the number of centers involved was not directly proportional to the number of procedures performed (Fig. 1).

In the therapeutic apheresis setting, a total of 13,439 procedures were recorded in 1997, including 387 LDL apheresis, 3,711 hematopoietic stem cell collections, 118 non-stem cell cytapheresis, 256 extracorporeal photochemotherapy/photopheresis, and 8,682 plasma exchange/treatment procedures, and 285 erythroaphesis. Despite the reduction in participating centers, the following years recorded a 75% increase in procedures (from 13,439 to 23,515), mainly represented by plasma exchange, offline photopheresis and haematopoietic stem cell collections (Table 2). From 2019–2024, total procedures increased by 54%, with notable rises in online photopheresis (176%) and offline photopheresis (90%), thrombocytopheresis (283%), red blood cell exchange (171%), and stem cell collection (autotransplantation) (58%). A

Table 2
Number of therapeutic apheresis procedures and type of procedure from 1997 to 2017 (manual recording).

YEAR	1997	2000	2009	2015	2017
Type of procedure	**MANUAL RECORDING**				
N° Procedures	**13,439**	**15,202**	**31,909**	**27,633**	**23,515**
Plasma exchange	data not available	7,496	13,659	11,797	10,679
Cascade filtration	data not available	759	1,263	1,190	610
Plasma adsorption (physical, chemical)	data not available	3	149	59	20
IgG / IgE Immunoadsorption	data not available	18	93	79	239
LDL apheresis	387	569	1,310	927	510
Lymphoplasmapheresis	118 (Lymphoplasmapheresis + Leukocyte -apheresis +Thrombocytapheresis)	32	0	4	21
Leukocyte -apheresis		103	0	279	121
Thrombocytapheresis		388	0	78	124
Granulocyte-Monocyte apheresis	0	0	751	1,204	398
Erythrocyte-exchange	0	128	776	1,300	505
Stem Cell Collection (autotransplant)	3,711	1,539	4,355	3,254	3,040
Erythro-apheresis	285	1,290	2,413	836	1,120
Online Photopheresis	256	376	1,098	1,427	1,556
Offline Photopheresis	0	328	6,042	5,179	4,286
Other	0	53	0	0	17

Table 3
Number of therapeutic apheresis procedures and type of procedure from 2019 to 2024 in SISTRA.

YEAR	2019	2020	2021	2022	2023	2024
Type of procedure	**SISTRA**					
Total	**23,715**	**28,673**	**34,734**	**35,205**	**36,868**	**36,631**
Plasma exchange	11,516	11,386	12,833	13,525	15,151	13,661
Cascade filtration	484	609	797	569	663	661
Plasma adsorption (physical, chemical)	0	0	274	96	109	139
IgG / IgE Immunoadsorption	235	138	192	43	39	34
Photopheresis online	1,624	2,774	3,012	3,770	4,525	4,479
Photopheresis offline	2,921	4,776	6,545	5,780	4,883	5,558
LDL-aferesi	377	441	657	584	670	468
Lymphoplasmapheresis	16	0	7	0	2	0
Leukocyte apheresis	199	75	98	75	82	86
Granulocyte-Monocyte apheresis	342	255	304	242	195	98
Thrombocytapheresis	12	30	41	21	55	46
Erythrocyte-exchange	1,274	2,110	2,298	2,392	2,699	3,458
Erythro-apheresis	2,457	2,787	3,361	3,421	2,999	3,614
Stem Cell Collection (autotransplant)	2,192	3,236	3,630	4,260	4,259	3,460
Other	66	56	685	427	537	869

Table 4
Number of procedures for clinical indications from 1997 to 2017.

YEAR	1997 (*)	2000	2009	2015	2017
	MANUAL RECORDING				
N° Procedures	**13,439**	**15,202**	**31,909**	**27,633**	**23,515**
Clinical indications					
Myasthenia Gravis	635	4,980	2,297	1,982	
Guillain-Barré Syndrome (GBS)	563	740	658		
Chronic inflammatory polyneuropathy	0	1,480	1,280		
Cryoglobulinemia	934	1,602	713	524	
Systemic vasculitis	0	829	219		
Thrombotic Thrombocytopenic Purpura (PTT) and other microangiopathies	607	2,123	2,110	1,632	
Glomerulonephritis/Kidney failure	137	0	389	262	
Hemolytic uremic syndrome	0	0	379	152	
Hypercholesterolemia	552	1,497	709	563	
Chronic inflammatory bowel disease	0	592	661	223	
AB0 incompatibile transplant	0	0	172	115	
Organ transplant rejection	0	2,816	780	697	
Autoimmune encephalitis/ other	0	0	434	215	
Systemic connective tissue disease /scleroderma	0	929	613	431	
Segmental focal glomerulosclerosis	0	0	419	496	
Multiple myeloma	0	0	278	0	
Syndrome HELLP	0	0	21	5	
Optic neuromyelitis	0	0	128	165	
Thyrotoxicosis	0	0	6	0	
Hyperbilirubinemia	0	0	88	0	
Pemphigus	0	0	53	217	
Hypertriglyceridemia	0	0	70	0	
Other	3,176	0	633	570	
HSC Collection					
Multiple myeloma	344	0	1,228	972	
Lymphoma	625	0	1,209	759	
Acute leukemia (Autograft/ Back up)	300	0	338	148	
Neuroblastoma	7	0	0	0	
Other solid tumor	46	0	54	42	
Other:	198	0	0	85	
Multiple myeloma	10	0	205	100	

(*) clinical indications were not recorded

reduction in IgG/IgE immunoadsorption procedures (-86%), granulocyte-monocyte apheresis (-71%), and leukocyte apheresis (-57%) was observed over the same period (Table 3).

In the collection of activity data from 2000 to 2017, the type of apheresis procedure was further detailed by including the clinical indications for each treatment, based on the ASFA Guidelines from the 2000 edition and subsequent editions published between 2007 and 2023 (six editions in total). (Table 4).

Clinical indications by area (2019–2024). Table 5 presents the clinical indications for apheresis procedures recorded in SISTRA from 2019 to 2024.

- Neurology: Procedures have increased, with the most frequent indications being myasthenia gravis, CIDP, and Guillain-Barré syndrome.
- Hematology: This area continues to require the highest number of procedures, totaling 11,908 in 2024 (32.5% of the total), primarily for graft-versus-host disease, erythrocytosis, and sickle cell disease. Treatments for thrombotic thrombocytopenic purpura have decreased following the introduction of new therapeutic protocols [4,5].
- Rheumatology: No significant changes were observed, with residual activity mainly for ANCA-associated glomerulonephritis, cryoglobulinemia, vasculitis, and scleroderma.
- Nephrology: No notable changes were recorded, with focal segmental glomerulosclerosis remaining the most frequent indication.
- Dermatology: Treatments for cutaneous T-cell lymphoma and pemphigus vulgaris have increased, while endocrinological indications remain negligible.
- Gastroenterology: Activity remains limited; in 2024, 40 procedures were performed for chronic inflammatory bowel disease and 48 for acute liver failure or fulminant hepatitis.
- Metabolic diseases: Despite new drug therapies, some patients with familial hypercholesterolemia and elevated Lp(a) continue to require therapeutic apheresis, likely due to inadequate response to PCSK9 inhibitors [6].
- Solid organ transplantation support: Apheresis activity is increasing; in 2024, 2318 procedures were performed, representing a 32.6% increase compared to 2023. Procedures for antibody-mediated rejection of lung transplants increased by approximately 300%, and ABO-compatible renal transplants by approximately 50%.
- Other indications: A total of 43 procedures were performed for conditions not included in the above areas: 9 for sudden deafness, 9 for drug or poison intoxication, 11 for sepsis and multiorgan failure, and 14 for hyperferritinemia or hemoglobinopathies. Among these,

Table 5
Number of procedures for clinical indications from 2019 to 2024 in SISTRA.

NEUROLOGY	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Acute disseminated encephalitis	118	70	100	115	233	304
CIDP - Chronic inflammatory demyelinated polyneuropathy	1,269	1,260	1,406	1,425	1,451	1,384
Chronic focal Rasmussen encephalitis	6	0	0	0	10	11
Guillain-Barré syndrome	666	645	695	1,182	1,307	1,115
Complex regional pain syndrome	0	0	3	3	9	0
Lambert-Eaton syndrome	7	9	97	69	109	78
Multiple Sclerosis	378	305	376	354	257	267
Myasthenia Gravis	2,938	2,787	2,412	2,808	2,740	3,308
Neuromyelitis optica	209	230	379	312	376	556
NMDAR- antibodies encephalitis	28	80	83	106	112	64
Paraneoplastic neurological syndromes	30	50	55	36	65	156
Paraproteinemic demyelinating neuropathies	100	117	187	115	121	77
PANDAS, Pediatric Neuropsychiatric Post-Streptococcal Syndrome	5	13	26	38	145	194
Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	0	1	0	0	4	0
VG-potassium channel (VGKC) antibody related Diseases	1	7	9	4	8	51
Stiff person syndrome	132	65	94	99	54	86
Other	228	314	229	325	280	323
Total	6,115	5,953	6,151	6,991	7,281	7,974
HEMATOLOGY	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Systemic amyloidosis	0	6	11	2	7	3
Autoimmune hemolytic anemia-Cold agglutinin disease	7	11	100	19	23	56
Coagulation factors inhibitors	1	14	0	0	1	2
Myeloma - acute renal failure	74	36	77	0	56	13
GVHD-Graft versus Host Disease	1,492	3,087	4,621	3,858	3,472	3,954
ABO-incompatible haematopoietic stem cell transplantation	29	62	110	81	85	110
Transplantation-haematopoietic stem cells, anti-HLA antibodies	3	24	48	76	53	43
Haemophagocytic syndromes	17	22	15	11	3	6
Thrombocytopaenia / thrombosis induced by heparin	0	0	3	1	0	0
Immunological thrombocytopaenias	8	0	0	0	0	11
Hyperviscosity in hipergammaglobulinaemia	72	114	152	115	129	217
Immunological thrombocytopenia	0	0	2	0	0	0
Polycythaemia vera-Erythrocytosis	1,972	2,225	2,846	2,810	1,926	3,067
Post-transfusion purpura	0	0	0	0	0	0
Red Cell Immunization, D-antigen-Prevention and treatment	0	0	0	0	0	0
Anti-D immunization in pregnancy	0	34	35	51	52	51
Acute Sickle Cell Disease	212	150	139	133	192	313
Sickle Cell Disease, non-Acute Sickle Cell Disease	811	1,441	1,175	1,571	1,697	2,089
Thrombocytosis	10	21	19	21	24	46
Thrombotic coagulation-mediated microangiopathy	24	42	15	28	25	12
Thrombotic complement-mediated microangiopathy	33	13	20	12	38	10
Thrombotic microangiopathy associated with drugs	0	0	0	0	2	0
Thrombotic microangiopathy associated with infection	9	13	52	0	9	17
Post-TMO thrombotic microangiopathy	1	50	34	49	62	51
Thrombotic thrombocytopaenia purpura, TTP	1,406	1,361	1,418	1,625	1,236	926
Malaria	0	0	0	0	0	9
Babesiosi	0	0	0	11	0	0
Erythropoietic porphyria	7	10	17	10	11	9
Hereditary haemochromatosis	107	208	208	304	208	305
Other	75	52	445	72	301	588
Total	6,370	8,996	11,562	10,860	9,612	11,908
RHEUMATOLOGY	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
ANCA-associated glomerulonephritis	200	158	343	175	126	167
Cryoglobulinemia	352	280	225	141	230	221
Schonlein-Henoch purpura	7	0	1	8	0	0
Vasculitis	186	231	208	247	270	192
Neonatal cardiac lupus	6	0	0	0	0	13
Catastrophic antiphospholipid syndrome	55	40	48	44	50	47
Scleroderma	414	264	98	105	61	100
Systemic Lupus erythematosus	63	70	114	52	48	54
Other	114	157	153	99	99	70
Total	1,397	1,200	1,190	871	884	864
NEPHROLOGY	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Goodpasture's syndrome	63	91	212	125	98	37
Focal segmental glomerulosclerosis	184	214	301	503	451	476
IgA nephropaty	0	18	20	20	15	7
Nephrogenic systemic fibrosis	0	0	0	0	0	0
Other	81	73	165	8	89	98
Total	328	396	698	656	653	618
DERMATHOLOGY	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Atopic dermatitis	5	1	3	0	0	10
Cutaneous T-cell lymphoma/Sezary syndrome	340	781	955	604	391	824
Pemphigus vulgaris	123	118	129	43	78	147
Pruritus due to biliary cirrhosis	12	4	0	3	0	14
Psoriasis	0	2	0	5	0	2

(*continued on next page*)

Table 5 (*continued*)

Toxic epidermal necrolysis (TEN) - drugs	13	4	0	7	0	10
Burn shock	0	0	0	0	0	0
Other	47	76	21	131	66	17
Total	540	986	1,108	793	535	1,024
ENDOCRINOLOGY	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Hashimoto's encephalopaty	0	0	0	4	0	0
Tyiroid storm	4	1	9	11	11	0
Other	45	7	0	0	1	6
Total	49	8	9	15	12	6
GASTROENTEROLOGY	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Acute liver failure-Fulminant hepatitis	26	62	66	93	48	48
Porphyria	0	0	0	2	0	0
Chronic inflammatory bowel disease	303	124	131	185	96	40
Fulminant Wilson's disease	0	0	0	13	0	0
Other	37	63	40	14	21	37
Total	366	249	237	307	165	125
METABOLISM	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Familial hypercholesterolemia	340	264	485	281	303	179
Pancreatitis with hypertriglyceridaemia	73	78	32	75	58	76
Hyper-Lp (a)	70	52	182	399	456	400
Peripheral vascular disease	48	36	32	0	0	8
Refsum's disease	0	0	0	0	0	0
Other	40	45	0	19	54	29
Total	571	475	731	774	871	692
SOLID ORGAN TRANSPLANT	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Heart Transplant-Recurrent Rejection	121	124	187	318	292	301
Heart transplant - Prophylaxis of rejection	185	421	402	138	161	157
Heart Transplant-Desensitization	0	7	17	48	0	17
Heart Transplant-Ab-mediated Rejection	45	40	129	53	50	42
Liver Transplant, ABO Desensitization (Living Donor)	0	1	0	0	0	0
Liver transplant, ABO Desensitization (deceased donor)	76	0	0	0	1	0
Liver transplant, Ab Rejection (ABO / HLA)	75	21	60	42	16	41
Lung Transplant-BOS	16	136	630	776	574	658
Lung Transplant-Ab-Mediated Rejection	26	39	86	62	167	288
Lung Transplant-Desensitization	0	0	12	1	0	2
ABO compatible kidney transplant - Ab mediated rejection	405	467	452	295	405	584
ABO compatible kidney transplant - Desensitization, living donor	17	31	7	91	44	68
ABO compatible kidney transplant - Desensitization, deceased donor	45	182	122	27	38	42
ABO Incompatible kidney transplant - Desensitization, living donor	116	134	162	68	117	81
ABO Incompatible Kidney Transplant-Ab mediated Rejection	35	2	46	60	2	25
Other	0	6	68	0	31	12
Total	1,162	1,611	2,380	1,979	1,898	2,318
OTHER	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Age-related macular degeneration	13	0	0	0	0	0
Dilated cardiomyopathy	0	0	0	0	0	0
Sudden hearing loss	0	18	24	14	0	9
HELLP syndrome	5	20	6	4	3	1
Overdose, envenomation, and poisoning	0	7	2	3	14	9
Sepsis with multiorgan failure	12	24	6	6	2	11
Other	0	0	7	40	13	27
Total	30	69	45	67	32	57

Table 6
Total adverse events to therapeutic procedures for the years 2000–2024.

YEAR	2000	2015	2017	2019	2020	2021	2022	2023	2024
Total adverse events									
N° Procedures	**15,202**	**27,633**	**23,515**	**23,715**	**28,673**	**33,681**	**34,702**	**36,208**	**36,631**
Mild*	5.34%	6.67%	5.50%	4.34%	3.41%	2.87%	2.74%	2.79%	3.86%
Moderate*	0.52%	0.88%	0.66%	0.32%	0.69%	0.32%	0.35%	0.12%	0.28%
Severe*	0.89%	0.35%	0.34%	0.07%	0.03%	0.03%	0.02%	0.02%	0.01%

* Percentage (%) of total procedures

sudden hearing loss and overdose/envenomation were the most prevalent indications.

Since 2000, information on adverse events has also been collected, classified into three levels of severity: mild, moderate, and severe [7].

Table 6 summarizes complete data collected manually in 2000, 2015, and 2017, as well as data recorded in SISTRA from 2019 to 2024. Mild complications, including symptomatic hypocalcemia, apheresis circuit clotting, hematoma at the venipuncture site, and insufficient blood flow in the circuit, occurred in 5–7% of procedures. Moderate complications, including allergic or hypersensitivity reactions, nausea or vomiting, fever with chills, and general malaise that could necessitate stopping the procedure, occurred in 0,1–0,9% of procedures. Severe complications, including shock, vasovagal reaction, hemolysis, cardiac rhythm disturbances, and the need for cardiopulmonary resuscitation, decreased from 0.89% to less than 0.45% of procedures. (Table 6).

Table 7 presents adverse events by procedure for 2024 showing that 92% were mild, 8% moderate and 0.4% severe.

In addition to safety data, the outcome of the apheresis treatment cycle has been recorded since 2015 for several pathological conditions.

Table 7
Adverse events related to each therapeutic procedure for year 2024.

Therapeutic procedure	Mild	Moderate	Severe	Total
Plasma exchange	639	48	2	689
Cascade filtration	10	8	0	18
Plasma adsorption (physical, chemical)	3	1	0	4
IgG / IgE Immunoadsorption	0	0	0	0
Photopheresis (online)	13	0	0	13
Photopheresis (off line)	53	2	0	55
Lipoprotein apheresis	18	1	0	19
Lymphoplasmapheresis	0	0	0	0
Cytoreductive leukapheresis	1	0	0	1
Granulocyte-monocytoapheresis	1	1	0	2
Therapeutic platelet apheresis	4	1	1	6
Erythrocyte exchange	37	8	0	45
Erythroapheresis	13	0	0	13
Haematopoietic Stem Cell Collection (HSCC- autotransplant)	247	16	2	265
Other:	15	0	0	15
Total	**1,054**	**86**	**5**	**1,145**

Although information on the subsequent evolution of the patient's disease is not available, the partial data indicate a favorable response (remission or improvement) in most patients. From 2019–2024, approximately 70% of patients experienced an improvement in their health conditions; 16% achieved complete remission, and 3% experienced disease progression (Table 8). These findings highlight that therapeutic apheresis is generally safe and effective across a range of clinical indications.

Evaluating responses by clinical area for the year 2024, the most favorable outcomes were achieved in hematology and rheumatology. A separate consideration applies to metabolic diseases, particularly familial hypercholesterolemia and hyper-LP(a), which are highly sensitive to apheresis. These are familial diseases in which the treatment rationale is primarily the removal of cholesterol with highly selective techniques. In contrast, most other diseases treated with apheresis are of dysimmune origin, where pathogenetic mechanisms are complex and not fully understood. In these cases, mainly based on plasmapheresis, with the removal of plasma in its entirety. Although more complex, this approach is effective because it eliminates the components clearly implicated in the disease, as well as other cofactors that may still be unidentified (Table 9).

A more detailed analysis of patient's outcomes, supported by a broader set of case studies, showed the highest clinical responses in Guillain-Barré syndrome (86.8% remission or improvement), sickle cell disease (93.2%), myasthenia gravis (78.1% positive response), and graft-versus-host disease (78.1% improvement).

4. Discussion

In Italy, therapeutic apheresis procedures were first performed in the 1970s, but only a decade later the Italian Society of Hemapheresis (SIdE) was founded, later SIdEM. Activity in TA has been recorded since the 1990s, with the establishment of IRTA. Today, TA activity is consolidated and carefully monitored through the IRTA within the SISTRA. Over the course of these nearly 30 years of monitoring activity, the clinical areas of application of TA have changed according to the evolution of scientific knowledge and the availability of new drugs. As widely reported in literature, in addition to its established role in hematology, primarily for oncological diseases, TA continues to find application in neurological field, where debilitating diseases, with both acute and chronic progression, are based on immune disorders. In many neurological conditions, pathogenetic mechanisms are unclear or specific medications are unavailable. Clinical indications for TA have evolved significantly over the years. For example, conditions such as Waldenström's macroglobulinemia and cryoglobulinemia, which were once main indications for apheresis, are now typically managed with targeted pharmacological therapies, except in special cases. For other diseases, treatment decisions must be made on an individual basis.

In terms of safety and outcome, in fact, TA is confirmed generally a highly safe treatment. When performed according to recognized guidelines, it allows for favorable clinical responses. Both therapeutic and productive apheresis procedures have proven to be well-controlled, despite being extracorporeal therapies. TA is a semi-intensive procedure requiring expertise in both the clinical assessment of indications and the technical and procedural management of patients. These aspects are confirmed by the low number of significant adverse events and the good clinical response rates.

An important indicator of quality and expertise is the number of procedures performed at each center, which correlates with the maintenance of clinical and technical skills among medical and nursing staff. In 1997, 70% of centers performed fewer than 100 procedures per year,

Table 8
Patient's outcome and number of assessable patients from 2015 to 2024.

YEAR	2015	2017	2019	2020	2021	2022	2023	2024
Total Outcome								
N° Procedures	**27,633**	**23,515**	**23,715**	**28,673**	**34,734**	**35,205**	**36,868**	**36,631**
Patients			**2,104**	**2,330**	**1,218**	**4,162**	**3,786**	**3,996**
Remission	22.50%	18.30%	14.35%	17.00%	16.22%	14.80%	16.50%	9.56%
Improved	51.50%	61.80%	73.43%	68.58%	65.14%	68.60%	70.60%	68.09%
Unchanged	21.20%	15.80%	10.51%	10.99%	15.65%	13.90%	10.50%	20.32%
Worsened	4.70%	4.00%	1.71%	3.43%	2.99%	2.70%	2.40%	2.03%

Table 9
Patient's outcome and number of assessable patients for year 2024.

2024	Procedures	Patients assessable	Remission	Improved	Unchanged	Worsened
Neurology	7,974	1,002	104	651	208	39
Hematology	11,908	2,508	227	1,764	490	27
Rheumatology	864	106	3	74	25	4
Nephrology	618	31	2	19	10	0
Dermatology	1,024	71	5	48	16	2
Endocrinologia	6	3	3	0	0	0
Gastroenterology	125	35	1	23	6	5
Metabolism	692	68	8	53	7	0
Solid Organ Transplant	2,318	152	29	84	35	4
Other	57	20	0	5	15	0
Total	**25,586**	**3,996**	**382**	**2,721**	**812**	**81**

Table 10
Categories of indications for treatment with therapeutic apheresis.

Indication categories for treatment with therapeutic apheresis Year 2000 and Year 2023 (*)			
Pathology	**Type of procedure**	**Category 2000**	**Category 2023**
Kidney and metabolic diseases			
Anti-basement membrane antibody disease	Plasma exchange	I	I Alveolar hemorrhage/ dialysis independent III Dialysis dependent
Rapidly progressive glomerulonephritis	Plasma exchange	II	III
Kidney transplant rejection	Plasma exchange	IV	I
Preparation for transplantion in immunized subjects	Plasma exchange	III	I
Focal segmental glomerulosclerosis	Plasma exchange	III	I
Heart transplant rejection	Plasma exchange	III	II
	Photopheresisis	III	II
Acute liver failure	Plasma exchange	III	I if High Volume III
Familial hypercholesterolemia	Selective apheresis	I	I/II
	Plasma exchange	II	N.I.
Autoimmune and rheumatic diseases			
Raynaud's phenomen	Plasma exchange	II	N.I.
Rheumatoid arthritis	Immunoadsorption	II	N.I.
	Linphoplasmaferesis	II	N.I.
	Plasma exchange	IV	N.I.
Systemic lupus erythematosus	Plasma exchange	III	II Severe
Hematological diseases			
Thrombotic thrombocytopenic purpura	Plasma exchange	I	I
Post-trasfusion purpura		I	III
Circulating coagulation inhibitor	Plasma exchange	II	III
Neonatal hemolytic disease	Plasma exchange	III	N.I.
Platelet refractoriness due to alloimmunisation	Immunoadsorption	III	N.I.
Neurological diseases			
Relapsing multiple sclerosis	Plasma exchange	III	II
IgG/IgA demyelinating polyneuropathy	Plasma exchange	I	I
	Immunoadsorption	III	N.I.
Sydenham's chorea	Plasma exchange	II	III
IgM polyneuropathy	Plasma exchange	II	I if Iperviscosity
	Immunoadsorption	III	N.I.
POEMS syndrome	Plasma exchange	III	N.I.
Systemic amyloidosis	Plasma exchange	IV	N.I.
Polymyositis and dermatomyositis	Plasma exchange	III	N.I.
	Leukapheresis	IV	N.I.
Myositis from foreign bodies	Plasma exchange	III	N.I.
	Leukapheresis	IV	N.I.

(*) Indication categories for treatment with therapeutic apheresis [7,8] N.I.: Not Indicated

highlighting the risks of low-volume activity at most centers. Higher procedural volume ensures greater expertise, improving both patient outcomes and the quality of service. A slow but continuous reorganization of activities has aimed to maintain adequate levels of activity across centers, ensuring the knowledge, skills, and safety necessary for effective therapy.

The ASFA guidelines have also evolved over time reflecting growing understanding of disease pathogenesis and the availability of targeted pharmacological treatments. Examples of diseases whose classification according to McLeod's principles (the four categories of evidence of clinical indication to treat with TA) has changed over the years are provided in Table 10. Some diseases have seen the therapeutic indication for apheresis strengthened, others have become less supported due to more effective pharmacological options, and some cases still require individual evaluation.

The analysis of IRTA data highlights the evolving indications for plasmapheresis in organ transplantation. In 2000, organ transplantation and the related scientific literature were still in an early stage.

Gained experience, increased procedural activity, and clinical results have progressively changed the indications for therapeutic apheresis. A striking example is kidney transplant rejection, classified as Category IV in 2000 and upgraded to Category I in 2023.

In conclusion, IRTA represents not only an excellent tool for monitoring apheresis activity at the national level, but also a valuable resource for anticipating future developments in the field. The low number of adverse events confirms the safety of the procedure, and the good clinical response attests to the correct indication. Emerging pathologies not yet addressed by current guidelines, particularly in neurology, as well as new applications of cellular therapies such as CAR-T, and advances in organ and tissue transplantation, are likely to represent the main challenges in the coming years [9].

CRediT authorship contribution statement

Angelo Ostuni: Writing – original draft, Conceptualization. **Luciana Teofili:** Writing – review & editing, Writing – original draft. **Liviana Catalano:** Writing – original draft, Validation, Supervision, Resources, Formal analysis, Data curation, Conceptualization. **Giustina De Silvestro:** Writing – original draft, Supervision, Resources, Formal analysis, Data curation, Conceptualization. **Giuseppe Marano:** Writing – original draft, Conceptualization. **Vanessa Piccinini:** Software, Formal analysis, Data curation. **Ursula La Rocca:** Writing – review & editing, Writing – original draft.

Acknowledgment

We would like to thank all the centers that contributed to insertion and validation of the data in SISTRA:

Sandro Macchi, Asti - Massimo Milan, Torino - Tiziana Francisci, Torino - Roberto Albiani, Torino - Pierangelo, Bescape', Novara - Paola Maria Manzini, Cuneo - Francesca Pollis, Alessandria - Franca Napoli, Orbassano - Sergio D'Antico, Verduno - Moreno Porcari, Cremona - Marco D'agostino, Lodi - Alessia Orsini, Milano - Flavio Arienti, Milano - Irene Cuppari, Legnano - Paola Lanzini, Sondrio - Daniele Prati, Milano - Anna Falanga, Bergamo - Antonio Lodato, Garbagnate - Cesare Perotti, Pavia - Ivo Beverina, Gallarate - Vincenzo La Vina, Lecco - Alessandra Livraghi, Vigevano - Milena Pintimalli, Bolzano - Manuela Rigno, Vicenza - Alessandro Spigariol, Treviso - Giulia De Fusco, Venezia - Anna Colpo, Padova - Maurizio Cantini, Verona - Bianca Robecchi, Rovigo - Ersilia Barbone, Belluno - Chiara Savignano, Udine - Massimo La Raja, Trieste - Rita Epifania Testa, Pordenone - Vanessa Agostini, Genova - Paola D'elia, La Spezia - Alessandro Cocchella, Genova - Attilio Cristallo, Imperia - Gino Tripodi, Genova - Annalisa Gabriele, Rimini - Cinzia Moretti, Ravenna - Maria Beatrice Rondinelli, Bologna - Francesco Romeo, Piacenza - Gianluca Lodi, Ferrara - Rino Biguzzi, Cesena - Erminia Di Bartolomeo, Reggio Emilia - Giovanni Ceccherelli, Modena - Maurizio Soli, Parma - Stefano Ermini, Firenze - Soana Moretti, Lucca - Elena Mori, Livorno - Silvia Ceretelli, Grosseto - Irene Bianco, Pisa - Mauro Marchesi, Perugia - Rosella Bencivenga, Ancona - Sabrina Tarulli, Terni - Adriana Maiello, Pesaro - Isabella Cantori, Civitanova - Nicola Piccirillo, Roma - Eleonora Ponte, Roma - Maria Rita Cassetta, Roma - Silvia Da Ros, Viterbo - Antonio Pavan, Roma - Angela Rinaldi, Roma - Maria Laura Foddai, Roma - Giorgia Guiducci, Roma - Ottavia Porzio, Roma - Stefania Vaglio, Roma - Michele Vacca, Roma - Anna Rughetti,

L'Aquila - Anna Quaglietta, Pescara - Antonio Leonardi, Napoli - Maria Mottola, Napoli - Carmine Oricchio, Nocera - Cosimo Nocera, Napoli - Angelo Ostuni, Bari - Leonardo Sardella, Bari - Marina D'Alagni, Barletta - Donato Canaris, Tricase - Giuliano D'andria, Taranto- Nicola Di Renzo, Lecce - Pierpaolo Negro, Gallipoli - Caterina Mancuso, Catanzaro - Alfonso Trimarchi, Reggio Calabria - Renato Messina, Trapani - Mario Lombardo, Catania - Sebastiano Gravina, Enna - Roberta Fedele, Palermo - Nunzio Marletta, Caltanissetta - Antonio Genovese, Siracusa - Paolo Sciarrone, Messina - Vincenzo Barbera, Piazza Armerina - Tommaso Aronica, Palermo - Elisabetta Scire', Palermo - Francesco Bennardello, Ragusa - Amalia Rosalba Assisi, Catania - Claudia Maria Rizzo, Messina - Maria Giulia Fadda, Cagliari - Anna Borgia, Carbonia - Adriana Ibba, Nuoro - Mauro Murgia, Oristano - Pietro Manca, Sassari.

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