DOI:10.23873/2074-0506-2019-11-2-128-140

Diagnostic capabilities of monitoring of redox potential in blood plasma of lung transplant patients

A.K. Evseev*[1], E.I. Pervakova[1], I.V. Goroncharovskaya[1], Y.A. Tarabrin[1], M.Sh. Khubutiya[1], M.M. Goldin[2]

[1]*N.V. Sklifosovsky Research Institute for Emergency Medicine, 3 Bolshaya Sukharevskaya Sq., Moscow 129090 Russia;*

[2] Glen Oaks Community College, MI 49032, Centreville, 62249 Shimmel Rd

*Correspondence to: Anatoliy K. Evseev, Dr. Chem. Sci., Leading Researcher of the Department for General Resuscitation, N.V. Sklifosovsky Research Institute for Emergency Medicine, e-mail: anatolevseev@gmail.com

Received: January 10, 2019

Accepted for publication: March 4, 2019

Introduction. *Monitoring of redox potential (platinum electrode open circuit potential) in biological media (serum, blood plasma) is one of the promising methods for diagnosing and predicting the development of complications in patients in the early post-transplantation period. The study of the diagnostic capabilities of this technique in patients after lung transplantation is highly relevant.*

The objective *was to assess the diagnostic and prognostic capabilities of monitoring platinum electrode open circuit potential in blood plasma of lung transplant patients.*

Material and methods. *The data obtained at monitoring of platinum electrode open circuit potential in blood plasma and clinical laboratory test results of 14 patients after double lung transplantation surgery were* *analyzed. The platinum electrode open circuit potential value in the blood plasma was measured by the potentiometric method.*

Results. *The study demonstrated the differences in the dynamics and values of platinum electrode open circuit potential in the blood plasma between the lung transplant patients with a favorable outcome and those with a fatal outcome. Wave-like segments on the relationship curves of the platinum electrode open circuit potential in blood plasma to time coincided with inflammatory markers (C-reactive protein, stab neutrophils, erythrocyte sedimentation rate) activation. Statistically significant correlations between platinum electrode open circuit potential values in blood plasma and clinical laboratory test results were revealed.*

Conclusion. *The informative value and diagnostic capabilities of the technique of the platinum electrode open circuit potential measurement in blood plasma of lung transplant patients have prospects of using its results as a criterion for assessing the patient's condition and improving the quality of therapy.*

Keywords: lung transplantation, open circuit potential, platinum electrode, blood plasma, inflammatory process, complication

Conflict of interests. Authors declare no conflict of interests

Financing. The study was performed without external funding

Evseev A.K., Pervakova E.I., Goroncharovskaya I.V., et al. Diagnostic capabilities of monitoring of redox potential in blood plasma of lung transplant patients. *Transplantologiya. The Russian Journal of Transplantation.* 2019;11(2):128–140. (In Russian). DOI:10.23873/2074- 0506-2019-11-2-128-140

MLV, mechanical lung ventilation

ABS, acid-base status

OCP, open circuit potential

ESR, erythrocyte sedimentation rate

ECMO, extracorporeal membrane oxygenation

ABE, actual bicarbonates

CHb, concentration of hemoglobin fraction

FCOHb, carboxyhemoglobin

FHHb, deoxyhemoglobin fraction

FMetHb, concentration of methemoglobin fraction

FO_2Hb, oxyhemoglobin fraction

pO_2, partial pressure of oxygen

pCO_2, partial pressure of carbon dioxide

sO_2, oxygen saturation

ctO_2, concentration of total oxygen

SBE, standard bicarbonates

Introduction

Lung transplantation is the generally accepted treatment of choice for end-stage pulmonary diseases such as chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, cystic fibrosis, etc. [1]. We emphasize that lung transplantation surgery and postoperative management of patients have a number of important features. Thus, donor lungs, unlike other solid organs, are characterized by the shortest storage period before transplantation (<8 h) [2]. In addition, transplanted lungs tend to developing edema, which is associated with an increased permeability of pulmonary vessels and impaired lymphatic drainage due to ischemic-reperfusion injury of the graft and its trauma due to surgery [3]. In this regard, the timely diagnosis of complications (inflammatory process, oxidative stress, graft dysfunction) developed in patients in the early postoperative period has been one of the key issues of clinical medicine.

One of the promising diagnostic methods is the measurement of the redox potential in biological media, which is an integral parameter of the balance between oxidizing agents (e.g. oxidized thiols, superoxide radical, hydroxyl radical, hydrogen peroxide, nitrogen oxide, peroxynitrite, transition metal ions) and reducing agents (e.g., free thiols, ascorbate, α-tocopherol, β-carotene, uric acid) in the body [4]. The most common method for determining the redox potential is the potentiometric method; but from the electrochemistry point of view, when analyzing biological media, it is more correct to use the term "open circuit potential" (OCP) that will be referred to hereinafter.

The diagnostic possibilities of measuring the platinum electrode OCP in blood plasma were shown earlier [5–7] by evaluating the probability of complications developed in patients with transplanted kidney and liver. We found that a change in the platinum electrode OCP value in plasma or serum of those patients more than by 25 mV indicated the development of complications [6]. In addition, using the probit-analysis of the data on OCP monitoring in blood plasma of patients after kidney transplantation, we determined the likelihood of complications in the early postoperative period [8].

Thus, the task of studying the diagnostic and prognostic capacity of monitoring the platinum electrode OCP in blood plasma of patients with transplanted lungs is very relevant.

Material and Methods

Fourteen patients were studied after bilateral lung transplantation performed in N.V.Sklifosofsky Research Institute for Emergency Medicine in 2013–2017 (Table 1).

Table 1. Characteristics of the study patients

	Favorable outcome	Fatal outcome
Number of patients	7	7
Age	32,4±5,4	37,6±14,9
Gender: Men	3	4
Women	4	3
Extracorporeal membrane oxygenation	Intraoperatively	Intraoperatively, and in 4 patients in the post-transplant period
The number of OCP measurements	117	60
The mean time of OCP monitoring, days	33	17
The main diagnosis and number of patients	Cystic fibrosis in **4 pts** Chronic obstructive pulmonary disease in **1pt** Primary pulmonary emphysema without α1-antitrypsin deficiency in **1 pt** Primary ciliary dyskinesia. Multiple bilateral broncho- and bronchiolectases in **1 pt**	Pulmonary fibrosis of various etiologies in **3 pts** Cystic fibrosis in **1 pt** Primary pulmonary emphysema without α1-antitrypsin deficiency in **1 pt** Lymphangioleiomyomatosis in **1 pt** Congenital cystic hypoplasia of the lungs in **1 pt**
Final diagnosis and number of patients		Multiple organ failure syndrome: acute cardiovascular insufficiency, acute respiratory failure, acute renal and hepatic failure in **7 pts** Bilateral pneumonia in **7 pts** Reactive pancreatitis and small-focal pancreonecrosis in **4 pts** Pulmonary graft dysfunction in **3 pts** Sepsis in **2 pts** Lactate acidosis in **1pt**

The equipment to measure OCP in blood plasma consisted of an IPS-compact potentiostat (Kronas ZAO [Close Joint Stock Company], Russia), a measuring platinum electrode, and a silver chloride electrode, being the reference electrode, according to the published methodology [9]. Experimental relationships of the platinum electrode OCP values to time were analyzed for the deviation from the calculated relationship, according to the methodology [10].

Whole blood was obtained using a vacuum system for blood sampling; Vacutainer® LH 102 IU tubes (BD, UK) containing lithium heparin anti-coagulant were used. Blood plasma was obtained by centrifuging the whole blood in a CR 3.12 centrifuge (Jouan, France) at 1500 g for 15 min. The amount of a plasma sample for the study was 2 ml. A total of 177 tests were made.

Clinical and laboratory tests (for acid-base status [ABS], the complete blood count, inflammatory markers) were performed according to standard techniques.

The experimental data were statistically processed by calculating the Pearson, Spearman, and Kendall correlation coefficients using Statistica 6.0 (StatSoft) software. The data are presented in $X \pm s$ form, statistically significant data are given for up to 25 days only for patients with a favorable outcome and up to 15 days for patients with a fatal outcome due to a small sample size at a later time.

Results and Discussion

Due to the characteristics specific for transplant patients associated with possible complications related to the ischemic-reperfusion injury of the transplanted organ, and to the immunosuppressive therapy, we can expect these factors to affect the balance of pro- and antioxidants in the body. It is known, for example, that immunosuppressive therapy may increase the concentration of active forms of oxygen; and, as a consequence, the risk of oxidative stress development may increase [11].

When monitoring the platinum electrode OCP in blood plasma of the patients in the early postoperative period after bilateral lung transplantation, we found a significant difference in the OCP changes throughout the treatment course between the patients with a favorable outcome and those with a fatal outcome (Fig. 1).

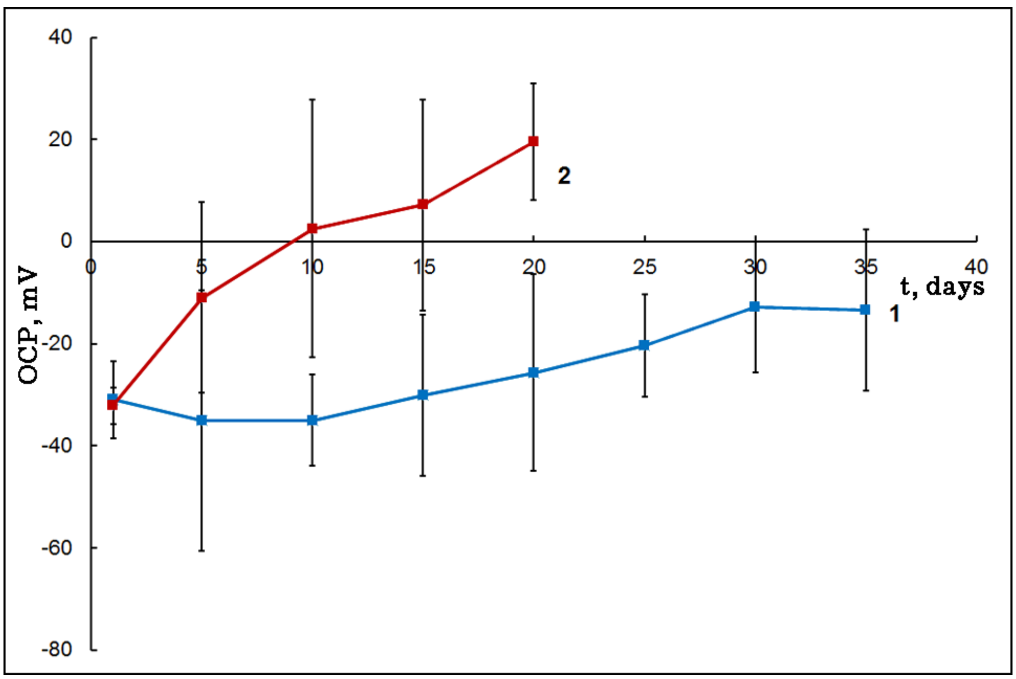

Fig. 1. Monitoring of the platinum electrode open circuit potential in blood plasma of patients with a favorable (1) or fatal (2) outcome

The patients with a favorable outcome (Fig. 1, curve 1) had the mean platinum electrode OCP values in the range of potentials –31.0 ± 19.1 mV in the early stages (first 2 weeks). Such negative values of OCP in blood plasma might probably have been related to the fact that due to the respiratory system dysfunction that might occur in the patients in the early postoperative period after lung transplantation, the hypo-oxygenation was observed resulting in the inhibition of the processes with the participation of reactive oxygen forms, which caused a shift in pro- and antioxidant balance towards the predominance of the body antioxidant system. By day 25, an insignificant shift of the OCP values had been observed to the region of more positive potentials up to values of -20.3 ± 17.1 mV. The shift in the platinum electrode OCP value averaged 10.7 mV. This observation may indicate the normalization of respiratory system function and the leveling of the pro-oxidant and antioxidant balance within the treatment of patients with transplanted lungs. In the long-term prognosis, one can expect that the platinum electrode OCP value should shift to the OCP values typical for patients with a transplanted kidney (+ 7.8 ± 24.5 mV) and liver (+ 9.1 ± 23.7 mV) [6]. This assumption was confirmed by the long-term results of monitoring the platinum electrode OCP in blood plasma of patient B. of 30 years old. The main diagnosis: "Primary ciliary dyskinesia, multiple bilateral broncho- and bronchioloectases." Concomitant diagnosis was "Chronic Hepatitis C". Surgery: orthotopic lung transplantation in conditions of ECMO. Complications: chronic respiratory failure 3 stage (hypercapnic type). Pulmonary bleeding of low intensity. Bilateral multisegmental pneumonia. Acute post-hemorrhagic anemia. Acute respiratory failure. Acute renal failure. Acute cardiovascular failure. Postpneumonic bilateral pleuritis. Acute pleural empyema on the left. Suppuration of postoperative wounds. It was shown that the platinum electrode OCP value was close to

+10.1 ± 7.6 mV at 2 months of post-transplantation follow-up, and –2.4 ± 5.2 mV at 6 months after the surgery.

Meanwhile, the patients after lung transplantation with a fatal outcome during the 1st week showed an abrupt shift of the OCP value closer to more positive potentials (Fig. 1, curve 2). So, on day 1 the platinum electrode OCP values in those patients were in the range of -32.2 ± 3.6 mV; later on, after 2 weeks there was a shift to +7.2 ± 20.6 mV, i.e. the shift in the platinum electrode OCP value averaged 39.4 mV. Based on the results of the previous studies that demonstrated a high probability of complications in the post-transplantation period in cases of OCP shifts more than by 25 mV [6], one could assume that such an abrupt shift in the platinum electrode OCP value in the patients with transplanted lungs indicated the development of serious complications in the postoperative period. Thus, not only the size of the platinum electrode OCP value had a diagnostic value, but also the dynamics of the changes in that parameter within 1–3 days did.

When comparing the results of the platinum electrode OCP monitoring and the dynamics of the inflammatory markers (Fig. 2), we found that the patients with a fatal outcome in the first two weeks showed the increases in the *C*-reactive protein concentration in blood to 175.7 ± 36.1 mg/L (Figure 2, a, curve 2) and the erythrocyte sedimentation rate up to mean 44.1±16.6 mm/h (Fig. 2, f, curve 2). At the same time, during the entire post-transplantation period, the leukocyte count was 16.0 ± 4.1×10^9 cells/L (Fig. 2, b, curve 2), the stab neutrophil percentage was 15.9 ± 5.7% (Fig. 2, c, curve 2). Thrombocytopenia at the level of 66.2 ± 29.7×10^9 cells/L was also characteristic for that group (Fig. 2, e, curve 2). All those signs may indicate the inflammatory process development.

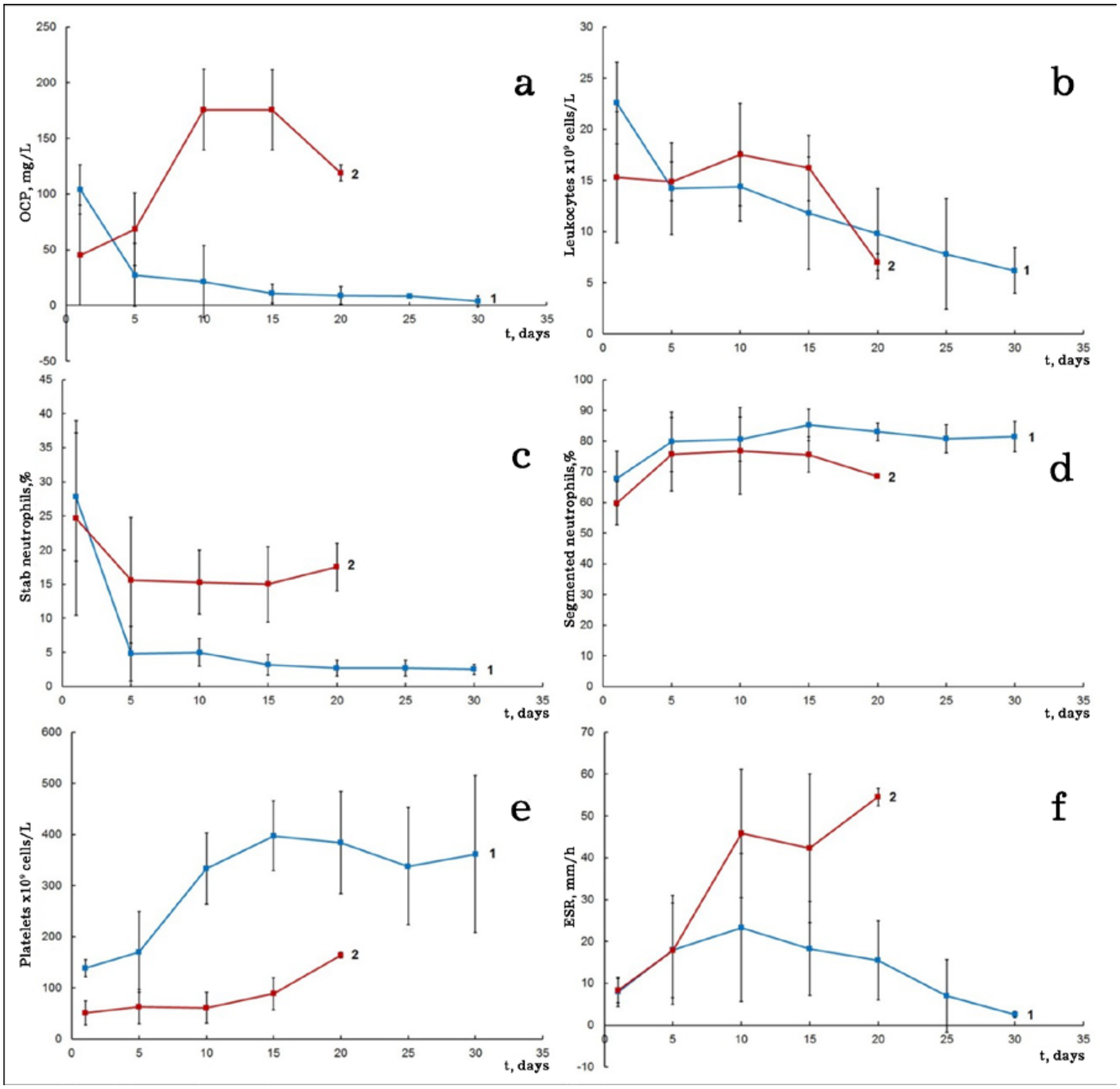

Fig. 2. The concentration of *C*-reactive protein (a), leukocyte count (b), stab neutrophils (c), segmented neutrophils (d), platelets (e) and erythrocyte sedimentation rate (f) in the patients with a favorable (1) or fatal (2) outcome

In patients with a favorable outcome, the most significant changes also occurred in the first 2 weeks after surgery (Fig. 2, curves 1), and resulted in gradual decreases of the *C*-reactive protein concentration in blood, leukocyte count, stab neutrophils, and the increase in platelet count. Further on, as demonstrated by the graphs, the curve showing the change in those values became flatter.

An important finding, from our point of view, was the detection of the undulating segments on the curves of the platinum electrode OCP to time (Fig. 3), which were predominantly manifested in the patients with a fatal outcome. The appearance of the such segments, as we have shown earlier [12], may indicate the inflammatory process development in the patients. Indeed, that phenomenon coincided in time or preceded by 1-2 days in some cases, to the laboratory signs of inflammation, namely, the increased C-reactive protein, stab neutrophils, and erythrocyte sedimentation rate.

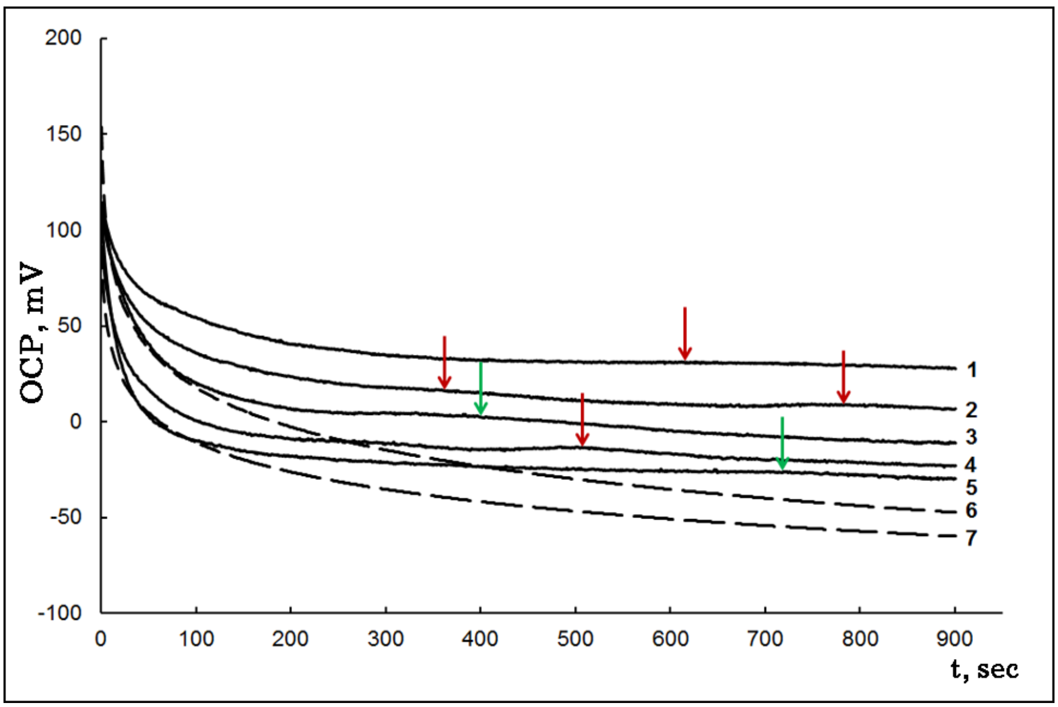

Fig. 3. The relationship curves of the platinum electrode open circuit potential value in blood plasma to time: 1–5, curves of patients after lung transplantation with favorable (No. 3, No. 5) and fatal (No. 1, No. 2, No. 4) outcomes; 6–7, curves of healthy people

* arrows ↓ and ↓ indicate wave-like segments for patients with favorable and fatal outcomes, respectively

Thus, the appearance of wave-like segments on the relationship curves of the platinum electrode OCP to time coincided with the activation of inflammatory markers, i.e. the electrochemical method used made it possible to suggest the presence of an inflammation in the body. We emphasize that, in contrast to the world analogues [4, 13, 14] operating with a discrete values of the platinum electrode OCP, the recording and analyzing of the "potential-time" relationship increases the informative value of the method, which is very important for diagnosing complications in seriously ill patients.

In addition to contrasting the results of platinum electrode OCP monitoring to the dynamics of inflammatory markers, we analyzed the relationship with the blood gas composition and oximetry, since the relationship of the blood redox potential to the partial oxygen pressure had been previously shown [15].

We found that significant changes in blood gas parameters (pO_2, pCO_2, sO_2, ctO_2) were observed for a group of patients with a favorable outcome during the first 5–10 days after surgery. The decreases in pO_2, sO_2, and ctO_2 were noted with a slight increase in pCO_2. That phenomenon could be associated with the fact of patients being on mechanical lung ventilation (MLV) on those days. After switching to spontaneous breathing, the so in venous blood averaged 60% without the insufflations of humidified oxygen, and increased to 65–70% after day 20 (the reference normal value being 70–75% [16]).

The patients from the fatal outcome group were provided with the oxygen support through the ventilator or ECMO during the entire post-transplantation period, which was reflected by a higher pO_2, exceeding 300 mm Hg in some cases, and a sO_2. In those conditions, tracing the correlation with the results of measuring the platinum electrode OCP seemed incorrect.

When assessing the blood oxygen transport parameters (FO_2Hb, FCOHb, FHHb, FMetHb) for patients with a favorable outcome, the most significant changes were noted for the ox hemoglobin and deoxyhemoglobin fractions (Fig. 4, b, d, curve 1). It was significant that the oxyhemoglobin fraction (FO_2Hb) decreased and the deoxyhemoglobin fraction (FHHb) increased in those patients during the first 5–10 days, which coincided with the above-mentioned weaning the patients from the ventilator support of respiration and switching them to spontaneous breathing. High values of deoxyhemoglobin fraction may indicate the presence of a large physiologic dead space in the lungs or an alveolar hypoventilation [17]. Subsequently, the oxyhemoglobin fraction stabilized at about 60%; and by day 20, there was a tendency to increase. Meanwhile, the deoxyhemoglobin fraction that was 37% on day 10, subsequently also tended to decrease by day 20 (Fig. 4, d, curve 2). The observed changes might have indicated the functional normalization of the transplanted organ.

In addition, the survived patients had a slight increase in hemoglobin concentration (Fig. 4, a, curve 1), and a decrease in the concentration of the methemoglobin fraction (Fig. 4, e, curve 1) in the first 2 weeks. We should emphasize that those data corresponded to the platinum electrode OCP monitoring results suggesting a positive outcome. No significant changes in the carboxyhemoglobin fraction (Fig. 4, c, curves 1) were seen.

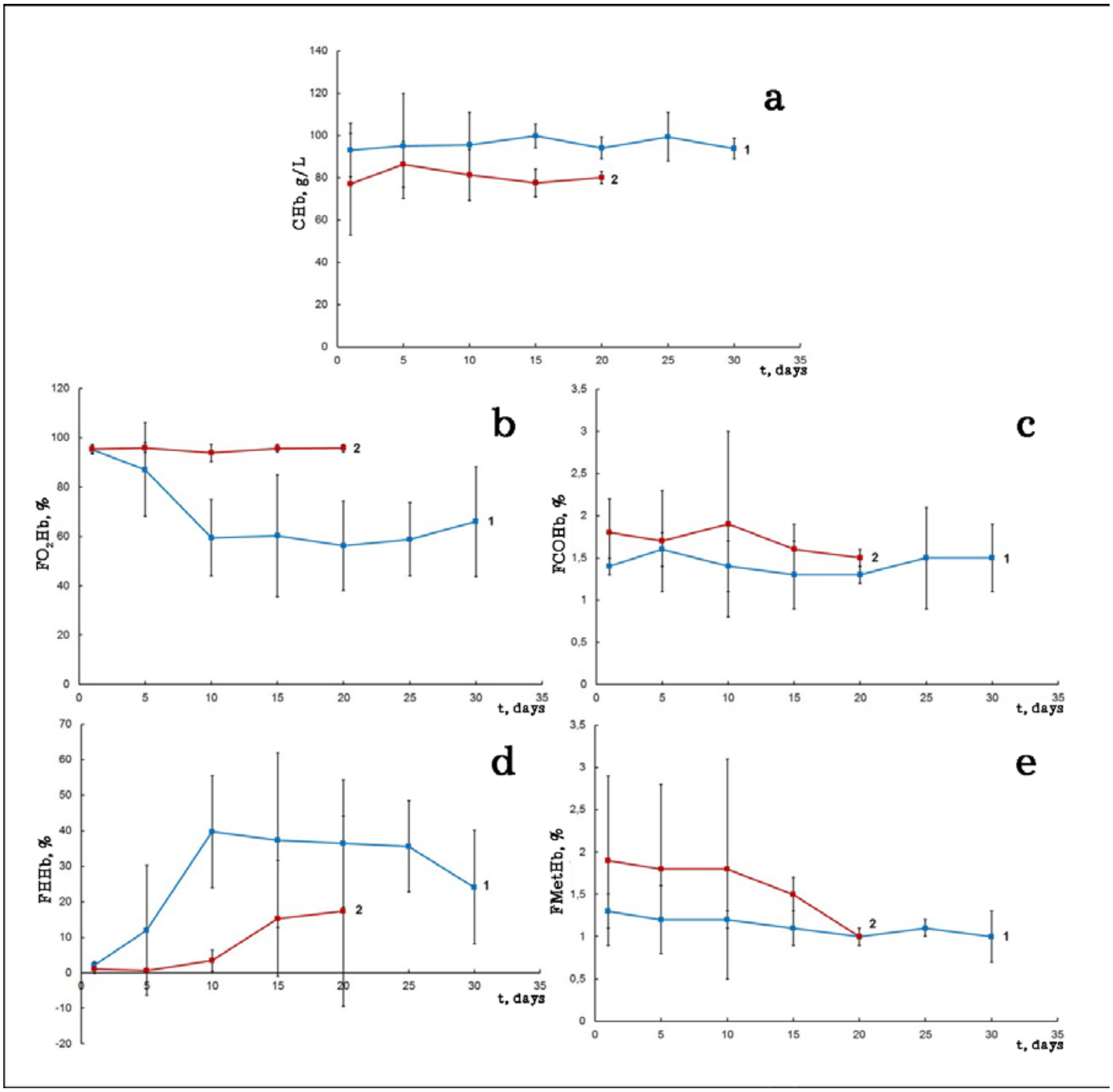

Fig. 4. The CHb (a), FO_2Hb (b), FCOHb (c), FHHb (d), and FMetHb (e) values in patients with favorable (1) and fatal (2) outcomes

The patients with a fatal outcome had a lower hemoglobin concentration compared to the patients with a favorable outcome: about 80 g/L versus 97 g/L. With the oxygen support provided by MLV or ECMO, similarly to the elevated pO_2 and sO_2 described above, it was quite natural for them to have the oxyhemoglobin fraction of at least 95% during the entire post-transplant period (Fig. 4, b, curve 2). In addition, the increased deoxyhemoglobin fraction was notable (Fig. 4, d, curve 2), despite the external support of the respiratory function. No significant changes were recorded in other parameters.

In general, assessing the oxygen status parameters, we identified the following pattern. The patients with a favorable outcome tended to have a positive prognosis at the end of the 2nd post-transplantation week as based on the data of platinum-electrode OCP monitoring; at the same time the blood gas parameters and the blood oxygen transport were stabilizing. In the same time of the post-transplant period, the patients with a fatal outcome showed the shift of the platinum electrode OCP values to the area of more positive potentials, which coincided with an increase in the deoxyhemoglobin fraction.

The blood acid-base status is another important parameter for patients with transplanted lungs. Earlier, Bernard C. et al. [18] showed a correlation between the redox potential and pCO_2 and blood pH, but they noted a complex nature of those correlations. Since their study subjects were the athletes at the age of 18–21 years old who could be characterized as practically healthy people, the analysis of case histories of patients with pathological conditions seems very reasonable.

We have shown that all studied parameters (pH, C_{HCO3-}, ABE, SBE) in the patients with a favorable outcome had only slight deviations from the norm in the post-transplantation period (Fig. 5, curves 1), whereas the fatal outcome patients had significant changes in all the parameters in the first 5–7 days, (Fig. 5, curves 2). Based on the pH effect on the platinum electrode potential [19], the pH decrease should lead to a shift in the platinum electrode OCP to the area of more positive potentials. We should emphasize that the change in solution pH by 1 point should lead to a shift in the platinum electrode OCP by 59.1 mV. The maximum shift in the pH value averaged 0.2, which should have led to a shift in the OCP by 12.0 mV; meanwhile the patients had higher values of the platinum electrode OCP shifts (Fig. 1, curve 2). Thus, we can conclude that a change in ABS parameters affect insignificantly the platinum electrode OCP value measured in blood plasma. However, taking the measured ABS parameters into the account when calculating the platinum electrode OCP values can improve the accuracy of the study.

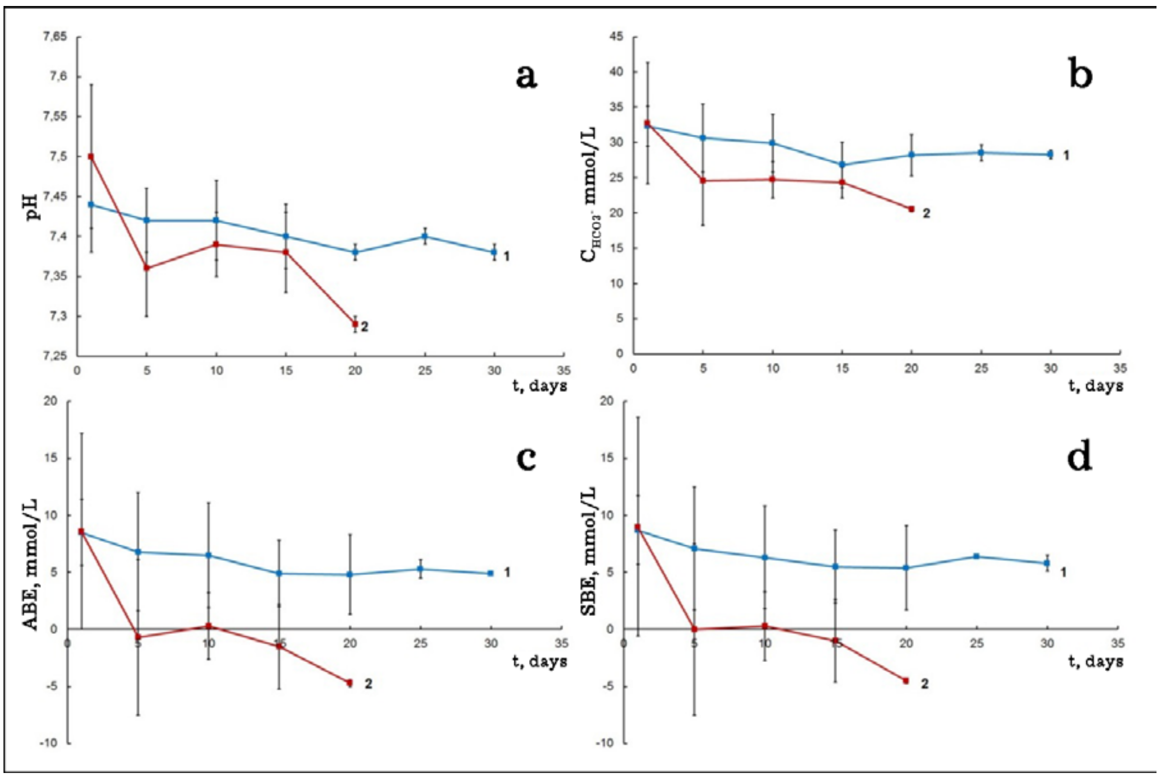

Fig. 5. PH (a), C_{HCO3}^{-} (b), ABE (c), and SBE (d) values in patients with favorable (1) and fatal (2) outcomes

We made a correlation analysis of the relationship between the OCP value and the clinical data, calculating the Pearson, Spearman, and Kendall correlation coefficients (Table 2). In the group of patients with a favorable outcome, there was a significant correlation of OCP values ($p < 0.05$) with the leukocyte count, platelets, segmented neutrophils, hemoglobin, and the ABS parameters (pH, C_{HCO3}^-, ABE, SBE) for all three coefficients. The correlation was significant between the OCP and the methemoglobin fraction when calculating the Spearman and Kendall coefficients, and with the pO2 only for the Pearson coefficient.

In the group of patients with a fatal outcome, a significant correlation for all three coefficients was found with the segmented neutrophils and the erythrocyte sedimentation rate. The correlation was significant with the carboxyhemoglobin fraction for the Pearson and Spearman coefficients, and with the stab neutrophils for the Pearson coefficient.

Table 2. Coefficients of correlation between OCP values and laboratory test results

Parameter	Pearson		Spearman		Kendall	
	Pts with favourable outcome	Pts with fatal outcome	Pts with favourable outcome	Pts with fatal outcome	Pts with favourable outcome	Pts with fatal outcome
C-reactive protein, mg/L	-0.13	0.25	-0.19	0.24	-0.11	0.14
Leukocytes, $x10^9$ cells/L	-0.28 *	0.18	-0.31 *	0.16	-0.22 *	0.1
Stabs,%	-0.01	-0.25 *	-0.01	-0.25	-0.003	-0.16
Segmented, %	-0.28 *	0.36 *	-0.28 *	0.34 *	-0.19 *	0.23 *
Platelets, $x10^9$ cells/L	0.35 *	0.02	0.26 *	0.18	0.17 *	0.14
Erythrocyte sedimentation rate (ESR), mm/h	-0.22	-0.33 *	-0.22	-0.29 *	-0.15	-0.18
pO_2, mm Hg	-0.23 *	-	0.001	-	0.01	-
pCO_2, mm Hg	-0.09	-0.01	-0.11	-0.04	-0.08	-0.02
sO_2, %	-0.02	-	-0.005	-	0.01	-
ctO_2, mmol/L	0.16	-	0.11	-	0.07	-
CHb, g/L	0.35 *	-0.002	0.33 *	0.02	0.22 *	0.01
FO_2Hb, %	-0.03	0.19	-0.01	-0.08	0.006	-0.06
FCOHb, %	0.03	0.31 *	0.02	0.26 *	0.02	0.16
FHHb, %	0.03	-0.22	0.02	0.11	0.001	0.09
FMetHb, %	-0.17	0.14	-0.29 *	0.04	-0.22 *	0.04

pH	-0.27 *	0.11	-0.26 *	0.14	-0.19 *	0.1
C_{HCO3}^{-} , mmol/L	-0.33 *	0.09	-0.32 *	0.16	-0.21 *	0.09
ABE, mmol/L	-0.33 *	0.09	-0.29 *	0.13	-0.20 *	0.08
SBE, mmol/L	-0.31 *	0.09	-0.27 *	0.13	-0.19 *	0.07

Pts, patients;
* Significant correlations at $p < 0.05$

The diagnostic efficacy of the method was evaluated using ROC analysis. As a model implying the absence of complications, we used data from the patients with a favorable outcome on monitoring day 20, i.e. the true negative cases were in the range of –25.7 ± 19.2 of the platinum electrode OCP values in blood plasma, and the true positive cases were outside that range. Based on the proposed model, we constructed a contingency table (Table 2) and a ROC curve (Fig .6).

Table 3. Fourfold Contingency Table

Model	Clinical and laboratory data	
	Any complication	No complications
Any complication	55	21
No complications	30	71

The sensitivity of the method (Se) was 64.5%, and the specificity (Sp) was 77.2%.

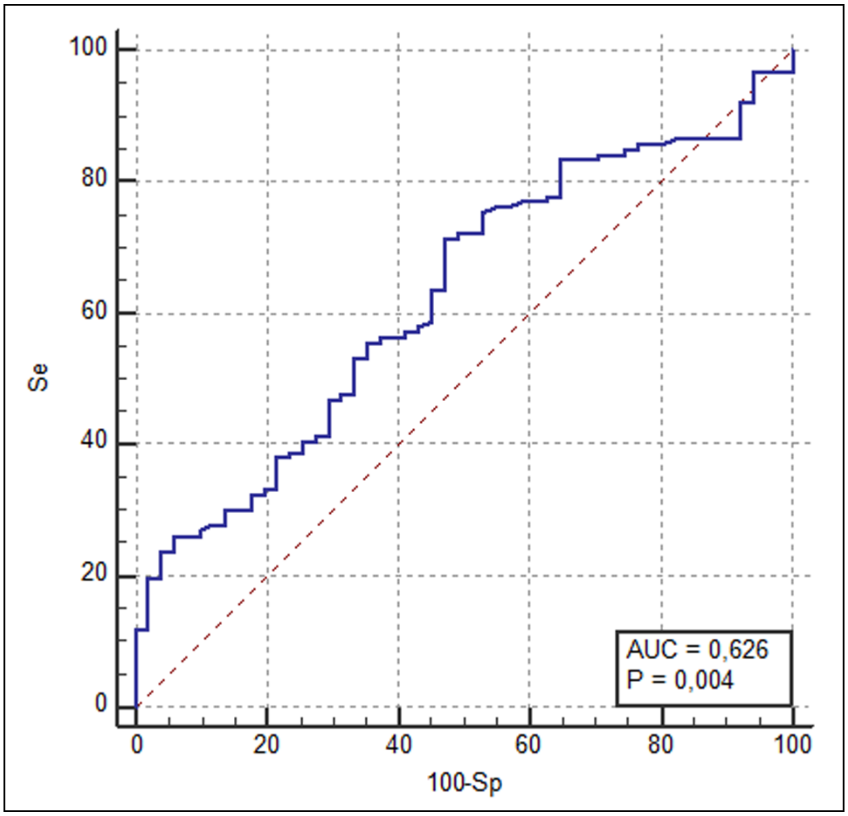

Fig. 6. ROC curve for predicting the development of complications by measuring the platinum electrode open circuit potential in blood plasma

This method can be assessed as providing a medium quality in predicting complications (0.6 <AUC <0.7).

Summary

Thus, the method of measuring the platinum electrode OCP in biological media, being simple in use and of low cost, is very informative in diagnosing the imbalance of pro- and antioxidant systems, as well as in predicting the complications in patients. The results of monitoring the platinum electrode OCP values in plasma of patients with transplanted lungs can be used as an additional criterion for assessing patient's condition in the post-transplant period.

Conclusions

1. The differences in the platinum electrode open circuit potential values in blood plasma and their dynamics were shown between the lung transplant patients with a favorable outcome and those with a fatal outcome.

2. Statistically significant correlations between the platinum electrode open circuit potential in blood plasma and the leukocyte count, platelets, segmented neutrophils, hemoglobin, methemoglobin fraction, pO_2, and acid-base parameters (pH, HCO_3^-, ABE, SBE) were shown in patients with a favorable outcome; and the correlations with the segmented neutrophils, stab neutrophils, the carboxyhemoglobin fraction, and the erythrocyte sedimentation rate were shown in patients with a fatal outcome.

3. Wave-like segments were found on the curves of the platinum electrode open circuit potential to time, which coincided with the activation of inflammatory markers in the patients.

4. We have proposed a model for predicting the risk of complications by platinum electrode open circuit potential measurement in blood plasma of patients with transplanted lungs in the early post-transplant period.

References

1. Gautier S.V., et al. *Russian Transplant Society. Lung Transplantation: National Clinical Guidelines*. Moscow, 2013. 51. Available at: http://transpl.ru/images/cms/data/pdf/nacional_nye_klinicheskie_rekomendacii_po_transplantacii_legkih_doc.pdf (In Russian).

2. Guibert E.E., Petrenko A.Y., Balaban C.L., et al. Organ Preservation: Current Concepts and New Strategies for the Next Decade. *Transfus Med Hemother*. 2011;38(2):125-142. PMID:21566713 DOI:10.1159/000327033

3. Cicco G., Panzera P.C., Catalano G., Memeo V. Microcirculation and reperfusion injury in organ transplantation. *Adv Exp Med Biol*. 2005;566:363-373. PMID:16594174 DOI:10.1007/0-387-26206-7_48

4. Rael L.T. Bar-Or R., Aumann R.M., et al. Oxidation-reduction potential and paraoxonase-arylesterase activity in trauma patients. *Biochem Biophys Res Commun*. 2007;361(2):561-565. PMID:17662690 DOI:10.1016/j.bbrc.2007.07.078

5. Gol'din M.M., Evseev A.K., El'kov A.N., et al. Development and efficacy evaluation of the electrochemical predictor of complications in patients after kidney transplantation. *Transplantologiya. The Russian Journal of Transplantation.*2015;(3):6-10.(In Russian).

6. Goldin M.M., Khubutia M.Sh., Evseev A.K., et al. Noninvasive Diagnosis of Dysfunctions in Patients After Organ Transplantation by Monitoring the Redox Potential of Blood Serum. *Transplantation*. 2015; 99(6):1288-1292. PMID:25606793DOI:10.1097/TP.0000000000000519

7. Sergiyenko V.I., Khubutiya M.Sh., Evseev A.K., et al. Diagnostic and Prognostic Possibilities of the Redox-Potential Electrochemical Measurements in Blood Plasma. *Vestnik Rossiiskoi Akademii Meditsinskikh Nauk = Annals of the Russian Academy of Medical Sciences.*2015;70(6):627-632. DOI:10.15690/vramn572(In Russian).

8. Kolesnikov V.A., Evseev A.K, El'kov A.N., et al. Prediction of Complication Development After Kidney Transplantation Using Blood

Plasma Redox Potential Monitoring. *Sovremennye tehnologii v medicine.* 2015;(4):84-90. DOI:10.17691/stm2015.7.4.11 (In Russian).

9. Khubutiya M.Sh., Evseev A.K., Kolesnikov V.A., et al. Measurements of platinum electrode potential in blood and blood plasma and serum. *Russian Journal of Electrochemistry*. 2010;46(5):569-573. (In Russian).

10. Evseev A.K., Pinchuk A.V., Andreev V.N., Gol'din M.M. Analysis of the dependency of platinum-electrode open-circuit potential on time in blood serum. *Protection of Metals and Physical Chemistry of Surfaces.* 2014;50(4):445-448. DOI:10.7868/S0044185614040020(In Russian).

11. Iyer A., Brown L. Is Mycophenolate more than just an Immunosuppressant? – An Overview. *Indian J Biochem Biophys*. 2009;46(1):25-30. PMID:19374250

12. Khubutiya M.Sh., Evseev A.K., Chzhao A.V., et al. Monitoring of the redox potential of blood serum for the diagnosis of complications in patients with liver transplants. *Transplantologiya. The Russian Journal of Transplantation.* 2012;(1-2):60-64. DOI:10.23873/2074-0506-2012-0-1-2-60-64(In Russian).

13. Zhi L., Hu X., Han C. Biphasic changes (overreduction and overoxidation) of plasma redox status and clinical implications in early stage of severe burns. *J Crit Care.*2014;29(6):1063-1068. PMID:25087859 DOI:10.1016/j.jcrc.2014.06.013

14. Spanidis Y., Goutzourelas N., Stagos D. Assessment of Oxidative Stress in Septic and Obese Patients Using Markers of Oxidation-reduction Potential. *In Vivo*. 2015;29(5):595-600. PMID:26359419

15. Grosz H.J., Farmer B.B. Reduction-oxidation potential of blood as a function of partial pressure of oxygen. *Nature*. 1967;213(5077):717-718. DOI:10.1038/213717a0

16. Toffaletti J.G. *Blood Gases and Electrolytes: Special Topics in Diagnostic Testing*. Washington: AACC Press, 2001. 82 p.

17. Hughes J.M.B. Pulmonary gas exchange. In: Gosselink R., Stam H. eds. Lung Function Testing. *Eur Respir Mon*. 2005;31:106-126.

18. Bernard C., Gallinet J.P., Conde C., et al. Interrelation between the blood redox potential and exercise induced variations of the biochemical characteristics of blood. *Bioelectrochem Bioenerg*. 1991;25(1)45-70. DOI:10.1016/0302-4598(91)87018-C

19. Pourbaix M.J.N., Van Muylder J., de Zoubov N. Electrochemical Properties of the Platinum Metals. A New Approach To Studies Of Corrosion Resistance And Cathodic Protection. *Platinum Metals Rev*. 1959;3(2):47-53.

Information about authors

Anatoly K. Evseev, Dr. Chem. Sci., Leading Researcher of the General Intensive Care Unit, N.V. Sklifosovsky Research Institute for Emergency Medicine, ORCID: 0000-0002-0832-3272;

El’za I. Pervakova, Cand. Med. Sci., Head of the Intensive Care Unit with Dialysis Methods for Patients after Organ Transplantation, N.V. Sklifosovsky Research Institute for Emergency Medicine, ORCID: 0000-0002-2163-5537;

Irina V. Goroncharovskaya, Cand. Chem. Sci., Researcher of the General Intensive Care Unit, N.V. Sklifosovsky Research Institute for Emergency Medicine, ORCID: 0000-0003-0113-306X;

Evgeniy A. Tarabrin, Cand. Med. Sci., Head of the Scientific Department of Urgent Thoracoabdominal Surgery, N.V. Sklifosovsky Research Institute for Emergency Medicine, ORCID: 0000-0002-9616-1161;

Mogeli Sh. Khubutiya, Acad. of RAS, Prof., Dr. Med. Sci., President of N.V. Sklifosovsky Research Institute for Emergency Medicine, ORCID:0000-0002-0746-1884;

Mark M. Goldin, Prof., Dr. Chem. Sci., Research Consultant of Glen Oaks Community College.