# SUMMARY

## Selected Indicators of Health Status and Quality of Life Monitored During Different Rehabilitation Procedures in Post-Sepsis Patients

### Introduction

In this project the significant problem is adressed of sepsis sequelae resulting in frequent hospital readmissions and higher mortality rate during the post-discharge period. However, neither specific diagnostic methods nor standards for rehabilitation of sepsis survivors have been yet introduced. Decades of failed randomized controlled trials involving sepsis patients has strongly suggested the need for a change in paradigm. Therefore, this study was designed as a prospective, interventional, controlled, pragmatic, patient-centred trial based on the principles of personalized medicine.

The aim of this study was to evaluate the effectiveness of two different multiparametermonitored rehabilitation treatments in order to improve health status and quality of life among sepsis survivors.

#### Methods

Thirty, post-sepsis patients after hospital discharge were individually assigned to a control group (group K, n = 10, without rehabilitation) and 2 groups with 3-month diagnostically monitored rehabilitation programs based either on recumbent cycloergometer training supplemented by individual specialistic exercises (group C, n = 10) or on intermittent hyperbaric oxygen therapy – iHBOT (group H, n = 10).

Due to the significantly reduced serum level of vitamin D3 at the time of qualification for the trial, according to doctors orders, all patients were supplemented with 2000 IU per day for 3 months and changes in its concentration were diagnostically monitored.

In all of the patients a wide range of physiological (spirometry, ECG/cycloergometer exercise test), haematological (microscopy) and biochemical (blood tests) parameters were assessed at hospital discharge and during the subsequent 3 months to monitor changes of their physical capacity, immunity and degree of post-sepsis organ damage/recovery. For quality of life monitoring a novel tool – "Life After Sepsis Survey" – was applied.

#### Results

There were no statistically significant variances in differential leukocyte count. However, the white blood cell (WBC) count in group H and the number of immature granulocytes (IGs) in groups C and H, were normalized. Whereas, in group K, an increase regarding the number of IGs above the norm after 3 months since the end of hospitalization was observed. Despite the lack of significant changes in the WBC count, blood smear analysis showed atypical and apoptotic neutrophils, eosinophils and atypical lymphocytes in all of the patients. Additionally, statistically significant decreases in vacuolated monocyte count after 2 months of iHBOT was observed in group H. Live blood cell analysis did not indicate any disorders of neutrophil spontaneous activity in groups C or H. However, in one of the patients from group K and shortly before the sepsis relapse, a significant decrease was demonstrated in spontaneous neutrophil crawling due to excessive platelet activation associated with large platelet-leukocyte aggregates and fibrous deposits.

In all of the analyzed groups (C, H, K), an increasing trend in red blood cell (RBC) count, hemoglobin (Hb) and hematocrit (Hct) levels was observed. However, the largest statistically significant increases in RBC count (+15.1%), Hb (18.3%) and Hct (+15.5%) levels were indicated in the group of patients who underwent iHBOT.

There were no statistically significant differences in oxidative stress indices, such as total oxidative status (TOS), total antioxidative status (TAS) and nitric oxide level (NO) in all analyzed groups (C, H, K). However, a statistically significant downward trend was noted with regard to glutathione level (GSH) in group K. Furthermore, in the group of patients undergoing iHBOT, an initial increase (+33.6%) of myeloperoxidase (MPO) concentration was observed, which was then followed by a statistically significant decrease (-39.7%) in its level related to the initiation and cessation of effective wound healing processes. In all of the analysed groups (C, H, K), a decreasing trend was also observed for the CRP value, but without its statistically significant changes over time.

After 3 months of specialized rehabilitation, a statistically significant increase in exercise duration [min] (+144.9 % in group C and +81.7 % in group H) and total work amount [kJ] (+303.9% in group C and +162% in group H) during the ECG cycloergometer exercise test were indicated. Additionally, a statistically significant increase in forced expiratory volume per 1 second – FEV 1 [l] (+19.3%), FEV1 [%] (+20.6%), forced vital capacity – FVC [l] (+20.5%), FVC [%] (+20.9%) in group C and peak expiratory flow – PEF [%] (+21.1% in group C and + 25.2% in group H) was noted. There were no statistically significant differences in FEV1/FVC ratio [%], time to peak expiratory flow (TPEF [sec]) or forced expiratory time (FET [sec]). There were no statistically significant changes in spirometry indices for group K.

Additionally, in patients from groups C and H, after 3 months of the individual rehabilitation program, statistically significant improvement in the quality of life of sepsis survivors from group C and H concerning the majority of assessed physiologic, physical and psychological function indices, was observed. The quality of life of patients from group K did not change significantly after 3 months of observation.

#### Conclusions

Critical analysis of past trials prompted the implementation of multiple improvements in tools and procedures, which contributed to the development of effective rehabilitation therapy addressing not only post-sepsis syndrome, but also the immune function of sepsis survivors. Both proposed forms of rehabilitation (personalized aerobic and functional training as well as intermittent hyperbaric oxygen therapy) contributed to significant improvement in selected health status indicators and quality of life. Importantly, iHBOT leads to significant increases in RBC count, Hb and Hct levels. Therefore, this form of rehabilitation should be recommended especially for patients with unhealed or non-healing wounds, for whom these indicators are still decreased or difficult to normalize.