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Risk factors influence the arterial line patency in ICU-bound patients during COVID-19 pandemic: An observational cohort study

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ABSTRACT

Background: There were increased claims of thrombotic events in ICU-bound patients with COVID-19. We designed this observational study to examine implementation of systemic anticoagulation on arterial catheter failure (ACF) and to identify contributing risk factors.

Methods: A total of 245 COVID-19 subjects were included in this observational study, 48 patients in the non-systemic, (Non-SA), anticoagulation cohort, and 197 patients in the systemic (SA), anticoagulation group. The first arterial line inserted on ICU admission for every patient was monitored regarding its duration of patency, number and location of consecutive arterial lines inserted during stay in ICU. Demographics of patients, ICU parameters and risk factors for ACF were analyzed.

Results: The percentage of ACF was significantly higher in Non-SA group, 45.8 % when compared to SA group, 25.9%, P = 0.007. The patients with ACF exhibited higher D-dimer, co-morbidities, diabetic patients, received aspirin and mortality than the patent group, respectively, p = 0.002, p = 0.002, p < 0.0001, p < 0.0001, and p < 0.0001. This group also received higher sedation and vasopressors consumption and more prone position on mechanical ventilation, respectively, p < 0.0001, p < 0.0001, and p < 0.0001 when compared to patent group. They had prolonged length of stay in ICU and hospital, respectively, p = 0.001 and p = 0.042. The cumulative incidence of index ACF was (Log-rank test 6.95, P = 0.008) when comparing SA group versus non-SA group, respectively, P = 0.007. On Cox-proportional hazard multivariate regression analysis, independent predictors of ACF were: platelets level (per 100.000 increase), (HR 1.40; 95% CI 1.12–1.74; p = 0.003), blind technique versus ultrasound in arterial line insertion (HR 4.12; 95% CI 1.60–10.67; p = 0.003), and prone position in ICU (HR 2.07; 95% CI 1.180–3.63; p = 0.011).

Conclusion: We observed three independent predictors of arterial line failure including platelets level and ultrasound use during arterial catheter insertion and prone position in ICU. Systemic anticoagulation was associated with more patency of arterial catheter than prophylactic therapy group.

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1. Introduction

The number of Coronavirus Disease 2019 (COVID-19) patients admitted to intensive care units has increased, and it has been noted that this epidemic is linked to high rates of thrombosis, which has exacerbated its effects on those critically ill patients [1,2]. A hypercoagulable state that promotes greater rates of arterial thrombosis is one explanation for the observed increased failure rate of arterial catheters in ICU patients with COVID-19. According to the information now available, individuals with COVID-19, and particularly those who need intensive care unit care have a higher frequency of thromboembolic events [3,4]. However, a recent study discussed the incidence of deep venous thrombosis among non-ICU subjects during COVID-19 epidemic [5].

During peak admission of patients with COVID-19 to ICU, some investigators initiated a dedicated invasive procedure team from anesthetists to provide a multidisciplinary, safe service for invasive vascular procedures, moreover, endotracheal intubations [6]. Because of these repeated attempts, doctors had to spend more time in patients' rooms placing arterial lines and/or managing malfunctioning lines, which increased their risk of contracting the SARS-COV-2 virus [7].

Invasive continuous arterial blood pressure monitoring is frequently used in the care of adult patients

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who are severely unwell and undergoing high-risk surgery [8]. Moreover, indwelling arterial catheters enable repeated blood gas analyses. Depending on clinical conditions, 10–97% of patients admitted to an intensive care unit (ICU) have an arterial monitoring [9].

The radial artery is the most typical insertion location (87%). In order to offer accurate monitoring and prevent the morbidity associated with recurrent punctures or catheter replacements, catheter patency is essential. Typically, flush solution is fed continuously into the arterial line. Nevertheless, after 3 days, 8–26% of patients experienced radial artery catheter failures [10], with median patency duration of 5–10 days [11]. Temporary artery blockage is a frequent side effect of radial catheters (19.7% frequency); however major adverse events are rare [9,12,13].

Invasive vascular access was employed for hemodynamic monitoring and management in patients undergoing high-risk surgery, especially in patients who were admitted to the intensive care unit [14].

There are various ways to lower the frequency of arterial line failure, such as using heparinized solutions [15]. The arterial line occlusion was reported when it was inserted for longer than 2–3 days [16]. One frequent consequence is a transient arterial blockage [9].

During COVID-19 crisis, other researchers noticed increased requests for arterial line insertions either in newly admitted or already present ICU patients with COVID-19. The repeated insertions of arterial lines may challenge the ICU provider as well as it increases risk of ischemic thrombosis and infectious events in the patient's limbs. However, there was one report about risk factors associated with arterial lines obstructions in patients with COVID-19 admitted to ICU [17].

Our ICU management committee suggested the use of systemic anticoagulation of ICU admitted patients starting on 20 March 2021 in response to the increased claims of thrombosis and pulmonary embolic events in patients with COVID-19 admitted to ICU in the second wave of this epidemic [18]. This observational study compares patients before and after implementing systemic anticoagulation to examine the effects of the medication on arterial line patency and the incidence of arterial line failure.

Identifying risk factors for impaired arterial line patency in both groups will be the secondary outcome.

2. Methods

2.1. Patients

Adult patients with COVID-19 diagnosed and admitted to an ICU at the Hazem Mubierik Hospital in Doha, Qatar, between 5 February 2021, and 30 April 2021 were the subject of an observational cohort study. On 1 February 2021, the approval of our Institutional Review Board (MRC #01-21-492) was confirmed. On 20 March 2021, the systemic anticoagulation protocol was started and implemented throughout the ICUs of this hospital, a tertiary COVID-19 facility in our healthcare corporation, as a quality improvement initiative in response to frequent cases of sudden pulmonary embolism in young patients with good physical capacity as well as an increasing demand for the on call team scheduled for invasive line placements due to arterial line failure and/or thrombosis. A multidisciplinary team from medical intensive care, pharmacy, and anesthesia worked on the development of our procedure. This systemic anti-coagulation (SA) protocol used was adjusted according to the D-dimer level as in the following sequence:

If D-dimer≤1.2; If body weight<90 kg; Enoxaparin 40 mg SC, Once daily. If body weight≥90 kg; Enoxaparin 60 mg SC, Once daily.

Moderate disease, PAO_2/FiO_2 ratio<200; If D-dimer≥1.2; If body weight<90 kg; Enoxaparin 40 mg SC, every 12 hours. If body weight≥90 kg; Enoxaparin 60 mg SC, every 12 hours. Severe disease, PAO_2/FiO_2 ratio<100; If D-dimer≥1.2; Enoxaparin 1 mg/kg SC, every 12 hours.

Eligibility of the study: Patients could be initiated on the protocol if they had fulfilled the above criteria and their first arterial line (index arterial line) inserted during their first day ICU admission was complicated by documented thrombosis or arterial line failure. Arterial line failure included; 1) severe arterial waveform dampening that did not improve with flushing or repositioning; 2) Inability to withdraw blood from the catheter, and/or; 3) Catheter malfunction requiring replacement with documented thrombosis on bedside ultrasound of the vessel [10]. They should have a peripheral artery cannulation with a suitable arterial cannula and a functional arterial line established after insertion. The duration of enrolment and start of Systemic Anticoagulation protocol implementation are as explained before.

The "index arterial line" (index a-line) defined as the first arterial line inserted on ICU admission, we monitored duration of the patent index a line, number of a lines inserted during stay in ICU, and location of a line.

Although all patients who satisfied these requirements were eligible for the protocol, it was only started once the ICU doctors had made their assessments. According to our hypothesis and to extend the duration of arterial line patency, inclusion criteria included all COVID-19 patients who either received non-systemic anticoagulation (prophylactic dose), group 1, or those who received systemic anticoagulation protocol (therapeutic dose), group 2, during their ICU admission. Ongoing hemorrhage, a history of cerebral hemorrhage, disseminated intravascular coagulopathy (DIC), and missing data were among the exclusion criteria for the SA procedure.

The sample size was divided into two groups as previously described and comprised all eligible patients during the planned time frame. Informed consent was waived for this observational cohort study with the approval of our Institutional Review Board (MRC #01-21-492). Data collection had been started after registry was approved on August 2021, NCT04992221.

2.2. Data collection

Age, sex, BMI, nationality, smoking, morbidities such as diabetes mellitus, hypertension, chronic kidney disease, hyperlipidemia, infections, and aspirin therapy; basal coagulation profile (PT, APTT, INR, D-dimer, platelet count); location of arterial line, (radial, dorsalis pedis, brachial, femoral); administration of vasopressors, daily number of arterial blood sampling gases and size of the arterial catheter per gauge. Level of awareness, mechanical ventilation, the patient's position (supine or prone), recent surgery (within 30 days), length of stay in the intensive care unit, and length of hospital stay were some of the patient's factors. Healthcare staff factors included seniority level as per years of experience; resident (1–4 years of experience), specialist, (5–7 years of experience), consultant (≥10 years of experience); time of procedure work shift, included morning, evening and night shift; use of the ultrasound device during arterial line insertion versus blind technique; degree of difficulty during insertion ranged from easy, moderate difficulty and challenging.

Outcome measures were to compare patients before and after the implementation of systemic anticoagulation in order to determine how systemic anticoagulation affected the incidence of arterial line failure and the patency of arterial lines. Risk variables for arterial line patency impairment are secondary outcome analysis.

All patients were monitored until the earliest of the following occurred: death, ICU discharge, or 45 days.

2.3. Statistical analysis

Descriptive statistics were used to summarize demographic, clinical, baseline laboratory features, comorbidities, and procedure-related parameters. Mean and standard deviation (SD) were used for normally distributed data, whereas median and inter-quartile-range (IQR) used for skewed data. Categorical data were summarized using frequencies and percentages. The Shapiro–Wilk test was used to examine whether a continuous variable follows a normal distribution. Associations between two or more qualitative variables were assessed using Chi-square ($\chi 2$) test, Fisher Exact, or Yates-corrected Chi-square tests as appropriate. Quantitative data and outcome measures between the two independent groups were analyzed using unpaired t or Mann–Whitney U-tests as appropriate depending on the data distribution. Survival functions were estimated with the Kaplan–Meier survival curve method followed by Log-rank test. Cumulative incidences of index arterial line failure between systemic and non-systemic anticoagulation groups were estimated and compared using Log-rank/Gray tests. All *P* values presented were two-tailed, and *P* values<0.05 were considered as statistically significant. All statistical analyses were carried out using statistical packages SPSS 28.0 (Armonk, NY: IBM Corp) and Epi-info (Centers for Disease Control and Prevention, Atlanta, GA) software.

3. Results

3.1. Patient characteristics

A total of 245 out of 260 patients were included, with 48 patients in the prophylactic (Non-SA) anticoagulation cohort, and 197 patients in the therapeutic (SA) anticoagulation group. Baseline characteristics of both cohorts are described in Table 1.

The percentage of arterial line failure was significantly higher in Non-SA group, (22/48) 45.8% when compared to SA group, (51/197) 25.9%, $P = 0.007$. The duration of index a-line patency and length of ICU stay were statistically insignificant. The fibrinogen level was higher in SA group versus Non-SA group, $P < 0.0001$. Majority of arterial line catheters were performed during morning time as per working shift comparison between the two groups, $P = 0.005$. Almost all other baseline parameters showed insignificant differences between SA and non-SA groups ($P > 0.05$) as shown in Table 1.

Analysis of failed arterial lines and when compared with patent arterial lines showed the following: the patency group showed a significantly higher percentage of receiving systemic anticoagulation regimen, 146 (84.9%) compared to patients with failed arterial line group, 51 (69.9%) ($P = 0.007$). The failed arterial line patients had higher D-dimer, fibrinogen, co morbidities, diabetic patients, on aspirin, and mortality than the patent group, respectively, $p = 0.002$, $P = 0.017$, $P = 0.002$, $P < 0.0001$, $P < 0.0001$ and $P < 0.0001$. They had significantly more sedated patients on mechanical ventilation and in prone position and received higher vasopressors drugs respectively, $p < 0.0001$, $p < 0.0001$ and $p < 0.0001$ when compared to patent group. They had higher arterial blood sampling when 3 times/day and 4 times/day after index arterial line insertion, $p < 0.0001$. There were prolonged length of stay both in ICU and hospital, respectively, $p = 0.001$ and $p = 0.042$ in failed arterial line patients when compared to patent group.

Table 1. Patients' characteristics of the two study groups: Systemic anticoagulation (therapeutic), group-1 and non-systemic anticoagulation (prophylactic), group-2 anticoagulation dose.

Item	Systemic anticoagulation (Therapeutic) n = 197	Non-systemic anticoagulation (Prophylactic) n = 48	*p value*
Male gender n (%)	156 (79.2)	41 (85.4)	0.33
Age/year median (IQR)	50.0 (42.0, 55.5)	48.0 (42.0, 58.0)	0.696
BMI/kg/m^2 median (IQR)	30.0 (27.0, 34.0)	28.0 (25.8, 33.2)	0.189
Basal Laboratory Data			
Platelets (K/uL) median (IQR)	239.0 (179.0, 315.0)	266.5 (171.3, 374.8)	0.195
INR median (IQR)	1.1 (1.0, 1.2)	1.1 (1.0, 1.2)	0.190
PT (seconds) median (IQR)	12.9 (11.8, 13.7)	12.9 (12.2, 14.3)	0.215
APTT (seconds) median (IQR)	29.3 (27.2, 32.5)	28.6 (25.4, 32.7)	0.402
D-Dimer (ng/mL) median (IQR)	0.9 (0.5, 3.2)	1.5 (0.5, 3.3)	0.671
Fibrinogen (mg/dL) median (IQR)	4.9 (3.8, 6.3)	4.0 (2.5, 4.2)	<0.0001
Ferritin (mcg/L) median (IQR)	991.5 (580.8, 1602)	1224 (417, 1716)	0.990
Anti-Xa level (IU/mL) median (IQR)	0.5 (0.4, 0.9)	1.1 (0.4, 1.1)	0.246
Associated morbidity and therapy			
Co morbidities n (%)	103 (52.3)	24 (50.0)	0.776
Malignancy n (%)	3 (1.5)	2 (4.2)	0.245
Diabetes Mellitus n (%)	99 (50.3)	23 (47.9)	0.772
Previous history of CNS stroke n (%)	3 (1.5)	2 (4.2)	0.245
Cardiovascular diseases n (%)	12 (6.1)	6 (12.5)	0.127
Hypertension n (%)	76 (38.6)	24 (50.0)	0.149
Pulmonary diseases n (%)	16 (8.1)	4 (8.3)	0.962
Recent hospitalization (<30 days) n (%)	25 (12.7)	6 (12.5)	0.972
Recent surgery (<30 days) n (%)	3 (1.5)	1 (2.1)	0.783
Sedated Mechanical ventilated n (%)	71 (36.0%)	19 (39.6)	0.648
Procedure Data			
Procedure duration/min median (IQR)	20.0 (15.0, 25.0)	20 (16.3, 30.0)	0.042
Physician 's Working Shift Time			
Morning	97 (49.2)	35 (72.9)	0.005
Afternoon	55 (27.9)	4 (8.3)	
Evening	45 (22.8)	9 (18.8)	
ASA scoring n (%)			0.176
ASA1	30 (15.2)	9 (18.8)	
ASA2	137 (69.5)	27 (56.2)	
ASA3	30 (15.2)	12 (25.0)	
Arterial Catheter insertion Ultra Sound – assisted n (%)	30 (15.2)	7 (14.6)	0.911
Vasopressor agents n (%)	61 (31.0)	9 (18.8)	0.093
Arterial line failure n (%)	51 (25.9)	22 (45.8)	0.007
Mortality n (%)	23 (11.7)	6 (12.5)	0.874
Duration of index A-line patency/day median (IQR)	5.0 (4.0, 9.0)	4.0 (3.0, 8.8)	0.184
Length of ICU stay/day median (IQR)	7.0 (4.0, 14.5)	9.0 (6.0, 16.5)	0.067
Length of Hospital stay/day median (IQR)	15.5 (7.3, 24.8)	16.0 (10.0, 28.0)	0.042

Abbreviations: Non-SA = Non Systemic anticoagulation (Prophylactic); SA = Systemic anticoagulation (Therapeutic); BMI = body mass index; INR = international normalized ratio; PT= prothrombin time; APTT; activated partial thromboplastin time; anti-Xa level = anti factor 10-a coagulation factor; ICU = intensive care unit; a-line = arterial line; ASA = American Society of Anaesthesia; IQR = inter quartile ratio. Statistically significant values at $p < 0.05$.

However, there were no significant differences ($P > 0.05$) in patients exhibited bleeding, who had recent hospitalization or surgery within 30 days as shown in Table 2.

The cumulative incidence of index arterial line failure was significantly lower in SA group compared to non-SA group (Log-rank test statistic 6.95, $P = 0.008$) with overall percentage of index arterial line failure was significantly lower in SA group (25.9%) compared to non-SA group (45.8%), respectively, $P = 0.007$, Figure 1. Furthermore, Kaplan–Meier survival estimated and showed that the median duration of index a-line patency was significantly higher in SA group (median 15 days, 95% CI 12.9, 17.1 days) compared to non-SA group (median 12 days, 95% CI 6.9, 17.1 days) (Log-rank $P = 0.008$) as shown in Figure 2.

Many univariate factors were associated with arterial line failure after Cox-proportional hazard regression analysis; systemic anticoagulation, ($p = 0.01$); aspirin therapy, ($p = 0.02$); platelets level, ($p < 0.0001$); fibrinogen level, ($p = 0.01$); number of arterial blood gases per day, ($p = 0.01$); and prone position in ICU, ($p < 0.0001$), as shown in Table 3.

On Cox-proportional hazard multivariate regression analysis, three independent predictors of arterial line failure were platelets level, ultrasound use during arterial line insertion and prone position in ICU (Table 4). However, no significant difference was detected in the hazard of systemic anticoagulation implementation therapeutic dose and standard prophylactic anticoagulation (adjusted hazard ratio (HR) [95% CI], 1.037 [0.558–1.925]; $P = 0.910$)

Platelets per 100.000 increase escalated the risk of arterial line failure (HR 1.40; 95% CI 1.12–1.74; $p = 0.003$). Blind technique versus ultrasound use in arterial line insertion exhibited more than four times increase risk of arterial line failure (HR 4.12; 95% CI 1.60–10.67; $p = 0.003$). Prone position in ICU had more than double the risk of arterial line failure than patients with supine position (HR 2.07; 95% CI 1.180–3.63; $p = 0.011$). Deaths within the first 45 days after arterial line insertion and its cause according to

Table 2. Patients' characteristics of the both failed and patent arterial lines.

Item	Failed arterial line n = 73	Patent arterial line n = 172	*p value*
Male gender n (%)	54 (74.0)	143 (83.1)	0.098
Age/year median (IQR)	51.0 (43.0, 55.0)	48.5 (42.0, 56.0)	0.201
Therapeutic measures	51 (69.9)	146 (84.9)	0.007
Systemic anticoagulant	22 (30.1)	26 (15.1)	
Non-Systemic anticoagulant			
BMI/kg/m^2 median (IQR)	29.0 (26.3, 34.0)	30.0 (27.0, 34.0)	0.581
ASA scoring n (%)			0.414
ASA1	15 (20.5)	24 (14.0)	
ASA 2	47 (64.4)	117 (68.0)	
ASA 3	11 (15.1)	31 (18.0)	
Basal Laboratory Data			
Platelets (K/uL) median (IQR)	252 (191, 381)	239 (175, 312.8)	0.074
INR median (IQR)	1.1 (1.0, 1.2)	1.1 (1.0, 1.2)	0.420
PT (seconds) median (IQR)	12.9 (12.2, 13.5)	12.9 (11.8, 14.1)	0.521
APTT (seconds) median (IQR)	28.1 (25.5, 32.1)	29.7 (27.4, 32.5)	0.080
D-Dimer (ng/mL) median (IQR)	1.7 (0.7, 3.8)	0.8 (0.5, 3.1)	0.002
Fibrinogen (mg/dL) median (IQR)	4.9 (3.6, 6.6)	4.1 (3.2, 5.3)	0.017
Ferritin (mcg/L) median (IQR)	816 (512, 1278)	1088 (591, 1688)	0.085
Anti-Xa level (IU/mL) median (IQR)	0.4 (0.4, 0.92)	0.56 (0.36, 1.08)	0.646
Associated morbidity and therapy			
Co-morbidities n (%)	49 (67.1)	78 (45.3)	0.002
Previous history of thrombosis n (%)	4 (5.5)	9 (5.2)	0.937
Renal Failure n (%)	5 (6.8)	8 (4.7)	0.483
Malignancy n (%)	0	5 (2.9)	0.141
Diabetes Mellitus n (%)	49 (67.1)	73 (42.4)	<0.0001
Previous history of CNS stroke n (%)	3 (4.1)	2 (1.2)	0.136
Cardiovascular diseases n (%)	7 (9.6)	11 (6.4)	0.381
Hypertension n (%)	31 (42.5)	69 (40.1)	0.732
Pulmonary diseases n (%)	3 (4.1)	17 (9.9)	0.131
Anticoagulation therapy n (%)	8 (11.0)	9 (5.2)	0.107
Aspirin therapy n (%)	20 (27.4)	12 (7.0)	<0.0001
Bleeding n (%)	6 (8.2)	5 (2.9)	0.066
Mortality n (%)	36 (49.3)	9 (5.2)	<0.0001
Recent hospitalization (<30 days) n(%)	10 (13.7)	21 (12.2)	0.748
Recent surgery (<30 days) n (%)	2 (2.7)	2 (1.2)	0.373
Procedure Data			
Procedure duration/min median (IQR)	20.0 (16.0, 28.0)	20.0 (15.0, 25.0)	0.046
Physician 's Working Shift Time			
Failure number n (%)			
Morning	43 (58.9)	89 (51.7)	0.12
Afternoon	20 (27.4)	39 (22.7)	
Evening	10 (13.7)	44 (25.6)	
ICU Prone Position n (%)	35 (47.9)	36 (20.9)	<0.0001
Arterial Catheter US assisted n (%)	7 (9.6)	30 (17.4)	0.116
Vasopressor agents n (%)	33 (45.2)	37 (21.5)	<0.0001
Sedated Mechanical ventilated n (%)	42 (57.5)	48 (27.9)	<0.0001
Arterial Catheter Size n (%)		0	0.066
Gauge −18 gauge	2 (2.7)	163 (94.8)	
Gauge −20 gauge	69 (94.5)	9 (5.2)	
Gauge −22 gauge	2 (2.7)		
No of arterial blood gas (ABG)/day n (%)			<0.0001
One time/day	7 (9.6)	63 (36.6)	
Two times/day	24 (32.9)	55 (32.0)	
Three times/day	24 (32.9)	32 (18.6)	
Four times/day	18 (24.7)	21 (12.2)	
Five times/day	0	1 (0.6)	
Duration of index A-line patency/day median (IQR)	4.0 (3.0, 9.0)	5.0 (4.0, 9.0)	0.079
Length of ICU stay/day median (IQR)	15.0 (4.0, 27.5)	7.0 (6.0, 12.0)	0.001
Length of Hospital stay/day median (IQR)	15.0 (4.0, 27.5)	7.0 (6.0, 12.0)	0.042

Abbreviations: Non- SA = Non-Systemic anticoagulation (Prophylactic); SA = Systemic anticoagulation (Therapeutic); BMI = body mass index; INR = international normalized ratio; PT= prothrombin time; APTT; activated partial thromboplastin time; anti-Xa level = anti factor 10-a coagulation factor; ICU = intensive care unit; a-line = arterial line; ASA = American Society of Anaesthesia; IQR = inter-quartile ratio. Statistically significant values at $p < 0.05$.

systemic anticoagulation and non-systemic anticoagulation were compared. There were increased percentages of cases with renal failure (83.3), heart failure, (83.3), $p = 0.019$ and $p < 0.0001$ in group of non-systemic anticoagulation, respectively as shown in Table 5. Deaths within the first 45 days after arterial line insertion and its reasons according to the failure of arterial line were analyzed. There were insignificant differences in mortality risk between patent and failed arterial lines as shown in Table 6.

4. Discussion

In this study, compared to critically ill COVID-19 patients who received therapeutic dosages of anticoagulation, patients with prophylactic dosages

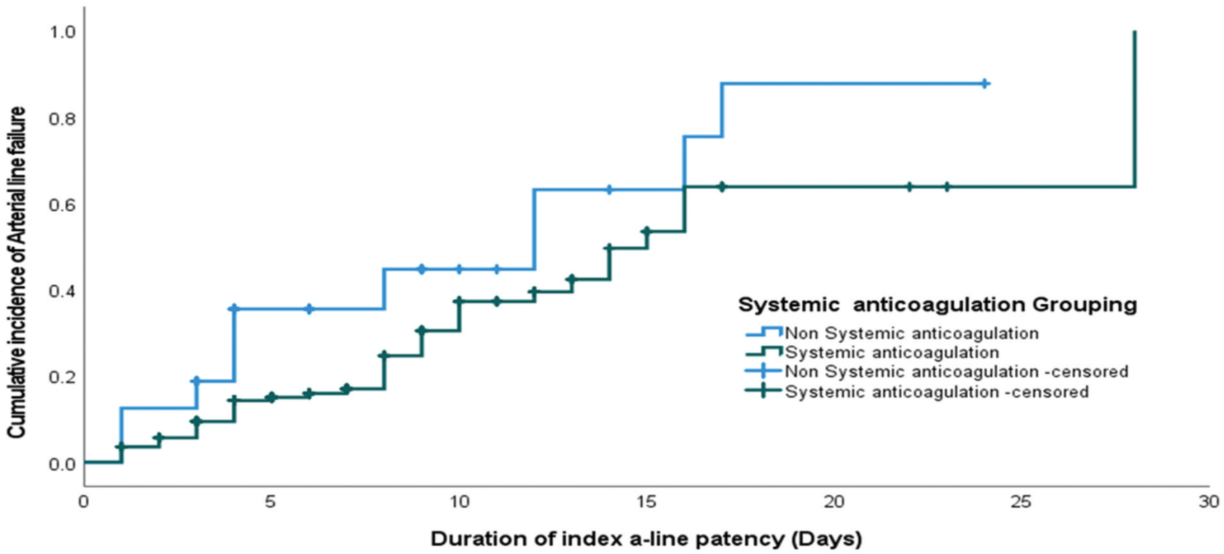

Figure 1. The cumulative incidence of index arterial line failure in the systemic anticoagulation (therapeutic), group-1 and non-systemic anticoagulation (prophylactic), group-2 anticoagulation dose, (log-rank test statistic 6.95, $P = 0.008$).

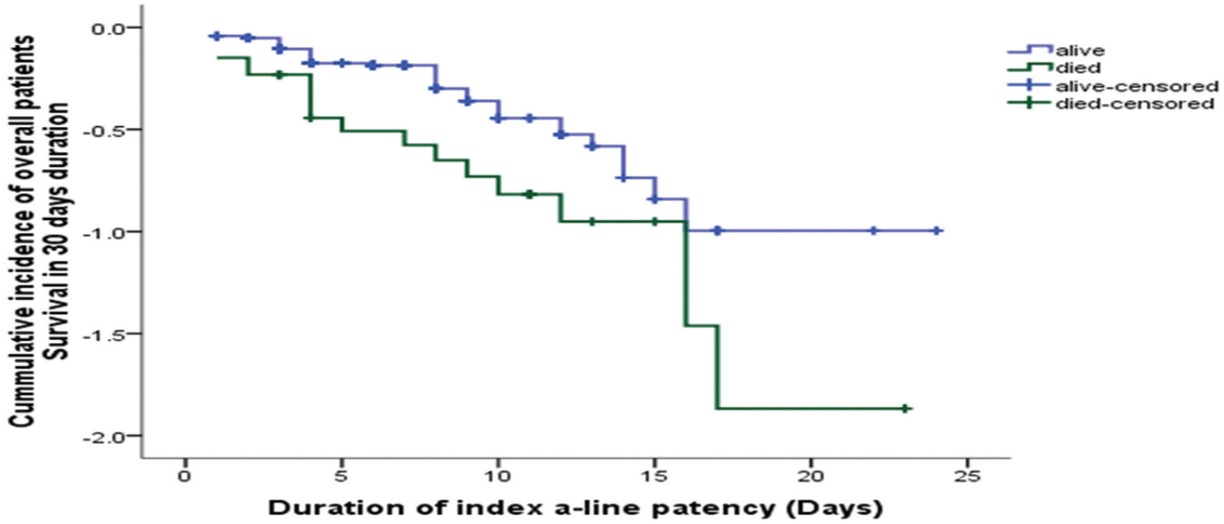

Figure 2. The median duration of index a-line patency in the systemic anticoagulation (therapeutic), group-1 and non-systemic anticoagulation (prophylactic), group-2 anticoagulation dose, with Kaplan–Meier survival estimated, (log-rank P=0.008).

showed a statistically significant high percentage of arterial line catheters that were failing Table 6.

The possibility of arterial line failure was independently higher in critically ill COVID-19 patients with thrombocytosis, ultrasound use during arterial catheter insertion, and prone positioning during mechanical ventilation. These observations may afford a new insight into the pathogenesis of arterial line failure in critically ill patients.

We found that failed arterial catheter group was more common in diabetics with co-morbidities and subjected to prone position during mechanical ventilation in ICU. Those individuals developed higher mortality and showed higher D-dimer and fibrinogen levels when compared with patent arterial line group.

Thrombocytosis may augment thrombus growth; we found that platelets per 100.000 increases augmented the risk of arterial line failure about 1.5 times. Vinholt et al. retrospective cohort study included 21,252 patients reported that 1.3-fold risk of ischemic stroke and peripheral vascular disease in patients with high platelet counts [19].

Thrombocytopenia may prevent thrombus growth and arterial line failure. However, the association between high platelet count and high risk of thromboembolic complications has not been consistently confirmed. Disseminated intravascular coagulopathy (DIC) is usually associated with increased risk of arterial thrombosis [20].

Bedford et al. (1977) reported that the probability of catheter failure was higher in female patients with intravascular thrombosis and increased proportionally to arterial blood sampling frequency and decreased in thrombocytopenia [17]. We observed associated increased arterial line failure with sampling frequency doing arterial blood gases in our cohort.

Table 3. Potential predictors of index arterial line failure: Univariate Cox-proportional hazard regression method.

	Univariate analysis	
Predictors	Unadjusted Hazard ratio (HR) (95% Confidence Interval)	*p* value
Age (years)	0.98 (0.98–1.02)	0.78
Gender		
Male	1.0 (reference)	
Female	1.51 (0.89–2.57)	0.12
Anticoagulant		
Systemic anticoagulant	1.0 (reference)	
Non-Systemic anticoagulant	1.9 (1.5–3.14)	0.01
Co-morbidities (versus none)	1.58 (0.97–2.58)	0.07
DM (versus none)	1.72 (1.05–2.81)	0.03
CVS disease (versus none)	0.63 (0.28–1.43)	0.27
HTN (versus none)	0.81 (0.51–1.29)	0.38
Pulmonary Disease (versus none)	0.54 (0.17–1.72)	0.30
Insulin Therapy (versus none)	0.85 (0.53–1.36)	0.49
Renal Disease (versus none)	0.72 (0.29–1.81)	0.49
Smoking (versus none)	0.29 (0.04–2.09)	0.22
Thrombosis History (versus none)	0.62 (0.23–1.71)	0.36
CNS Stroke (versus none)	2.0 (0.61–6.24)	0.26
Malignancy (versus none)	0.05 (0–22.5)	0.33
BMI>30	1.0 (reference)	0.10
BMI≤30	0.68 (0.42–1.10)	
Aspirin Therapy (versus none)	1.89 (1.12–3.18)	0.02
INR	1.20 (0.58–2.49)	0.62
PT	1.01 (0.95–1.08)	0.67
APTT	0.99 (0.94–1.03)	0.52
D-dimer	1.0 (0.98–1.03)	0.80
Platelets level	1.00 (1.00–1.01)	<0.0001
Fibrinogen level	0.83 (0.72–0.96)	0.01
Ferritin	1.00 (1.00–1.00)	0.55
Anti-Xa level	0.67 (1.7–2.65)	0.57
Procedure Duration (min)	1.01 (0.99–1.04)	0.33
Physician Working Shift Time		
Morning	1.0 (reference)	
Afternoon	1.06 (0.62–1.80)	0.84
Evening	0.69 (0.35–1.39)	0.30
Performing Physician Seniority		
Group 1	1.0 (reference)	
Group 2	0.73(0.35–1.53)	0.40
Group 3	1.91 (0.98–3.73)	0.06
Cannula insertion: ultrasound use versus Blind technique	4.06 (1.67–9.85)	0.002
Number ABG/day		
Number ABG/day (1)	1.0 (reference)	
Number ABG/day (2)	1.92 (0.82–4.49)	0.133
Number ABG/day (3)	3.09 (1.31–7.29)	0.01
Number ABG/day (4)	2.04 (0.83–5.04)	0.122
Number ABG/day (5)	–	–
ICU Position		
Prone Position	1.0 (reference)	
Supine position	2.36 (1.48–3.75)	<0.0001
Sedated		
Mechanical ventilation	1.0 (reference)	
Awake	1.17 (0.71–1.94)	0.54

Abbreviations: Non-SA = Non-Systemic anticoagulation (Prophylactic); SA = Systemic anticoagulation (Therapeutic); ASA = American Society of Anaesthesiologists; DM = diabetes mellitus; CVS = cardiovascular system disease; HTN = hypertension; CNS = central nervous system; BMI = body mass index; INR = international normalized ratio; PT= prothrombin time; APTT; activated partial thromboplastin time; ABG= arterial blood gas.
Performing Physician Seniority was divided into three groups according to years of working experience Group 1: Resident (1–4 Y experience), Group 2: Specialist (5–7 Y experience) and Group 3: Consultant (10+ Y experience)
Statistically significant at $p < 0.05$.
At protocol start for Systemic anticoagulation and at index arterial line failure.

The third independent factor for arterial line failure was the use of ultrasound guidance to insert arterial line. The standardization of ultrasound guidance in arterial catheterization promotes vessel health and patient safety through device and site optimization [21]. Ultrasound has demonstrated unequivocal efficacies and safety with the procedure, improving first attempt success rates with obese or patients with unstable clinical vital signs and shock. Moreover, anatomic variations of the radial artery are not rare, and ultrasound-guided catheterization reduces the incidence of insertion-related complications such as hematoma, posterior wall puncture, intimal dissection, and radial nerve injury. The intimal injury is considered as the trigger for thrombus generation. In addition, ultrasound guidance offers several immediate benefits by enhancing the most appropriate insertion techniques, allows for the correct catheter to vessel ratio

Table 4. Potential predictors of index arterial line failure: multivariate Cox-proportional hazard regression method.

Predictors	Adjusted Hazard ratio (HR) (95% Confidence Interval)	*p* value
Platelets (per 100.000 increase)	1.40 (1.12–1.74)	0.003
Arterial Catheter Insertion		
Ultrasound	1.0 (reference)	
Blind technique	4.12 (1.60–10.67)	0.003
ICU Position		
Supine position	1.0 (reference)	
Prone Position	2.07 (1.18–3.63)	0.011

Normal platelets count 150.000–450.000 × 10^9/L

Table 5. Deaths within the first 45 days after arterial line insertion and its cause according to systemic anticoagulation (therapeutic) and non-systemic anticoagulation (prophylactic).

Item	Systemic anticoagulation (Therapeutic) n = 23	Non-Systemic anticoagulation (Prophylactic) n = 6	*p value*
Sepsis/Septic shock n (%)	10 (43.5)	3 (50.0)	0.775
Cerebral lesion n (%)	1 (4.3)	0	0.603
COVID pneumonia n (%)	22 (95.7)	6 (100.0)	0.041
ARDS/respiratory failure n (%)	11 (47.8)	2 (33.3)	0.525
PCA ischemic infarction n (%)	2 (8.7)	0	0.454
DKA n (%)	1 (4.3)	0	0.603
Multiorgan failure n (%)	11 (47.8)	5 (83.3)	0.119
Renal failure n (%)	7 (30.4)	5 (83.3)	0.019
Coagulopathy n (%)	1 (4.3)	0	0.603
Heart failure n (%)	2 (8.7)	5 (83.3)	<0.0001

Table 6. Deaths within the first 45 days after arterial line insertion and its reasons according to the failure of arterial line.

Item	Failed arterial line *N* = 20	Patent arterial line *N* = 9	*p value*
Sepsis/Septic shock n (%)	7 (35.0)	6 (66.7)	0.113
Cerebral lesion n (%)	0	1 (11.1)	0.129
COVID pneumonia n (%)	20 (100)	8 (88.9)	0.129
ARDS/respiratory failure n (%)	6 (30.0)	7 (77.8)	0.017
PCA ischemic infarction n (%)	1 (11.1)	1 (5.0)	0.548
DKA n (%)	0	0 (5.0)	0.495
Multiorgan failuren (%)	10 (50.0)	6 (66.7)	0.404
Renal failure n (%)	7 (35.0)	5 (55.6)	0.298
Coagulopathy n (%)	1 (5.0)	0	0.495
Heart failure n (%)	5 (25.0)	2 (22.2)	0.872

Abbreviations: COVID = Coronavirus Disease; ARDS = adult respiratory distress syndrome; PCA = Posterior cerebral artery; DKA = diabetic ketoacidosis.

measurements to be performed, and reduces the angle of insertion, which may affect catheter failure due to inappropriate catheter length. Catheter to vessel ratio is considered as an important factor for arterial line failure [22]. Furthermore, a deeper and more proximal cannulation site at least 4 cm from wrist joint, avoiding the area of wrist flexion, reduces mechanical complications related to patient movements and may improve catheter functionality, patency duration and well along with a better area for stabilization and securement [23]. In our study, we found that blind arterial line insertion augmented the risk of arterial line failure, more than four times (HR 4.12 4.68; 95% CI 1. (1.60–10.67); $p =$ 0.003).

PROSEVA trial showed that in patients with severe ARDS, early application of prolonged prone positioning sessions significantly decreased 28-day and 90-day mortality. Additionally, prone positioning is a sign of a severe COVID-19 pneumonia, which is linked to a higher risk of thrombosis [24]. Prone positioning is another independent risk factor for arterial line failure, it exhibited nearly double the risk of arterial line failure than patients with supine position in our cohort (HR 2.068; 95% CI (1.179–3.627); $p = 0.011$).

Prone positioning is frequently considered to improve oxygenation of severe ARDS critically ill COVID-19 patients, which are normally at higher risk of thromboembolic complications secondary to their illness or their co-morbidities. Severe ARDS COVID-19 patients require frequent blood sampling which may facilitated arterial catheter failure even with proper catheter flushing post each sampling. Fibrin deposits may develop within the arterial line catheter from blood backflow, owed to repeated sample collection, a kinked catheter or decreased flush pressure; consequently, fibrin might be flashed away into the vessel during fast flushing. Ultimately, the stream of the fast-flush solution versus pulsatile blood flow might cause local shear stress disruptions, damage adjoining endothelial glycocalyx, and modulate shear-dependent endothelial expression of mediators involved in platelet aggregation. Moreover, frequent catheter manipulations and wrist flexion during prone positioning may lead to catheter kinking and displacement [25].

Chances for patency are greatest in men with long femoral lines who receive other anticoagulants or thrombolytics and heparinized flush solutions. Risks are greatest in women with short non-femoral lines who do not receive other antioagulants or thrombolytics and have non-heparinized flush solutions [10]. It has been shown that the incidence of radial obstruction increases linearly with the ratio of outer diameter to vessel lumen diameter [22]. This might explain the higher incidence of radial occlusion in female patients, who generally have vessels of smaller diameter [17,26]. However, we did not find impact of gender in our cohort. Similar to our study, the age of adult patients does not appear to be a risk factor [8].

Thrombus formation and occlusion of the artery appear to be caused by changes in the integrity of the vessel wall induced by the presence of the catheter [26]. The incidence of thrombus appears to be related to the degree to which the catheter fills the arterial lumen [27]. Bedford 1977 found that the incidence of arterial occlusion increases linearly as the ratio of cannula outer diameter to vessel-lumen diameter increases [22]. In our cohort, 20-gauge arterial catheters showed a significant higher percentage in systemic anticoagulation grou; however, they had insignificant impact on patency of the arterial catheters. Multiple punctures for catheter insertion were shown to be a risk factor for complications in one study [8] but this could not be confirmed in another [16].

An important factor with regard to arterial occlusion is the duration of cannulation [8,16]. In our analysis, we observed that systemic anticoagulation shortened the hospital length of stay; however, the arterial line patency was associated with less ICU and hospital stay.

Even in critically ill patients before COVID-19 condition, Fleury et al. 2018 found that arterial blood sampling frequency as important factor affected the patency of arterial catheters [28]. We investigated size of catheter and frequency of arterial blood sampling in our cohort. The majority of arterial catheters were Gauge 20 in both groups and the frequency of sampling showed significant difference when achieved three and four times per day. Although the majority of arterial lines in our cohort were inserted during morning time shift, we did not observe any impact of neither working shift time, or the level of physician's seniority who inserted the lines.

5. Strengths

The placement of the arterial line is crucial for managing the critically ill COVID-19 patients, who typically arrive with severe ARDS and necessitate frequent sampling and minute-by-minute blood pressure monitoring. Knowing the risk factors for arterial line failure is crucial in order to maintain arterial line and extend its life expectancy, which lowers the risk of infection by limiting caregiver interaction with patients. Therefore, our study is considered a foundation to analyze risk factors of arterial line failure and a prospective analysis of such important subject with comprehensive investigation for anticoagulation rule is warranted.

6. Limitations

There are several limitations in our study, being retrospective with small-sized study limited our ability to recognize small-sized effect and raise the probability of confounders that may have affected the effect we noticed. The small sample size presented challenges to extensive, granular confounder modification given low prevalence co-morbidities and concerns for over fitting. Precipitously developing guidelines during the second wave of COVID 19, for instance, providing intermediate prophylactic dose of anticoagulation to all critically ill COVID-19 patients may also have confounded our results. Furthermore, the impact of other COVID-19 interventions and medications on our observation was not assessed.

In addition, no scoring system was used to assess the severity of recruited patients. As the study was retrospective during exceptional situation, some data were missed which prevented us from using SOFA score or APACHE II score.

Moreover, we considered that all arterial failure cases were secondary to thrombosis and couldn't confirm that with ultrasound prospectively as the study was observational retrospective.

Finally, the study population were recruited second wave of COVID 19, and the following breaks may have had altered pathophysiology as well as clinical characteristics. Given these limits, our observations should be considered as hypothesis generating.

7. Conclusion

In our study, there are three independent predictors of arterial line failure including platelets level, and ultrasound use during arterial catheter insertion and prone position during mechanical ventilation in ICU. Therapeutic anticoagulation was associated with higher patency of the arterial catheters than prophylactic dosages.

Disclosure statement

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All the investigators mentioned as co-authors gathered the data. The statistical analysis was performed by Hanaa Nafady-Hego and Prem Chandra. The paper was written by Hanaa Nafady-Hego, Hamed Elgendy, and Adel Ganaw. The paper was submitted to all the co-authors who made substantial contributions and agreed to submit to Egyptian j of Anaesthesia. All authors read and approved the final manuscript.

References

[1] Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thromb Res. 2020;191:9–14.
[2] Klok FA, Kruip M, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145–147. DOI:10.1016/j.thromres.2020.04.013
[3] Llitjos JF, Leclerc M, Chochois C, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost. 2020;18(7):1743–1746. DOI:10.1111/jth.14869
[4] Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. Blood. 2020;136(4):489–500. DOI:10.1182/blood.2020006520
[5] Santoliquido A, Porfidia A, Nesci A, et al. Incidence of deep vein thrombosis among non-ICU patients hospitalized for COVID-19 despite pharmacological thromboprophylaxis. J Thromb Haemost. 2020;18(9):2358–2363. DOI:10.1111/jth.14992
[6] Albutt K, Luckhurst CM, Alba GA, et al. Design and impact of a COVID-19 multidisciplinary bundled procedure team. Ann Surg. 2020;272(2):e72–3. DOI:10.1097/SLA.0000000000004089
[7] Zon RL, Merz LE, Fields KG, et al. Thrombosis-related loss of arterial lines in the first wave of COVID-19 and non–COVID-19 intensive care unit patients. Anesth Analg. 2022;136(1):70–78. DOI:10.1213/ANE.0000000000006214
[8] Davis FM, Stewart JM. Radial artery cannulation. A prospective study in patients undergoing cardiothoracic surgery. Br J Anaesth. 1980;52(1):41–47.
[9] Scheer B, Perel A, Pfeiffer UJ. Clinical review: complications and risk factors of peripheral arterial catheters used for haemodynamic monitoring in anaesthesia and intensive care medicine. crit care. 2002;6(3):199–204.
[10] AACN. Evaluation of the effects of heparinized and nonheparinized flush solutions on the patency of arterial pressure monitoring lines: the AACN thunder project. By the American association of critical-care nurses. Am J Crit Care. 1993;2(1):3–15. DOI:10.4037/ajcc1993.2.1.3.
[11] Del Cotillo M, Grane N, Llavore M, et al. Heparinized solution vs. saline solution in the maintenance of arterial catheters: a double blind randomized clinical trial. Intensive care Med. 2008;34(2):339–343.
[12] Martin C, Saux P, Papazian L, et al. Long-term arterial cannulation in ICU patients using the radial artery or dorsalis pedis artery. Chest. 2001;119(3):901–906.
[13] Gunther SC, Schwebel C, Hamidfar-Roy R, et al. Complications of intravascular catheters in ICU: definitions, incidence and severity. A randomized controlled trial comparing usual transparent dressings versus new-generation dressings (the ADVANCED study). Intensive care Med. 2016;42(11):1753–1765. DOI:10.1007/s00134-016-4582-2
[14] Cannesson M, Pestel G, Ricks C, et al. Hemodynamic monitoring and management in patients undergoing high risk surgery: a survey among North American and European anesthesiologists. crit care. 2020;15(4):R197.
[15] Zevola DR, Dioso J, Moggio R. Comparison of heparinized and nonheparinized solutions for maintaining patency of arterial and pulmonary artery catheters. Am J Crit Care. 1997;6(1):52–55.
[16] Slogoff S, Keats AS, Arlund C. On the safety of radial artery cannulation. Anesthesiology. 1983;59(1):42–47.
[17] Maurer LR, Luckhurst CM, Hamidi A, et al. A low dose heparinized saline protocol is associated with improved duration of arterial line patency in critically ill COVID-19 patients. J Crit Care. 2020;60:253–259.
[18] Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020;18(5):1094–1099.
[19] Vinholt PJ, Hvas AM, Frederiksen H, et al. Platelet count is associated with cardiovascular disease, cancer and mortality: a population-based cohort study. Thromb Res. 2016;148:136–142.
[20] Nopp S, Moik F, Jilma B, et al. Risk of venous thromboembolism in patients with COVID-19: a systematic review and meta-analysis. Res Pract Thromb Haemost. 2020;4(7):1178–1191.
[21] Bardin-Spencer AJ, Spencer TR. Arterial insertion method: a new method for systematic evaluation of ultrasound-guided radial arterial catheterization. J Vasc Access. 2021;22(5):733–738.
[22] Aminian A, Saito S, Takahashi A, et al. Impact of sheath size and hemostasis time on radial artery patency after transradial coronary angiography and intervention in Japanese and non-Japanese patients: a substudy from RAP and BEAT (radial artery patency and bleeding, efficacy, adverse event) randomized multicenter trial. Catheter Cardiovasc Interv. 2017;92:844–851.
[23] Imbriaco G, Monesi A, Spencer TR. Preventing radial arterial catheter failure in critical care — Factoring

updated clinical strategies and techniques. Anaesth Crit Care Pain Med. 2022;41(4):101096.

[24] Ayzac L, Girard R, Baboi L, et al. Ventilator-associated pneumonia in ARDS patients: the impact of prone positioning. A secondary analysis of the PROSEVA trial. Intensive care Med. 2016;42(5):871–878. DOI:10.1007/s00134-015-4167-5

[25] Guerin C, Albert RK, Beitler J, et al. Prone position in ARDS patients: why, when, how and for whom. Intensive care Med. 2020;46(12):2385–2396. DOI:10.1007/s00134-020-06306-w

[26] Roy S, Kabach M, Patel DB, et al. Radial artery access complications: prevention, diagnosis and management. Cardiovasc Revasc Med. 2022;40:163–171.

[27] Schachinger V, Kasper W, Wollschlager H, et al. Incidence, predisposing factors, acute complications and prognostic significance of intracoronary thrombus formation during PTCA. Z Kardiol. 1993;82(11):712–720.

[28] Fleury Y, Arroyo D, Couchepin C, et al. Impact of intravascular thrombosis on failure of radial arterial catheters in critically ill patients: a nested case-control study. Intensive care Med. 2018;44(5):553–563. DOI:10.1007/s00134-018-5149-1