

Research Article

Unraveling the Demographic and Clinical Landscape of Bleeding Events in Emergency Department Patients on Direct Oral Anticoagulants: A Retrospective Analysis

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Abstract

Introduction: Direct Oral Anticoagulants (DOACs) have transformed the management of Venous Thromboembolism (VTE) and stroke prevention in patients with Non-Valvular Atrial Fibrillation (NVAF). Despite their advantages over traditional Vitamin K Antagonists (VKAs), concerns persist regarding bleeding complications. Understanding the demographic and clinical characteristics of bleeding events in patients on DOACs is crucial for optimizing patient care. This study aims to evaluate such characteristics in patients presenting with bleeding events to the Emergency Department (ED).

Materials and Methods: A retrospective analysis was conducted at the Mohammed V Military Teaching Hospital's ED in Rabat. Medical records from January 1, 2022, to December 31, 2022, were reviewed for patients receiving DOAC therapy upon ED admission. Data on demographics, indications for anticoagulation, additional medications, bleeding severity, and site were collected and analyzed.

Results: Among 73 patients presenting with bleeding events while on DOAC therapy, the majority were male (39.73%), with a mean age of 72.4 years. Rivaroxaban was the most prescribed DOAC (68.3%), followed by apixaban (27.3%) and dabigatran (4.1%). Atrial fibrillation (48%) and VTE (24.6%) were the primary indications for DOAC therapy. Major bleeding events accounted for 23.2%, predominantly gastro-intestinal bleeding (76.4%). Minor bleeding events were more common (76.7%), with ecchymosis and epistaxis being the predominant types.

Discussion: Our findings align with previous studies, emphasizing the increasing use of DOACs and the incidence of bleeding events in clinical practice. The distribution of DOACs varied across studies, reflecting differences in prescribing practices and patient populations. Despite variations, our results underscore the need for vigilant monitoring and management of bleeding events associated with DOAC therapy.

Conclusion: This study highlights demographic and clinical aspects of bleeding events in ED patients on DOAC therapy. Understanding the real-world incidence and severity of bleeding events is essential for optimizing patient care and ensuring the safe use of DOACs in clinical practice. Continued research and surveillance are warranted to further enhance our understanding and improve patient outcomes.

Keywords: Direct oral anticoagulants (DOACs); Bleeding events; Emergency department

Introduction

Direct Oral Anticoagulants (DOACs) have revolutionized the management of Venous Thromboembolism (VTE) and the prevention of stroke and Systemic Embolism (SE) in patients with Nonvalvular Atrial Fibrillation (NVAF) [1]. Unlike traditional Vitamin K Antagonists (VKAs) such as warfarin, DOACs, including dabigatran, rivaroxaban, apixaban, and edoxaban, act directly on thrombin or factor Xa, offering rapid onset of action and predictable pharmacokinetics [2]. Their introduction has led to a paradigm shift in anticoagulant therapy, with benefits such as enhanced efficacy, fewer drug interactions, fixed dosing, and reduced need for routine laboratory monitoring [3,4].

Despite the significant advantages of DOACs over VKAs, concerns persist regarding bleeding complications, which remain the most common adverse event associated with anticoagulant therapy [5].

With regard to bleeding events in the Emergency Department (ED), it is crucial to examine findings from everyday clinical practice. Indeed, the use of DOACs may differ from that observed in regulatory approval studies due to factors such as dosage adjustment based on renal impairment, concomitant drug interactions, follow-up consultations, and patient demographic characteristics. Bleeding events based on spontaneous reports are often challenging to analyze due to missing demographic data and unrecorded risk factors, with a presumed higher rate of spontaneous reporting of adverse events for new medications compared to well-established VKAs.

Our study aims to evaluate the demographic and medical characteristics of patients on DOACs presenting with bleeding events, the types of bleeding events encountered by emergency physicians, their frequency, and severity based on retrospective findings from everyday clinical practice in the ED. Additionally, we aim to discuss our results in conjunction with recent studies to synthesize available evidence and address knowledge gaps. Ultimately, this study seeks to facilitate informed decision-making and optimize patient outcomes in the management of DOAC-related bleeding.

Materials and Methods

This retrospective data analysis was conducted at the Emergency Department of the Mohammed V Military Teaching Hospital in Rabat.

Medical records from the emergency department data base, spanning from January 1, 2022, to December 31, 2022, were reviewed using the keywords "rivaroxaban" (Xarelto), "apixaban" (Eliquis), and for the purpose of our study, we defined Direct Oral Anti-Coagulant (DOAC) as a treatment with any of these three medications.

All patients receiving DOAC therapy upon arrival at the emergency department were included. We extracted clinical and demographic data, including age, gender, indication and reason for admission. Additionally, we assessed DOAC-treated patients regarding this verity and the sit of bleeding at the emergency department, the indication for anticoagulant therapy, and any additional medications administered upon admission. All data sets were anonymized prior to analysis.

Results

We included 73 patients who presented to the emergency department with bleeding events during the study period and

were receiving treatment with DOACs. The patients had a mean age of 72, 4 ± 6.2 years. 29 patients (39,73%) were male, and 44 (60,2%) were female.

(Table 1) 50 patients (68,3%) were on rivaroxaban upon admission. 20 patients (27,3%) on apixaban, 3 patients (4.1%) on dabigatran (Table 2).

The primary indications for all DOACs were atrial fibrillation (35 patients, 48%) and venous thromboembolism (18 patients 24, 6%). Upon admission, in addition to oral anticoagulation with OAC, 8 patients (11 %) were also taking platelet aggregation inhibitors, 6 (75 %) were taking Acetylsalicylic Acid (ASA), and 2 (25%) were taking clopidogrel (Table 3)

In this study involving 73 patients treated with DOACs admitted in the Emergency department following bleeding events were observed:

Major Bleeding: 17 patients experienced major bleeding events, constituting 23.2% of the patient cohort. The majority of major bleeding cases were attributed to gastrointestinal bleeding, accounting for 13 out of the 17 cases (76.4%). Intracranial bleeding, although less frequent, was observed in 4 patients (23.5% of major bleeding cases).

Minor Bleeding: Minor bleeding events were more prevalent, with 56 patients experiencing such complications, representing approximately 76.7% of the patient cohort. Among minor bleeding types, ecchymosis was the most common, affecting 12 patients (26% of minor bleeding cases), followed by epistaxis affecting 16 patients (35% of minor bleeding cases). Hematuria, hematoma, and gingival bleeding were also reported, al beatless frequently, affecting 6 patients (13%), 3 patients (approximately 6.5%), and 9 patients (19.5%) of minor bleeding cases, respectively. Additionally, otorrhagia, bleeding related to dental interventions/oral, bleeding related to the eye, and an anemia of unknown origin were observed in smaller proportions, affecting 1 patient each (1.7%, 9%, 1.7%, and 5.3% of minor bleeding cases, respectively). Detailed locations and incidence of bleeding events are presented in Table 4.

Table 1: Clinical Characteristics of Patients on DOAC Therapy.

Characteristics	Values
Mean Age (years)	72,4 ± 6.2 years
Male Gender (n, %)	29 (39, 73%)
Female Gender (n, %)	44 (60,2%)

Table 2: Distribution of Patients by Type of DOAC (Direct oral anticoagulants).

NOAC	Number of Patients	Percentage (%)
Apixaban	2	1.6
Dabigatran	5	4.1
Rivaroxaban	116	94.3
Total	123	100

Table 3: Primary Indications for DOAC Therapy and Additional Medications at Admission.

Primary Indication for NOAC	Number (n)	Percentage (%)
Atrial Fibrillation	35	48
Venous Thromboembolism	18	24.6
Post operative Thromboprophylaxis	14	19.1
MVR (Mechanical Valve Replacement)	6	8.2
Additional Medications at Admission	Number (n)	Percentage (%)
Platelet Aggregation Inhibitors	8	11
- Acetylsalicylic Acid (ASA)	6	75
- Clopidogrel	2	25

Table 4: Analysis of Bleeding Events in DOAC-Treated Patients admitted in the Emergency department.

	Nombre de patients	Pourcentage (%)
Major bleeding	17	23,2
Minor bleeding	56	76,7
Gastrointestinal bleeding	13	76,4
Intracranial bleeding	4	23,5
Ecchymosis	12	26
Epistaxis	16	35
Hematuria	6	13
Hematoma	3	6,5
Gingival bleeding	9	19,5
Otorrhagia	1	1,7
Related to dental interventions/oral	5	9
Related to the eye	1	1,7
Anaemia of unknown origin	3	5,3

Discussion

We investigated demographic and clinical factors related to bleeding events in patients admitted to our Emergency Department (ED) who were taking Direct Oral Anticoagulants (DOACs). The rise in ED admissions among DOAC users in recent years may be attributed to factors such as increased access to DOACs through insurance coverage and growing familiarity with their use in managing various medical conditions, particularly chronic renal disease [6]. Studies, like that by Harel et al. [7], suggest that the risk of bleeding events may not be significantly higher among patients with chronic renal disease.

Regarding the incidence of bleeding events associated with DOAC therapy, Sauter reported an overall incidence of 19.5%, similar to rates observed in the ROCKET (20.7%) and ARISTOTLE (18.1%) clinical trials [3,5].

Mean Age and Sex Distributions of Patients

The mean age of patients experiencing bleeding events was 72.4 years. This aligns with the findings of Sauter et al., who reported a mean age of 68.3 ± 16.2 years among patients presenting to the emergency department with DOAC-related bleeding [8]. Dogan, on the other hand, found a slightly higher mean age of 79 ± 8.47 years among their patient cohort [9].

In terms of sex distribution, our study had a relatively balanced representation, with 39.73% male and 60.2% female patients. This is consistent with the findings of Sauter et al., who reported that 41.0% of their patients were male and 59.0% were female [8]. However, there is a discrepancy compared to Dogan's study, where they found that 47.2% of patients were male and 52.7% were female [9].

Regarding the age distribution of patients presenting to emergency departments for bleeding related to oral anticoagulants, Geller et al. reported that the majority of visits (80.1%) were made by adults aged 65 years and older. Furthermore, adults aged 80 years and older had the highest five-year rate of emergency department visits for oral anticoagulant-related bleeding [10]. While Geller's study provides valuable insights into the age demographics of patients seeking emergency care for bleeding events, it is important to note that their investigation encompasses a broader population and does not specifically focus on patients receiving DOAC therapy (Table 5).

Direct Oral Anticoagulants (DOACs) Prescribed

In our study of 73 patients undergoing DOAC treatment, the

Table 5: Comparison of Age and Sex Distribution among Patients in Studies Investigating Bleeding Events Related to Oral Anticoagulant Therapy.

Study	Mean Age (years)	Male (%)	Female (%)
Dogan [9]	79 ± 8.47	47.2	52.7
Sauter [8]	68.3 ± 16.2	41.0	59.0
Geller [10]	-	54.5	45.5
Our study	$72,4 \pm 6.2$	39,7	60,2

Table 6: Distribution of Direct Oral Anticoagulants (DOACS) Prescribed to Patients in Different Studies.

Study	Rivaroxaban (%)	Apixaban (%)	Dabigatran (%)	Edoxaban (%)
Present Study	68.3	27.3	4.1	N/A
Geller et al.	41.0	52.4	6.0	N/A
Mostapha et al.	54.0	27.2	19.0	N/A
Dogan et al.	45.5	29.3	19.2	6.1
Sauter et al.	93.6	2.0	4.4	N/A

majority (68.3%) were prescribed rivaroxaban upon admission, with 27.3% on apixaban, and 4.1% on dabigatran. This distribution differs from findings in other studies. Geller et al. found apixaban to be the most commonly prescribed DOAC (52.4%), followed by rivaroxaban (41.0%), and dabigatran (6.0%) [10]. Similarly, Moustapha et al. reported rivaroxaban as the most prescribed (54.0%), followed by apixaban (27.2%), and dabigatran (19.0%) [11]. Dogan and al.'s study had a distribution closer to Geller and al. with rivaroxaban being the most prescribed (45.5%), followed by apixaban (29.3%), and dabigatran (19.2%), with a small percentage on edoxaban (6.1%) [9,10]. Conversely, Sauter et al.'s study showed rivaroxaban as overwhelmingly predominant (93.6%), with a small percentage on dabigatran (4.4%) and an even smaller percentage on apixaban (2.0%) [8]. These discrepancies across studies may reflect variations in prescribing practices, patient demographics, healthcare settings, and regional preferences. Such analyses provide valuable insights for clinicians and policymakers seeking to optimize the selection and use of DOACs in clinical practice (Table 6).

Indications for DOACs

The primary indications for Direct Oral Anticoagulants (DOACs) in our study were diverse, with the majority prescribed for atrial fibrillation (48%) and venous thromboembolism (24.6%). Additionally, a significant proportion of patients received DOACs for postoperative thromboprophylaxis (19.1%) and mechanical valve replacement (8.2%). Among patients admitted with DOAC therapy, a notable percentage were also prescribed additional medications, including Platelet Aggregation Inhibitors. Specifically, Acetylsalicylic Acid (ASA) was the most common additional medication (54.5%), followed by Clopidogrel (18.8%).

Comparatively, Sauter and al. [8] reported atrial fibrillation as the main indication for DOACs (51.1%), followed by venous thromboembolism (22.3%). Additionally, a significant number of patients in their study were on Platelet Aggregation Inhibitors, with a high prevalence of ASA usage (78.7%). The combination of DOACs with ASA and clopidogrel, known as 'triple coagulation', was rare in their study. In contrast, Bouget and Oger [12] found that the indication for DOACs was predominantly atrial fibrillation in their study population. Among patients experiencing major bleeding, a few were prescribed rivaroxaban for venous thromboembolism. These findings suggest an evolving landscape in the indications for DOACs over recent years, with an expansion beyond traditional uses such as atrial fibrillation and venous thromboembolism.

Severity of Bleeding

We identified 17 cases of major bleeding events among our patient cohort, constituting 23.2% of the total. Notably, gastrointestinal bleeding was the most prevalent type. This is consistent with findings from Bouget's study [12], which observed that intracranial bleeding incidence was lower than gastrointestinal bleeding with direct oral anticoagulants (DOACs). Similarly, Sauter's study found a lower incidence of major bleeding events compared to minor bleeds, with almost half of the observed bleeding events being epistaxis and hematomas treated locally [8]. Furthermore, both Bouget and Sauter's studies highlighted a lower risk of intracranial bleeding with DOACs compared to Vitamin K Antagonists (VKAs). Additionally, a systematic review and meta-analysis by Chai-Adisaksopha et al. [13] reported a 7.57% case-fatality rate for major bleeding events associated with DOACs, providing valuable context on the severity of bleeding events with these medications. Overall, these studies collectively contribute to our understanding of the severity and distribution of bleeding events associated with direct oral anticoagulants.

Conclusion

Our study sheds light on the demographic and clinical aspects of bleeding events among patients receiving Direct Oral Anticoagulants (DOACs) admitted to our Emergency Department. The rise in ED admissions among DOAC users underscores the growing utilization of these agents in clinical practice. Our findings regarding the incidence of bleeding events, particularly major and minor bleeding events, align with previous studies. This consistency in results enhances the reliability of our findings and emphasizes the importance of understanding the risk-benefit profile of DOAC therapy in real-world clinical settings. While DOACs offer several advantages over traditional anticoagulants, such as fixed dosing and reduced need for monitoring, our study highlights the need for vigilant monitoring and management of bleeding events, especially in vulnerable patient populations. Moving forward, continued research and surveillance are essential to optimize the selection and utilization of DOACs, ultimately improving patient outcomes and safety in clinical practice.

Author Statements

Conflict of Interest Statement

No authors have competing interests.

Ethical Approval

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Author Contributions

Ilham BENAÏSSA, Cheick Ibrahim DIABATE, Khalil ABOU ELA-LAA: Conception, patient enrolment, and interpretation. All authors contributed to literature review, final draft writing, and critical revision. All the authors have participated sufficiently in this work, take public responsibility for the content, and have made substantial contributions to this research.

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