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BRIEF COMMUNICATION

A brief clinical case of monitoring of oxygenator performance and patient-machine interdependency during prolonged veno-venous extracorporeal membrane oxygenation

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Abstract Monitoring veno-venous extracorporeal membrane oxygenation (vvECMO) during 76 days of continuous support in a 42-years old patient with end-stage pulmonary disease, listed for double-lung transplantation. Applying a new monitor (Landing®, Eurosets, Medolla, Italy) and describing how measured and calculated parameters can be used to understand the variable interdependency between artificial membrane lung (ML) and patient native lung (NL). During vvECMO, in order to understand how the respiratory function is shared between ML and NL, ideally we should obtain data about oxygen transfer and CO_2 removal, both by ML and NL. Measurements for NL can be made on the mechanical ventilator. Measurements for ML are typically made from gas analysis on blood samples drawn from the ECMO system before and after the oxygenator, and therefore are non-continuous. Differently, the Landing monitor provides a continuous measurement of the oxygen transfer from the ML, combined with hemoglobin level, saturation of drained blood and saturation of reinfused blood. Moreover, the Landing monitor provides hemodynamics data about circulation through the ECMO system, with blood flow, pre-oxygenator pressure and post-oxygenator pressure. Of note, measurements include the drain negative pressure, whose monitoring may be particularly useful to prevent hemolysis. Real-time monitoring of vvECMO provides data helpful to understand the complex picture of a patient with severely damaged lungs on one side and an artificial lung on the other side. Data from vvECMO monitoring may help to adapt the settings of both mechanical ventilator and vvECMO. Data about oxygen transfer by the oxygenator are important to evaluate the performance of the device and may help to avoid unnecessary replacements, thus reducing risks and costs.

Keywords ECMO monitoring · Oxygenator performance · $V'O_2$ monitoring · Respiratory support · Membrane lung function

1 Introduction

Extracorporeal membrane oxygenation (ECMO) should be considered a support for the vital functions of the organism, rather than a therapy. This support technique has proved to be effective in reducing mortality of patients suffering from potentially reversible heart failure and/or severe acute respiratory failure unresponsive to mechanical ventilation with maximal medical and pharmacological treatment [1–3]. ECMO in veno-venous configuration (vvECMO), by providing extracorporeal oxygenation and carbon dioxide (CO_2) removal, can accomplish partial or even total substitution of the gas exchange function of the lungs. During vvECMO the assessment of the respiratory function of the native lung (NL) cannot rely just on the two-dimensional relationship between mechanical ventilation settings (tidal and minute ventilation, inspired oxygen fraction and positive end expiratory pressure –PEEP–) and arterial blood gases (arterial oxygen partial pressure –PaO_2– and arterial carbon dioxide partial pressure –$PaCO_2$–). A three dimensional approach is

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required, taking into account also the extracorporeal gas exchange provided by the membrane lung (ML). The contribution of the membrane lung to the total respiratory gas exchange can be quantified by calculating the oxygen transfer to the blood and the CO_2 removal from the blood provided by the membrane lung ($V'O_2ML$ and $V'CO_2ML$ respectively) [4]. Typically these data are obtained by a double blood sampling for gas analysis from the ECMO circuit, before and after the oxygenator, combined with simultaneous measurement of blood flow rate through the ECMO circuit. During ECMO the measurement of blood pressures within the circuit is also important. The relevant points for pressure measurement are before the pump (drainage pressure), before the oxygenator (pre-oxygenator pressure) and after the oxygenator (post-oxygenator pressure). These data are helpful to prevent haemolysis due to excessive pressures, especially excessive subatmospheric pressures applied to the drainage cannula. In turn, pre- and post-oxygenator pressures are useful especially to assess the resistance through the oxygenator, typically increasing with the duration of use [5]. These kinds of measurements are typically performed by perfusionists during the periodical checks of the ECMO system scheduled to prevent or detect problems that might arise during the treatment. Non continuous measurements, however, may fail timely detection of critical issues. If we consider the severity of the underlying disease of the patients assisted by ECMO and the risks connected with the invasiveness of extracorporeal circulation, continuous monitoring of ECMO systems might be an important step forward, by improving safety and adding relevant clinical information, especially interesting in case of long duration ECMO. The present study deals with the clinical application of an ECMO circuit monitor recently proposed to the market; this monitor allows continuous measurement of a set of critical parameters and might reduce the need for blood sampling from the circuit.

2 Materials and methods

In the intensive care unit (ICU) of a tertiary university hospital, we used a Landing® monitor for the first time during a long term vvECMO assistance. The Landing® monitor (Eurosets™, Medolla –MO–, Italy) (Fig. 1) was originally designed as a monitor for short term applications on heart–lung machines during cardiac surgery, to provide information about oxygen consumption, oxygen transport, venous and arterial oxygenation, as well as on extracorporeal circuit pressures and blood flow. With a capability to update data every 5 s, it is conceived to guide the medical team in making decisions about the management of the cardiopulmonary bypass.

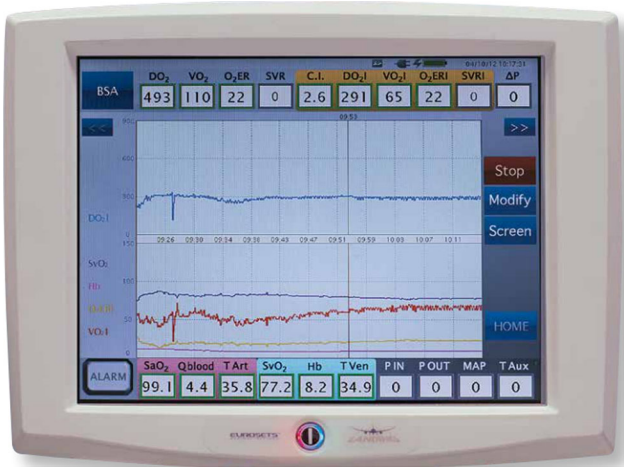


Fig. 1 Frontal view of Landing® monitor

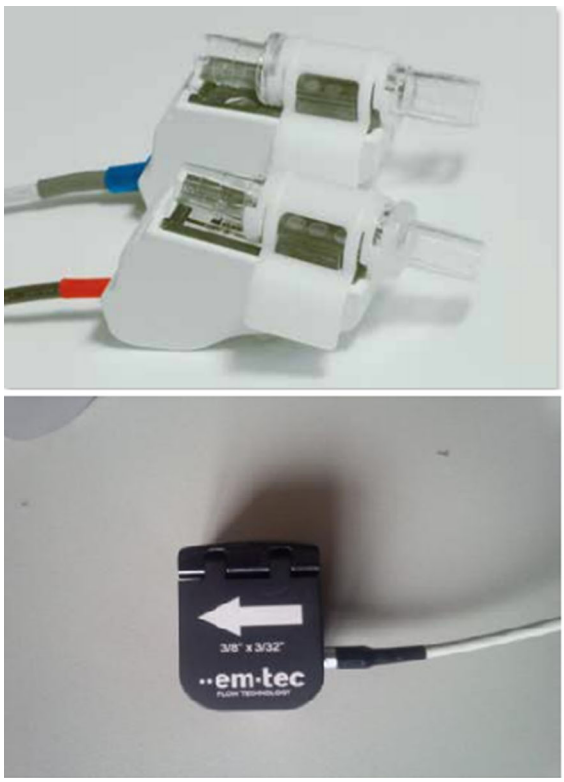
During the assembly of the ECMO circuit, two cuts must be made in the drainage and the reinfusion line respectively, in order to insert two specific 3/8" adapters for probes. Probe A, denoted as venous probe (Fig. 2), provides the measurement of haemoglobin (Hb), pre-oxygenator (venous) oxygen saturation (SvO_2) and temperature (Tven). Probe B, denoted as arterial probe (Fig. 2), provides the measurement of post-oxygenator (arterial) oxygen saturation (SaO_2) and temperature (Tart). A ultrasound flowmeter provides the measurement of extracorporeal blood flow (Fig. 2). The Landing® monitor manages also three pressure transducers that were connected to the ECMO circuit ports before the pump for the measurement of drainage pressure, before the oxygenator for pre-oxygenator pressure and after the oxygenator for post-oxygenator pressure.

From measured values, the Landing® monitor calculates several parameters that are relevant during cardiopulmonary bypass (Fig. 3). Among these calculated parameters, the one denoted as $V'O_2$ maintains a validity also during vvECMO, here expressing the oxygen transfer provided by the membrane lung, i.e. $V'O_2ML$. The Landing® monitor calculates this $V'O_2$ value according to the following simplified equation:

$$V'O_2 = (k*Hb*SaO_2) - (k*Hb*SvO_2) * \text{blood flow}$$

with $k = 13.8$ for $V'O_2$ expressed as ml/min, Hb as g/dl and Blood flow as l/min

Besides the continuous measurements provided by the Landing® monitor, we performed also measurements of the CO_2 removed by the native lung ($V'CO_2NL$) and by the membrane lung ($V'CO_2ML$). $V'CO_2NL$ was obtained by the volumetric capnometry function embedded in a Hamilton S1 mechanical ventilator (Hamilton Medical, Bonaduz, Switzerland). $V'CO_2ML$ was calculated on a daily basis by



TECHNICAL DATA	VENOUS PROBE
SvO_2 measurement method	Spectrophotometric
Temperature measurement	Infrared sensor
Size (H x W x D)	45 x 80 x 28 mm
Weight	50 g
Cable lenght	180 cm
Connectors sizes	1/2"; 3/8"; 1/4"

TECHNICAL DATA	ARTERIAL PROBE
SaO_2 measurement method	Spectrophotometric
Temperature measurement	Infrared sensor
Size (H x W x D)	45 x 80 x 28 mm
Weight	50 g
Cable lenght	180 cm
Connectors sizes	3/8"; 1/4"

TECHNICAL DATA	FLOW SENSOR EM-TEC
Blood Flow measurement method	Ultrasound
Size (H x W x D)	25 x 33 x 45 mm
Weight	100 g
Cable lenght	280 cm
Connectors sizes	3/8"; 1/4"

Fig. 2 Venous probe, arterial probe and blood flow sensor, with technical specifications

volumetric capnometry applied to the membrane lung, achieved by measuring the CO_2 content in the gas coming out of the exhaust port of the oxygenator, multiplied by the sweep gas flow. The measurement of oxygen transfer from the native lung ($V'O_2NL$) would have required a pulmonary artery catheter and was not performed.

3 Clinical case

A 42-year old man (height 176 cm, body weight 80 kg, body surface area 1.964 m^2) was submitted to vvECMO for amiodarone-related pneumonitis with fast evolution to fibrosis. ECMO was applied by a Rotaflow centrifugal pump (Maquet, Rastatt, Germany) through a 31-Fr Avalon Elite^{tm} cannula (Maquet Getinge Group) inserted into the right internal jugular vein. The patient was on ECMO support for 76 days and Fig. 4 shows the values of ECMO blood flow and sweep gas flow during this time. ECMO was started with a polymethylpentene hollow-fiber ECMO Adult Oxygenator (Eurosets^{tm}) with biopassive phosphorylcholine coating. The patient was tracheostomized on day 5 and it was kept ventilated in pressure controlled mode with a tidal volume of 1.5 ml/kg, respiratory rate of 8 breaths/min, PEEP of 12 cmH2O, a FiO2 of 80 % and a peak pressure of 28 cmH2O. He was sedated during all time for the impossibility to obtain a satisfactory patient/ventilator interaction. We also considered the possibility of extubate the patient, but the increasing of the oxygen consumption due to the awakening, it resulted in a too low arterial oxygen saturation. On day 37 the first ECMO circuit replacement took place, this time with a polymethylpentene hollow-fibre PLSi oxygenator (Maquet Getinge Group) with bioactive covalently-bonded heparin coating. On day 70 the circuit was replaced another time, with an ECMO Adult Oxygenator again. On day 15 of ECMO the lung disease was considered as not reversible and the patient was listed for double lung transplantation, that was performed on day 71. ECMO was discontinued on day 4 after transplantation (day 76 of ECMO). On day 7 after transplantation the patient suffered from bowel ischemia and underwent a small bowel resection. On day 32 after transplantation he died for septic shock due to massive intestinal bacterial translocation, with multiple isolation of Klebsiella pneumoniae carbapenemase-producing (KPC) from blood cultures.

4 Discussion and analysis

During vvECMO, the artificial lung and the native lung work in-series and cooperate in transferring oxygen to the body and eliminating CO_2. How these tasks are shared, it depends on the functional state of membrane lung and

MEASURED PARAMETER	UNIT	RANGE	RESOLUTION	ACCURACY
SaO_2	%	90 - 100	1	± 3%
SvO_2	%	60 - 90	1	± 3%
Q Blood	l/min	0,5 - 8,0	0,1	± 3%
Hb	g/dl	5 - 16	0,1	± 0,5 g/dl
Ta	°C	4 - 42 °C	0,1	± 0,5 °C %
Tv	°C	4 - 42 °C	0,1	± 0,5 °C %
P in	mmHg (kPa)	0 - 800	1	± 3% mmHg
P out	mmHg (kPa)	0 - 800	1	± 3% mmHg
MAP	mmHg (kPa)	0 - 800	1	± 3% mmHg
Taux	°C	4 - 42 °C	0,1	± 1 °C %

CALCULATED PARAMETER	UNIT	RANGE	RESOLUTION
DO_2	ml/min	300 - 900	1
VO_2	ml/min	10 - 300	1
O_2ER	%	5 - 50	1
SVR	dyne*sec/cm^5	600 - 2500	1
C.I.	l/min/m^2	0,5 - 3	1
DO_2i	ml/min/m^2	100 - 500	1
VO_2i	ml/min/m^2	10 - 150	1
O_2ERi	%	5 - 50	1
SVRi	dyne*sec/cm^5/m^2	600 - 2500	1
dP	mmHg (kPa)	0 - 800	1
B.S.A.	m^2 (ft^2)	0,5 - 3,2	1

Fig. 3 Data measured and calculated by Landing® monitor

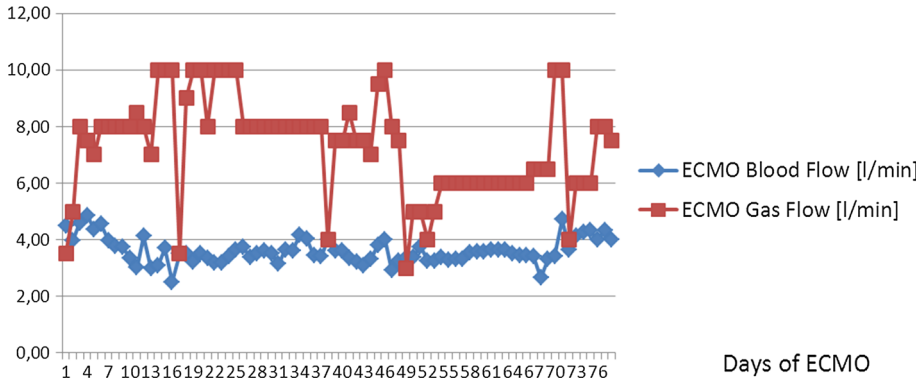


Fig. 4 Daily values of ECMO blood flow and gas flow

native lung respectively, as well as on how ECMO is set (namely blood flow, sweep gas flow and oxygen fraction) and mechanical ventilation is set (here a number of parameters play a role). $V'O_2ML$, as provided by the Landing® monitor, is an important piece of information of the complex puzzle represented by vvECMO in severe respiratory failure. It may help making decisions about the setting of ECMO controls and the time of oxygenator replacement. Indirectly, it may also help making decisions about how to set the mechanical ventilator. Continuous $V'O_2ML$ measurement provided by Landing® monitor can be used in daily clinical practice to evaluate the oxygenator efficiency, a critical point especially when the oxygenator is running beyond its certification period. In our clinical case the first oxygenator was used for 37 days. Figure 5 shows how, during this long time, $V'O_2ML$ was well maintained even past the first 15-days corresponding to the certification period the oxygenator. Although actual $V'O_2ML$ was frequently below the theoretical relationship between $V'O_2ML$ and blood flow of the ECMO Adult Oxygenator (Fig. 6) obtained in benchmark condition, the time analysis shown in Fig. 5 indicates no substantial

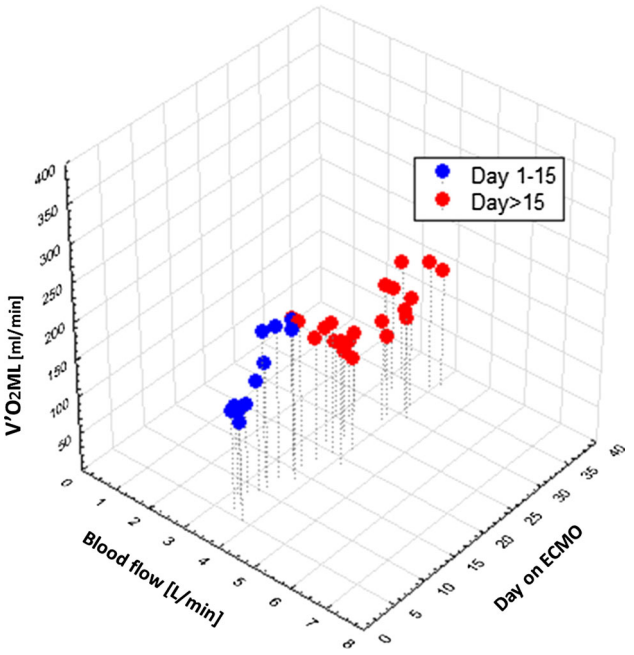


Fig. 5 3-D plot of oxygen transfer from membrane lung ($V'O_2$ ML) during the entire period of use of the first oxygenator, an ECMO Adult Oxygenator (by Eurosets^{TM}) certified up to 15 days

decline of oxygen transfer capacity during the 37 days of use. On day 37 the oxygenator was working very close to its theoretical specifications, being still able to provide a $V'O_2ML$ of approximately 200 ml/min at a blood flow around 4 l/min. Meticulous control of anticoagulation might have played an important role in preserving such a high performance, like daily monitoring of D-Dimer, anti-

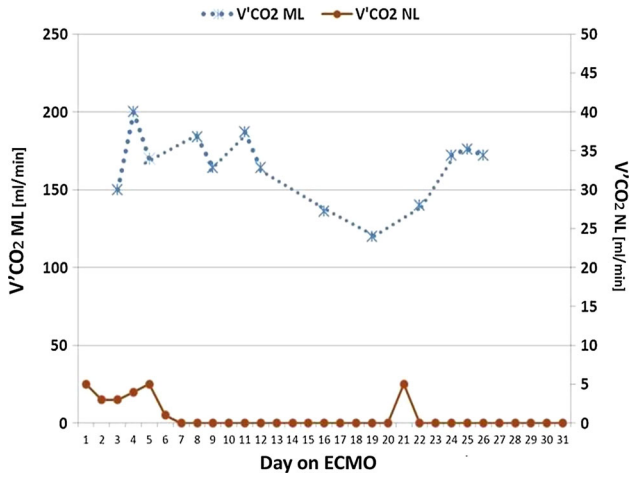


Fig. 7 Sharing of carbon dioxide removal between membrane lung ($V'CO_2ML$) and native lung ($V'CO_2NL$)

thrombin III (ATIII), Activate Clotting Time (ACT), aPPT ratio, INR and prothrombin percentage (PT %). Ideally, the information about $V'O_2ML$ should be completed by the complementary information about $V'O_2NL$. This was not available in our case, but we tried to clarify the picture by adding measurements for $V'CO_2ML$ and $V'CO_2NL$. Figure 7 shows how the lungs were kept at rest: as soon as ECMO was started, most of task of CO_2 removal was shifted to the membrane lung, the latter warranting the entire CO_2 removal after day 6 of ECMO. Total CO_2 removal was higher in the first days of ECMO and around days 24–26. In both cases the acceleration of metabolism was associated with an inflammatory state witnessed by an

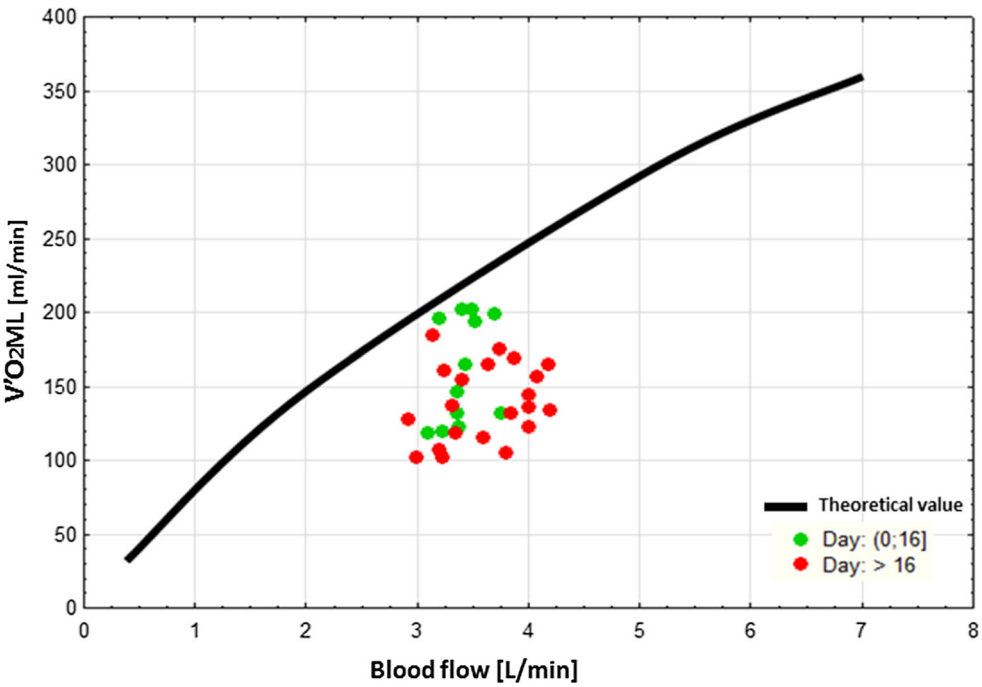


Fig. 6 Oxygen transfer from membrane lung ($V'O_2ML$) during the entire period of use of the first oxygenator, an ECMO Adult Oxygenator (by Eurosets^{TM}). Actual values are obtained with a gas flow/blood flow ratio of 1:1 and a FiO_2 of 100 %. The values are plotted together with the factory theoretical relationship between $V'O_2ML$ and blood flow (the theoretical values are obtained with bovine blood at 37 °C, with venous oxygen saturation of 65 % and total Hb of 12 g/dl and a venous CO_2 partial pressure of 45 mmHg, the gas flow/blood flow ratio were 1:1 and the FiO_2 100 %)

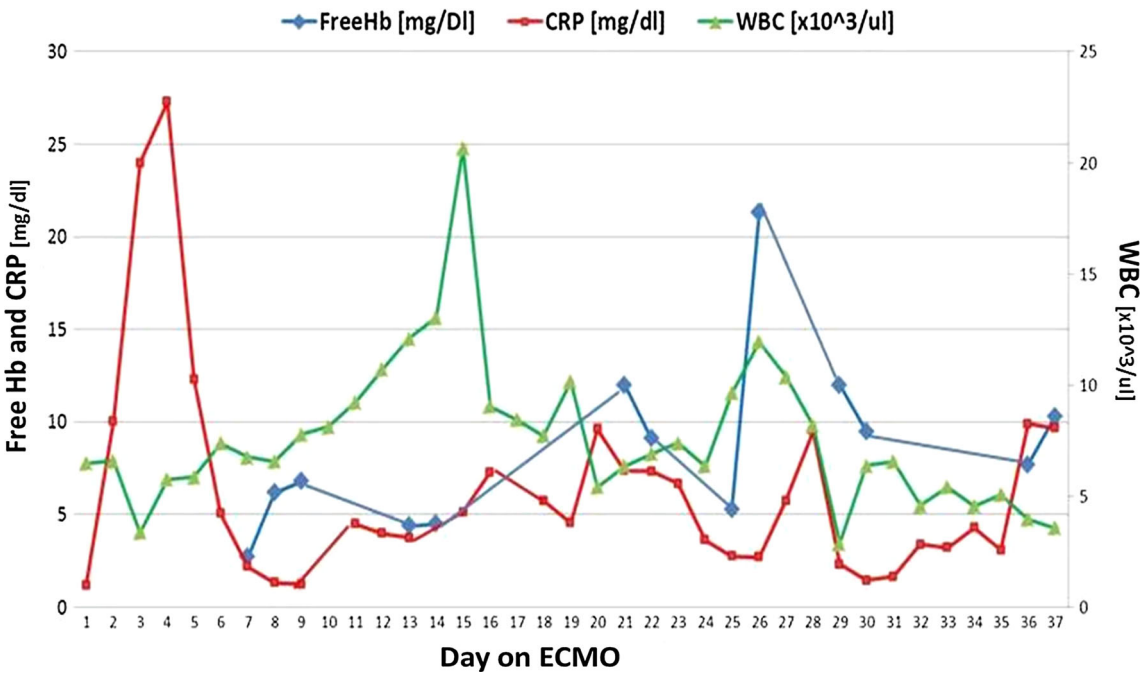


Fig. 8 White blood cells (WBC) count, C-reactive protein (CRP) level and free hemoglobin (FreeHb) level during the entire period of use of the first oxygenator

increase of C-reactive protein (Fig. 8), most likely due to sepsis in the first period and secondary to haemolysis in the second one [5]. Former versions of the Landing® monitor were able to read only positive pressures. In the version used in the present trial, the measurement of sub-atmospheric pressures is enabled in one channel for continuous monitoring of drainage pressure. Information about level and stability of negative pressure in the ECMO circuit may help to prevent cavitation phenomena and consequent haemolysis, as well as to judge about adequate position of the drainage cannula or need for blood volume expansion. The peak of free haemoglobin found on day 25 (Fig. 8) was associated with instability of drainage pressure due to partial displacement of the drainage cannula. Drainage pressure monitoring allowed early detection of the problem and guided us in optimizing blood drain and thus stopping haemolysis.

5 Conclusions

ECMO technology is rapidly evolving and the addition of monitoring components to ECMO machines is part of this continuous evolution. While during cardiopulmonary bypass the heart–lung machine works under the direct and continuous supervision of the perfusionist, an ECMO machine works non-stop even for several weeks and is not continuously attended; for this reason a monitoring system with alarms may be particularly important during ECMO.

Like for the patient vital signs monitor, or the mechanical ventilator monitor, an ECMO monitor has a double purpose: early detection of dysfunctions and critical states, but also source of information for understanding pathophysiological phenomena and following the patient course. The version of Landing® monitor used in the present trial provides an interesting combination of parameters, including drainage pressure and oxygen transfer provided by the membrane lung. The former parameter is critical for the assessment of blood drainage adequacy and haemolysis risk. The second parameter may play an important role in decision-making about oxygenator replacement, thus helping to reduce risks while saving money.

In the present trail the measurement of $V'CO_2ML$, made intermittently by volumetric capnometry with independent equipment, gave useful insights into the degree of respiratory function substitution actually operated by the vvECMO system. In a future perspective, the combination of $V'CO_2ML$ as a continuous measurement provided by the Landing® monitor would be an ideal complement of the functions presently offered by the apparatus. Besides the lack of measurement of CO_2 removal, another limitation of the Landing® monitor is due to the fact that the ECMO circuit must be slightly modified, by cutting the drainage and reinfusion lines in order to insert the adapters for the venous and arterial optical probes. This is a minor problem when done before starting the ECMO circuit priming. On the contrary, should the Landing® monitor be connected to

an ECMO circuit not prepared for that and already running, circuit adaptation would require a short stop of extracorporeal circulation and extremely high attention paid during the insertion of the adapters; in that case, benefits of monitoring should be weighted with caution against risks. The possible benefits suggested by the present trial with Landing® monitor on vvECMO require confirmation by further experiences possibly extended also to the different context of veno-arterial ECMO. Extended monitoring should warrant advantages, especially when correctly conceived as a tool to help, and not to replace, the process of clinical observation of the patient.

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Compliance with ethical standards

Conflict of interest Dr. M. Belliato received honoraria from Eurosets™ srl (Medolla, Italy) for lecturing at congresses and meetings. Dr. A. Degani, Dr. C. Pellegrini, Dr. G.A. Iotti, Dr. A. Buffa, Dr. M. Pagani and Dr. F. Sciutti have no conflicts of interest.

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