



The Italian registry of therapeutic apheresis: year of activity 2021

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ABSTRACT

In 2019, the Italian National Blood Center (NBC), at the request of the Italian Scientific Society of Haemapheresis and Cell Manipulation (*SidEM*), included the Italian Registry of Therapeutic Apheresis (IRTA) in the Information System of Transfusion Services (SISTRA), whose activity is coordinated by the NBC.

The IRTA provides institutions and scientific societies with a wide range of information including therapeutic procedures and outcomes of treated patients.

The Italian National Health Service offers therapeutic apheresis for patients with various conditions, but it is mainly the patient with haematological and/or neurological disorders who turns to the apheresis centres as evidenced by the activity data of 2021. In the haematological field, the apheresis centres mainly supply haematopoietic stem cells for autologous or allogeneic transplantation as well as mononuclear cell collection for extracorporeal photopheresis (ECP), a therapeutic approach of II line in post-transplant Graft versus Host Disease.

The activity of 2021 in the neurological field confirms the data of 2019, the pre-pandemic year, and indicates that myasthenia, chronic inflammatory demyelinating polyneuropathy and Guillain-Barré syndrome along with other neurological pathologies related to immune disorders are the diseases in which apheresis procedures are most used.

In conclusion, the IRTA is a valuable tool for monitoring the activity of apheresis centres carried out at a national level and above all for providing an overall picture of how the use of this therapeutic tool evolves and changes over time.

1. Introduction

Therapeutic apheresis is an extracorporeal treatment used to remove cells or substances in the blood as well as to administer cells or plasma constituents. It is successfully employed to treat haematologic, neurologic, renal, rheumatic and metabolic disorders, for which therapeutic alternatives are not available or effective.

The Italian Registry of Therapeutic Apheresis (IRTA) provides institutions and scientific societies with a wide range of information including therapeutic procedures and outcomes of treated patients.

Since most of the apheresis procedures are performed within the transfusion services, the IRTA has been included in the information system of the transfusion services (SISTRA), which collects data on all transfusion activity.

SISTRA is the Information System of the Transfusion Services,

developed as a strategic support for the achievement of the objectives established by the Italian law regulating blood transfusion. It is managed by the National Blood Centre (NBC) and uses the infrastructure of the Italian Ministry of Health [1].

This choice certainly represented a great operational advantage also for the Italian Society of Haemapheresis and Cell Manipulation (*SidEM*), which found in the SISTRA an effective tool for collecting information and data available for further scientific activities. The previous operating years of IRTA, i.e. 2019 and 2020, have been the subject of a previous publication [2]. Data for 2021 is presented in this manuscript.

2. Material and methods

The data collection software was created as a section of SISTRA and called "Italian Registry of Therapeutic Apheresis" (IRTA). The types of

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procedures and diseases are identified by a specific code generated within SISTRA. Participation in the survey was voluntary and participants were asked to enter data for the year 2021.

All collected data, were analysed by descriptive analysis. Patients' outcome rates were calculated as percentage of all examined patients.

In this paper we report therapeutic apheresis procedures including emergency procedures, number of treated patients including paediatric patients, adverse events to therapeutic apheresis, disciplines in which these procedures were used, as well as patients' outcome.

3. Results

One hundred thirty-eight therapeutic apheresis centers are registered in SISTRA, of which 102 (74%) have entered their data. The number of registered centres is in line with expectation.

In 2021, a total of 33681 procedures were registered (Table 1), of which therapeutic plasma exchange, with 12562 procedures, represents 37.3%, extracorporeal photopheresis, with 9064 procedures, represents 26.9%, erythrocyte exchange and erythro-apheresis, respectively with 2203 and 3300 procedures, represent 16.3%, while the collection of autologous stem cells for autotransplantation, with 3548 procedures, represents 10.5%. Also, there were reported 657 lipoprotein removal procedures.

Among the procedures in which filters are used, cascade filtration, with 797 procedures, is the most representative, much less representative are plasma-adsorption and immunoadsorption, with 240 and 192 procedures, respectively.

Adverse events occurred in 1083 procedures (Tables 2), 3.2% of the total. The most of them were mild and predominantly referred to hypocalcemia (89.3% of all events), while severe events constituted only 0.8% of all adverse effects and occurred during therapeutic plasma exchange (4 events), off-line extracorporeal photopheresis (2 events) and peripheral stem cell collection (3 events). These procedures were involved to a greater extent in mild and moderate adverse events (Table 2).

The collection of haematopoietic stem cells (HSCC) is an important part of the apheresis activity. Myeloma and lymphoma are the main indications for autologous transplantation which is a very valid therapeutic option in these haematological disorders (Table 3).

In 2021, HSCC was used in 2413 patients. Regarding erythro-apheresis, a cyto-apheresis procedure by which erythrocytes (red blood cells) are separated from whole blood, polycythemia/erythrocytosis is the main application (2272 procedures in 630 patients), followed by erythrocyte exchange in patients with sickle cell disease

Table 2

Adverse events to therapeutic apheresis procedures year 2021.

Therapeutic procedure	Mild ^a	Moderate ^b	Severe ^c
1 - Therapeutic plasma exchange	487	75	4
2 - Cascade filtration	31	1	0
3 - Plasma adsorption (physical, chemical)	0	0	0
4 - IgG / IgE Immunoadsorption	4	0	0
5 - Extracorporeal photopheresis (online)	28	2	0
6 - Extracorporeal photopheresis (off line)	115	10	2
7 - Lipoprotein apheresis	4	2	0
8 - Lymphoplasmapheresis	1	0	0
9 - Cyto-reductive leukapheresis	1	0	0
10 - Granulocyte-monocytoapheresis	27	0	0
11 - Therapeutic platelet apheresis	0	0	0
12 - Erythrocyte exchange	25	1	0
13 - Erythroapheresis	11	0	0
14 - Haematopoietic Stem Cell Collection (HSCC-autotransplant)	230	16	3
15 - Other	3	0	0
Total	967	107	9

^a **Mild:** hypocalcemic symptoms, blood circuit clotting, hematoma at puncture site, insufficient blood flow rate;

^b **Moderate:** allergic/hypersensitivity reactions, digestive disorders, nausea/vomiting, fever and chills, general discomfort;

^c **Severe:** cardiovascular collapse, vaso vagal reaction/fainting, hemolysis, arrhythmias, use of resuscitation maneuvers.

(1792 procedures in 347 patients) (Table 3).

Extracorporeal photopheresis is particularly used in the treatment of GvHD (5656 procedures in 379 patients), followed by organ transplant rejection (1529 procedures in 192 patients) and cutaneous T-cell lymphoma (936 procedures in 68 patients). Its use in autoimmune diseases is still limited, with only 42 patients treated with 199 procedures (Table 3).

The 2021 data of the IRTA shows that the apheresis procedures are mainly used in haematology with 10941 procedures performed in 1934 patients, followed by neurology, with 5974 procedures in 871 patients, and solid organ transplantation with 2368 procedures in 304 patients (Table 4).

As reported in the reference guidelines of the American Society of Apheresis (ASFA, 2019) [3], the specialty areas of use of therapeutic apheresis are numerous.

In haematology, most of the patients treated with therapeutic apheresis had polycythemia vera (41.9%), GvHD (14.4%), Sickle Cell Disease, non-Acute Sickle Cell Disease (9.5%), Thrombotic thrombocytopenia purpura, TTP (8.9%) (Table 5).

Table 1

Therapeutic apheresis procedures and number of patients treated, including paediatric patients and emergency procedures: year 2021.

Therapeutic procedure	N. Procedures (including emergency procedures)	N. Patients (including paediatric patients)	N. paediatric patients	N. Emergency procedures
1 - Therapeutic plasma exchange	12562	2103	73	1068
2 - Cascade filtration	797	108	0	2
3 - Plasma adsorption (physical, chemical)	240	7	5	0
4 - IgG / IgE Immunoadsorption	192	22	1	67
5 - Extracorporeal photopheresis (online)	3012	184	10	5
6 - Extracorporeal photopheresis (off line)	6052	689	47	10
7 - Lipoprotein apheresis	657	58	4	0
8 - Lymphoplasmapheresis	7	5	0	0
9 - Cyto-reductive leukapheresis	98	63	5	46
10 - Granulocyte-monocyto-apheresis	294	42	3	0
11 - Therapeutic platelet apheresis	36	19	0	0
12 - Erythrocyte exchange	2203	534	86	160
13 - Erythro-apheresis	3300	1099	2	37
14 - Autologous Stem Cell Collection	3548	2455	147	31
15 - Other	683	496	36	2
Total	33681	7884	419	1428

Table 3

Haematopoietic Stem Cell collection (HSCC), Cyto-apheresis and Photopheresis: number of procedures and number of patients by disorders year 2021.

HSC Collection	N. Procedures	N. Patients
700 - Multiple myeloma	1700	1083
701 - Lymphoma	1192	935
702 - Acute leukaemia (Autograft / Back up)	148	116
703 - Neuroblastoma	54	43
704 - Other solid tumour	243	167
799 - Other	116	69
Total	3453	2413
Cytoapheresis	N.	N.
	Procedures	Patients
710 - Sickle Cell Disease (Erythrocyte Exchange)	1792	347
711 - Malaria (Erythrocyte Exchange)	0	0
712 - Polycythaemia / Erythrocytosis (Erythro-apheresis)	2272	630
713 - LAM (cytoreductive leukapheresis)	46	29
714 - ALL (cytoreductive leukapheresis)	19	10
799 - Other	73	14
Total	4202	1030
Photopheresis	N.	N.
	Procedures	Patients
720 - GvHD	5656	379
721 - Rejection of solid organ	1529	192
722 - Cutaneous T lymphoma / Sezary syndrome	936	68
723 - Autoimmune diseases	199	42
799 - Other	7	1
Total	8327	682

Table 4

Specialty areas of therapeutic apheresis use, number of patients and procedures.

	N° Procedures	N° Patients
Haematology	10941	1934
Neurology	5974	871
Solid Organ Transplant	2368	304
Rheumatology	1146	171
Dermatology	1057	75
Metabolism	731	51
Nephrology	691	75
Gastrointestinal System	228	48
Other	45	29

The 811 patients with polycythemia vera underwent 2789 procedures (average 3.44 procedures/patient) with a positive response in 85% of evaluated patients.

The largest number of procedures was performed for the treatment of GvHD, with 4179 in 279 patients and an average of 15 procedures/patient. Of 209 evaluated patients, 24.8% was in remission.

Therapeutic apheresis was confirmed as a widely used therapy in thrombotic thrombocytopenic purpura with 1409 procedures in 172 patients and an average of 8.1 procedures/patient. The outcome, available for 129 of these patients, was 95% of positive responses with 70% of remissions and 25% of improvements.

Patients with acute renal failure associated with myeloma also responded positively. Of 44 patients for whom we had outcome data, 75% showed remission or improvement of clinical conditions.

The response to the treatment of inherited hemochromatosis was equally positive. Of 63 treated patients, 97% had a positive response.

The overall outcome for the haematological disorders was available for 1528 patients (79%) with 298 remissions (19%) and 992 improvements (65%) (Table 5).

In neurology (Table 6), myasthenia (2298 treatments), chronic inflammatory demyelinating polyneuropathy (CIDP) (1369 treatments) and Guillain-Barré syndrome (GBS) (682 treatments) are the pathologies for which therapeutic apheresis has been used most frequently. From the analysis of the available outcome data, the best response was for Myasthenia, with 87% of improvements or remissions, followed by GBS (80%) and CIDP (64%). The results considered as a whole were positive.

In fact an improvement or remission was obtained in 76% of the patients, most of whose were on maintenance therapy or recovering from disease flares. The outcome was available for 721 patients (83%): of these, 93 underwent remission (13%) and 455 improvement (63%).

In rheumatology (Table 7), the most represented pathology is ANCA-associated glomerulonephritis with 343 procedures in 59 patients and an average of 5.8 treatments per patient.

The outcome is available for 53 patients, with remission or improvement in 79% of cases. Thirty-four patients had a picture of vasculitis and were treated with 203 procedures (6 procedures/patient). Most of these patients experienced an improvement (60%) or stabilization of the clinical picture (24%).

Similar results were obtained in patients with cryoglobulinemia, with stabilization of the clinical picture in 66% of cases and remission in 8% of cases.

The overall outcome is available for 151 patients (88%) with 93 remissions (8%) and 98 improvements (65%).

In the field of transplantation (Table 8), in 2021, 2368 treatments were performed in 304 patients, with 7.8 procedures per patient. Ab-mediated ABO-compatible kidney transplant rejection involved a large number of patients, with 442 procedures per 84 patients (27%). However, the largest number of treatments was in lung transplant patients, followed by bronchiolitis obliterative syndrome (BOS), with 630 procedures in 85 patients (7.4 procedures/patient).

Prophylaxis of heart transplant rejection was performed in 16 patients, who underwent 402 treatments (25 treatments per patient).

Recurrent heart rejection was the indication for 23 patients, who underwent 187 treatments.

Desensitization for HLA or ABO antibodies involved patients scheduled for transplant of liver (13 patients, 58 procedures), kidney (39 patients, 291 procedures), heart (3 patients, 17 procedures) and lung (1 patient, 12 procedures).

Among the kidney transplant recipients, 30 were ABO-incompatible and required 162 procedures.

The overall outcome of the apheresis treatment is available for 261 patients (86% of the total); in 209 of these (80%), the outcome was remission of the clinical picture (16%) or, in any case, its improvement (64%).

Collectively, as regards the outcome of all treated patients for the 4 specialty areas considered (Table 9), the outcome data was received for 2661 patients, of whose about 80% had a positive response, with disease remission in 16.7% of patients and improvement in 64.3%. Only 2.9% of patients worsened, an effect not attributable to the procedure but to the evolution of the disease.

4. Discussion

The therapeutic apheresis activity has certainly been affected by the Covid-19 pandemic we have experienced, and which still involves us. However, despite SARS-CoV-2 infection has engaged all hospital departments and healthcare workers, apheresis procedures carried out within the Italian transfusion system increased from 23657 in 2019–33681 in 2021.

Among the disciplines that mainly use the apheresis centres, haematology has a central place due to the growing demand for the collection of haematopoietic stem cells for autologous or allogeneic transplantation as well as extracorporeal photopheresis, a therapeutic approach of second line in post-transplant Graft versus Host disease.

The activity data of 2021 also shows that, in the haematological field, the demand of apheresis procedures for patients with thrombotic thrombocytopenic purpura is stable as well as the use of erythrocyte exchange in the treatment of sickle cell disease. In contrast, the use of apheresis procedures for the treatment of polycythemia vera is growing rapidly. It is also of interest to note that the item "Other" in Table 1 includes as many as 317 lymphocytoapheresis procedures for CAR-T therapy: In 2021 there are 18 authorized Centers for these treatments

Table 5

Haematological disorders: number of procedures, number of patients treated, number of patients at first diagnosis and patients outcome: year 2021.

Haematology	N. Procedures	N. Patients	N. Patients at first diagnosis	Patients outcome			
				Remission	Improved	Unchanged	Worsened
17 - Systemic amyloidosis	11	7	5	2	0	3	0
18 - Autoimmune haemolytic anaemia- Cold agglutinin disease	100	15	3	5	4	2	2
19 - Coagulation factors inhibitors	0	0	0	0	0	0	0
20 - Myeloma - acute renal failure	77	48	29	17	16	5	6
21 - GVHD-Graft versus Host Disease	4179	279	124	52	103	38	16
22 - ABO-incompatible haematopoietic stem cell transplantation	102	39	10	6	13	1	0
23 - Transplantation-haematopoietic stem cells, anti-HLA antibodies	48	15	9	2	6	2	0
24 - Haemophagocytic syndromes	15	3	2	0	1	0	2
25 - Thrombocytopenia / thrombosis induced by heparin	3	1	0	0	0	0	0
26 - Immunological thrombocytopenias	0	0	0	0	0	0	0
27 - Hyperviscosity in hipergammaglobulinaemia	152	45	19	2	21	7	1
28 - Immunological thrombocytopenia	2	2	0	0	2	0	0
29 - Polycythaemia vera-Erythrocytosis	2789	811	93	32	591	110	0
30 - Post-transfusion purpura	0	0	0	0	0	0	0
31 - Red Cell Immunization, D-antigen-Prevention and treatment	0	0	0	0	0	0	0
32 - Anti-D immunization in pregnancy	35	3	1	1	1	0	0
33 - Acute Sickle Cell Disease	138	76	15	26	39	0	0
34 - Sickle Cell Disease, non-Acute Sickle Cell Disease	1081	184	11	39	76	13	0
35 - Thrombocytosis	14	10	1	1	6	2	0
36 - Thrombotic, coagulation-mediated microangiopathy	15	5	5	1	3	0	1
37 - Thrombotic, complement-mediated microangiopathy	20	7	6	1	1	4	0
38 - Thrombotic microangiopathy associated with drugs	0	0	0	0	0	0	0
39 - Thrombotic microangiopathy associated with infection	52	7	6	1	4	1	1
40 - Post-TMO thrombotic microangiopathy	34	4	3	0	2	1	1
41 - Thrombotic thrombocytopenia purpura, TTP	1409	172	82	90	32	4	3
42 - Malaria	0	0	0	0	0	0	0
43 - Babesiosi	0	0	0	0	0	0	0
44 - Erythropoietic porphyria	17	2	1	1	1	0	0
45 - Hereditary haemochromatosis	204	63	9	5	56	2	0
992 - Other	444	136	23	14	14	5	5
Total	10941	1934	457	298	992	200	38

Table 6

Neurological pathologies: number of procedures, number patients treated, number of patients at first diagnosis and patients outcome: year 2021.

Neurology	N. Procedures	N. Patients	N. Patients at first diagnosis	Patients outcome			
				Remission	Improved	Unchanged	Worsened
1 - Acute disseminated encephalitis	100	23	14	1	7	8	1
2 - CIDP - Chronic inflammatory demyelinated polyneuropathy	1369	166	52	7	87	50	3
3 - Chronic focal Rasmussen encephalitis	0	0	0	0	0	0	0
4 - Guillain-Barré syndrome	682	133	90	32	49	15	3
5 - Complex regional pain syndrome	3	1	0	0	0	1	0
6 - Lambert-Eaton syndrome	97	7	2	0	6	0	0
7 - Multiple Sclerosis	376	67	17	1	41	15	0
8 - Myasthenia Gravis	2298	306	87	39	185	27	6
9 - Neuromyelitis optica	366	59	42	7	35	10	0
10 - NMDAR- antibodies encephalitis	83	13	7	2	5	3	0
11 - Paraneoplastic neurological syndromes	55	13	9	1	2	7	0
12 - Paraproteinemic demyelinating neuropathies	187	31	11	1	14	5	2
13 - PANDAS, Paediatric Neuropsychiatric Post-Streptococcal Syndrome	26	3	2	0	2	1	0
14 - Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	0	0	0	0	0	0	0
15 - VG-potassium channel (VGKC) antibody related Diseases	9	2	1	0	1	0	0
16 - Stiff person syndrome	94	10	1	1	6	3	0
991 - Other	229	37	13	1	15	10	3
Total	5974	871	348	93	455	155	18

and are distributed throughout Italy.

In the neurological field, the activity data of 2021 are in line with those of the pre-pandemic year 2019. Myasthenia, chronic inflammatory demyelinating polyneuropathy and Guillain-Barré syndrome are the diseases in which apheresis procedures are mostly used. Stable is their use for neurological pathologies related to immune system disorders.

The use of therapeutic apheresis in organ transplantation is also increasing. In fact, the possibility of overcoming the immunological

barrier of HLA incompatibility and ABO incompatibility has represented a further possibility for the many patients on the waiting list, especially for kidney transplantation. The use of apheresis remains stable in rheumatology, a medical specialty in which therapeutic progress linked to the availability of biological drugs has determined the use of therapeutic apheresis exclusively in cases that do not respond to pharmacological therapy. On the other hand, apheresis, a procedure with extremely high levels of safety, is in any case an invasive procedure

Table 7

Rheumatological pathologies: number of procedures, number of patients treated, number of patients at first diagnosis and patients outcome: year 2021.

Rheumatology	N. Procedures	N. Patients	N. Patients at first diagnosis	Patients outcome			
				Remission	Improved	Unchanged	Worsened
46 - ANCA-associated glomerulonephritis	343	59	44	3	39	8	3
48 - Cryoglobulinemia	186	26	14	2	16	5	1
49 - Schonlein-Henoch purpura	1	1	6	0	0	0	1
50 - Vasculitis	203	34	19	0	20	8	5
51 - Cardiac neonatal lupus	0	0	0	0	0	0	0
52 - Catastrophic Antiphospholipid-Acute Syndrome	48	12	7	0	6	1	1
53 - Scleroderma	98	10	3	1	5	2	1
54 - Systemic lupus erythematosus	114	14	9	1	8	3	0
994 - Other	153	15	2	6	4	1	0
Total	1146	171	104	13	98	28	12

Table 8

Solid organ transplant: number of procedures, number of patients treated, number of patients at first diagnosis and patients outcome: year 2021.

Solid organ transplant	N. Procedures	N. Patients	N. Patients at first diagnosis	Patients outcome			
				Remission	Improved	Unchanged	Worsened
77 - Heart Transplant-Recurrent Rejection	187	23	2	1	17	1	3
78 - Heart transplant - Prophylaxis of rejection	402	16	0	0	16	0	0
79 - Heart Transplant-Desensitization	17	3	1	0	1	1	0
80 - Heart Transplant-Ab-mediated Rejection	129	16	7	4	2	0	1
81 - Liver Transplant, ABO Desensitization (Living Donor)	0	0	0	0	0	0	0
82 - Liver transplant, ABO Desensitization (deceased donor)	0	0	0	0	0	0	0
83 - Liver transplant, Ab Rejection (ABO / HLA)	58	13	11	5	5	2	1
84 - Lung Transplant-BOS	630	75	8	0	49	21	3
85 - Lung Transplant-Ab-Mediated Rejection	86	8	5	4	0	2	0
86 - Lung Transplant-Desensitisation	12	1	0	0	0	1	0
87 - ABO compatible kidney transplant - Ab mediated rejection	442	84	43	4	53	6	1
88 - ABO compatible kidney transplant - Desensitization, living donor	7	2	0	2	0	0	0
89 - ABO compatible kidney transplant - Desensitization, deceased donor	122	7	2	4	3	0	0
90 - ABO Incompatible kidney transplant - Desensitization, living donor	162	30	20	16	6	1	0
91 - ABO Incompatible Kidney Transplant-Ab mediated Rejection	46	12	12	2	6	3	0
990 - Other	68	14	10	0	9	5	0
Total	2368	304	121	42	167	43	9

Table 9

Patients outcome and number of assessable patients.

Specialty	N° assessable patients	Patients outcome			
		Remission	Improved	Unchanged	Worsened
Haematology	1528	298	992	200	38
Neurology	721	93	455	155	18
Rheumatology	151	13	98	28	12
Solid organ transplant	261	42	167	43	9
Total	2661	446	1712	426	77
% outcome	100%	16.7%	64.3%	16.0%	2.9%

which does not alter the pathogenesis of the disease. This explains why, in the presence of new effective drugs, the specialist is oriented towards the use of such drugs.

Regarding the adverse effects of apheresis procedures, the data from this study confirm that therapeutic apheresis is a safe procedure with an extremely limited number of adverse events, especially severe ones. The greatest number of adverse events occurs during therapeutic plasma exchange, which on the other hand is the most frequent treatment (37.3% of the total): in almost all cases these are mild adverse events attributable to hypocalcemia. To this regard it should be noted that all the Centers adopt measures for the treatment of symptoms of hypocalcemia and in many Centers the administration of Ca++ in a continuous infusion pump is used for the prevention of symptoms. Likewise, for each patient and each procedure, all the parameters necessary for the

prevention of adverse events are verified: weight, hematocrit, plasmatic volume, flow rate, extracorporeal volume. SiDEM over the years has also paid great attention to the training aspects dedicated to the safety of procedures. With regard to efficacy, data from this study show that therapeutic apheresis is associated with a general improvement of clinical conditions.

Another additional feature of our study is worth commenting on. Immunoglobulin therapy, whose immunomodulatory effect is well known [4,5], represents a valid therapeutic strategy in some neurological pathologies. However, after the pandemic and especially in 2022 there was a reduced availability of the drug [6,7], a plasma-derived medicine obtained from the plasma of a donor [8]. It is therefore probable that in 2022 a greater number of patients, especially in the neurological field, were treated with plasmapheresis rather than

immunoglobulins, thus increasing the activity of the apheresis centres. This is a question we will try to answer when we will be able to analyze the data relating to the year 2022.

For the organizational and management aspects of the activity, it has been observed that some regions have concentrated therapeutic apheresis procedures in the main hospitals which therefore perform many procedures/year; to the contrary, in other regions, the activity is spread over the territory with many hospitals performing few procedures. Of the total number of Centers that have joined the IRTA, 4 hospitals carry out more than 1500 procedures/year, most of the hospitals carry out a number of procedures between 101 and 500 procedures/year, and there are still many hospitals which carry out less than 100 procedures/year. In some of these only erythroapheresis procedures are performed.

In conclusion, the IRTA is a valid tool for monitoring the activity of the apheresis centres carried out at national level and above all for providing an overall picture of how the use of apheresis procedures evolves and changes over time.

CRediT authorship contribution statement

Liviana Catalano: Conceptualization, Methodology, Software validation, Writing. **Giustina de Silvestro:** Conceptualization, Methodology, Software validation, Writing. **Giuseppe Marano:** Conceptualization, Methodology, Software validation, Writing. **Vanessa Piccinini:** Data curation. **Livia Cannata:** Data curation.

Angelo Ostuni: Supervision. **Vincenzo de Angelis:** Supervision.

References

- [1] Catalano L., Piccinini V., Pati L., Masiello F., Barone F., Marano G., et al. 2021: Activity data, haemovigilance and epidemiological surveillance Roma: Istituto Superiore di Sanità; 2022 (Rapporti ISTISAN 22/25) 88pp.
- [2] de Silvestro G, Catalano L, Marano G, Piccinini V, Pupella S, Ostuni A, et al. The Italian registry of therapeutic apheresis enters the information system of transfusion services –SISTRA. *Transfus Apher Sci* 2022;61(1):1–8.
- [3] Padmanabhan A, Padmanabhan L, Aqui N, Balogun RA, Klingel R, Meyer E, et al. Guidelines on the use of therapeutic apheresis in clinical practice - evidence-based approach from the writing committee of the american society for apheresis: the eighth special issue. *J Clin Apher* 2019;34(3):171–354.
- [4] Maddur MS, Othy S, Hegde P, Vani J, Lacroix-Desmazes S, Bayry J, et al. Immunomodulation by intravenous immunoglobulin: role of regulatory T cells. *J Clin Immunol* 2010;1(S4–8):84–8. Suppl.
- [5] Norris PAA, Kaur G, Lazarus AH. New insights into IVIg mechanisms and alternatives in autoimmune and inflammatory diseases. *Curr Opin Hematol* 2020;27(6):392–8.
- [6] N'kaoua E, Attarian S, Delmont E, Campana-Salort E, Verschuere A, Grappone AM, et al. Immunoglobulin shortage: Practice modifications and clinical outcomes in a reference centre. *Rev Neurol* 2022;178(6):616–23.
- [7] Sasongko PL, van Kraaij M, So-Osman C. Using a scenario approach to assess for the current and future demand of immunoglobulins: an interview and literature study from The Netherlands. *Transfus Med* 2022;1–12.
- [8] Di Giorgio D., Traversa G., Trotta M.P. et al. Guideline on the use of human immunoglobulins in case of shortages (<https://www.centronazionalesangue.it/wp-content/uploads/2022/05/Guidelines-on-the-use-of-human-immunoglobulins-in-case-of-shortages.pdf>) 2022 Feb;1–33.