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Evaluation of direct oral anticoagulant continuation versus switching to a parenteral anticoagulant in critically ill patients: a retrospective cohort study

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Abstract

Background Direct oral anticoagulants (DOACs) are widely used as first-line agents in various clinical settings. However, there is very little evidence regarding their use in critically ill patients in the intensive care unit (ICU), given the gap in the literature regarding their safety in this population and the concerns of bleeding and alterations in pharmacokinetics. Therefore, this study aimed to evaluate the prescribing pattern and safety of DOAC use in critically ill patients.

Methods This was a single-centre retrospective chart review study involving critically ill patients with confirmed prehospital use of DOACs who either continued their use of DOACs or switched to a therapeutic parenteral anticoagulant agent (enoxaparin or heparin) during the admission to the medical ICU and/or coronary care unit (CCU). The primary outcome was the incidence of major bleeding (MB) events. The secondary outcomes included the incidence of new thrombosis and medical ICU/CCU mortality and hospital and medical ICU/CCU lengths of stay (LOS).

Results A total of 675 patients were screened for inclusion. A total of 302 patients were included in the final analysis, with 167 patients in the DOAC group and 135 patients in the parenteral anticoagulant group. There were no differences between the groups in terms of the incidence of MB (11% vs. 9%, $p=0.61$) or new thrombosis (1% vs. 3%, $p=0.50$). The overall medical ICU/CCU mortality rate was lower in the DOAC group compared to the parenteral anticoagulant group (7% vs. 15%, $p=0.03$). Additionally, the DOAC group had shorter medical ICU/CCU stays (6 days [4–11] vs. 11 days [5–24], $p<0.001$) and shorter hospital stays (7 days [5–13] vs. 13 days [7–35], $p<0.001$), respectively.

Conclusion Compared with the use of parenteral anticoagulants, the use of DOACs in critically ill patients was associated with a similar incidence of MB and new thrombotic events. The observed differences in mortality and LOS between the groups may be attributed to variability in physician decision-making regarding anticoagulation strategies, potentially influenced by patient-specific factors and severity of illness. Further prospective studies to determine the optimal anticoagulation strategy in critically ill patients are warranted.

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Keywords DOACs, Anticoagulant, Bleeding, Thrombosis, Critical care

Introduction

Direct oral anticoagulants (DOACs) are a class of anticoagulation agents that have been of interest over the past decade. DOACs are currently the preferred oral anticoagulants due to their stable pharmacokinetics, lower drug–drug and drug–food interactions, and superior efficacy to warfarin in treating acute VTE or preventing stroke in atrial fibrillation (Afib) patients [1, 2, 3]. However, there is very little evidence regarding their use in critically ill patients in the intensive care unit (ICU), which requires careful consideration and monitoring due to the potential risks and benefits.

Critically ill patients are known to be more prone to thrombosis compared to non-critically ill hospitalized patients [4]. Many factors increase the risk of thrombosis during ICU admission, including significant past medical history, such as stroke or cancer; age; immobilization; inflammation; intravenous catheters; positive-pressure ventilation; concomitant medications; sepsis; heart failure; and surgery or trauma [5, 6, 7, 8, 9]. Due to this increased risk, thromboprophylaxis is an essential part of the usual care provided to this population. Critically ill patients are also prone to bleeding due to hepatic or renal dysfunctions, the use of renal replacement therapy, concomitant medications, surgeries, and the presence of catheters and tubes [10, 11, 12]. Additional risk factors include thrombocytopenia, which impacts clot formation, and a lack of enteral feeding, which could cause gastrointestinal mucosal atrophy, leading to an increased risk of bleeding [13, 14].

Currently, there is a gap in the literature concerning the safety of DOACs in critically ill patients, as this population is often excluded from observational studies and clinical trials due to concerns of bleeding risks and alterations in pharmacokinetics and pharmacodynamics. A recent observational study described the prescribing patterns of DOACs in ICU patients who were on these medications prior to their admission [15]. The study revealed that 41% of patients discontinued DOACs without transitioning to another agent, 20% of patients transitioned to parenteral anticoagulation, and 39% were kept on DOACs during their ICU admission. The rate of major bleeding reported in the study was 12.7%. Another observational study compared the incidence of bleeding in the ICU between patients receiving prehospital use of DOACs and those receiving warfarin [16]. They reported a lower risk of major bleeding in the DOAC group. However, not all patients receive DOACs consistently during their ICU stay, rendering their results ungeneralizable to all patients administered DOACs in the ICU.

Despite these findings, there is a gap in the literature concerning the use of DOACs in the ICU setting, and clinicians are hesitant to use them in critically ill patients, even those who are haemodynamically stable [17, 18]. A common practice in the ICU is to hold oral anticoagulants and switch patients to parenteral agents. There are wide variations across clinicians in terms of when to resume patients' prehospital DOAC regimens. Some clinicians recommend restarting DOACs immediately before discharge from the ICU, whereas others prefer to defer the decision until the patient is transferred to the general ward or step-down units. Currently, there is a trend toward the utilization of DOACs during the ICU stay given the increased understanding of their pharmacodynamics and pharmacokinetics and the availability of reversal agents [15, 16]. However, evidence of the prescribing patterns of DOACs in the ICU and the outcomes associated with their use in critically ill patients is still lacking. This uncertainty underscores the need for further research to inform clinical practice and ensure the best possible outcomes for critically ill patients. This study addresses this gap by evaluating the clinical outcomes of using DOACs in critically ill patients, providing evidence to guide clinical design-making. The aim of this study was to evaluate the safety of continuing DOACs in critically ill patients compared with switching to therapeutic parenteral anticoagulant agents.

Methods

Patients and study design

This was a retrospective cohort study of adult patients with a documented prescription for a direct oral anticoagulant (DOAC), such as apixaban, rivaroxaban, dabigatran, or edoxaban, as one of their outpatient medications upon their initial admission to the medical ICU or coronary care unit (CCU) at King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia. The study was approved by King Abdullah International Medical Research Center (KAIMRC) in December 2023 with reference number NRC23R/779/12. System-generated reports were used to identify patients who were admitted to the medical ICU or CCU and with a documented prescription for a DOAC as one of their outpatient medications upon their initial admission from January 1, 2021, to December 31, 2023. All identified patients were manually screened for the inclusion criteria by two reviewers. Participants were included if they were at least 18 years of age, had prehospital use of a DOAC identified through the medication list and either continued their DOAC agent or switched to a therapeutic parenteral anticoagulant agent (enoxaparin or heparin) during medical ICU/

CCU admission. Patients who were initially started on parenteral anticoagulants and then switched back to their outpatient DOACs during their medical ICU/CCU stay were classified under the DOAC group. Patients were excluded if they were admitted or transferred to the surgical units, which are defined as units dedicated to patients who are either undergoing or recovering from surgery, such as the surgical ICU and cardiac surgery ICU; who are receiving renal replacement therapy; or who died within 3 h of admission. Patients who were treated with reduced-dose (prophylactic-dose) anticoagulants, defined as heparin 5000 units twice or three times daily or enoxaparin 30 mg or 40 mg every 24 h, were excluded. Patients who had a DOAC listed as outpatient medication but not actively taking it prior to admission were also excluded; this was performed by a clinical pharmacist through medication reconciliation during the admission process, which is a standard practice at our institution. No standardized treatment protocol was in place for restarting or continuing DOACs, and all medication changes were made at the physician's discretion.

Study variables and data collection

The primary outcome of this study was the incidence of major bleeding (MB) events in critically ill patients with prehospital use of DOACs who continued their DOAC agent during medical ICU/CCU admission compared with patients who were switched to a therapeutic parenteral anticoagulant. Therapeutic parenteral anticoagulant was defined as enoxaparin given as 1 mg/kg subcutaneously every 12 h or 1.5 mg/kg subcutaneously every 24 h, or unfractionated heparin administered as a continuous infusion on the basis of nurse-driven protocols to target activated partial thromboplastin time (aPTT) of 50–70 s or 60–80 s, as determined at the discretion of the physician. The aPTT was monitored every 6 h until the therapeutic range was achieved and then every 12 h thereafter. The definition of major bleeding follows the criteria of the International Society on Thrombosis and Haemostasis (ISTH), which include fatal bleeding; bleeding involving a critical organ (i.e., intraspinal, intracerebral, intraocular, retroperitoneal, or intramuscular); and transfusion of ≥ 2 units of blood or a decrease in haemoglobin level of at least 2 g/dL [19]. The secondary outcomes included the incidence of new thrombosis (deep vein thrombosis, pulmonary embolism, or ischaemic stroke), ICU/CCU mortality, and hospital and ICU/CCU lengths of stay (LOS). Bleeding and thrombotic events were identified based on physician's clinical notes, radiology reports, echocardiogram reports, or imaging studies, and they were manually extracted from the electronic health system by two authors (AA and FA) and confirmed by a third author (AA).

Demographic and clinical data, including outpatient and hospital anticoagulant agents, primary indications for anticoagulation, vital signs, and comorbidities according to ICD-10 classification, were collected. The comorbidities included cancer, diabetes mellitus, congestive heart failure, chronic pulmonary disease, moderate to severe chronic kidney disease (defined as an estimated glomerular filtration rate less than 60 mL/min/1.73 m^2), cerebrovascular accidents, peptic ulcer disease, anaemia, peripheral vascular disease, and liver disease (defined as chronic cirrhosis, including all stages). Hypercoagulable disorders, defined as inherited thrombophilias or acquired conditions known to increase the risk of thrombosis, such as antiphospholipid syndrome, were also recorded. The laboratory parameters collected included the Acute Physiology and Chronic Health Evaluation III (APACHE III) score; haemoglobin (g/L); haematocrit (%); platelets ($\times 10^9$/L); serum creatinine (μmol/L); creatinine clearance (mL/min), which was calculated via the Cockcroft-Gault method; blood urea nitrogen (mmol/L); international normalized ratio (INR); prothrombin time (seconds); and activated partial thromboplastin time (aPTT) (seconds).

Data analysis

Continuous variables were analysed via the Mann–Whitney U test and are presented as medians (interquartile ranges). Categorical data were analysed via Pearson's chi-square test or Fisher's exact test and are presented as frequencies and percentages. All variables with a Pvalue < 0.05 were associated with a significant impact on the endpoints. Missing data were handled by utilizing listwise deletion for cases in which data were missing completely, and multiple imputations were applied for patterns of missing data to ensure robust results. Sensitivity analysis was conducted to assess the robustness of the findings by comparing the DOAC group (excluding 22 patients who were initially started on parenteral anticoagulants and then switched to DOAC) with the parenteral anticoagulant group. All the data were analysed via Stata/SE statistical software version 15.1 (StataCorp LLC, College Station, Texas, USA).

Results

During the study period, 675 patients were identified with at least one DOAC listed on their outpatient medication list. Among these patients, 373 patients were excluded for various reasons: 120 patients were not included for not actively taking DOACs prior to their index hospital admission, 89 patients were on prophylactic anticoagulants only, 77 patients were on renal replacement therapy, 67 were admitted to surgical units, and 15 patients died within 3 h of admission (Fig. 1); this resulted in the inclusion of 302 patients in the final analysis, with 167 patients

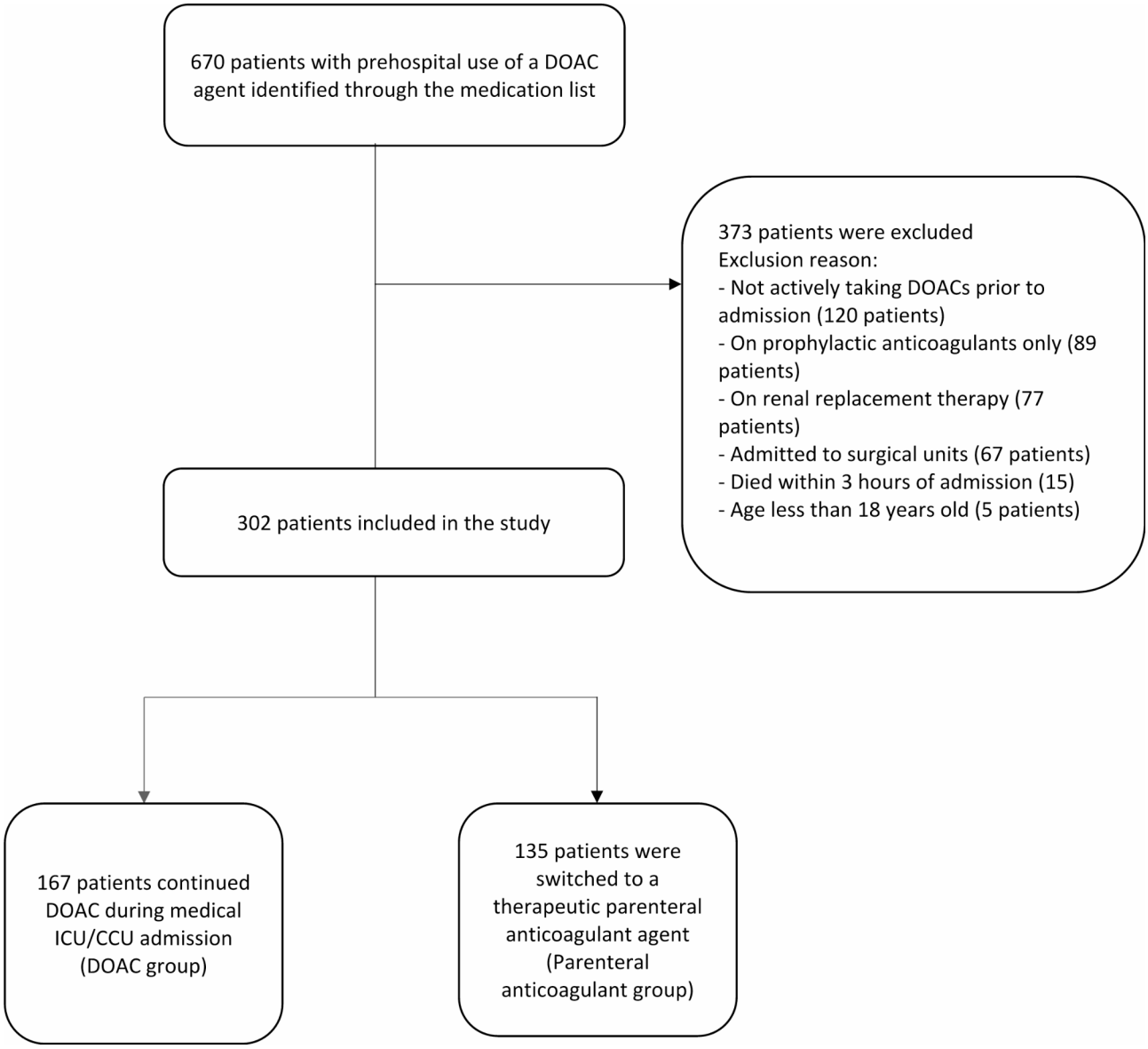

Fig. 1 Flowchart of the patients included in the study

in the DOAC group and 135 patients being switched to a therapeutic parenteral anticoagulant agent.

Baseline characteristics

Table 1 presents the baseline characteristics of patients who were receiving DOAC therapy prior to their index hospitalization. The median age for patients who continued DOAC therapy was 70.5 years, whereas it was 71 years for those who switched to therapeutic parenteral anticoagulants. The APACHE III score at admission was slightly higher in parenteral anticoagulant group (44 vs. 41) but was not statistically significant. Congestive heart failure (CHF) was significantly more prevalent in the DOAC group (59% vs. 47%, $p = 0.04$). No other statistically significant differences were observed in comorbidities, including chronic pulmonary disease (22% vs. 27%), moderate to severe chronic kidney disease (24% vs. 30%), cancer (8%), and diabetes mellitus (70% vs. 61%).

The laboratory findings were similar between the two groups. The most common admission diagnosis for both groups was cardiovascular conditions (42% vs. 37%), followed by respiratory failure (27% vs. 25%). Sepsis/infections were significantly more common in the parenteral group than in the DOAC group (27% vs. 12%, $p = 0.014$). Apixaban was the most common DOAC agent used in both groups (93% vs. 96%), and the most common indication for anticoagulation was nonvalvular atrial fibrillation (78% vs. 84%).

Table 1 Baseline characteristics

Characteristic	DOAC group ($n=167$)	Parenteral anticoagulant group ($n=135$)	*P* value
Age, years, Median (Q1-Q3)	70.5 (60–79)	71 (63–81)	0.4
Body Mass Index, kg/m², Median (Q1-Q3)	28.75 (24.2–35)	30 (26.4–36.5)	0.97
Gender, male, n (%)	83 (50)	52 (39)	0.07
Admission Unit, n (%)			0.39
Medical ICU	101 (60)	89 (66)	
Coronary Care Unit	66 (40)	46 (34)	
Admission Diagnoses, n (%)			**0.01**
Respiratory failure	45 (27)	34 (25)	
Sepsis and infections	20 (12)	37 (27)	
Cardiovascular conditions	70 (42)	50 (37)	
Renal and metabolic conditions	12 (7)	7 (5)	
Hepatic conditions	3 (2)	1 (1)	
Other	17 (10)	6 (4)	
Comorbidities, n (%)			
Cancer	14 (8)	11 (8)	1
Diabetes mellitus	117 (70)	83 (61)	0.15
Congestive heart failure	99 (59)	63 (47)	0.04
Chronic pulmonary disease	36 (22)	37 (27)	0.3
Moderate to severe chronic kidney disease	40 (24)	41 (30)	0.26
Cerebrovascular accident	24 (14)	10 (7)	0.09
Peptic ulcer disease	2 (1)	0 (0)	0.57
Anaemia	1 (1)	0 (0)	1
Peripheral vascular disease	7 (4)	5 (4)	1
Liver disease	4 (2)	2 (1)	0.88
Hypercoagulable disorders	5 (3)	8 (6)	0.34
APACHE III Score, Median (Q1-Q3)	41 (29.2–52)	44 (34–58)	0.34
Laboratory at admission, Median (Q1-Q3)			
Haemoglobin, g/L	119 (103–138)	112 (99–134)	0.11
Haematocrit, %	37 (32–43)	35 (31–43)	0.14
Platelets, $\times 10^9$/L	222 (182–280)	258 (177–320)	0.63
Creatinine clearance, mL/min	59 (31–78)	58 (33–89)	0.87
Blood urea nitrogen, mmol/L	8.4 (5.7–16.2)	8.3 (5.6–14.9)	0.83
INR	1.1 (1-1.3)	1.1 (1-1.3)	0.91
Prothrombin time, seconds	12.2 (11.6–13.6)	12.1 (11.4–14.2)	0.76
aPTT, seconds	29 (26–34)	28 (25–33)	0.01
Outpatient DOAC Agent, n (%)			
Apixaban	156 (93)	130 (96)	0.29
Rivaroxaban	14 (8)	4 (3)	0.06
Edoxaban	0 (0)	0 (0)	NA
Dabigatran	2 (1)	1 (1)	1
Primary DOAC indication, n (%)			
Nonvalvular Atrial fibrillation	130 (78)	113 (84)	0.18
History of deep vein thrombosis	12 (7)	6 (4)	0.32
History of pulmonary embolism	18 (11)	6 (4)	0.06
Acute myocardial infarction*	6 (4)	8 (6)	0.39
Other thrombosis	1 (1)	2 (1)	0.58

Abbreviations: DOAC: Direct Oral Anticoagulant; APACHE III: Acute Physiology and Chronic Health Evaluation III; INR: International Normalized Ratio; aPTT: Activated Partial Thromboplastin Time; NA: Not Applicable

* The chronic DOAC regimen was initiated as part of long-term management following a previous acute myocardial infarction

Note: No variables in the dataset have more than 1% missing data

Table 2 Primary and secondary outcomes

Outcomes	DOAC group (*n* = 167)	Parenteral anticoagulant group (*n* = 135)	*P* value	DOAC group (Excluding patients initially on parenteral anticoagulant) (*n* = 145)*	*P* value
In-hospital major bleeding, n (%)	19 (11)	12 (9)	0.61	15 (10)	0.83
Gastrointestinal	10 (6)	8 (6)	1	8 (6)	1
Intracranial	4 (2)	3 (2)	1	3 (2)	1
Intraspinal	2 (1)	0 (0)	0.57	1 (1)	1
Retroperitoneal	3 (2)	1 (1)	0.77	2 (1)	1
In-hospital new thrombosis, n (%)	2 (1)	4 (3)	0.50	2 (1)	0.62
Ischaemic stroke	2 (1)	0 (0)	0.57	1 (1)	1
Deep vein thrombosis	0 (0)	2 (1)	0.39	0 (0)	0.47
Pulmonary embolism	0 (0)	2 (1)	0.39	0 (0)	0.47
Medical ICU/CCU mortality, n (%)	11 (7)	20 (15)	0.03	9 (6)	0.03
Medical ICU/CCU length of stay, days, Median (Q1-Q3)	6 (4–11)	11 (5–24)	< 0.001	6 (4–11)	< 0.001
Hospital length of stay, days, Median (Q1-Q3)	7 (5–13)	13 (7–35)	< 0.001	7 (5–12)	< 0.001

Abbreviations: ICU: Intensive Care Unit, CCU: Coronary care unit

*Sensitivity analysis was conducted after excluding 22 patients who were initially started on parenteral anticoagulants and then switched to DOAC

In-Hospital prescription practice and outcomes

The in-hospital trend of DOAC continuation or switching to parenteral anticoagulants during medical ICU/CCU admission was analysed. Among the patients on prehospital DOAC therapy ($n = 302$), 55% ($n = 167$) continued their DOACs during their medical ICU/CCU admission, whereas 45% ($n = 135$) were transitioned to alternative therapeutic parenteral anticoagulants. Among patients who transitioned to alternative therapeutic parenteral anticoagulants, 63% ($n = 85$) were switched to unfractionated heparin, and 37% ($n = 50$) were switched to therapeutic low-molecular-weight heparin (enoxaparin).

In-hospital major bleeding occurred in 11% ($n = 19$) of the DOAC group and 9% ($n = 12$) of the parenteral anticoagulant group ($p = 0.61$). The most common major bleeding event was gastrointestinal bleeding, which was similar between the two groups and occurred in 6% ($n = 10$) of the DOAC group compared with 6% ($n = 8$) of the parenteral anticoagulant group ($p = 1.00$). The incidence of new thrombosis was also similar between the two groups: 1% ($n = 2$) in the DOAC group and 3% ($n = 4$) in the parenteral anticoagulant group ($p = 0.5$). The overall medical ICU/CCU mortality rate among patients on DOAC therapy was 7% ($n = 11$), whereas it was 15% ($n = 20$) for those who switched to therapeutic parenteral anticoagulants ($p = 0.03$). Compared with the parenteral anticoagulant group, the DOAC group had shorter medical ICU/CCU stays (6 days [4, 5, 6, 7, 8, 9, 10, 11] vs. 11 days [5–24], $p < 0.001$) and shorter hospital stays (7 days [5, 6, 7, 8, 9, 10, 11, 12, 13] vs. 13 days [7–35], $p < 0.001$). After conducting the sensitivity analysis, excluding 22 patients who were initially started on parenteral anticoagulants and then switched to DOAC, there were no significant differences in the outcomes between the DOAC group and the parenteral anticoagulant group except for overall medical ICU/CCU and medical ICU/CCU and hospital stays, which were consistent with the primary analysis (Table 2).

Discussion

Our findings reveal variations in prescribing practices for DOACs in the medical ICU/CCU patient population. Approximately half of the patients (167 [55%]) continued their DOAC therapy, whereas the remaining patients (135 [45%]) had their DOAC switched to a parenteral agent. A key finding is the lack of a significant association between bleeding risk and the use of DOAC therapy in critically ill patients with rates of 11% in the DOAC group and 9% in the parenteral anticoagulant group ($p = 0.61$). Gastrointestinal bleeding was the most common type of major bleeding in both groups, which aligns with the findings of previous studies [15, 19, 20]. Additionally, there was no notable difference in the incidence of new in-hospital thrombotic events, including ischaemic stroke, DVT, and PE, between the groups. This finding is consistent with prior research that highlights the challenge of balancing bleeding risk with the need for effective thromboprophylaxis [15, 20, 21]. Together, these findings provide indirect support for existing studies that suggest similar bleeding risk profiles for anticoagulant use among critically ill patients in the medical ICU/CCU. Given the complexity of patients during acute illness, careful monitoring of DOACs, including considerations of their pharmacodynamics and pharmacokinetics, in the ICU setting is essential. However, it is important to highlight the variability in physician decision-making regarding whether to continue DOAC therapy or transition to parenteral anticoagulants remains unclear and may

reflect differences in patient-specific factors, perceived risks, or familiarity with DOAC use in critically ill populations. This distinction likely contributes to the observed differences in the outcomes, as patients transitioned to parenteral anticoagulants may have had more severe illness or contraindications to DOACs.

The management of anticoagulation in critically ill patients remains challenging due to the variability in patient responses and the complexity of their conditions [15, 20, 21]. A retrospective study of critically ill patients receiving prehospital DOAC therapy reported that the incidence of bleeding was 12.7% among patients who were admitted to the ICU, including those who continued their DOACs during ICU admission [15]. The rate of major bleeding was similar to our findings. Furthermore, we found no difference in the rate of major bleeding events between patients who continued DOAC therapy and those who switched to a parenteral agent during their ICU admission. Notably, the overall incidence of major bleeding in our cohort was greater than that reported in previous studies of critically ill patients, which reported an incidence of approximately 5% [22, 23]. This difference could be attributed to the high percentage of patients who remained on therapeutic anticoagulation for conditions such as atrial fibrillation as well as the exclusion of patients who were switched to prophylactic doses of anticoagulants.

The percentage of patients who died in the DOAC group was 7%, which was comparable to that reported in a similar study in which the rate of ICU mortality was 6.1% among patients who were started on DOACs during ICU admission [15]. However, the study did not include a comparator anticoagulant group and was mainly descriptive. In our study, we found an increased rate of medical ICU/CCU mortality in the parenteral anticoagulant group compared with the DOAC group. This could be due to the greater severity of illness in patients who were switched from DOACs to therapeutic parenteral anticoagulants.

It is important to note that patients who were switched to parenteral anticoagulants had significantly longer medical ICU/CCU and hospital stays. The median medical ICU/CCU LOS was 11 days in the parenteral anticoagulants group compared with 6 days in the DOAC group ($P<0.001$), and the median hospital LOS was 13 days for parenteral anticoagulant group compared with 7 days for DOAC group ($P<0.001$). These prolonged stays could contribute to the higher mortality rates observed in patients who were switched to parenteral anticoagulants. Furthermore, the symptoms of critically ill patients who were switched to parenteral anticoagulants may be due to the severity of illness and disrupted pharmacokinetics and pharmacodynamics. However, there was no significant difference in the APACHE III score between the groups, which may indicate a similar severity of illness. While our study did not find a significant difference in the incidence of major bleeding between the two groups, it is possible that the longer hospital and medical ICU/CCU stays observed in the parenteral anticoagulant groups are related to the need for closer monitoring and the management of other complications during admission.

The main limitation of this study is its single-centre, retrospective design and relatively small sample size. There are no standardized protocols for continuing DOACs or switching to parenteral anticoagulants, and treatment decisions are made at the discretion of the treating physician without standardized protocols for continuing DOACs or switching to parenteral anticoagulants. The retrospective nature of the study further limits the ability to establish causal relationships between the anticoagulation strategy and patient outcomes, as more severely ill patients or those at higher risk of bleeding may have been more likely to be switched to parenteral anticoagulants. Furthermore, the study did not address variations in the pharmacokinetics and pharmacodynamics of DOACs in critically ill patients, who often experience altered drug metabolism due to organ dysfunction and drug interactions; this could have affected the efficacy and safety of the anticoagulants used. Additionally, screening for new thrombosis was performed at the clinician's discretion based on presence of signs and symptoms or risk factors rather than via a standardized screening protocol, which may explain the lower incidence of thromboembolic events among critically ill patients than in critically ill patients reported in previous studies [23]. We acknowledge that the lower incidence of documented thrombosis could be attributed to possible decreased motivation to investigate for new thrombosis, as that would not alter the existing therapy since patients are already on anticoagulant therapy. It could also be due to the fact that all patients received therapeutic anticoagulation, which may have contributed to the low rate of thrombosis. Furthermore, it is important to highlight that the majority of patients in the DOAC group were on apixaban, which could limit the generalizability of our findings to other DOACs given their different pharmacokinetic and pharmacodynamic profiles. Finally, the inclusion of both medical ICU and CCU patients and the differences in admission diagnoses between the two groups may have introduced heterogeneity in the patient population, which could influence the choice of anticoagulation therapy. Despite these limitations, our study provides insights into different anticoagulation practices across a diverse population of critically ill patients and provides real-world data that could serve as a starting point for future prospective studies with standardized protocols to better evaluate anticoagulation strategies in

critically ill patients given the scarcity of evidence regarding the use of DOACs in this population.

Conclusion

Compared with the use of parenteral anticoagulants, the use of DOACs in critically ill patients was associated with a similar incidence of MB and new thrombotic events. The observed differences in mortality and LOS between the groups may be attributed to variability in physician decision-making regarding anticoagulation strategies, potentially influenced by patient-specific factors and severity of illness. Further prospective studies to determine the optimal anticoagulation strategy in critically ill patients are warranted.

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Author contributions
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Data availability
The data supporting the findings of this study will be made available by the corresponding author, upon request.

Declarations

Ethics approval and consent to participate
This study was approved by the Institutional Review Board of the King Abdullah International Medical Research Center (protocol # NRC23R/779/12). The study was conducted in accordance with the protocol and ethical principles derived from international guidelines, including the Declaration of Helsinki. Owing to the retrospective nature of the study, the ethics committee waived the need to obtain informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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