



# Effect of Aspirin Use on clinical Outcome among Critically Ill Patients with COVID- 19

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## ABSTRACT

**Background:** Critically ill COVID-19 patients are at risk of developing major complications with high mortality rate. Aspirin might have favorable effects in severe COVID-19 via various mechanisms besides inhibition of platelet aggregation. The role of aspirin as adjuvant therapy in critically ill patients with COVID-19 has not been studied. In this study, we investigated the correlation between aspirin use and the clinical outcome in critically ill COVID-19 patients.

**Methods:** This is a retrospective cohort observational study of critically ill COVID-19 Egyptian patients. Participants were divided into two groups: patients who received aspirin, 150 mg per day orally, upon admission to the intensive care unit, and those who did not. The primary outcome in this study was the shift to invasive ventilatory support.

**Results:** A total of 1190 patients were involved in the study, 660 patients received aspirin, while 530 patients did not. Among aspirin group compared to non-aspirin group, invasive ventilatory support, DVT, PE, stroke, ACS, ARDS, AKI, septic shock, and mortality were less frequent, and the differences were significant except for ACS, AKI, and septic shock. Major bleeding was non-significantly more frequent. The length of ICU stay was significantly longer among non-survivors, and shorter among survivors. The variations between the two groups were significant among subgroups  $\geq 40$  or 60.

**Conclusions:** In critically ill patients with COVID-19, aspirin has the potential role as an adjuvant therapeutic, lowering the risk of mechanical ventilation, thromboembolic events, ARDS, and ICU mortality. Patients older than 40 years were a significant category that might benefit from aspirin.

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Aspirin; critically ill; COVID- 19; clinical outcome

## 1. Introduction

Severe COVID-19 infection is a multisystem inflammatory disease that is linked to immune dysfunction, hypercoagulation, and thrombosis [1]. Critically ill COVID-19 patients are at risk of developing major complications with a high mortality rate [2]. They are prone to thrombotic events, which occur despite standard thrombo-prophylaxis [3]. Platelet activation has been involved in the COVID-19 inflammatory response. Aspirin has multiple mechanisms of action; it provides tissue protection in addition to inhibition of platelet aggregation. Thus, it may have substantial potential to prevent COVID-19 complications [4]. However, the role of aspirin in critically ill patients with COVID-19 is not clear and has not been studied. In this study, we investigated the correlation between aspirin use and the clinical outcome among critically ill COVID-19 patients and subdivided patients according to age.

### 1.1. Patients and methods

This is a retrospective cohort observational study of critically ill COVID-19 adult Egyptian patients admitted to Ain Shams University quarantine hospital, the Obour specialized hospital's intensive care units between

April 2020 and September 2021. The Ethical Research Committee at Ain Shams University approved the study and permitted data usage and analysis after protection of patient privacy and anonymity, FMASU R08/2021.

Diagnosis of COVID-19 was established via a nasopharyngeal polymerase chain reaction test. Critical illness necessitated ICU admission was considered in case of clinical signs of severe pneumonia including fever, respiratory rate greater than 30 breaths/min, or SpO<sub>2</sub> less than 93% on room air or the ratio of arterial partial pressure of oxygen to fraction of inspired oxygen less than 300 mmHg or patients with more than 50% lung infiltrate progression within 24–48 hours in high-resolution computed tomography associated with respiratory failure requiring respiratory support, presence of shock, sepsis, other organ failure that requires monitoring and treatment in the ICU. Patients with history of aspirin allergy or patients who were receiving either antiplatelets or anticoagulants for any other comorbidities before diagnosis of COVID were excluded from the study. Likewise, pregnant women, those with coagulopathy, or recent history of major bleeding were excluded.

All the critically ill patients admitted to the ICU received full care in accordance with the COVID

management protocol at Ain Shams University Hospital. Available antiviral drug was administered, Lopinavir–Ritonavir (200/50 mg) two tablets bid for 5–10 days or Favipiravir if available 1600 mg twice day 1 then 600 mg twice for 9 days. If cytokine storm was diagnosed, tocilizumab was added as 8 mg/kg and the response was assessed, if the patient needed second dose it was calculated as 4 mg/kg after 12 hrs. If tocilizumab was not available, methylprednisolone 1–2 mg/kg/day IV up to 500 mg/day intravenous infusion for 5 days was given, followed by half the previous dose for 2 days then gradual withdrawal in the following days. Self-prone positioning was encouraged for all patients as tolerated unless there was a contraindication. All patients received oxygen therapy, which was escalated depending on the patient's condition to non-invasive mechanical ventilation (NIMV) for lung recruitment using high-flow nasal oxygen (HFNO) administration or non-invasive positive pressure ventilation (NIPPV) to reach the target oxygen saturation level of greater than 94%. If the tidal volume for patients utilizing NIPPV exceeded 9 ml/kg of predicted body weight or the ROX index score, the ratio of oxygen saturation/fraction of inspired oxygen to respiratory rate fell below 3.85 for patients utilizing HFNO therapy and switch to invasive mechanical ventilation with lung protective methods was decided.

While the study investigators were blinded to the aggregated outcome data, neither the participants or their guardians nor the attending intensivists were. Participants were divided into two groups, Aspirin group: patients who received aspirin at the dose of 150 mg per day orally on admission to the ICU because the attending intensivist believed the patient would benefit from aspirin and non-aspirin group: patients who did not receive aspirin. Aspirin was administered until ICU discharge at the decision of the attending intensivist according to the clinical outcome. The patients were excluded if the occurrence of an adverse event necessitated discontinuation of aspirin therapy, which was started as a component of COVID-19 therapy. On the other hand, the patients were excluded if it was clinically necessary to start aspirin for a standard indication other than COVID-19. All the study participants received prophylactic anticoagulation that was escalated to therapeutic anticoagulation if their D-dimer was greater than 1 mg/L.

The primary outcome in this study was the need for invasive ventilatory support. The secondary outcomes included the length of ICU stay and the clinical outcomes. Further, subgroup analyses were done for the primary and secondary outcome according to age.

Patient data were collected from the medical records retrospectively, including age, sex, comorbidities, the Acute Physiology and Chronic Health Evaluation II (APACHE II) score and Sequential Organ Failure Assessment (SOFA) score on ICU admission, and clinical

outcomes. Comorbidities included obesity, hypertension, diabetes, severe renal impairment (defined as estimated glomerular filtration rate lower than 30 ml/min/1.73 m<sup>2</sup>), cardiac disease (defined as angina, myocardial infarction, heart failure, heart valve problems, major cardiac arrhythmias, stroke, or transient ischemic attack), chronic liver disease (defined as Childs-Pugh score equal to or greater than 1), and chronic lung disease (defined as asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, and pneumonitis).

## 1.2. Statistical methods

Using the PASS 11 program for sample size calculation, setting power at 80% and alpha error at 0.05. According to "Chow et al., 2021" [5], the expected rate of mechanical ventilation among patients receiving aspirin is 35.7% and among other patients is 48.4%. According to estimates, a sample size of 175 patients in each group is sufficient to distinguish between two groups. However, the availability of data that were extracted from the medical record yielded an overall study cohort size of 1190 patients, 660 in the aspirin group and 530 in the control group.

Using IBM SPSS statistics (Statistical Package for Social Sciences) software, version 28.0, IBM Corp., Chicago, USA, 2021, the collected data were statistically analyzed. The Shapiro–Wilk test was used to check the normality of the quantitative data. As the collected data were normally distributed, they are expressed as mean and standard deviation (mean ± SD) and compared using independent t-test. Qualitative data are presented as numbers and percentages and were compared using Chi-square test or Fisher's Exact test if the number of observations was 5 or less. A comparison of ICU mortality rates was done using the log rank test. P values below 0.050 were considered significant.

## 1.3. Results

There were 1,019 patients included in the trial, 660 of whom received aspirin (55.46%) and 530 of whom did not (44.54%). Regarding their initial clinical and demographic characteristics, the patients in the two groups were comparable (Table 1). Table 2 shows different results: IMV > NIMV in subgroups >60y and all cases.

Regarding thrombosis parameters, among all patients in group A compared to group C, DVT, PE, stroke, and ACS were less frequent, and the differences were significant except for ACS, whereas major bleeding was non-significantly more frequent among group A compared to group C. In patient subgroup analysis by age, DVT and PE were significantly less frequent among group A compared to group C in the 40–79 age subgroups while for Stroke in the 40–59 age subgroups. For ACS and major bleeding, there were non-significant differences between group A compared to group C across all age groupings (Table 3).

**Table 1.** Baseline clinical and demographic characteristics.

Variables		Group A (n = 660)	Group C (n = 530)	p-value
Age (years)		62.8 ± 13.1	63.8 ± 13.4	0.176
Age categories (years)	20–39	37 (5.6%)	33 (6.2%)	0.832
	40–59	191 (28.9%)	142 (26.8%)	
	60–79	379 (57.4%)	314 (59.2%)	
	≥ 80.0	53 (8.0%)	41 (7.7%)	
Sex	Male	351 (53.2%)	293 (55.3%)	0.470
	Female	309 (46.8%)	237 (44.7%)	
Diabetes mellitus		308 (46.7%)	240 (45.3%)	0.634
Hypertension		380 (57.6%)	319 (60.2%)	0.363
Severe renal impairment		232 (35.2%)	185 (34.9%)	0.930
Chronic lung disease		206 (31.2%)	162 (30.6%)	0.811
Heart diseases		143 (21.7%)	121 (22.8%)	0.631
Chronic liver disease		60 (9.1%)	54 (10.2%)	0.523
SOFA score, Mean ± SD		7.1 ± 1.1	7.2 ± 1.2	0.462
APACHE score, Mean ± SD		15.3 ± 2.2	15.4 ± 2.2	0.264
CORAD	IV	306 (46.4%)	245 (46.2%)	0.962
	V	354 (53.6%)	285 (53.8%)	

Data are expressed by either mean ± SD or number (%). P ≥ 0.05 = non-significant difference.

n = The number of patients in each group. SOFA: Sequential Organ Failure Assessment scores. APACHE II: Acute Physiology and Chronic Health Evaluation II score.

**Table 2.** Ventilatory support parameters.

Age	Type	Group A (n = 660)	Group C (n = 530)	p-value	Relative effect RR (95% CI)
20–39	NIMV	16 (43.2%)	16 (48.5%)	0.660	0.89 (0.54–1.49)
	IMV	21 (56.8%)	17 (51.5%)		
40–59	NIMV	92 (48.2%)	81 (57.0%)	0.109	0.84 (0.69–1.04)
	IMV	99 (51.8%)	61 (43.0%)		
60–79	NIMV	217 (57.3%)	226 (72.0%)	<b>&lt;0.001*</b>	0.80 (0.71–0.89)
	IMV	162 (42.7%)	88 (28.0%)		
≥ 80.0	NIMV	33 (62.3%)	35 (85.4%)	<b>0.013*</b>	0.73 (0.57–0.93)
	IMV	20 (37.7%)	6 (14.6%)		
All cases	NIMV	358 (54.2%)	358 (67.5%)	<b>&lt;0.001*</b>	0.80 (0.73–0.88)
	IMV	302 (45.8%)	172 (32.5%)		

Data are expressed by number (%). \* P < 0.05 = significant difference. Relative effect: Effect of group A relative to group C. RR: Relative risk. CI: Confidence interval. n = The number of patients in each group. NIMV: non-invasive mechanical ventilation, IMV: invasive mechanical ventilation.

**Table 3.** Comparison regarding major bleeding and thrombosis parameters.

Events	Age	Group A (n = 660)	Group C (n = 530)	p-value	Relative effect RR (95% CI)
Major bleeding	20–39	2 (5.4%)	0 (0.0%)	0.494	NA
	40–59	8 (4.2%)	3 (2.1%)	0.365	1.98 (0.54–7.34)
	60–79	31 (8.2%)	18 (5.7%)	0.211	1.43 (0.81–2.50)
	≥ 80.0	6 (11.3%)	3 (7.3%)	0.727	1.55 (0.41–5.82)
	All cases	47 (7.1%)	24 (4.5%)	0.061	1.57 (0.97–2.54)
DVT	20–39	2 (5.4%)	2 (6.1%)	0.999	0.89 (0.13–5.98)
	40–59	6 (3.1%)	22 (15.5%)	<b>&lt;0.001*</b>	0.20 (0.08–0.49)
	60–79	18 (4.7%)	45 (14.3%)	<b>&lt;0.001*</b>	0.33 (0.20–0.56)
	≥ 80.0	5 (9.4%)	7 (17.1%)	0.271	0.55 (0.19–1.62)
	All cases	31 (4.7%)	76 (14.3%)	<b>&lt;0.001*</b>	0.33 (0.22–0.49)
P E	20–39	0 (0.0%)	2 (6.1%)	0.219	Not applicable
	40–59	4 (2.1%)	14 (9.9%)	<b>0.002*</b>	0.21 (0.07–0.63)
	60–79	10 (2.6%)	27 (8.6%)	<b>&lt;0.001*</b>	0.31 (0.15–0.62)
	≥ 80.0	5 (9.4%)	4 (9.8%)	0.999	0.97 (0.28–3.38)
	All cases	19 (2.9%)	47 (8.9%)	<b>&lt;0.001*</b>	0.32 (0.19–0.55)
Stroke	20–39	0 (0.0%)	0 (0.0%)		Not applicable
	40–59	1 (0.5%)	7 (4.9%)	<b>0.023*</b>	0.11 (0.01–0.85)
	60–79	5 (1.3%)	11 (3.5%)	0.057	0.38 (0.13–1.07)
	≥ 80.0	0 (0.0%)	1 (2.4%)	0.436	Not applicable
	All cases	6 (0.9%)	19 (3.6%)	<b>0.001*</b>	0.25 (0.10–0.63)
ACS	20–39	2 (5.4%)	0 (0.0%)	0.494	Not applicable
	40–59	1 (0.5%)	1 (0.7%)	0.999	0.74 (0.05–11.79)
	60–79	3 (0.8%)	7 (2.2%)	0.199	0.36 (0.09–1.36)
	≥ 80.0	0 (0.0%)	2 (4.9%)	0.188	Not applicable
	All cases	6 (0.9%)	10 (1.9%)	0.146	0.48 (0.18–1.32)

Data are expressed by number (%). \* P < 0.05 = significant difference. Relative effect: Effect of group A relative to group C. RR: Relative risk. CI: Confidence interval. n = The number of patients in each group. DVT: deep vein thrombosis, PE: pulmonary embolism, ACS: acute coronary syndrome.

**Table 4.** Comparison regarding clinical outcome parameters.

Events	Age	Group A (n = 660)	Group C (n = 530)	p-value	Relative effect RR (95% CI)
AKI	20–39	1 (2.7%)	2 (6.1%)	0.599	0.45 (0.04–4.70)
	40–59	8 (4.2%)	6 (4.2%)	0.987	0.99 (0.35–2.79)
	60–79	15 (4.0%)	14 (4.5%)	0.743	0.89 (0.44–1.81)
	≥ 80.0	5 (9.4%)	6 (14.6%)	0.525	0.64 (0.21–1.97)
ARDS	All cases	29 (4.4%)	28 (5.3%)	0.475	0.83 (0.50–1.38)
	20–39	3 (8.1%)	3 (9.1%)	0.999	0.89 (0.19–4.12)
	40–59	19 (9.9%)	24 (16.9%)	0.061	0.59 (0.34–1.03)
	60–79	45 (11.9%)	55 (17.5%)	<b>0.035*</b>	0.68 (0.47–0.98)
	≥ 80.0	7 (13.2%)	13 (31.7%)	<b>0.030*</b>	0.42 (0.18–0.95)
Septic shock	All cases	74 (11.2%)	95 (17.9%)	<b>&lt;0.001*</b>	0.63 (0.47–0.83)
	20–39	1 (2.7%)	2 (6.1%)	0.599	0.45 (0.04–4.70)
	40–59	20 (10.5%)	13 (9.2%)	0.691	1.14 (0.59–2.22)
	60–79	46 (12.1%)	48 (15.3%)	0.228	0.79 (0.55–1.16)
	≥ 80.0	11 (20.8%)	10 (24.4%)	0.675	0.85 (0.40–1.81)
Mortality	All cases	78 (11.8%)	73 (13.8%)	0.314	0.86 (0.64–1.16)
	20–39	6 (16.2%)	6 (18.2%)	0.828	0.89 (0.32–2.50)
	40–59	29 (15.2%)	34 (23.9%)	<b>&lt;0.001*</b>	0.63 (0.41–0.99)
	60–79	98 (25.9%)	133 (42.4%)	<b>&lt;0.001*</b>	0.61 (0.49–0.76)
	≥ 80.0	19 (35.8%)	29 (70.7%)	<b>&lt;0.001*</b>	0.51 (0.34–0.76)
All cases	152 (23.0%)	202 (38.1%)	<b>&lt;0.001*</b>	0.60 (0.51–0.72)	

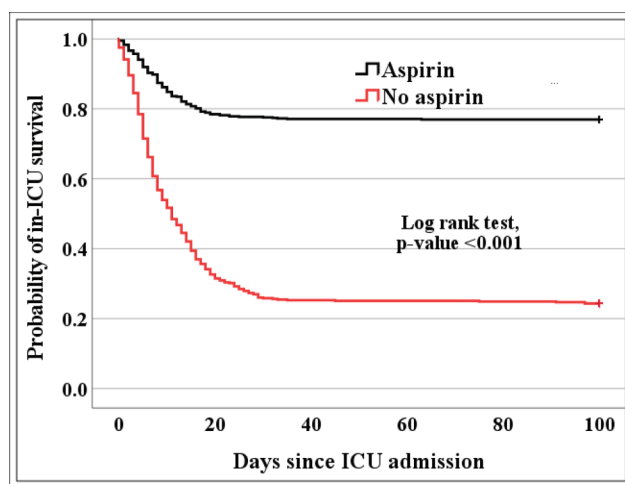
Data are expressed by number (%). \*  $P < 0.05$  = significant difference. Relative effect: Effect of group A relative to group C. RR: Relative risk. CI: Confidence interval. n = The number of patients in each group. AKI: acute kidney injury, ARDS: Acute respiratory distress syndrome.

Regarding clinical outcome parameters, all patients in the group A experienced ARDS, AKI, septic shock, and ICU mortality at a lower rate than those in group C. The differences were significant for ARDS, and mortality, but not for AKI, and septic shock. In subgroup analysis of patients according to age, ARDS was significantly less frequent among group A compared to group C in subgroup older than 60 years while for mortality in subgroups older than 40 years. There were no statistically significant differences between group A compared to group C for AKI and septic shock across all age groupings (Table 4). Figure 1 demonstrates that among all patients who received aspirin, ICU mortality was significantly less frequent.

Among non-survivors, the length of ICU stay was longer in group A compared to group C, as well as the subgroup of patients older than 60 years. Conversely, among survivors, ICU stay was significantly shorter among all patients in group A compared to group C, and for the subgroup of patients older than 40 years (Table 5).

## 2. Discussion

In the present study, allocation to aspirin was associated with a lower risk of shifting to invasive mechanical ventilation among all patients and patients older than 60 years. Likewise, there was a lower risk of thromboembolic manifestations, ARDS, and ICU mortality. Nevertheless, ACS incidence was not significantly lower among all patients who received aspirin. In subgroup analysis of patients according to age, there was emphasis on patients who were between 40 and 79 years for DVT and PE while for stroke among patients who were between 40 and 59 years. The length of ICU stay among non-survivors was significantly longer among all patients in aspirin group compared to non-aspirin group, and among patients who were older than 60 years. On the other hand, among survivors, ICU stay was significantly shorter among all patients in aspirin group compared to non-aspirin group, and among patients who were older than 40 years.



**Figure 1.** Kaplan Meier curve for ICU mortality rate.

**Table 5.** Comparison regarding length of ICU stay.

Age	Type	Group A (n = 660)	Group C (n = 530)	p-value	Relative effect RR (95% CI)
<b>Non-survivors</b>					
20–39	1 week	1 (16.7%)	2 (33.3%)	0.999	0.50
	> 1 week	5 (83.3%)	4 (66.7%)		(0.06–4.15)
40–59	1 week	10 (34.5%)	17 (50.0%)	0.215	0.69
	> 1 week	19 (65.5%)	17 (50.0%)		(0.38–1.26)
60–79	1 week	45 (45.9%)	91 (68.4%)	<0.001*	0.67
	> 1 week	53 (54.1%)	42 (31.6%)		(0.53–0.86)
≥ 80.0	1 week	12 (63.2%)	28 (96.6%)	0.004*	0.65
	> 1 week	7 (36.8%)	1 (3.4%)		(0.46–0.93)
All cases	1 week	68 (44.7%)	138 (68.3%)	<0.001*	0.65
	> 1 week	84 (55.3%)	64 (31.7%)		(0.54–0.80)
<b>Survivors</b>					
20–39	1 week	27 (87.1%)	19 (70.4%)	0.117	1.24
	> 1 week	4 (12.9%)	8 (29.6%)		(0.94–1.64)
40–59	1 week	105 (64.8%)	51 (47.2%)	0.004*	1.37
	> 1 week	57 (35.2%)	57 (52.8%)		(1.09–1.73)
60–79	1 week	184 (65.5%)	81 (44.8%)	<0.001*	1.46
	> 1 week	97 (34.5%)	100 (55.2%)		(1.22–1.76)
≥ 80.0	1 week	16 (47.1%)	1 (8.3%)	0.034*	5.65
	> 1 week	18 (52.9%)	11 (91.7%)		(0.84–38.14)
All cases	1 week	332 (65.4%)	152 (46.3%)	<0.001*	1.41
	> 1 week	176 (34.6%)	176 (53.7%)		(1.24–1.61)

Data are expressed by number (%). \*Significant. Relative effect: Effect of group A relative to group C; Relative risk. CI: Confidence interval.

Critical illness represents 6–19% of COVID-19 patients [5]. Handling critically ill patients with COVID-19 in the ICU requires preventing COVID-19 related complications. Despite global vaccination, COVID-19 treatments are still crucial, particularly in patients with severe disease or critically ill. The critically ill patients who are admitted to the ICU are usually elderly or presenting with considerable comorbidities [6]. Managing these patients could help to improve the clinical outcomes and reduce morbidity and mortality.

COVID-19 is a systemic disease that causes vascular endothelial cell dysfunction involving the pulmonary capillary endothelium and endothelial cells in multiple organs in addition to escalating the procoagulant tendency [7,8]. There is interest in the use of antiplatelet drugs in patients with COVID-19 because endothelial injury and inflammation result in significant platelet activation [4].

Acetylsalicylic acid, the active ingredient in aspirin, is a well-tolerated, affordable, widely accessible, and safe drug. Aspirin may benefit patients with severe COVID-19 through diverse mechanisms. Since aspirin is cyclooxygenase-1 enzyme inhibitor, which reduces thromboxane A<sub>2</sub> synthesis and platelet aggregation, it can reduce thrombotic occurrences in the veins and the arteries. Aspirin moreover possesses anti-inflammatory characteristics that can lessen the likelihood of cytokine storm. Aspirin reduces the synthesis of prostaglandins, interleukin-6, C-reactive protein, and macrophage colony-stimulating factor, which are all inflammatory molecules [9,10]. Further, aspirin might have antiviral effect against DNA and RNA viruses [11]. Likewise, aspirin could have a favorable potential in targeting ARDS.

Aspirin reduces platelet-neutrophil aggregates in the lungs, reduces inflammation, and promotes lipoxin synthesis, which restores pulmonary endothelial cell function [12,13].

Studies on the effectiveness of chronic prehospital admission aspirin therapy on the course of COVID-19 infection [14] addressed the possibility that aspirin could prevent and even treat COVID-19 problems; aspirin users had a considerably lower risk of mortality. In a retrospective, observational cohort analysis [5] of adult patients admitted with COVID-19, 314 patients did not receive aspirin, while 98 patients received aspirin within the first day of admission or a week before admission. Aspirin use was associated with less mechanical ventilation and lower rates of ICU admission. There were no differences in major bleeding or thrombosis between aspirin users and non-aspirin users.

In the RECOVERY trial [11], aspirin was given to 7351 COVID-19 patients and usual care was given to 7541 patients. Most patients had non-critical conditions. To our knowledge, this is the only trial that excluded patients who were already using chronic aspirin therapy before being admitted to the hospital, which is consistent with the present study's methodology. The 28-day mortality rate and aspirin use were not correlated. The risk of bleeding somewhat increased, although the risk of thrombotic events barely changed. These findings support those of the current study.

Likewise, the REMAP-CAP investigators found that antiplatelet therapy enhanced survival to hospital discharge in 1557 critically ill adult patients with COVID-19, with a 97% likelihood. Patients who received antiplatelet therapy were more likely to experience major bleeding. A rise in the number of patients receiving



short-term organ support for less than 6 days was observed though was associated with decrease in mortality [15]. These results are in line with those of the present investigation.

Noteworthy in the present study, invasive ventilatory support and ARDS were significantly less frequent among patients who received aspirin and particularly who were older than 60 years. Additionally, we found that all patients who were given aspirin had lower rates of DVT, PE, and stroke. These reductions were particularly noticeable in patients between the ages of 40 and 79 for DVT and PE and 40 and 59 for stroke. This could be because of aspirin's non-exclusive effect on arterial circulation. Aspirin has been demonstrated to decrease the risk of recurrent DVT [16,17] as well as the risk of PE after arthroplasty [18]. Age-related increases in COVID-19 mortality have been shown in several studies [19,20]. In one study, aspirin use on the first day of hospitalization was associated with lower in-hospital mortality only in patients older than 60 with moderate COVID-19 [6]. The results of this study are consistent with these findings, which should provide further insight on the role of aspirin at that specific age group. Even though patients with COVID-19 are typically hypercoagulable, aspirin may increase the risk of bleeding, particularly when combined with systemic heparinization. Patients using aspirin in our study did not significantly show a rise in major bleeding. The results of other studies [4,6,12] support this observation. Consequently, given that the risk of death and severe COVID-19 variants rises with advancing age, aspirin's potential benefits in this high-risk group of people should be considered.

The fact that this research involved COVID-19 patients who were critically ill as well as its age-based patient segmentation were both merits. The findings of the current study indicate that any potential benefit of aspirin in patients with COVID-19 will depend on the age of the targeted population. However, the retrospective cohort design was one of the trial's limitations.

### 3. Conclusions

In critically ill patients with COVID-19, aspirin has the potential role to serve as an adjuvant therapeutic, lowering the need of mechanical ventilation, thromboembolic symptoms, ARDS, and ICU mortality. Patients older than 40 years were a significant category that might benefit from aspirin.

### Disclosure statement

No potential conflict of interest was reported by the author(s).

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