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Modern ECMO: why an ECMO programme in a tertiary care hospital

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Extracorporeal Membrane Oxygenation (ECMO) represents a useful tool to support the lungs and the heart when all conventional therapies failed and the patients are at risk of death. While the Extracorporeal Life Support Organization (ELSO) collects data from different institutions that joined the Registry and reports overall outcome, individual centres often collide with results below expectations, either in adults and in paediatric population. Some authors suggest that poor outcomes could be overcome with a programme dedicated to ECMO, with specialized professionals adequately trained on ECMO and with a consistent number of procedures. In 2012, The IRCCS PSD ECMO Programme was instituted with the specific aim of achieving better results than hitherto obtained. After only 1 year of activity, the results justified the programme, with a better survival rate for each group investigated, particularly in adults, but surprisingly in paediatrics too, where the results were better than what reported by ELSO. Although the number of patients treated with ECMO is still growing up, the effects of the ECMO programme continue to exert a positive action on outcome even now. The present article reports data on survival, blood loss, and blood consumption during ECMO in the last few years at our institution.

Introduction

Extra Corporeal Membrane Oxygenation (ECMO) is component of the larger world of extracorporeal life support. In the ECMO procedure, respiratory function or cardiac function (or both) are temporarily replaced. The kind of support is determined by the organ which has to be replaced: if lungs alone are the affected, ECMO can be used in a veno-venous (V-V) configuration in which blood is drained by a venous site before the heart, oxygenated by the artificial lung and returned to the right heart.

If heart alone or heart and lungs are affected, ECMO should be used in a veno-arterial (V-A) configuration: blood is drained similarly to V-V ECMO but is returned to the arterial circulation providing circulatory support too.

First described in the clinical setting in the mid-1970[1] ECMO got its fortune cyclically, both as respiratory support in newborns affected by different grading of acute respiratory distress syndrome (ARDS), mainly congenital diaphragmatic hernia, meconium aspiration, multi-factorial pneumonia, and as cardiac support in patients suffering from acute heart failure.

In the early 1990s, it partially lost its appeal: complications associated with ECMO runs, the improvement in ventilators and ventilation setting and the possibility

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to support single failing ventricles with temporary ventricular assist devices (VAD), reduced the clinical use of ECMO.

In the last few decades, the onset of new aggressive influenza virus (AH1N1 pandemia and its modified flu strains) led to severe pneumonia: a new wide spread use of ECMO begun for respiratory distress treatment. Several trials demonstrated the efficacy of ECMO with respect to conventional therapy.[2]

New technology, powered by growing numbers, provided easily deployable devices: time to set up, to prime, and connect to the patient, particularly in percutaneous fashion, was so improved to treat with V-A ECMO patients suffering from cardiogenic shock or cardiac arrest,[3] so defined extracorporeal cardiopulmonary resuscitation (E-CPR).

ECMO has so become nowadays a widespread, well-accepted strategy. Guidelines have been developed by the Extracorporeal Life Support Organization (ELSO)[4] which is also responsible to maintain an International Registry: data submitted by centres are intended to support clinical research, regulatory agencies, and support individual ELSO centres. However, single centres generally adopt these guidelines with some modification according to internal institutional policies.

ECMO in the IRCCS Policlinico San Donato: history

The IRCCS Policlinico San Donato (PSD) is a private tertiary hospital in the south area of Milan, fully accredited by the public Healthcare System and strongly characterized by cardiac surgery activity.

Heart transplantation is not performed, and no VAD programme is active, yet. The majority of paediatric ECMOs is implanted as circulatory support; no external patients are referred to our centre for ARDS, and V-V ECMO is usually applied to ARDS acquired in the post-operative course.

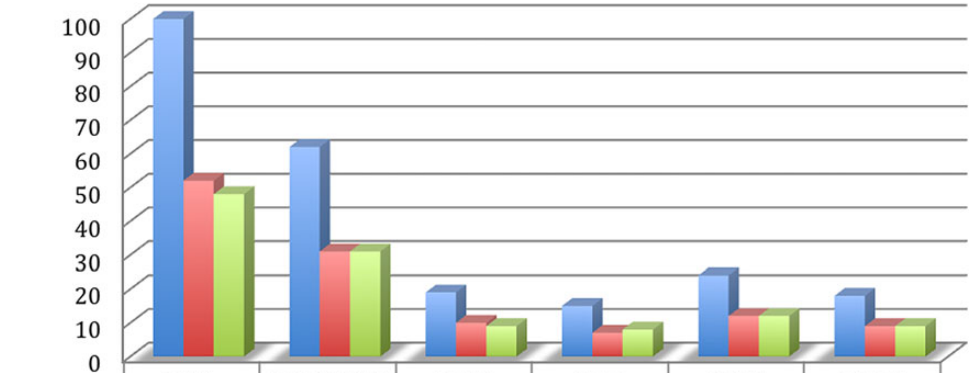
The ECMO strategy in PSD has followed the growing up activity of cardiac surgery, but in the early era this procedure was limited by the alternative use of left or right VAD to support one single ventricle: this strategy is less invasive and requires less aggressive anticoagulation protocols, compared with ECMO. There was no specific ECMO training and given the technology at that time the balance between anticoagulation, bleeding, and thrombotic complication was cumbersome. The ECMO indications were based on the presence of an inappropriate lung function and/or biventricular support was required. The main indications were bridge to recovery and in rare cases bridge-to-bridge.

In the 1990s, no more than two to three ECMO/years were implanted, generally on paediatric patients, and the indications were mainly bi-ventricular failure following cardiac surgery (failure to wean from cardiopulmonary bypass). All patients received ECMO support through central cannulation, and the chest was left open. Respiratory V-V ECMO was totally absent, and no standardized data collection was established.

Starting with the new millennium, the ECMO runs grew up to five to seven procedures per year: the general approach remained in favour of central cannulation for both paediatric and adult patients. The indications were again mainly inability to wean from cardiopulmonary bypass or cardiogenic shock following cardiac surgery: an internal protocol-guided indications and timing, but no clear contraindications or exclusion criteria, were considered.

By the end of 2009, the increasing age and the worsening pattern of the patients led to some cases of severe pneumonia following cardiac surgery: first attempts of respiratory V-V ECMO were performed, but the results were not satisfactory.

The lack of clear contraindications and exclusion criteria associated with some new easily deployable devices induced to implant more ECMOs, often in a compassionate way particularly on adult patients. As a consequence, the



	TOT	2012-2015	2012	2013	2014	2015*
ECMO #	100	62	19	15	24	18
ad	52	31	10	7	12	9
ped	48	31	9	8	12	9

Figure 1 The overall number of ECMO procedures at San Donato hospital divided by year. For year 2015, only the first 7 months are considered. Ad, adult; ped, paediatric.

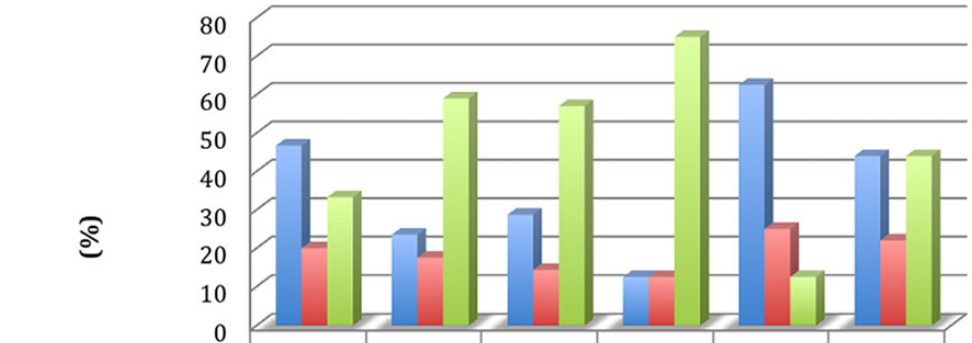
results were so poor as to suggest the clinicians to reflect on the opportunity to continue in such a resource-consuming direction.

The IRCCS Policlinico San Donato ECMO programme

Recently, some authors[5,6] reported that patients receiving ECMO at hospitals with more than 30 adult annual ECMO cases had significantly lower odds of mortality (adjusted odds ratio, 0.61; 95% confidence interval, 0.46–0.80) compared with adults receiving ECMO at hospitals with less than six annual cases.

This could be associated either to improved skills due to a larger number of cases, but also to the development of strict protocols providing guidelines for indications, contraindications, and exclusion criteria.

According to this philosophy, in October 2012 the IRCCS PSD instituted the PSD ECMO Team, including nine professionals identified within anaesthesiologists, surgeons, and perfusionists. Following the ELSO Guidelines for ECMO Centres,[7] a general structure was defined with a Medical Director and a Staff Coordinator.



	pre ECMO Team All (15)	post ECMO Team All (17)	pre ECMO Team Ped (7)	post ECMO Team Ped (8)	pre ECMO Team Ad (8)	post ECMO Team Ad (10)
died on ECMO (%)	46,7	23,5	28,7	12,5	62,5	44
died weaned (%)	20	17,5	14,3	12,5	25	22
discharge alive (%)	33,3	59	57	75	12,5	44

Figure 2 Comparative outcomes between before and after the ECMO Team establishment. Ad, adult; ped, paediatric.

ECLS Registry Report
International Summary
July, 2015

Extracorporeal Life Support Organization
2800 Plymouth Road
Building 300, Room 303
Ann Arbor, MI 48109

Overall Outcomes

	Total Patients	Survived ECLS		Survived to DC or Transfer	
Neonatal					
Respiratory	28,271	23,791	84%	20,978	74%
Cardiac	6,046	3,750	62%	2,497	41%
ECPR	1,188	766	64%	489	41%
Pediatric					
Respiratory	6,929	4,579	66%	3,979	57%
Cardiac	7,668	5,084	66%	3,878	51%
ECPR	2,583	1,432	55%	1,070	41%
Adult					
Respiratory	7,922	5,209	66%	4,576	58%
Cardiac	6,522	3,661	56%	2,708	42%
ECPR	1,985	791	40%	589	30%
Total	69,114	49,063	71%	40,764	59%

Figure 3 The overall ECMO outcomes as described by the Extracorporeal Life Support Organization Report 6/2015 (with the permission of Extracorporeal Life Support Organization).

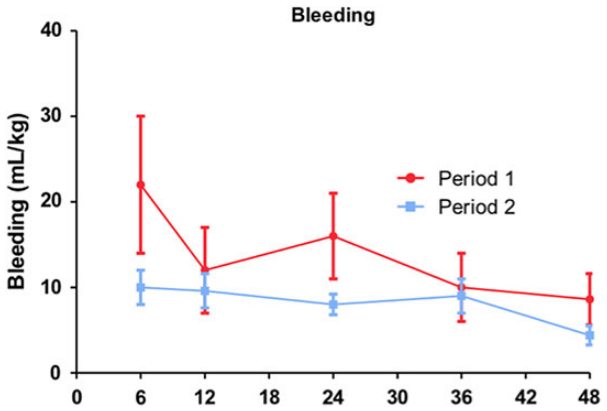


Figure 4 The overall bleeding on ECMO before and after the ECMO Team establishment. Period 1, pre-ECMO Team era, Period 2, post-ECMO team institution.

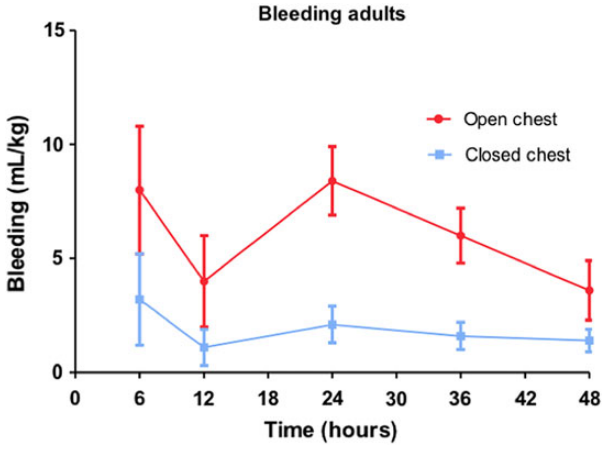


Figure 5 The overall bleeding in adult population on ECMO splitted between open vs. close chest status.

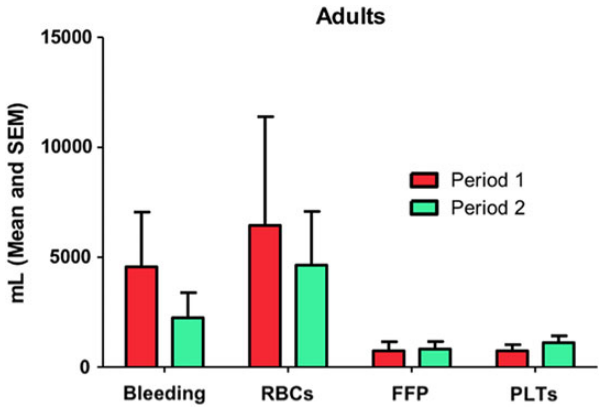


Figure 6 The overall bleeding and blood product consumption in adult population on ECMO. Period 1, pre-ECMO Team era, Period 2, post-ECMO team institution. RBC, red blood cells, FFP, fresh frozen plasma, PLT, platelet concentrates.

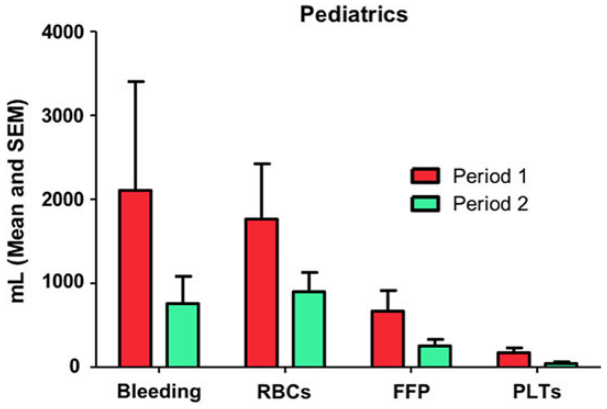


Figure 7 The overall bleeding and blood product consumption in paediatric population. Period 1, pre-ECMO Team era, Period 2, post-ECMO team institution. RBC, red blood cells, FFP, fresh frozen plasma, PLT, platelet concentrates.

The primary aims of the Team were to (i) retrospectively analyse the ECMO-run history, identifying any possible cause of failure and (ii) prospectively perform ECMO within a restricted group of people to minimize data loss. The second aim was to modify methods and technical aspects and to produce documents for internal guidelines. After 1-year of activity, in a public clinical audit, the results were reported with an analysis 'before and after' the ECMO Team era (*Figure 2*).

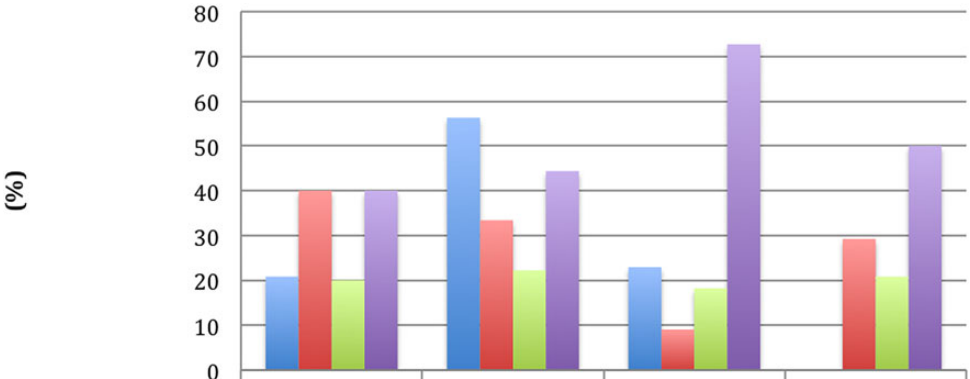
While working on the Clinical Audit, an ECMO database was built in order to collect objective data on the ECMO activity: more than 370 fields for each run were filled in, and the database now works in a continuous access protocol modality. Every ECMO-run is included, even if two or more on the same patient. To date, data from 100 patients are registered in the ECMO database (July 2015).

For every ECMO patient, it is now available a specific ECMO file comprising data about the ECMO course: this allows the team to get information anytime simply requesting the patient file. Unfortunately, no ECMO file was recorded in the previous era so that data on the oldest runs are pretty uncompleted or totally lost. In June 2015, the ECMO Programme of PSD joined ELSO.

The ECMO programme results

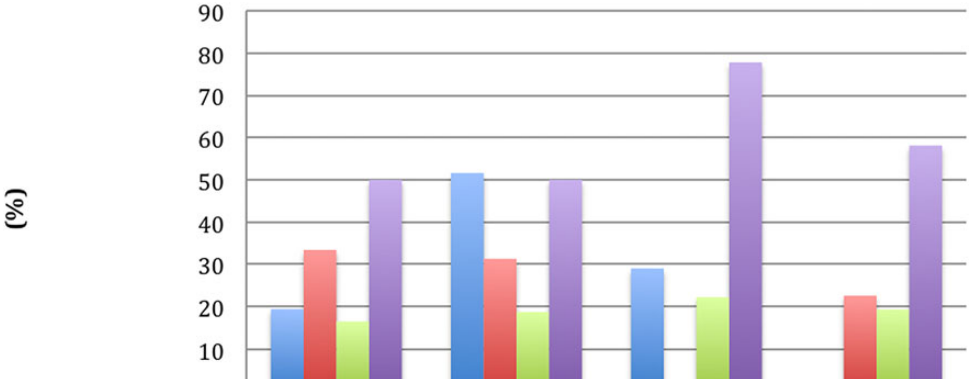
The retrospective review of the ECMO activity confirmed the positive effects of a structured programme dedicated to ECMO. ECMOs increased in number year by year (*Figure 1*): the reduction in 2013, compared with the previous trend, reflects the conservative approach following more strict indications and the application of exclusion criteria after the ECMO Team institution. The ratio between paediatric and adult cases remains quite the same across the time frame investigated.

In the public clinical audit, held in November 2013, the data were presented comparing a frame of 1 year before (Oct 2011–Oct 2012) and after (Oct 2012–Oct 2013) the ECMO Team institution (*Figure 2*): the results obtained justified the efforts done and the establishment of the ECMO Programme. All cases were included; the outcome was defined as mortality on



	<30 days (10)	30 days-1year (27)	>1 year (11)	TOT (48)
TOT (%)	20,8	56,3	22,9	
died on ECMO (%)	40	33,4	9,1	29,2
died weaned (%)	20	22,2	18,2	20,8
discharge alive (%)	40	44,4	72,7	50

Figure 8 The overall outcome in paediatric population in 2008–15.



	<30 days (6)	30 days-1year (16)	>1 year (9)	TOT (31)
TOT (%)	19,4	51,6	29	
died on ECMO (%)	33,4	31,3	0	22,6
died weaned (%)	16,6	18,7	22,2	19,3
discharge alive (%)	50	50	77,8	58,1

Figure 9 The overall outcome in paediatric population after ECMO Team establishment (October 2012–July 2015).

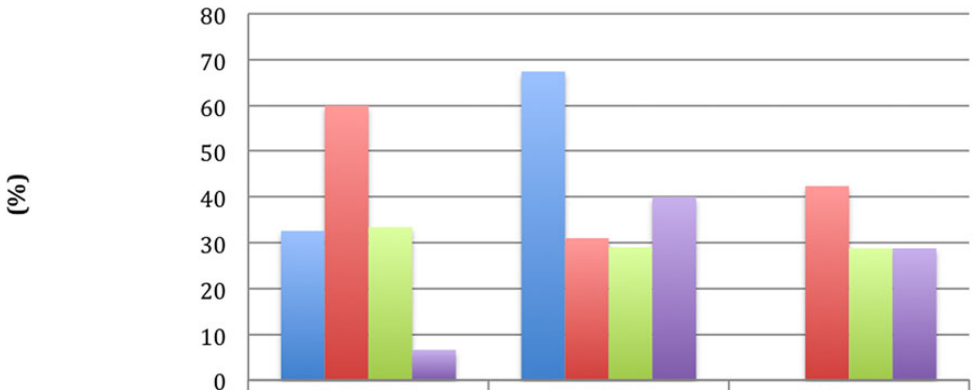
ECMO and survival to discharge or transfer, as reported in the ELSO Registry.

Survival to discharge was better for each cohort in the ECMO Team era: in all cases (59 vs. 33%) but particularly in the adult patient population (44 vs. 12%). Surprisingly, the new approach was able to ameliorate survival rate even in paediatrics (75 vs. 57%) where results were already pretty good enough according to the ELSO Registry (*Figure 3*).

Bleeding, intended as blood loss from chest tube, was lower in the second period (*Figure 4*). One of the possible interpretations is that since the ECMO Team was instituted, the preferred cannulation site in adult patients has moved from a central, open chest approach to a widespread use of peripheral cannulation or the use of transthoracic VAD cannula in adult patients, keeping the chest close (*Figure 5*) even in patients following cardiac surgery.

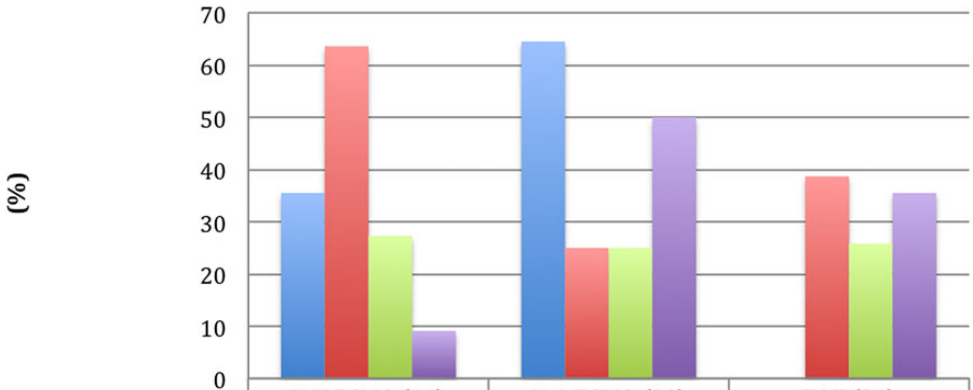
In no adult patients, by rule, the chest was left open and, when left venting was needed, a left ventricular apex cannula was inserted through a left thoracotomy. In some cases, left ventricular venting was obtained by a pigtail catheter inserted directly via a femoral artery with a percutaneous approach in Cath-lab.

The containment of bleeding was more prominent in the first hours after the ECMO implantation: this finding reflects a more aggressive behaviour towards coagulation



	V-V ECMO	V-A ECMO	TOT cases
TOT (%)	32,6	67,4	
died on ECMO (%)	60	31	42,4
died weaned (%)	33,4	29	28,8
discharge alive (%)	6,6	40	28,8

Figure 10 The overall outcome in adult population in 2008–15.



	V-V ECMO (11)	V-A ECMO (20)	TOT (31)
TOT (%)	35,5	64,5	
died on ECMO (%)	63,6	25	38,7
died weaned (%)	27,3	25	25,8
discharge alive (%)	9,1	50	35,5

Figure 11 The overall outcome in adult population after ECMO Team establishment (October 2012–July 2015).

disorders. The ECMO Team and the intensive care unit personnel were strongly involved in haemostatic control. The management of the haemostatic balance was based on coagulation point of care (POC) tests.

In adult ECMO (*Figure 6*), red blood cells consumption reflects the overall trend, with a reduction of transfused volumes (mL/kg/day or total bank units number). In paediatric ECMO (*Figure 7*), both bleeding and transfusions were lower in the ECMO Team era.

In general, many paediatric ECMO patients were treated with a different anticoagulation protocol based on the direct thrombin inhibitor Bivalirudin (Angiox^{R}). This strategy carried a better coagulation profile, less bleeding, and allogeneic transfusions, even if some caution should be applied.[8,9]

Some technical improvements were done in order to reduce red blood cells damage, particularly in the paediatric cohort, but it is unclear if these changes really affected bleeding and transfusions.

The above reported results seem to be correlated with multi-factorial causes: on one side, again, a strict control of hemostasis by POC tests and goal directed therapy; on the other side, an aggressive policy on bleeding treatment that led to prompt surgical re-exploration once POC tests were not suggestive for medical bleeding.

No patient on ECMO in the ECMO Team Era left the operating room with active uncontrolled bleeding. The general outcome has been investigated comparing overall (since 2008) results before and after the ECMO team era: the

primary endpoints were survival to ECMO (weaning rate) and survival to discharge/transfer.

In the paediatric group (*Figures 8* and *9*), survival to ECLS (patient weaned from ECMO) was higher in the ECMO Programme period (77 vs. 70%), even when analysed for each age subgroup. Survival to discharge follows the same trend (58 vs. 50% for all age groups). Moreover, these results are similar or better than what reported in the ELSO Registry (*Figure 3*).

The same outcome data were compared in the adult population (*Figures 10* and *11*), splitting V-V from V-A ECMO as subgroups. In the overall adult patient population ($N = 52$), the rate of patients weaned from ECMO was higher post-ECMO Team (61 vs. 57%) as well as the discharge rate (35 vs. 28%). The analysis of subgroups included only 46 patients due to an incomplete data acquisition relative to support mode in the early cases. In the period after the establishment of the ECMO Team, the rate of patients discharged alive was 50% in V-A ECMO and 9% in V-V ECMO. Both these values are higher than what obtained before the ECMO Team. The results of the A-V ECMO are in line with what reported by the ELSO Registry, while that of V-V ECMO are disappointingly poorer. Our interpretation is that our patients with respiratory problems are basically not pure ARDS patients, conversely being almost always cardiac surgery patients with multiple organ dysfunction. However, efforts have been done to improve these results by involving the General Intensive Care staff in the treatment of ARDS patients.

Conclusions

ECMO is a resource-consuming strategy that allows supporting failing heart or lungs while primary healing therapy is running. Its efficacy has been well established, but results reported in international registries are referred to high-skilled, high-experienced centres. In the real world, good results accord to strict protocol and guidelines, modified for Institutional policies. A programme based on multi-disciplinary experts team, dedicated and adequately trained on these disciplines, could offer a good option to optimize resource utilization. An internal ECMO database may be useful not only to report data of outcome but also to determine predictive variables of outcome.

Conflict of interest: none declared.

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