ORIGINAL ARTICLES
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UDC: 616.98:617-089.168-085.8-036.82
DOI: https://doi.org/10.2298/VSP231228033S

Early rehabilitation challenges of surgical patients with COVID-19 infection – a single-arm study

Izazovi u ranoj rehabilitaciji hirurških bolesnika sa COVID-19 infekcijom – *single-arm* studija

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Abstract

Background/Aim. A very limited amount of data regarding the rehabilitation outcome of surgical patients with COVID-19 is available in the current literature. The aim of this study was to point out the characteristics of early rehabilitation of these patients and determine the predictors of rehabilitation outcomes. **Methods**. The study was designed as a prospective clinical trial. It included patients who had surgical treatment from April 1, 2022, to March 31, 2023, at the University Clinical Center of Vojvodina, Serbia and either had positive results for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) preoperatively or developed coronavirus disease 2019 (COVID-19) within 72 hrs after surgery. The rehabilitation program was planned for each patient according to the type of surgical treatment, age, clinical presentation and severity of the COVID-19, length of immobilization, and comorbidities. Rehabilitation treatment (RT) started with a minimum of one 30-minute daily session, up to three 30-minute sessions daily. Patients were assessed at the beginning of RT and discharge. Outcomes were assessed with the Modified Borg Scale (MBS) for dyspnoea, Barthel index (BI) for activities of daily living, Six-Minute Walk Test (6MWT) for exercise tolerance, and Timed up and Go (TUG) test for balance and lower limb mobility. **Results.** A total of 81 patients were included in the study. RT was successful for 42 patients (24 female and 18 male) with an average age of 62.10 ± 20.07 years. These patients exhibited significant functional improvement, which was measured by all tests that assessed rehabilitation outcome at discharge: BI ($p < 0.001$), MBS ($p < 0.001$), 6MWT ($p < 0.001$), and TUG test ($p < 0.001$). The remaining 31 patients had unsuccessful RT. The binary logistic regression analysis has shown that age ($p = 0.009$), cardiovascular disease ($p = 0.017$), and malignancy ($p = 0.022$) were significant predictors of rehabilitation outcome. **Conclusion**. Results of the present study implicate that individually tailored RT during the acute phase of COVID-19 in surgical patients is very challenging. Advanced age, cardiovascular disease, and malignancy are predictors of unfavorable outcomes, and careful consideration is needed when planning the treatment for these patients.

Key words:
covid-19; general surgery; rehabilitation; treatment outcome.

Apstrakt

Uvod/Cilj. U aktuelnoj literaturi dostupno je veoma malo podataka o ishodu rehabilitacije hirurških bolesnika obolelih od COVID-19. Cilj istraživanja bio je da ukaže na karakteristike rane rehabilitacije ovih bolesnika i da se utvrde prediktori ishoda rehabilitacije. **Metode.** Studija je bila osmišljena kao prospektivno kliničko ispitivanje i obuhvatila je bolesnike koji su bili hirurški lečeni od 1. aprila 2022. do 31. marta 2023. godine u Univerzitetskom kliničkom centru Vojvodine, Srbija, a koji su bili pozitivni na *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) preoperativno ili su razvili koronavirusnu bolest 2019 (COVID-19) u roku od 72 sata nakon operativnog tretmana. Program rehabilitacije planiran je za svakog bolesnika pojedinačno, shodno vrsti hirurškog lečenja, uzrastu, kliničkoj slici i težini COVID-19, dužini imobilizacije i komorbiditetima. Tretman rehabilitacije (TR) je počinjao sa najmanje jednom sesijom od 30 minuta dnevno, do tri dnevne sesije od po 30 minuta. Bolesnici su procenjivani na početku TR i pri otpustu iz bolnice. Za procenu ishoda korišćene su modifikovana Borgova skala

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(MBS) za dispneju, Bartelov indeks (BI) za aktivnosti svakodnevnog života, Šestominutni test hoda (*Six-Minute Walk Test*-6MWT) za toleranciju vežbanja i test Ustani i kreni (*Timed up and Go*-TUG), za ravnotežu i pokretljivost donjih ekstremiteta. **Rezultati.** U studiju je bilo uključeno ukupno 81 bolesnika. TR je bio uspešan kod 42 bolesnika (24 žene i 18 muškaraca) prosečne starosti 62,10 ± 20,07 godina. Ovi bolesnici su pokazali značajno funkcionalno poboljšanje koje je izmereno svim testovima za procenu ishoda rehabilitacije, pri otpustu: BI (p < 0,001), MBS (p < 0,001), 6MWT (p < 0,001) i test TUG (p < 0,001). Preostalih 31 bolesnika nije imalo uspešan TR. Binarna logistička regresiona analiza pokazala je da su starost (p = 0,009), kardiovaskularne bolesti (p = 0,017) i malignitet (p = 0,022) značajni prediktori ishoda rehabilitacije. **Zaključak.** Rezultati ove studije ukazuju da je individualno prilagođen TR tokom akutne faze COVID-19 kod hirurških bolesnika veoma izazovan. Starije životno doba, kardiovaskularne bolesti i malignitet su prediktori nepovoljnog ishoda i potrebno je pažljivo razmatranje prilikom planiranja lečenja ovih bolesnika.

Ključne reči:
covid-19; hirurgija, opšta; rehabilitacija; lečenje, ishod.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) pandemic has placed healthcare systems throughout the world under considerable strain, with a substantial effect on patients who require surgical care. Furthermore, surgical treatment of patients diagnosed with COVID-19 increases the risk of perioperative morbidity and mortality. Doglietto et al. [1] in their study demonstrated that the 30-day mortality risk for patients with COVID-19 undergoing surgery, as well as the odds for pulmonary and thrombotic complications, were significantly higher compared with patients without COVID-19. So far, very limited data are available in the current literature regarding the outcome of patients who undergo surgical intervention and either have positive results for COVID-19 or develop positive results soon after surgery.

Early respiratory rehabilitation is of vital value for hospitalized COVID-19 patients recovering from surgery to improve dyspnoea, prevent complications, decrease morbidity, reduce anxiety and depression, and prevent muscle weakness and physical performance impairment [2]. Rehabilitation treatment (RT) needs to be individually tailored for each patient according to the type of surgery, age, comorbidities, and respiratory status. Evaluation and monitoring of the patient need to be performed at all times during the RT. However, early respiratory rehabilitation is often delayed in critically ill patients while their condition is unstable and in progressive decline [3]. Furthermore, respiratory manifestations, complications of intensive care and hospitalization, and neurological sequelae necessitate the need for early RT in surgical COVID-19 patients [4].

The aim of this study was to point out the challenges of early rehabilitation of surgical patients with COVID-19, to determine the outcome of the treatment and functional status (FS), and to ascertain the predictors of rehabilitation outcome. That would enable us to gain insight into which patients most benefit from the RT, when the best moment is to begin, how to conduct the treatment, and for how long.

Methods

Patients who received surgical treatment from April 1, 2022, to March 31, 2023, at the University Clinical Center of Vojvodina, Serbia, and either had positive results for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) preoperatively or developed coronavirus disease 2019 (COVID-19) within 72 hrs after surgery were included in the study. Patients received early RT postoperatively, after team evaluation by a surgeon, physiatrist, and specialist of internal medicine. The research was conducted as a prospective study; all patients gave written consent at the beginning of the RT, and the study was approved by the Ethics Committee of the University Clinical Center of Vojvodina, in Novi Sad, Serbia (No. 600-66, from March 25, 2022).

Inclusion criteria were surgical treatment, positive nasopharyngeal swab test for SARS-CoV-2 obtained by real-time reverse transcription polymerase chain reaction (RT-PCR) method preoperatively or within 72 hrs after surgery, ability to participate in early RT defined by oxygen saturation (SpO_2) over 94% on admission, body temperature under 37.5°C, and clinical stability defined as the ability to perform active bedside mobilization with SpO_2 > 92%. Patients who underwent minor procedures such as lumbar puncture, tracheostomy, minor gynecological interventions, and suturing of superficial wounds were excluded from the study. Other exclusion criteria were age below 18, SARS-CoV-2-positive surgical patients who were treated non-operatively, patients who had lethal outcomes, patients who were unable to tolerate RT due to clinical instability, reduction of SpO_2 lower than 94% on admission and moderate and severe heart failure (New York Heart Association classes III and IV), and impaired cognitive function.

Data collection

The following data were recorded for all patients: gender, age, medical comorbidities, pathology and type of surgery, length of hospital stay, the beginning of RT, and the duration of RT. For all patients, evidence of SARS-CoV-2 infection was recorded, as well as chest radiograph or computerized tomography (CT) findings. The need for oxygen therapy and type of oxygen therapy (nasal cannula or oxygen mask, continuous positive airway pressure, high flow nasal cannula, or mechanical ventilation) was also noted for each patient.

Rehabilitation treatment

The rehabilitation program was planned for each patient individually, according to the type of surgical treatment, age, clinical presentation and severity of the disease, length of immobilization, and comorbidities. Treatment started from a minimum of one 30-minute daily session and up to three 30-minute daily sessions. RT began with patient positioning, breathing exercises, and postural drainage. It was followed by a range of motion exercises to preserve the mobility of the upper and lower extremities adjusted to the individual needs of the patient. At the beginning of each session, the patient was positioned either in a lying supine position with legs bent at the knees or in a semi-sitting or sitting position, depending on type of the surgery and respiratory status. Patients were instructed to relax their neck and shoulder muscles. Training in diaphragmatic breathing was used to improve breathing control, reduce the energy needed to breathe, and enhance lung ventilation. The patients were instructed to do deep inspiration through the nose, followed by a passive prolonged exhale through the half-open mouth. Expiration was prolonged, so it was two to three times longer than the inspiration, leading to a decrease in respiratory rate. Forced expiration techniques were included for patients to help eliminate secretions from airways. Breathing exercises were followed by exercises for peripheral circulation and range of motion exercises for upper and lower extremities lasting for 10–20 minutes. Depending on the clinical stability of the patient and type of surgery, mobilization exercises were applied, as well as walking with or without aid and balance exercises. Subjects were assessed every day so that the type and intensity of the treatment could be adjusted to the patient's condition. SpO_2, respiratory rate, heart rate, and blood pressure were measured before and after each session. Rehabilitation sessions would be ended if patients complained of any chest discomfort, palpitations or dyspnea scored as 4 or above on a Modified 10-point Borg Scale [5, 6] (MBS), shortness of breath, blurred vision, or dizziness.

Measurement of outcome

At the beginning of the RT and before discharge from the hospital, patients underwent a functional and physical evaluation by a specialist in physical and rehabilitation medicine. Functional assessment was performed by measurement of the following outcome parameters, along with all the safety procedures and appropriate personal protective equipment: MBS for dyspnea assessment was used to determine the patient's subjective exertion and provide feedback for exercise intensity. It consists of ten numerical values ranging from 0 to 10 (0 – no breathlessness, 10 – maximum breathlessness) [5, 6]. Independence in activities of daily living (ADL) was measured by the Barthel index (BI). The total BI score ranges from 0 (which represents the maximum level of dependency) to 100 (indicating complete autonomy). A score lower than 70 is considered to correspond to severe disability [7].

Six-Minute Walk Test (6MWT) was used to assess exercise tolerance as well as cardiovascular and respiratory function [8]. The patients were instructed to walk on a flat surface for six minutes and the walking distance was recorded. Patients who were unable to perform the test were given a value of 0 for analysis. Timed up and Go test (TUG) was administered to evaluate balance and lower limb mobility [9].

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (IBM, USA). Continuous variables were reported as mean ± standard deviation, and categorical variables were presented as frequencies and percentages. Comparisons between baseline and discharge values of numerical variables were performed using a *t*-test for paired samples or a Wilcoxon signed-rank test where appropriate. Differences in categorical variables among the two groups were determined with the Chi-square (χ^2) test. An independent sample *t*-test or Mann-Whitney *U* test was used for comparing continuous variables between the two groups. Binary logistic regression was used to assess the predictive significance of various factors/parameters for the success of RT. All *p*-values < 0.05 were considered statistically significant.

Results

The study flow chart is shown in Figure 1. Out of 81 patients who were assessed for eligibility, 42 completed the rehabilitation program with successful outcomes. Eight patients refused to participate in the study. The remaining 31 patients had unsuccessful rehabilitation outcomes: 5 patients

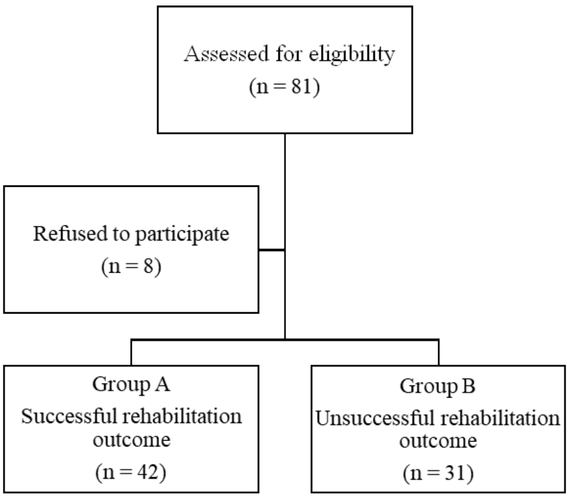

Fig. 1 – The flow chart of the study.

died, 12 patients had medical complications that prevented further RT, and 14 patients were unable to participate in the RT due to worsening of their clinical status and inability to tolerate physical exertion. Patients were divided into two groups according to the rehabilitation outcome: group A – successful rehabilitation and group B – unsuccessful rehabilitation. Group A included 42 patients, 24 (57.1%) women and 18 (42.9%) men, with an average age of 62.10 ± 20.07 years. Patients in group B were significantly older, with a mean age of 75.87 ± 6.40 years. No significant difference according to gender was found between the two groups.

The most common comorbidities in group A were hypertension (54.76%), cardiovascular diseases (16.67%), and diabetes (11.90%). There were significant differences regarding comorbidities between the groups. Patients in group B had a higher incidence of hypertension, cardiovascular disease, diabetes, and comorbidities in general. Chest radiographs and CT findings imply that bilateral and multiple lobe lesions were seen in most surgical patients with COVID-19. No significant differences were found between the two groups concerning radiological characteristics. In group A postoperatively, 10 (23.80%) patients required invasive mechanical ventilation (IMV), 5 (11.90%) received high-flow oxygen or non-invasive ventilation (NIV), and 28 (66.67%) needed oxygen support *via* an oxygen mask or nasal cannula. In group B, a significantly higher number of patients required oxygen support *via* NIV or high-flow nasal cannula, and 25 (80.65%) and 20 (64.52%) patients needed IMV. The demographics and clinical characteristics of the patients are shown in Table 1.

Most patients (16; 38.10%) in group A underwent abdominal surgery procedures. In comparison, 9 (21.43%) patients had orthopedic interventions, 7 (16.67%) had vascular surgery treatment, 6 (14.29%) had neurosurgical procedures, 2 (4.76%) had gynecological interventions, 1 (2.38%) had a urological procedure, and 1 (2.38%) patient had thoracic surgery. In group B, the most common interventions were orthopedic in 8 (25.81%) patients, while 7 (22.58%) patients had abdominal surgery procedures, 5 (16.13%) had vascular procedures, another 5 (16.13%) had neurosurgical interventions, 2 (6.45%) had urological procedures, another 2 (6.45%) had thoracic surgery, and 2 (6.45%) patients had cardiosurgical interventions. Types of surgery and underlying pathologies are presented in Table 2. One patient in group A had two types of operation: endovascular coiling and evacuation of intracranial hemorrhage. No significant differences were found between the groups regarding underlying pathology and type of intervention.

The mean length of hospital stay for the patients in group A was 21.74 ± 16.02 days, and the mean duration of RT was 13.67 ± 11.64 days. In group B, patients had longer hospitalization, with a mean value of 29.13 ± 13.46 days; rehabilitation onset was delayed, with a mean onset of 11.77 ± 6.66 days; the duration of RT was shorter, with a mean dura-

Table 1

Demographic and clinical characteristics of the patients

Variable	Group A (n = 42)	Group B (n = 31)	Statistics
Age, years	62.10 ± 20.07	75.87 ± 6.40	t = -3.680; p = 0.000
Gender			
female	18 (42.86)	13 (41.94)	χ^2 = 0.006; p = 0.937
male	24 (57.14)	18 (58.06)	
Comorbidity			
hypertension	23 (54.76)	24 (77.42)	χ^2 = 3.993; p = 0.046
cardiovascular disease	7 (16.67)	15 (48.39)	χ^2 = 8.524; p = 0.004
diabetes	5 (11.90)	11 (35.48)	χ^2 = 5.794; p = 0.016
cerebrovascular disease	4 (9.52)	7 (22.58)	χ^2 = 2.376; p = 0.123
malignancy	3 (7.14)	7 (22.58)	χ^2 = 3.596; p = 0.058
COPD	2 (4.76)	5 (16.13)	χ^2 = 2.658; p = 0.103
chronic kidney disease	1 (2.38)	4 (12.90)	χ^2 = 3.095; p = 0.079
No comorbidity	11 (26.19)	0 (0.00)	χ^2 = 9.560; p = 0.002
Radiological characteristics			
unilateral pneumonia	3 (7.14)	5 (16.13)	χ^2 = 1.476; p = 0.224
bilateral pneumonia	26 (61.90)	18 (58.06)	χ^2 = 0.110; p = 0.740
single lung lobe	4 (9.52)	1 (3.23)	χ^2 = 1.109; p = 0.292
multiple lung lobes	28 (66.67)	14 (45.16)	χ^2 = 3.376; p = 0.066
ground glass opacity	18 (42.86)	10 (32.26)	χ^2 = 0.847; p = 0.357
patchy shadows	7 (16.67)	9 (29.03)	χ^2 = 1.594; p = 0.207
normal radiological findings	13 (30.95)	8 (25.81)	χ^2 = 0.230; p = 0.631
Postoperative oxygen support			
nasal cannula or oxygen mask	28 (66.67)	28 (90.32)	χ^2 = 5.587; p = 0.018
duration, days	10.11 ± 8.55	13.39 ± 8.26	U = 278.5; p = 0.062
NIV or high-flow nasal cannula	5 (11.90)	25 (80.65)	χ^2 = 34.815; p = 0.000
duration, days	7.60 ± 2.88	7.76 ± 3.05	U = 47.5; p = 0.019
IMV	10 (23.80)	20 (64.52)	χ^2 = 12.209; p = 0.000
duration, days	4.10 ± 5.38	5.55 ± 3.38	U = 47.50; p = 0.019

COPD – chronic obstructive pulmonary disease; NIV – non-invasive ventilation; IMV – invasive mechanical ventilation; *U* – Mann-Whitney *U* test; *t* – Student's t-test; χ^2 – Chi-square test.
Data are presented as numbers (percentages) or mean ± standard deviation.

Table 2

Descriptive statistics of preoperative features and type of operation

Variable	Group A (n = 42)	Group B (n = 31)	Statistics
Pathology			
acute appendicitis	9 (21.43)	0 (0.00)	
femoral fracture	6 (14.29)	6 (19.35)	
ischemia of the lower limb	3 (7.14)	2 (6.45)	
acute cholecystitis	3 (7.14)	1 (3.23)	
gastric cancer	2 (4.76)	1 (3.23)	
subdural hematoma	2 (4.76)	2 (6.45)	
ruptured abdominal aortic aneurysm	2 (4.76)	1 (3.23)	
humeral fracture	2 (4.76)	1 (3.23)	
lower limb gangrene	2 (4.76)	2 (6.45)	
ruptured cerebral aneurysm	2 (4.76)	1 (3.23)	
uterine myoma	1 (2.38)	0 (0.00)	
gallbladder cancer	1 (2.38)	1 (3.23)	$\chi^2 = 22.725$
IMSCT	1 (2.38)	0 (0.00)	$p = 0.477$
endometrial carcinoma	1 (2.38)	0 (0.00)	
brain tumor	1 (2.38)	2 (6.45)	
bladder cancer	1 (2.38)	0 (0.00)	
intestinal occlusion	1 (2.38)	1 (3.23)	
tibia fracture	1 (2.38)	1 (3.23)	
lung cancer	1 (2.38)	1 (3.23)	
colon cancer	0 (0.00)	2 (6.45)	
rectal cancer	0 (0.00)	1 (3.23)	
breast cancer	0 (0.00)	1 (3.23)	
myocardial infarction	0 (0.00)	2 (6.45)	
prostate cancer	0 (0.00)	2 (6.45)	
Surgery procedure/intervention name *			
laparoscopic appendectomy	9 (21.43)	0 (0.00)	
femur fixation with a nail	4 (9.52)	2 (6.45)	
lower limb amputation	5 (11.90)	4 (12.9)	
hip hemiarthroplasty	2 (4.76)	4 (12.9)	
laparoscopic cholecystectomy	2 (4.76)	0 (0.00)	
open cholecystectomy	2 (4.76)	2 (6.45)	
subtotal gastrectomy	2 (4.76)	1 (3.23)	
evacuation of ICH	3 (7.14)	3 (9.68)	
aortic replacement	2 (4.76)	1 (3.23)	$\chi^2 = 25.704$
humerus fixation	2 (4.76)	1 (3.23)	$p = 0.315$
endovascular coiling	2 (4.76)	0 (0.00)	
total hysterectomy	2 (4.76)	0 (0.00)	
IMSCT resection	1 (2.38)	0 (0.00)	
craniotomy and tumor resection	1 (2.38)	2 (6.45)	
cystectomy	1 (2.38)	0 (0.00)	
adhesiolysis	1 (2.38)	1 (3.23)	
tibia fixation	1 (2.38)	1 (3.23)	
lobectomy	1 (2.38)	1 (3.23)	
open hemicolectomy	0 (0.00)	2 (6.45)	
hartmann procedure	0 (0.00)	1 (3.23)	
radical prostatectomy	0 (0.00)	2 (6.45)	
radical unilateral mastectomy	0 (0.00)	1 (3.23)	
CABG surgery	0 (0.00)	2 (6.45)	
Type of surgery procedure/intervention			
abdominal surgery	16 (38.10)	7 (22.58)	
vascular surgery	7 (16.67)	5 (16.13)	
neurosurgical procedures	6 (14.29)	5 (16.13)	
gynecological interventions	2 (4.76)	0 (0.00)	$\chi^2 = 7.177$
orthopedic	9 (21.43)	8 (25.81)	$p = 0.411$
urological procedures	1 (2.38)	2 (6.45)	
thoracic surgery	1 (2.38)	2 (6.45)	
cardiosurgical interventions	0 (0.00)	2 (6.45)	

IMSCT – intramedullary spinal cord tumor; ICH – intracranial hemorrhage; CABG – coronary artery bypass graft; χ^2 – Chi-square test. Data are presented as numbers (percentages).

***one patient in group A had two types of operation: endovascular coiling and evacuation of ICH.**

tion of 6.77 ± 4.71 days. Data regarding the duration of treatment and discharge destination are shown in Table 3. The length of hospital stay is shown in Figures 2 and 3, and the duration of RT is shown in Figures 4 and 5.

The physical condition of our patients at the beginning of RT was severe, judging by the baseline values of the assessed outcome parameters. The baseline value of BI in group A was 35.60 ± 18.88, which indicates the patients' severe disability in all areas of ADL. Rehabilitation led to an increase in BI at discharge 76.09 ± 21.12, with most patients exhibiting only mild or moderate disability in ADL. In group B, the baseline value of BI was significantly lower (26.29 ± 13.16, $p = 0.016$), which indicates an even more pronounced disability. The comparison of the values of outcome parameters at the beginning of RT between groups is shown in Table 3. Furthermore, a comparison between baseline values of outcome

Table 3

Clinical characteristics related to rehabilitation

Parameter	Group A (n = 42)	Group B (n = 31)	Statistics
Length of hospital stay, days			
min–max	4.0–74.0	7.0–68.0	t = -2.082
median	15.00	29.00	p = 0.041
mean ± SD	21.74 ± 16.02	29.13 ± 13.46	
Onset of rehabilitation, days			
min–max	2.0–25.0	3.0–27.0	
median	6.00	10.00	t = -2.716
mean ± SD	7.93 ± 5.43	11.77 ± 6.66	p = 0.008
Duration of rehabilitation, days			
min–max	2.0–51.0	2.0–21.0	U = 358.0
median	10.00	6.00	p = 0.001
mean ± SD	13.67 ± 11.64	6.77 ± 4.71	
Discharge destination, n (%)			
home	30 (71.43)	14 (45.16)	
other healthcare facility	12 (28.57)	12 (38.71)	χ^2 = 9.373
death	0 (0.00)	5 (16.13)	p = 0.009
Outcome test results at the beginning of rehabilitation treatment, mean ± SD			
MBS (0–10)	2.76 ± 0.43	2.90 ± 0.30	U = 559.0; p = 0.121
BI (0–100)	35.60 ± 18.88	26.29 ± 13.16	t = 2.480; p = 0.016
6MWT (m)	210.62 ± 144.02	29.52 ± 45.07	t = 7.657; p = 0.000

MBS – Modified Borg Scale; BI – Barthel Index; 6MWT – Six-Minute Walk Test; SD – standard deviation; *U* – Mann-Whitney *U* test; t – Student's *t*-test; χ^2 – Chi-square test.

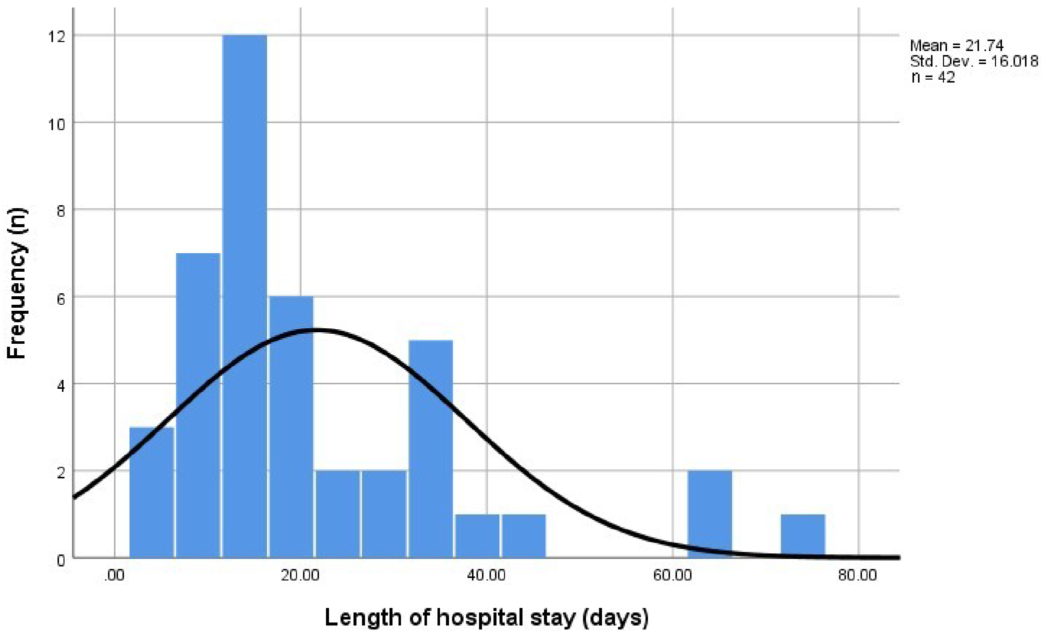

Fig. 2 – Length of hospital stay for group A (successful rehabilitation outcome).
n – number.

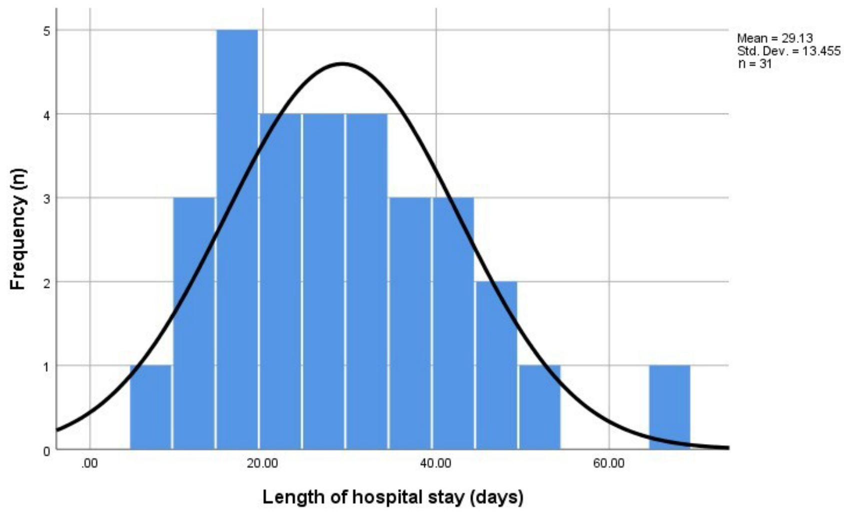

Fig. 3 – Length of hospital stay for group B (unsuccessful rehabilitation outcome). n – number.

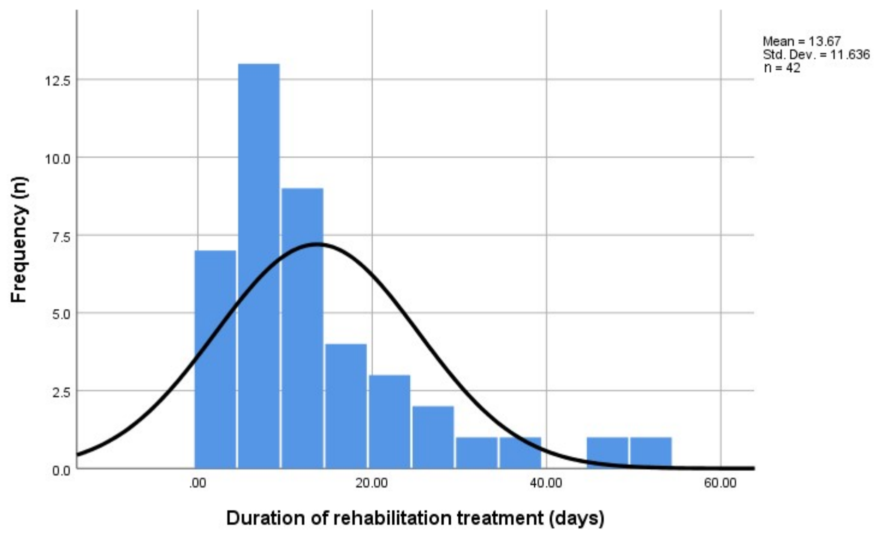

Fig. 4 – Duration of rehabilitation treatment for group A (successful rehabilitation outcome). n – number.

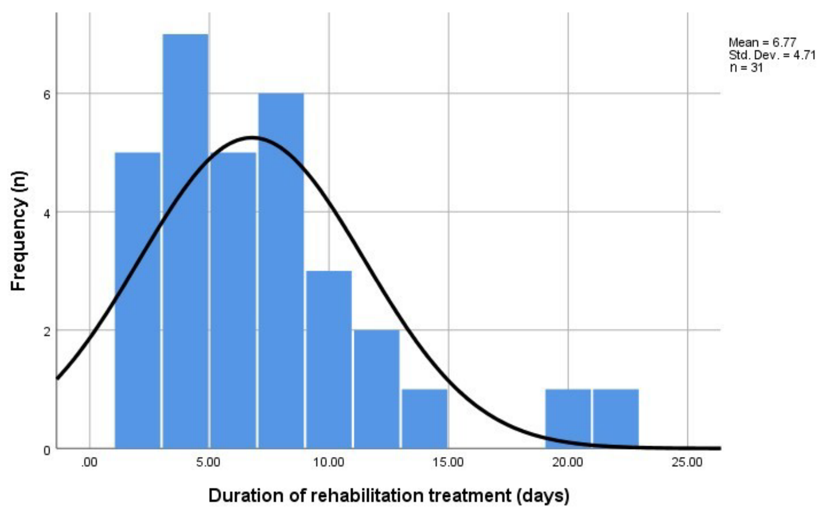

Fig. 5 – Duration of rehabilitation treatment for group B (unsuccessful rehabilitation outcome). n – number.

Table 4

Outcome test results at the beginning of rehabilitation treatment (T1) and discharge (T2) for patients with successful rehabilitation (group A)

Variable	Time point		*p*-value
	T1	T2	
MBS (0–10)	2.75 ± 0.86	0.78 ± 0.68	< 0.001*
6MWT (m)	210.04 ± 46.67	307.79 ± 74.32	< 0.001**
TUG (sec)	35.37 ± 7.27	22.78 ± 54.04	< 0.001**
BI (0–100)	35.60 ± 18.88	76.09 ± 21.12	< 0.001**

TUG – Timed Up and Go. For other abbreviations, see Table 3. Data are presented as mean ± standard deviation. *Paired Student's *t*-test; ** Wilcoxon signed-rank test.

Table 5

Results of binary logistic regression analysis for predicting rehabilitation outcome – model significance and partial contribution of predictors

Parameter	B	SE	Wald	Sig	Exp(B) / OR	95% CI for Exp(B)	
						LL	UL
Age (years)	0.08	0.03	6.77	**0.009**	1.08	1.02	1.15
Hypertension	0.32	0.74	0.19	0.666	1.38	0.32	5.90
CVD	1.80	0.75	5.74	**0.017**	6.04	1.39	26.28
Diabetes	1.11	0.83	1.82	0.178	3.05	0.60	15.38
Malignancy	2.19	0.96	5.21	**0.022**	8.92	1.36	58.39
LOS (days)	0.01	0.03	0.11	0.741	1.01	0.95	1.07
Onset of RT (days)	0.05	0.08	0.36	0.550	1.05	0.90	1.23
BI on the beginning of RT	0.01	0.03	0.22	0.641	1.01	0.96	1.07
Constant	-8.46	2.93	8.35	0.004	0.00	/	/

CVD – cardiovascular disease; LOS – length of hospital stay; RT – rehabilitation treatment; BI – Barthel Index; B – coefficient for the constant (also called the "intercept") in the null model; SE – standard error; Wald – Wald test; Sig – significance (*p*-value); OR – odds ratio; Exp(B) – exponentiation of the B coefficient (prognostic values for each predictor); CI – confidence interval; LL – lower limbs; UL – upper limbs.

Bolded values are statistically significant.

and values of outcome measured at discharge for patients with successful rehabilitation (MBS, BI, 6MWT, and TUG) shows a significant improvement after RT ($p < 0.001$ for all variables). The values of outcome parameters at the beginning of RT and discharge are shown in Table 4.

The last step in statistical analysis was to evaluate which clinical variables best predict the success of the RT of surgical patients with COVID-19 infection. For this purpose, logistic regression was conducted. Given the limited sample size, those variables that showed significant relationships with the criterion of rehabilitation outcome at the univariate level were included in the final list of predictors. The group of predictors consisted of the patient's age, comorbidities: hypertension, cardiovascular disease, diabetes, and malignancy, length of hospital stay, the onset of RT, and BI at the beginning of RT. The forced entry method was used. The test of the final model compared to zero proved to be statistically significant [$\chi^2(8) = 32.766$, $p < 0.001$, Nagelkerke $R^2 = 0.486$], so it can be concluded that the model significantly contributes to the prediction of the treatment outcome. The model corresponds with the data [$\chi^2(8) = 5.347$, $p = 0.720$). The prediction success rate, based on the model, was 81%. Based on the Wald's indicator, the following predictors were statistically significant: age [$p = 0.009$, odds ratio (OR) = 1.08; 95% confidence interval (CI): 1.02–1.15], cardiovascular disease ($p = 0.017$, OR = 6.04; 95% CI: 1.39–26.28) and malignancy ($p = 0.022$, OR = 8.92; 95% CI: 1.36–58.39). Results of binary logistic regression analysis for the prediction of rehabilitation outcome, model significance, and partial contribution of predictors are shown in Table 5. The surface area under the receiver operating characteristic (ROC) curve was AUC = 0.866 ($p < 0.001$), which shows that the tested final model contributes well to the prediction of the outcome of RT (successful vs. unsuccessful). The ROC curve of the treatment success prediction model is shown in Figure 6.

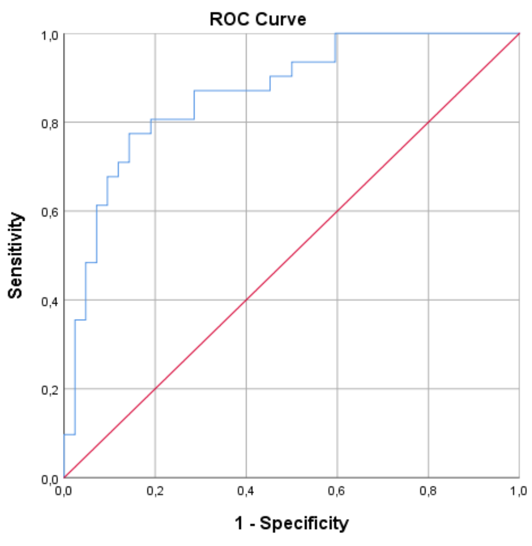

Fig. 6 – Receiver operating characteristic (ROC) curve of the treatment success prediction model.

Discussion

Recent studies have shown that COVID-19 patients who underwent surgical procedures had higher mortality rates and more complications compared to patients who had negative results for SARS-CoV-2 [1, 10, 11]. However, there is currently no data available on the effect of RT on surgical patients with COVID-19. Our results imply that COVID-19 surgical patients had prolonged hospital stays and severe dependence on ADL at the beginning of RT. Lei et al. [12], in their study regarding outcomes of patients undergoing surgeries during the incubation period of COVID-19, also reported prolonged hospitalization due to numerous complications such as acute respiratory distress syndrome-ARDS, arrhythmia shock, and acute cardiac injury.

Severe disability in COVID-19 patients is often the result of muscle weakness caused by prolonged immobility, post-intensive care myopathy and polyneuropathy, nutritional status, and underlying health conditions [4, 13]. Results from the current studies on the role of acute rehabilitation in COVID-19 patients suggest that rehabilitation has a beneficial effect on respiratory and FS [14–16]. In our research, we report a significant improvement in the independence in ADL measured by BI and exercise tolerance and cardiovascular and respiratory function evaluated by the 6MWT after completing early RT. Zampogna et al. [2], in their research on the effect of pulmonary rehabilitation in patients recovering from COVID-19, report a similar increase in the values of BI and 6MWT after RT. However, patients in our study had lower baseline results, which can be attributed to the additional effect of surgical treatment. However, a study by Curci et al. [17] on 32 post-acute COVID-19 patients showed that BI was not significantly increased after RT. Patients in this study were significantly older than patients in our research, which can explain the difference in our findings. In a study on patients who suffered from severe and critical COVID-19 pneumonia, Güler et al. [18] showed that patients gained significant functional independence during RT (mean BI improved from 44.8 to 88.4). We also noted significant improvement in lower limb function at the end of RT (mean TUG values reduced from 35.37 at baseline to 22.78 ± 54.04 at discharge). Similar results were obtained in a study by Rodrigues et al. [19], who reported a significant increase in lower limb and respiratory muscle strength, balance, and exercise capacity measured by TUG, 6MWT, and Functional Independence Measure. These findings underline the need for early rehabilitation for functional recovery of surgical COVID-19 patients.

In our study, patients with unsuccessful rehabilitation outcomes were significantly older than patients with successful rehabilitation, while they also had a higher overall incidence of comorbidities, in particular hypertension, cardiovascular disease, diabetes, and malignancy. Bellou et al. [20], in their random-effects meta-analysis of 263 studies, found that female gender, obstructive sleep apnoea, history of venous thromboembolism, coronary heart disease, cancer, chronic liver disease, chronic obstructive pulmonary disease-COPD, dementia, peripheral arterial disease, and rheumatological disease were associated with adverse outcomes in patients with COVID-19. Barbieri et al. [21], in their retrospective cohort study, reported a significant decrease in the level of disability in both motor and cognitive functioning after a multidisciplinary patient-tailored rehabilitation program. However, neither motor and nutritional characteristics nor comorbidities played a significant role in predicting the overall positive change registered after rehabilitation. Furthermore, our research showed that patients with adverse rehabilitation outcomes more often required oxygen support *via* nasal cannula, oxygen mask, high-flow nasal cannula, NIV, and IMV. Paneroni et al. [22], in their cross-sectional study on the sample of 184 patients, determined that the predictors for impaired FS in patients with COVID-19 were age, previous disability, comorbidity, and use of both IMV and NIV. Similarly to our results, a study by SeyedAlinaghi et al. [23] showed that patients who required IMV due to COVID-19 had a prolonged hospitalization duration and poor outcomes. In their research, Piquet et al. [24] demonstrated that grip strength was negatively correlated with the number of days spent in the intensive care unit-ICU, both on admission and at discharge. However, their findings suggest that an ICU or longer acute stay did not hamper responsiveness to rehabilitation. Our results imply that patients with unsuccessful rehabilitation had lower values of the BI and 6MWT at the beginning of RT. In their study, Trevisson-Redondo et al. [25] found that the BI total results could potentially be used to predict the related quality of life after recovering from COVID-19. In our research, after binary logistic regression analysis was performed, age, cardiovascular disease, and malignancy emerged as factors with predictive significance of rehabilitation outcome. Ikebuchi et al. [26], in their research on a sample of 57 patients with the severe form of COVID-19, determined that predictive factors for mobility after early rehabilitation were chronic lung disease, renal impairment, heart disease, and the presence of cerebrovascular disorder. Based on the results of this study, early rehabilitation of surgical patients with COVID-19 is very challenging due to underlying pathology, which often leads to severe disability, impaired respiratory function, comorbidities, and age of the patients. Although most patients achieved significant functional improvement at the end of RT, caution is needed when planning RT for patients with advanced age, cardiovascular comorbidity, and malignancy. Patients with successful rehabilitation had an earlier onset of RT, implying that the treatment should be started as soon as the patient is stable enough to prevent possible complications that can lead to adverse outcomes. Patients with favorable rehabilitation outcomes also had longer durations of RT, which can account for their significant functional gain.

This study has several limitations. As a single-arm study, it is methodologically insufficient in proving the effectiveness of RT because there are no results of a similar control group of surgical patients with COVID-19 who were not included in RT for comparison. However, because of the pandemic, a clinical trial of a rehabilitation group as opposed to a ‘sham rehabilitation’ control group was not considered ethical. The follow-up period is limited (only during hospitalization), and only early outcomes can be investigated. Moreover, the cohort of patients is small and does not allow detailed subpopulation analyses. To address these limitations, further controlled trials with a larger sample size at multiple centers are required to understand better the role of RT in the long-term recovery of surgical patients with COVID-19.

Conclusion

Results of the present study have indicated that individually tailored RT during the acute phase of COVID-19 in surgical patients is very challenging. At the end of RT, most patients achieved significant improvement in their FS, greater independence in the activities of daily living, better balance, and lower limb mobility. In addition to functional benefits and reduction of disability, patients demonstrated a significant decrease in dyspnoea and better tolerance of physical exertion. However, a significant number of patients had unfavorable outcomes. Binary logistic regression analysis has shown that age, cardiovascular disease, and malignancy are predictors of unfavorable outcomes and that caution is needed when devising a RT for these patients.

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Received on December 28, 2023
Revised on March 19, 2024
Revised on March 26, 2024
Accepted on April 9, 2024
Online First May 2024