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CLINICAL STUDY

Platelet mitochondrial function and endogenous coenzyme Q_{10} levels are reduced in patients after COVID-19

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ABSTRACT

BACKGROUND: After an acute treatment for coronavirus disease (COVID-19), some symptoms may persist for several weeks, for example: fatigue, headaches, muscle and joint pain, cough, loss of taste and smell, sleep and memory disturbances, depression. Many viruses manipulate mitochondrial function, but the exact mechanisms of SARS-CoV-2 virus effect remain unclear. We tested the hypothesis that SARS-CoV-2 virus may affect mitochondrial energy production and endogenous biosynthesis of coenzyme Q_{10} (CoQ_{10}).

METHODS: Ten patients after COVID-19 and 15 healthy individuals were included in the study. Platelets isolated from peripheral blood were used as an accessible source of mitochondria. High-resolution respirometry for the evaluation of platelets mitochondrial function, and HPLC method for CoQ_{10} determination were used. Oxidative stress was evaluated by TBARS concentration in plasma.

RESULTS: Platelet mitochondrial respiratory chain function, oxidative phosphorylation and endogenous CoQ_{10} level were reduced in the patients after COVID-19.

CONCLUSION: We assume that a reduced concentration of endogenous CoQ_{10} may partially block electron transfer in the respiratory chain resulting in a reduced adenosine triphosphate (ATP) production in the patients after COVID-19. Targeted mitochondrial therapy with CoQ_{10} supplementation and spa rehabilitation may improve mitochondrial health and accelerate the recovery of the patients after COVID-19. Platelet mitochondrial function and CoQ_{10} content may be useful mitochondrial health biomarkers after SARS-CoV-2 infection *(Tab. 3, Fig. 3, Ref. 46)*. Text in PDF *www.elis.sk*

KEY WORDS: SARS-CoV-2, platelet, mitochondria, OXPHOS, coenzyme Q_{10}, oxidative stress.

Introduction

In March 2020, the World Health Organization declared a global pandemic caused by the SARS-CoV-2 virus. Since the first cases of the disease were reported in November 2019, until March 20, 2021, there were 122 million infected people in the world, 99 million patients have been cured and 2.708 million deaths have been reported. Since the beginning of the pandemic in Slovakia, 346.149 people have been infected, 255.300 patients have been cured and 8.894 deaths have been recorded. The numbers are rapidly growing, and the data are continuously updated (https://www.worldometers.info/coronavirus/country/slovakia/).

The first new coronavirus originated from the southeast China in 2003 (SARS – Severe Acute Respiratory Syndrome). The second coronavirus originated from Middle East in 2012 (MERS – Middle East Respiratory Syndrome) (1). Mortality of COVID-19 patients increases with age, in the presence of comorbidities such as hypertension, cardiovascular diseases, diabetes mellitus, obesity, chronic obstructive pulmonary diseases and cancer (2, 3, 4, 5). The main clinical symptoms of coronavirus disease COVID-19 include fever, dry cough, headache, dyspnoea, muscle pain, fatigue, loss of taste and smell (2, 6, 7, 8).

After overcoming an acute COVID-19, many symptoms may persist in patients for weeks, even new symptoms may occur. The main symptoms include: general fatigue, exhaustion, headaches, muscle and joint pain, cough, loss of taste and smell, sleep and memory disturbances, depression, sensitivity to sound and light. The symptoms may persist regardless of the severity of acute COVID-19. These health complications are known as *Post-COVID-19 Syndrome or „Long COVID"*. Long-term symptoms after SARS-CoV-2 viral infection occur with a higher incidence in the patients with comorbidities such as: diabetes mellitus, obesity, cardiovascular disease, chronic lung disease and cancer (9, 10, 11, 12).

The SARS-CoV-2 virus has a crown-like appearance, it mutates at high speed. With the help of surface "spike" proteins, which bind to angiotensin converting enzyme 2 (ACE2), the virus can

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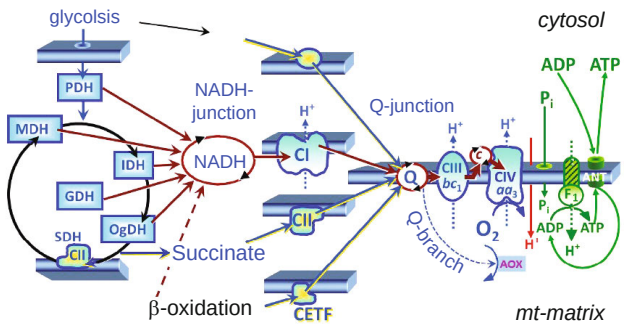

Fig. 1. Mitochondrial electron transfer system – convergent electron transfer at the NADH-junction and Q-junction (35, with permission). Electrons flow to oxygen from Complex I (CI), or from Complex II (CII) and other flavoproteins, providing multiple entries into the Q-cycle (Q-junction). Advanced SUIT protocols are designed for reconstitution of tricarboxylic acid (TCA) cycle function and sequential separation of segments of mitochondrial pathways for OXPHOS analysis (35). PDH-pyruvate dehydrogenase, MDH – malate dehydrogenase, IDH – isocitrate dehydrogenase, GDH – glutamate dehydrogenase, OgDH – 2-oxoglutarate dehydrogenase, SDH – succinate dehydrogenase (CII), CETF – electron transfer flavoprotein Complex, CGpDH – glycerophosphate dehydrogenase Complex, Gp – glycerophosphate.

pass through the mucous membranes of nose, larynx, and airways into the lungs (13).

Many viruses affect mitochondrial metabolism. Mitochondria play the key role in cellular metabolism and immune responses. They have been implicated in antiviral defence by activating immune response through mitochondrial antiviral signalling protein (MAVS) (14). It has been shown that viruses manipulate mitochondrial dynamics, bioenergetics, membrane potential and modulate mitochondrial function (15). Mitochondria damaged by the virus produce more reactive oxygen species, cause oxidative stress, cytokine storm, and stimulate inflammation (16). Mitochondrial dysfunction contributes to the symptoms of muscle pain, muscle weakness, weakening the function of individual organs such as: heart, brain, lungs, kidneys, liver and others. The mechanisms, by which SARS-CoV-2 affects its host, remain unclear (16). It is assumed that SARS-CoV-2 targets mitochondria (17).

Platelets isolated from peripheral blood are an accessible source of mitochondria and their use for the assessment of mitochondrial health is extensively studied. Platelet mitochondrial dysfunction has been documented in various diseases, such as in major depression (18), amyotrophic lateral sclerosis (19), chronic kidney disease (20, 21), in patients after kidney transplantation (22). Mitochondrial bioenergetics has been shown to be reduced in monocytes and peripheral blood mononuclear cells (PBMC) of the patients with COVID-19 (23, 24). SARS-CoV-2 virus may manipulate mitochondrial function in the patients with COVID-19 (25), and the manipulation may persist in patients after COVID-19 for an extended time.

We performed studies to test the hypothesis that platelet mitochondrial bioenergy function and endogenous biosynthesis of coenzyme Q_{10} (CoQ_{10}) may be affected by SARS-CoV-2 virus in the patients after COVID-19.

Material and methods

Subjects

Ten patients after COVID-19 in Bratislava in January and February 2021 were included in this study, 7 women and 3 men, aged 41 to 81 years with the mean age 59.9 ± 5.4 years (the Post-COVID-19 group). The patients had mild to moderate course of COVID-19 and all managed their symptoms at home taking vitamins and medications according to recommendation of a doctor. The supplemental therapy of all the patients in acute COVID-19 consisted of high daily doses of vitamin C (1000–2000 mg/day), vitamin D_3 (2000–4000 IU/day), Zn (50–100 mg/day). At the time of blood sampling, the patients were without infection, 4–7 weeks (4.70 ± 0.38) after being diagnosed SARS-CoV-2 virus infection.

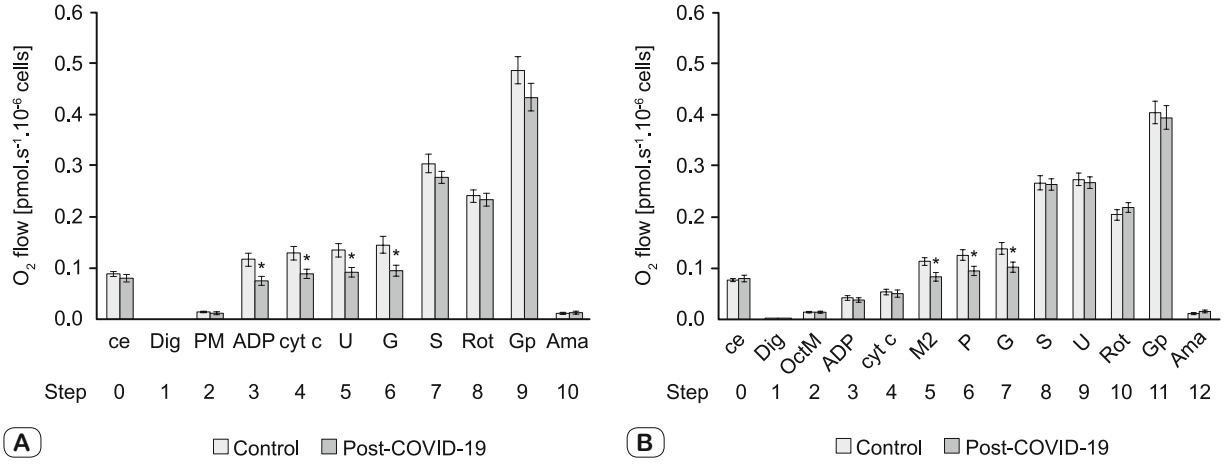

Fig. 2. The parameters of mitochondrial respiration in human platelets following SUIT reference protocol RP1 A), and modified RP2 B). The names on x-axis represent titration steps in the SUIT protocol (see the methods section). The bars show the mean±sem of mitochondrial respiration after titration step shown on x-axis. * p <0.05 – statistically significant difference vs control group.

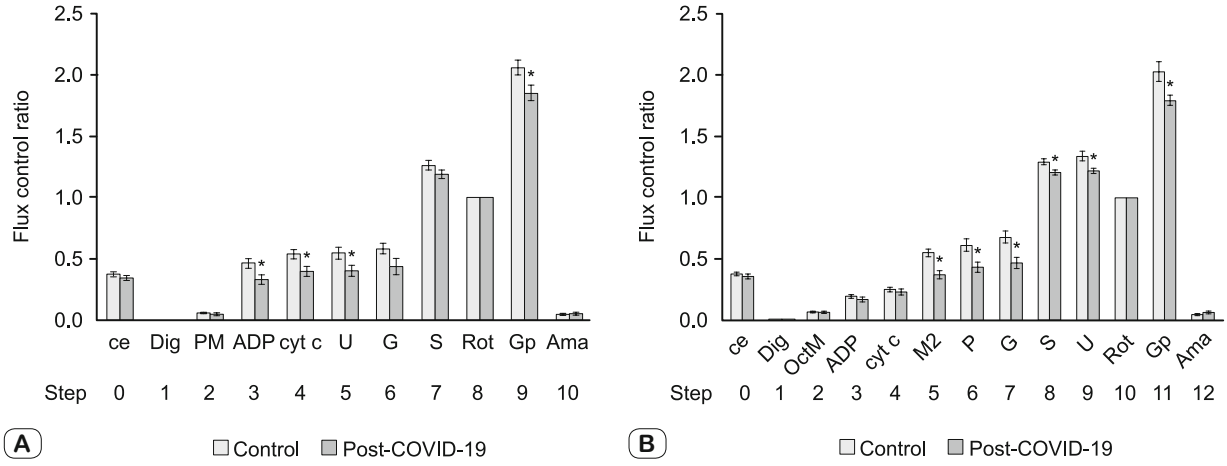

Fig. 3. Flux control ratios (FCR) – the parameters of mitochondrial respiration in human platelets normalized for CII-linked noncoupled respiration (Rot). A) FCR from SUIT protocol RP1, B) FCR from modified RP2. The names on x-axis represent steps in the SUIT protocol (see the methods section). The bars show the mean ± sem of mitochondrial respiration after titration step shown on x-axis, normalized for mitochondrial respiration after Rot. * p < 0.05, ** p < 0.01 – statistically significant difference vs control group.

The main symptoms at this stage were fatigue (7/10), cough (1/10), loss of smell (2/10), impaired breathing during exercise (2/10), loss of appetite accompanied with a significant weight loss (2/10) 7 and 10 kg. The control group consisted of 15 healthy individuals (6 men and 9 women), aged 38 to 67 years with the mean age of 51.3±2.3 years.

The study was carried out according to the principles expressed in the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of National Cancer Institute in Bratislava. Written informed consent form was obtained from each subject before enrolment in the study.

Blood count and biochemical parameters

In all the subjects, blood count and biochemical parameters, such as: blood lipid parameters, metabolites, minerals, and enzymes, were determined.

Coenzyme Q_{10} and oxidative stress

Coenzyme $Q_{10\text{-TOTAL}}$ (ubiquinol+ubiquinone) in whole blood, plasma and isolated platelets were determined using HPLC method with UV detection (26), modified by authors (27, 28). A parameter of oxidative stress – thiobarbituric acid reactive substances (TBARS) was determined by spectrophotometric method (29).

Platelets isolation

Platelets were isolated from the whole blood (30) as described previously (22) and counted on hematological analyzer Mindray BC-6200 (Mindray, China).

High-resolution respirometry

Mitochondrial respiration was determined with a high-resolution respirometry method (31, 32). For respirometric analysis, 200×10^6 platelets were used in a 2 mL chamber of an O2k-Respirometer (Oroboros Instruments, Austria). The respiration was measured in mitochondrial respiration medium MiR05 (31) with 20 mM creatine at 37 °C under continuous stirring at 750 rpm. Two different substrate-uncoupler-inhibitor (SUIT) protocols – the reference protocol 1 (RP1) and RP2 (33, 34) were applied with common cross-linked respiratory states, allowing for harmonization of both protocols (35).

Platelet mitochondrial respiration and oxidative phosphorylation (OXPHOS) by RP1

The protocol RP1 (33) described in detail previously (22) included the following titration steps: 1 – Digitonin (Dig, 0.20 µg 10^{-6} cells); 2 – pyruvate+malate (PM, 5 mM+2mM); 3 – adenosine diphosphate (ADP, 1 mM); 4 – cytochrome c (cyt *c*, 10 µM); 5 – uncoupler carbonyl cyanide p-trifluoro-methoxyphenyl hydrazone (FCCP) (U, 0.5 µM steps); 6 – glutamate (G, 10 mM); 7 – succinate (S, 10 mM); 8 – rotenone (Rot, 1 µM); 9 – glycerophosphate (Gp, 10 mM); 10 – antimycin A (Ama, 2.5 µM). The steps in the protocol serve as names on x-axis in the results Figures 2A and 3A.

Platelet mitochondrial respiration and OXPHOS by RP2

The modified protocol RP2 (34) included the following titration steps: 1 – digitonin (Dig, 0.20 µg·10^{-6} cells); 2 – octanoylcarnitine+malate (OctM, 0.5mM+0.1 mM); 3 – ADP (1 mM); 4 – cytochrome *c* (cyt *c*, 10 µM); 5 – malate (M2, 2 mM); 6 – pyruvate (P, 5 mM), 7 – glutamate (G, 10 mM); 8 – succinate (S, 10 mM); 9 – uncoupler FCCP (U, 0.5 µM steps); 10 – rotenone (Rot, 1 µM); 11 – glycerophosphate (Gp, 10 mM); 12 – antimycin A (Ama, 2.5 µM). The steps in the protocol serve as names on x-axis in the results Figures 2B and 3B.

The application of these two protocols allowed a comprehensive evaluation of mitochondrial pathways. The RP1 allowed a stepwise evaluation of Complex I (CI)-linked pathway (N-pathway) followed by the evaluation of CI&CII-linked pathway

(NS-pathway), Complex II (CII)-linked pathway (S-pathway) and SGp-pathway. The RP2 allowed the evaluation of fatty acid oxidation (FAO)-pathway (F-pathway) followed by addition of malate-anaplerotic pathways, N-pathway, S-pathway (together FNS-pathway). Next, S-pathway and SGp-pathway were evaluated. A schematic illustration of mitochondrial electron transfer system with dissected mitochondrial pathways is on Figure 1.

Data analysis

Unpaired Student´s t-test was applied to evaluate the difference between parameters of Post-COVID-19 and the control group. p-values <0.05 were considered statistically significant. The results are expressed as the mean±sem.

Results

Demographic and physical characteristics of groups

Demographic characteristics of the participants are shown in Table 1. In the Post-COVID-19 group, in total three patients had comorbidities and their adequate drug treatment. One patient had 3 comorbidities: Diabetes mellitus, hypertension and dyslipoproteinemia. Other 7 participants were healthy before COVID-19. The control group consisted of healthy volunteers without chronic diseases (Tab. 1).

Tab. 1. Demographic characteristics of the groups.

Characteristics	Control	Post-COVID-19
N (number)	15	10
Age	51.3±2.3	59.9±5.4
Sex(M/F)	6/9	3/7
BMI (kg/m^2)	25.2±0.9	27.2±1.4
Comorbidities	0/15	3/10
Diabetes mellitus	0	1
Hypertension	0	2
Heart disease	0	1
Dyslipoproteinemia	0	1
Drugs	0/15	3/10
Statins	0	0
Beta-blockers	0	1
ACE-inhibitors	0	2
Anticoagulants	0	2

BMI – body mass index

Blood count and biochemical parameters

The biochemical parameters and parameters of blood counts of both groups were within the control range. However, differences in several parameters between Post-COVID-19 and the control group were found. Albumin and total proteins were lower and the activity of gamma-glutamyltransferase (GMT) was higher in the Post-COVID-19 group (Tab. 2), indicating a reduced liver function. The parameters of red blood cells, MCV and MCH, were higher in the Post-COVID-19 group (Tab. 2), indicating a larger size of erythrocytes.

Platelet mitochondrial respiration and oxidative phosphorylation (OXPHOS)

The results of respirometric analysis of platelet bioenergetics by following the SUIT protocol RP1 are shown in Figure 2A. The protocol revealed a difference between the Post-COVID-19 and the control group in CI-linked respiration associated with adenosine triphosphate (ATP) production (OXPHOS) and noncoupled respiration. The CI-linked OXPHOS in the Post-COVID-19 group reached only 65.0 % of the control values (Step 3, p=0.027), and stayed lower (at 69.0 % of control values) also after addition of cytochrome *c* (Step 4, p=0.040). CI-linked noncoupled respiration (uncoupled from OXPHOS) reached 68 % and 65.3 % of control values (Steps 5–6, p=0.036 and p=0.038). These differences reflect deficit in CI-linked OXPHOS- and electron transfer (ET)-capacity in the Post-COVID-19 group. After addition of CII-linked substrate succinate, the respiration representing ET-capacity with CI-and CII-linked substrates did not differ between the groups (Step 7, S) suggesting that CI-deficit could be compensated by CII-linked substrate. The CII-linked ET-capacity (Step 8, Rot) was nearly the same in both groups, and the ET-capacity after addition of Gp was slightly lower (n.s.) in the Post-COVID-19 group (Step 9, Gp).

The data from modified protocol RP2 (Fig. 2B) showed that neither *Routine* respiration of intact cells (Step 0, ce), nor FAO (Step 2, 3, 4) were affected by SARS-CoV-2 infection, but deficit in mitochondrial respiration occurred, when malate-anaplerotic pathways were tested (Step 5, M2). Mitochondrial respiration after addition of 2 mM malate was reduced in the Post-COVID-19 group to 73.1 % of the control value (p=0.017). After addition of pyruvate (Step 6, P), the OXPHOS respiration stayed at 75.4 % of the control value (p=0.046), and after addition of glutamate (Step 7, G) on 73.6 % of control value (p=0.043). The deficit in FN-linked OXPHOS respiration was compensated by addition of succinate (Step 8, S). No difference between the groups was revealed in FNS-linked ET-capacity (Step 9, U), CII-linked ET-capacity (Step 10, Rot) and SGp-linked ET-capacity (Step 11, Gp).

As CII-linked ET-capacity did not differ between the groups in either of the SUIT protocols, this respiratory flux (the mitochondrial respiration after addition of rotenone) was used in both protocols for internal normalization of each measurement. These Flux control ratios (FCR) (35) confirmed already described deficit associated with CI-linked and malate-anaplerotic pathways in Post-COVID-19 group (Fig. 3A, B). In addition, the FCR in RP2 (Fig. 3B) showed a decreased FNS-linked OXPHOS- and ET-capacity (Step 8, S and 9, U) in Post-COVID-19 group by 7.5% and 12.2 % (p=0.021 and p=0.008) vs control group indicating that the deficit in electron transfer may not be fully compensated by addition of succinate. Importantly, the FCR revealed also a deficit in SGp-linked ET-capacity in both RP1 (–9.9 %, p=0.036) and RP2 (–11.4 %, p=0.026) in the Post-COVID-19 group (Fig. 3A, B) indicating a deficit in Gp-linked pathway. The FCR showed a difference in the respiratory pattern between Post-COVID-19 and the control group indicating that downregulation of several pathways of intermediary metabolism could be seen shortly after acute COVID-19.

Tab. 2. Biochemical and blood count parameters different between groups.

	control range	Control	Post-COVID-19	p
Metabolites				
Albumin (g/L)	32-48	46.79±0.67	42.92±1.74	0.023
Total proteins (g/L)	57-82	71.89±0.71	66.46±1.31	0.002
GMT (μkat/L)	0-1.22	0.38±0.06	0.75±0.018	0.032
Blood count				
MCV (fL)	80-100	87.14±0.65	91.94±1.81	0.051
MCH (pg)	28-34	29.95±0.28	31.20±0.70	0.074

GMT – gamma-glutamyltransferase, MCV – mean corpuscular volume, MCH – mean corpuscular hemoglobin

Tab. 3. Endogenous coenzyme $Q_{10\text{-TOTAL}}$ and TBARS.

	Control	Post-COVID-19	p	% of control
$CoQ_{10\text{-TOTAL}}$				
Platelets (pmol.10^{-9} cells)	84.1±5.3	58.9±3.60	0.002	70.0
Blood (μmol.L^{-1})	0.313±0.020	0.217±0.030	0.014	69.1
Plasma (μmol.L^{-1})	0.516±0.030	0.394±0.043	0.034	76.3
TBARS (μmol.L^{-1})	5.035±0.213	4.619±0.225	0.2	91.7

Coenzyme $Q_{10\text{-TOTAL}}$ and TBARS

Endogenous concentration of $CoQ_{10\text{-TOTAL}}$ (ubiquinone + ubiquinol) in whole blood and plasma of the Post-COVID-19 group was decreased to 69.1 % (p=0.014) and 76.3 % (p=0.034) of the control group values. Moreover, the decline of this important antioxidant concentration in platelets to 70.0 % of control reached a high statistical significance (p = 0.002). The concentration of TBARS in plasma was slightly (n.s.) lower in the Post-COVID-19 group (Tab. 3).

Discussion

COVID-19 complications include acute respiratory distress syndrome, thrombosis, cardiovascular diseases, overproduction of mitochondrial reactive oxygen radicals, inflammation, and induction of mitochondrial metabolism dysregulation.

ACE2 serve as receptors for SARS-CoV-2 entry into target organs such as the lungs, heart, renal system, and gastrointestinal tract (13). The binding of SARS-CoV-2 spike proteins to ACE2 initiates endocytosis of the virus. ACE2, which cleaves angiotensin II into angiotensin 1-7, regulates mitochondrial function. Decline in ACE2 function in aged individuals results in chronic metabolic disorders like diabetes or cancer and may make the host more vulnerable to SARS-CoV-2 infection, health complications and mortality (36). SARS-CoV-2 may manipulate mitochondrial function indirectly by ACE2 regulation, and after entering the host cell directly through open-reading frames proteins such as ORF-9b (36, 37). The ORF-9b protein encoded by SARS-CoV virus genome localizes to mitochondria of the host cell, causes mitochondrial elongation, and disrupts mitochondrial antiviral signalling protein (MAVS), an essential component of cellular antiviral defence system and antiviral innate immunity (38). ORF-9b protein manipulates host cell mitochondria and mitochondrial function (37). The mechanisms by which SARS-CoV-2 proteins enter mitochondria is not well understood (16).

The current study was undertaken to determine the effect of SARS-CoV-2 infection on mitochondrial function, CoQ_{10} concentration and parameters of oxidative stress in patients 4-7 weeks after overcoming acute COVID-19. Isolated platelets served as a source of human mitochondria. Our results indicate that mitochondrial function is modulated after SARS-CoV-2 infection. By using two different SUIT protocols we showed that CI-linked ADP-stimulated mitochondrial respiration, which is associated with ATP production, was reduced in platelets of Post-COVID-19 patients to 65.0 %, and CI-linked ET-capacity was reduced to 65.3 % of control group values. The Complex II-linked respiration was not affected (Fig. 2A, B). The deficit in CI-linked OXPHOS could be caused by a decreased activity of Complex I due to its impairment, by decreased activities of dehydrogenases upstream of CI, or by impaired electron transfer from CI through CoQ to Complex III (CIII). The highly reduced concentration of CoQ_{10} in platelets in the Post-COVID-19 group (to 70.0 % of control group value, p = 0.002) indicates that its deficit could be limiting for the electron transfer from CI to CIII. The organization of the respiratory complexes into super complexes with different interactions with membrane lipid environment and CoQ pool (39, 40) could explain that the deficit in electron transfer was not seen for CII-pathway.

In addition, our measurements showed a high activity of malate-anaplerotic pathway in platelets. This pathway includes malic enzyme (ME) catalysing oxidative decarboxylation of L-malate to pyruvate that re-enters the tricarboxylic acid (TCA) cycle. In the presence of ME, malate alone can support CI-linked respiration (35). It is not clear from our experiment whether also ME was downregulated in Post-COVID-19 group, but it is interesting to mention that downregulation of its mitochondrial form (ME2) leads to a strong induction of senescence (41).

The relative contribution of Gp-linked pathway into respiration was lower in the Post-COVID-19 group (Fig. 3A, B). Mitochondrial glycerophosphate dehydrogenase (mGpDH) is the key enzyme connecting OXPHOS, glycolysis and fatty acids metabolism. mGpDH catalyses the rate limiting step of glycerophosphate shuttle involved in oxidation of cytosolic NADH, converting glycerol-3-phosphate to dihydroxyacetone phosphate with two electrons transferred to Q-cycle (40). mGpDH is a site of considerably high reactive oxygen species (ROS) production (42). The relative deficit in mGpDH activity in patients Post-COVID-19 indicate a switch in the intermediary metabolism.

SARS-CoV-2 virus utilizes glucose as the main substrate for energy production and its own replication (24). SARS-CoV-2 has been shown to impair mitochondrial metabolism, increase glycolytic metabolism and TCA intermediates concentration in endothelial cells to ensure a successful virus replication (24, 43). In PBMCs of the patients with COVID-19, a decreased mitochondrial membrane potential, mitochondrial dysfunction, and an increased rate of glycolysis has been shown (24). The results of our

study are consistent with these findings and indicate that deficit of CoQ_{10} in the patients after COVID-19 may contribute to the reduced ATP production by OXPHOS and to reprogramming of OXPHOS to glycolysis.

Endogenous CoQ_{10} level was decreased in whole blood to 69.1 % (p=0.014) and in plasma to 76.3 % (p=0.034) of the control group value in the patients after COVID-19. Mechanisms by which the deficit of CoQ_{10} is caused by SARS-CoV-2 viral infection are not fully known. One possibility could be mutations of one or more of the genes responsible for CoQ_{10} biosynthesis, resulting in a damage to mitochondrial bioenergetics (25). Reduced endogenous CoQ_{10} biosynthesis can contribute to the reduction of electron transport in mitochondrial respiratory system and to the preferential use of glycolysis rather than OXPHOS for ATP production. We propose that a reduced concentration of endogenous CoQ_{10} may partially block electron transfer in the respiratory chain resulting in reduced ATP production in the Post-COVID-19 patients.

Viral infections induce inflammation, production of ROS, and increased ROS may contribute to the alterations in mitochondrial function and immune response (37, 44, 15). In our patients in the Post-COVID-19 group, the parameter of oxidative stress – TBARS concentration, was within normal range and slightly lower than in the control group. We assume that the supplementary therapy with high daily doses of vitamin C, vitamin D_3, Zn, as a strategy for COVID-19 treatment, reduced oxidative stress in the Post-COVID-19 group.

Preventive treatments based on therapies improving mitochondrial turnover, dynamics and activity would be essential to protect against COVID-19 severity (45). Mitochondrial health, induced by a healthy lifestyle, could be a key factor in resisting the virus and for those people, who are perhaps not in optimal health, treatments that could support mitochondrial function might be pivotal for their long-term recovery (37).

We assume that impaired mitochondrial function and CoQ deficiency persisting after SARS-CoV-2 infection contribute to development of health complications of Post-COVID-19 Syndrome. CoQ is an essential component of mitochondrial respiratory system necessary for electron transfer in the process of ATP production and an important lipophilic antioxidant. Supplementation with CoQ_{10} has been shown to improve mitochondrial respiration also when Complex I was impaired, and CoQ deficiency was not demonstrated (46). We propose that supplementation with CoQ_{10} may be effective for boosting mitochondrial function and for faster recovery of the patients after COVID-19.

Conclusion and perspective

Our results showed that platelet mitochondrial respiration, oxidative phosphorylation, and endogenous CoQ_{10} concentration were reduced by SARS-CoV-2 virus in patients shortly after acute COVID-19. We assume that a decreased mitochondrial function may be involved in the pathogenesis of Post-COVID-19 Syndrome. Several strategies to target mitochondrial bioenergetics and antioxidant defence (as pharmacological interventions, spa rehabilitation, moderate exercise, and supplementary therapy with CoQ_{10}) are important for improving mitochondrial health and for acceleration of the recovery in patients after COVID-19. Our study showed that platelet mitochondrial function and CoQ_{10} content may be useful biomarkers for mitochondrial health after SARS-CoV-2 virus infections.

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