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Case Report

The Tuscany Population Based Cohort Study on Bleeding Events to the Emergency Department

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Abstract

Background: Data on bleeding events to the Emergency Department has been limited to clinical trial and the real life scenario about clinical characteristics eventually associated with treatment strategies and outcomes is still lacking. **Methods:** Inclusion criterion was the presence of any bleeding events regardless of comorbidities and ongoing treatment strategy. Clinical variables, site of bleeding, ongoing antithrombotics and outcomes were prospectively collected. Primary endpoint was in-hospital death; secondary endpoints were the composite of in-hospital death or admission, and the need of reversal treatment or blood transfusions. **Results:** Out of 155.320 visits, 2.592(1.7%) patients were enrolled (mean age 64.9 ± 20.3 year). Of these, 441(17%) showed gastrointestinal bleeding, 413(16%) intracranial, 278(11%) haematuria, 189(7%) gynecological bleeding, 87(3%) hemoptysis, 1184(46%) bleeding of minor clinical interest. Major bleeding account for 668(26%) patients. Ongoing antithrombotics were more likely associated with major bleeding ($p<0.001$) and to receive reversal treatment or blood transfusion ($p<0.05$). Overall, in-hospital deaths accounted for 30(1.2%) patients; in those with intracranial hemorrhage accounted for 5%. Overall, 696(27%) patients needed observation or admission. On the multivariate analysis, major bleeding (Odds Ratio, OR 7) was predictor of in-hospital death; major bleeding (OR 37) and age (OR 1.1) of the composite of death or admission; major bleeding (OR 38) and warfarin (OR 6) of the composite of reversal treatment or transfusion. **Conclusions:** Major bleeding was more likely to predict primary and secondary endpoints in patients presented to the Emergency Department with any bleeding events; age or use of warfarin were more likely to predict secondary endpoints. One in four patients needed prolonged in-hospital stay.

Keywords: Haemorrhage; Anticoagulation; Emergency department; Prognosis; Epidemiology

Introduction

Antithrombotics in the setting of coronary heart disease, deep venous thrombosis and pulmonary embolism have effectively reduced adverse event rates. However, antithrombotics are substantially linked to increased risk of bleeding. As longer courses of powerful regimens are used, increased efficacy may be offset by increases in any bleeding. Risk of events and risk of bleeding are two sides of the coin in prevention of thrombosis and thromboembolism. Concern regarding net clinical benefit in the setting of prevention still represents a major problem in clinical practice, due to bleeding events especially in aged population and patients with comorbidities [1-4]. Data shows that bleeding complications frequently and independently affect adverse outcomes, carry similar importance in adversely influencing mortality as ischemic events. Clinical characteristics associated with increased bleeding risk include older age, female gender, major bleeding, comorbidities as hypertension, renal disease, anemia, diabetes mellitus and previous history of bleeding [5-7]. Nowadays, evidence-based decision making should result in the choice of appropriate pharmacologic strategies including antiplatelets, indirect antithrombin therapy (vitamin K antagonist) and direct oral anticoagulants (Dabigratan, Rivaroxaban, Apixaban, and Edoxaban) that will offer the best balance of benefit and risk with the goal of optimizing outcomes. However, structured data on patients presented with bleeding events has been limited to the setting of controlled clinical trials; In the setting of the general population, the knowledge of how many patients were given antithrombotics is lacking [8].

Aim of present study was to analyze clinical characteristics which could be associated with any treatment regimens and adverse outcomes in patients with any bleeding

events as the main reason of presentation to the Emergency Department of the public healthcare.

Patients and Methods

Setting

The study was conducted at three academic and six large medical centers with an annual Emergency Department census ranging from 40,000 to 100,000. The three academic and six community hospitals involved in the study play are referral centers in as many health districts with a catchment area of 2 million people overall, and approximately half a million visit per year, in the Tuscany public healthcare, in Italy.

Study design

The three-month survey period was between March and April 2016. Clinical data of all patients presenting to the Emergency Department were prospectively inserted in a structured medical chart review. Inclusion criterion was the presence of any recent-onset bleeding event regardless of ongoing treatment strategy and comorbidities. Exclusion criterion was age less than 18 years. Each patient gave informed consent to participate in the study and publication of personal data. The study was conducted in accordance with good clinical practice and principles of the Declaration of Helsinki. The Emergency Department Institutional Review Board of Careggi University Hospital of Florence and Apuane General Hospital of Massa-Carrara approved the protocol. Departmental sources supported the work and no contributorship or competing interest existed.

Data collection and management of patients

Subgroup analysis based on clinical variables, major or minor bleeding, site of bleeding, ongoing anti-thrombotic treatment strategy, need of reversal treatment or transfusion, and adverse outcomes including admission to hospital and death were prospectively collected. Major bleeding was defined according to the statement of the International Society of Thrombosis and Haemostasis [6,7]. All the patients underwent clinical evaluation, serial blood tests and ECG, on presentation. Clinical data, comorbidities and pharmacological treatment were self-reported and confirmed after reviewing the clinical charts. The direct oral anticoagulants considered in the study and used by study participants were dabigratan, rivaroxaban, apixaban and edoxaban; the vitamin-k-antagonist considered in the study was warfarin. Patients were most likely to submit to instrumental evaluation, observation or discharged on the basis of clinical evolution. The therapeutic approach and disposition were at the discretion of the physician on duty. All the patients with haemodynamic instability were considered for reversal treatment and blood transfusion, and eventually admitted. Haemodynamic instability was defined according to latest version of the guidelines in "Adult Advanced Cardiovascular Life Support 2010., American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care [9], and by the presence of systolic blood pressure less than 100 mmHg, associated with cutaneous or neurological or renal signs of tissue hypoperfusion; or with eventually reduction of the usual systolic blood pressure value of 40 mmHg, at least.

Endpoint

The primary endpoint was in-hospital death; secondary endpoints were the composite of admission and death and the composite of need of reversal treatment or transfusions.

Statistical analysis

Summary data are expressed as absolute numbers and percentage for categorical variables while mean ± SD for continuous values. Statistical comparisons of demographic and clinical features were performed using the χ^2 test and the Pearson exact test for categorical variables, whereas the Student's t-test was used for continuous variables (Wilcoxon rank-sum test). P-values <0.05, from a two-sided test, were considered to indicate statistical significance. Cox analysis regression model was performed to identify independent predictors for primary end point. Sensitivity analyses using backward logistic regression for all the clinical variables and comorbidities considered in the study were carried out; the clinical variables which were found to have a probability value <0.05 were subjected to multivariate backward logistic regression analysis. Receiver Operator Curve analysis was obtained for patients presenting with major bleeding and for patients who died during in-hospital stay. Calculations were performed using SPSS version 21(SPSS Inc., Chicago, Illinois, USA) for all analyses.

Results

Study population

Out of 155,320 visits, 2,592(1.7%) patients presented to the Emergency Department with any bleeding events were analyzed. Mean age was 64.9 ± 20.3 year (range 18-105 year), and female numbers were 911(35.1%). The chart of time to clinical evaluation, management and main outcomes during in-hospital stay in patients presented with any bleeding event is shown in the Figure 1. Overall 179(6.9%) patients received reversal treatment or blood transfusion as follows: reversal treatment (108, 4.2%), transfusions (86, 3.4%) and vitamin K (30, 1.2%); Of these, one-third were given ongoing antitrombotics; 59(21.5%) patients received anticoagulants (p<0.001 versus others) and 43(10.9%) were given antiplatelets (p=0.049 versus others). Overall, one in four patient needed prolonged in-hospital stay as follows; 193(7.4%) patients needed observation and 503(19.4%) needed admission. In-hospital death accounted for 30(1.2%) patients. Baseline clinical characteristics and outcomes of patients stratified according to the presence of major or minor bleeding are shown in the Table 1. Values of mean age, female gender, heart rate, systolic arterial pressure, creatinine, haemoglobin, treatment with aspirin, warfarin, anti-platelets,

anticoagulants but direct oral anticoagulants were higher in patients presented with major bleeding as compared to minor bleeding. Patients stratified according to the different sites of bleeding are shown in the Figure 2.

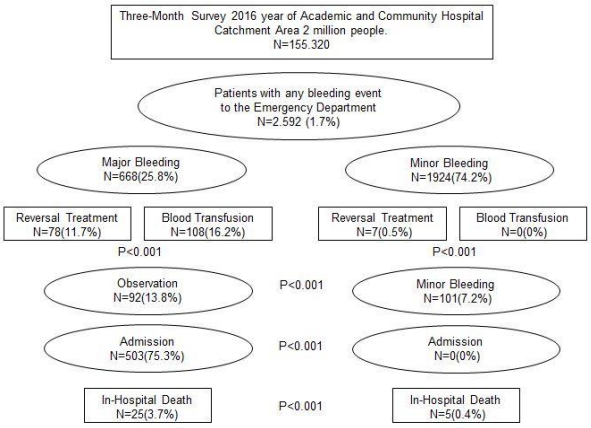

Figure 1: The chart of time to clinical evaluation, management and main outcomes during in-hospital stay in 2,592 patients presented with any bleeding events to the Emergency Departments of Tuscany HealthCare.

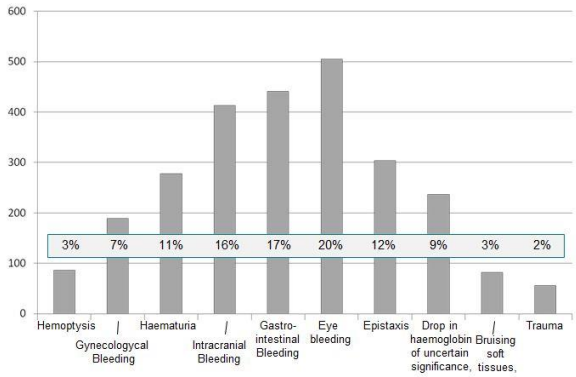

Figure 2: Patients stratified according to the different sites of bleeding (n=2592).

Of note, gastro-intestinal bleeding and intra-cranial bleeding account for 20% and 17%, respectively. Outcomes of patients stratified according to the different sites of bleeding of major clinical interest are shown in the Figure 3.

In patients with gastro-intestinal bleeding and intra-cranial bleeding death account for 0.7% and 5%, respectively; the composite of reversal treatment or blood transfusion for 20.5% and 93.6%, respectively; the composite of death or admission in 57.8% and 90.3%, respectively.

Bleeding events and pharmacological treatment strategies

Bleeding events based on pharmacological treatment in patients with ongoing antiplatelets or anticoagulants are shown in Figure 4. Of note, among anticoagulants, 115 patients received low molecular weight Heparin, 155 received Warfarin, 10 Dabigratan, 21 Rivaroxaban, and 10 Apixaban; Among antiplatelets, 334 patients received Aspirin and 106 Clopidogrel. Overall, patients who received antithrombotics were more likely to show major bleeding events when compared to others (Table 1).

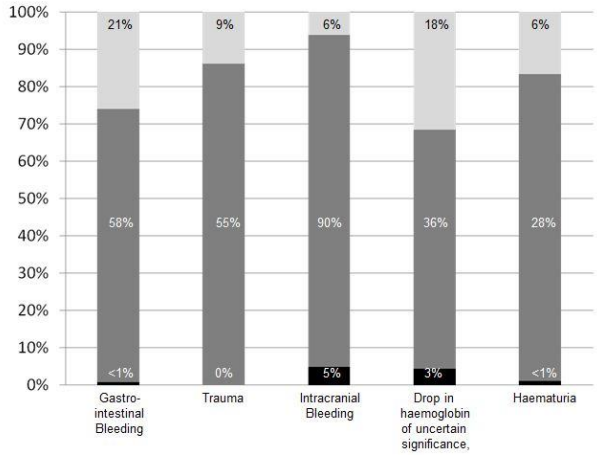

Figure 3: Outcomes of patients stratified according to the different sites of bleeding of major clinical interest (n=2,592).

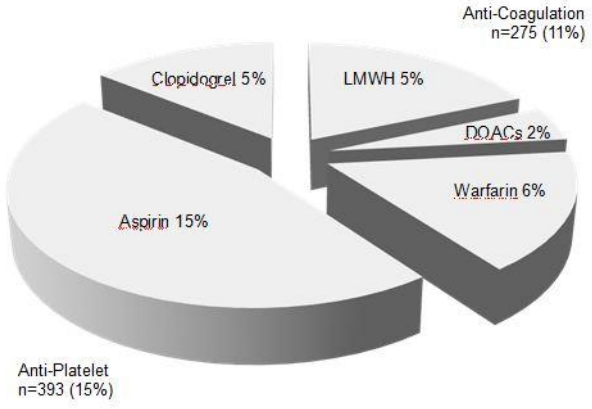

Figure 4: Bleeding events based on pharmacological treatment in patients with ongoing antiplatelets or anticoagulants; antiplatelets, n=393, including patients with both Aspirin and Clopidogrel; anticoagulants, n=275, including patients with overlap with LMWH and anticoagulation.

However, among the 668 major bleeding reports, patients taking antiplatelets showed higher rate of events when compared to patients taking anticoagulants (171 versus 127, respectively; $p<0.005$). Of note, from the patients taking anticoagulants, 64 major bleeding occurred in patients taking Low Molecular Weight Heparin (9.6% of major bleeding and 55.7% in patients taking Low Molecular Weight Heparin); 63 in patients taking Warfarin (9.4% and 40.6%, respectively); 18 in patients taking direct oral anticoagulants (2.7% and 43.9%, respectively); of which 6 in patients taking Dabigratan (0.9% and 60.0%, respectively); 7 in patients taking

Rivaroxaban (1.0% and 33.3%, respectively); 5 in patients taking Apixaban (0.8% and 50%, respectively).

	Total (n=2592)	**Major Bleeding (n=668)**	**Minor Bleeding (n=1396)**	**p value**
Mean Age (years ± SD)	64.9 ± 20.3	72.5 ± 17.3	62.3 ± 20.3	<0.001
Systolic Arterial Pressure, (mean ± SD; mmHg)	137 ± 26	134 ± 24	136 ± 20	<0.001
Female Gender, n(%)	911 (35.1)	253 (37.9)	636 (45.6)	0.001
Heart Rate, (mean ± SD; bpm	81±15	82 ± 17	78 ± 13	0.001
Creatinine (mean ± SD; mg/dL)	1.07±0,75	1.11 ± 0.74	1.00 ± 0.54	0.002
Haemoglobin, g/dL	12.1±2.5	11,6 ± 2,9	12.5 ± 2.1	<0.001
Aspirin, n(%)	394 (15.2)	145 (21.7)	187 (13,4)	<0.001
Warfarin, n(%)	160 (6.2)	63(9.4)	92(6,6)	0.025
DOACs, n(%)	41(1,6)	18 (2.7)	23 (1.6)	0.129
Anti–platelets, n(%)	393 (15.2)	171 (25.6)	222 (15.9)	<0.001
Anti-coagulants, n(%)	275(10.6)	127 (19.0)	147 (10.5)	<0.001

Table 1: Baseline clinical characteristics and outcomes of 2,592 patients stratified according to the presence of major or minor bleeding.

Among patients taking antiplatelets, 145 major bleeding occurred in patients taking Aspirin (21.7% and 43.7%; respectively) and; 47 in patients taking Clopidogrel (7.0% and 44.3%, respectively). When patients taking Low Molecular Weight Heparin, Warfarin, Aspirin and Clopidogrel were compared to others statistical analysis showed p=0.010; conversely, patients taking oral direct anticoagulants when compared to others showed non- significance (p=0.129).

Predictors of adverse outcome and Receiver Operator Characteristics (ROC) analysis

The independent predictors of the primary (in-hospital death) and the secondary endpoints (the composite of in-hospital death or admission) and (the composite of reversal treatment and blood transfusion) in the cohort of patients presented to the Emergency Department with any bleeding events are showed in the Table 2.

Independent predictors of in-hospital death						
	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*p value*	OR	95% CI	*p value*
Major Bleeding	10.8	4.12–28.4	<0.001	6.77	2.33-19.69	<0.001
Age ≥ 65 year	6.04	1.83–19.9	0.003	3.13	0.93-10.55	0.066
Age	1.05	1.02–1.08	0.001			
Systolic Arterial Pressure	1.01	1.00–1.03	0.032			
Anti-Platelets	2.15	1.00-4.64	0.050			
Independent predictors for the composite of in-hospital death and admission						
	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*p value*	OR	95% CI	*p value*
Major Bleeding	101.8	74.3–139.0	<0.001	36.9	26.1-52.2	<0.001
Age	1.05	1.02–1.08	0.001	1.01	1.00-1.02	0.004
Male Gender	0.69	0.57-0.83	<0.001			
Anti-Platelets	2.02	1.61-2.52	<0.001			
Creatinine	1.39	1.11-1.73	0.003			
Anti-Coagulants	1.93	1.49-2.49	<0.001			
Independent predictors for the composite of reversal treatment and blood transfusion						
	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*p value*	OR	95% CI	*p value*
Major Bleeding	68.8	32.1–147.5	<0.001	38.2	16.5-88.6	<0.001
Warfarin	5.21	3.53-7.70	<0.001	5.82	3.42-9.91	<0.001
Age	1.031	1.02–1.04	<0.001			
Anti-Coagulants	3.83	2.71-5.39	<0.001			
Creatinine	1.31	1.07-1.61	0.009			

Table 2: Independent predictors of the primary (in-hospital death) and the secondary (the composite of in-hospital death and admission) or (the composite of reversal treatment and blood transfusion) endpoints in the cohort of patients presenteding to the Emergency Department with any bleeding events (n=2.592).

On the multivariate analysis, only major bleeding was independent predictor of in-hospital death; major bleeding and age were independent predictors of the composite of in-hospital death or admission; major bleeding and warfarin were independent predictors of the composite of reversal treatment and blood transfusion. Receiver Operator Characteristics (ROC) analysis built for in-hospital death and major bleeding are shown in the Table 3. Age, major bleeding and systolic arterial pressure showed larger area as compared to other parameters when the curve was built for in-hospital death; age and creatinine showed larger area as compared to other variables when the curve was built for major bleeding.

Patients submitted to reversal treatment or blood transfusion according to treatment strategy

Among patients taking anticoagulants and who were submitted to reversal treatment or blood transfusion, 16 (8.9%) out of 117 were on low molecular weight Heparin (p=0.060 versus others), 44 (24.6%) out of 115 were on Warfarin (p<0.001 versus others), 3 (1.7%) out of 10 were on Dabigratan (p=0.006 versus others), 3 (1.7%) out of 18 were on Rivaroxaban (p=0.006 versus others), and 3 (1.7%) out of 10 were on Apixaban (p=0.006 versus others).

Endpoint: Death					
Variables	Area	Standard Error	Significance	95% Confidence Intervals	
				Inferior Limit	Superior Limit
Aspirin	0.548	0.063	0.431	0.424	0.672
Haemoglobin	0.494	0.066	0.925	0.364	0.624
Creatinine	0.528	0.069	0.648	0.392	0.663
Blood Transfusion	0.452	0.055	0.431	0.344	0.560
Reversal (Coagulation)	0.487	0.060	0.837	0.371	0.604
Anti-Platelets	0.527	0.062	0.658	0.405	0.649
Anti-Coagulants	0.514	0.062	0.815	0.393	0.635
DOACs	0.507	0.062	0.914	0.386	0.627
Age ≥ 65 year	0.622	0.050	0.045	0.524	0.720
Age	0.646	0.048	0.016	0.553	0.740
Systolic Arterial Pressure	0.645	0.076	0.017	0.497	0.793
Reversal treatment or Blood Transfusion	0.446	0.055	0.379	0.338	0.555
Major Bleeding	0.646	0.051	0.016	0.546	0.747
Endpoint: Major Bleeding					
Variables	Area	Standard Error	Significance	95% Confidence Intervals	
				Inferior Limit	Superior Limit
Male Gender	0.434	0.018	0.000	0.399	0.469
Age	0.622	0.017	0.000	0.588	0.656
Systolic Arterial Pressure	0.528	0.018	0.122	0.493	0.563
Warfarin	0.494	0.018	0.717	0.458	0.529
DOACs	0.499	0.018	0.976	0.464	0.535
Aspirin	0.506	0.018	0.726	0.471	0.541
Haemoglobin	0.426	0.018	0.000	0.391	0.460
Creatinine	0.551	0.018	0.005	0.516	0.585
Anti-Platelets	0.510	0.018	0.587	0.475	0.545
Anti-Coagulants	0.504	0.018	0.818	0.469	0.539
Age ≥ 65 year	0.586	0.018	0.000	0.551	0.620

Table 3: Receiver Operator Characteristics (ROC) analysis built for death and major bleeding in patients presenting with any bleeding events to the Emergency Departments (n=2.592).

Among patients taking antipaltelets and who were submitted to reversal treatment or blood transfusion, 36 (20.1%) out of 334 were on Aspirin (p=0.137 versus others), and 14 (7.8%) out of 106 were on Clopidogrel (p=0.108 versus others). Among patients submitted to reversal treatment or blood transfusion, 19.6% were submitted to observation and 52.5% were admitted. Of note, only 2.2% of all patients who were given reversal treatment or blood transfusion died (p=0.321).

Discussion

The present large prospective multicenter study, based on nine academic or community hospitals in Tuscany, with a catchment area of 3 million inhabitants, and approximately half a million visit per year, shows a picture update of the real life of any bleeding events in patients presented to the Emergency Department. Patients were enrolled irrespective to comorbidities or ongoing treatment strategy including antithrombotic. To the best of our knowledge, the present

study is the first that investigates the incidence of any bleeding in a population-based survey.

General results show low rate of in-hospital mortality. Death was driven by major bleeding regardless of any treatment strategy. Final disposition shows that about one in ten patients received reversal treatment or blood transfusions, and one in four needed prolonged in-hospital stay, facing high impact on health resources. Interestingly, patients with ongoing antiplatelet medication were more likely to show bleeding events and patients with anticoagulants were more likely to receive reversal treatment or blood transfusion. Of these, one in five was submitted to observation and one half was admitted, suggesting a pivotal role of ongoing treatment strategy in determining poor outcomes. Overall, bleeding events of clinical interest like gastro-intestinal and intra-cranial bleeding account for one in three. As expected, intracranial bleeding was associated with high incidence of death (5%) and admission (90%). Eventually, Receiver Operator Characteristics (ROC) shows larger areas of age, major bleeding and systolic arterial pressure versus areas of others variables, when built for in-hospital death; age and creatinine, when built for major bleeding.

Very few studies were reported discussing the incidence of bleeding in general population presented to the Emergency Department with bleeding as the main reason of presentation. The report of "The National Surveillance of Emergency Department Visits for outpatient drug event" showed that warfarin and aspirin have gained the first places as cause of visit to the Emergency Department, and the "Emergency Hospitalizations for Adverse Drug Events in Older Americans" showed that warfarin have gained the first place in the hospitalization for adverse drug events in older population, at least [10,11].

Only some Authors have published studies with comparison of major bleeding events among patients treated with old and new anticoagulation regimens in prevention of stroke. In the recent report "Management and outcomes of bleeding events in patients in the emergency department taking warfarin or a non-vitamin k antagonist oral anticoagulant", 437 patients presented to the Emergency Department of a large suburban medical center with an annual Emergency Department census of roughly 100,000 were identified, during a period of about three years [12]. Mortality was low and outcomes were comparable among patients with gastrointestinal or intracranial haemorrhage taking direct oral anticoagulants when compared with warfarin. However, the overall case fatality rate was higher for intracranial haemorrhage. Also in the "Major bleeding with vitamin K antagonists or direct oral anticoagulant in real-life", similar results in patients outside clinical trials were reported [13]. Admission for gastrointestinal major bleeding was more frequent for direct oral anticoagulants as compared to vitamin-k antagonist patients and mortality was lower in patients with major bleedings while on direct oral anticoagulants than vitamin-k antagonist, but this finding varies across different types of major bleedings. In addition, the survey of Swiss general internal medicine practitioners on anticoagulation shows that bleeding complications were rare in the population submitted to anticoagulation and could mostly be handled without hospital admission [14].

Many authors have published large trials dedicated to compare warfarin and direct oral anticoagulants in prevention of systemic or pulmonary embolism. A meta-analysis that included more than seventy thousands patients with atrial fibrillation showed direct oral anticoagulants significantly reduced all-cause mortality up to 10% and intra cranial haemorrhage up to 48% when compared with warfarin, however gastrointestinal bleeding increased up to 25% [8]. Another two meta-analysis both of about fifty thousands patients with atrial fibrillation found that direct oral anticoagulants significantly reduced the risk of intra cranial haemorrhage when compared to warfarin and without no significant difference among the different direct oral anticoagulants [15,16].

In addition, a meta-analysis of 20 trials found that fatal bleeding was more likely to be associated with warfarin, favoring the direct oral anticoagulants who showed an odds ratio of 0.65 [17]. Laliberte and coworkers matched 3654 patients on rivaroxaban to 14,616 patients on warfarin from a claims database and found similar rates of major, intracranial, and gastrointestinal bleeding [18]. With regard to gastrointestinal bleeding, most studies have found an increased risk among patients taking direct oral anticoagulant. A meta-analysis of 43 controlled trials including 151,578 patients compared the rates of gastrointestinal bleeding among patients treated with warfarin or a direct oral anticoagulant [19]. The overall odds ratio for gastrointestinal bleeding among patients taking a direct oral anticoagulant was 1.45. In contrast, a retrospective, propensity-matched cohort of near one-hundred thousand patients taking an anticoagulant outside of well-controlled trials found that the risk of gastrointestinal bleeding related to direct oral anticoagulants was similar to that of warfarin [20]. However, among patients older than 75 years receiving direct oral anticoagulants, the risk of gastrointestinal bleeding was greater than for warfarin. Therefore, the risk of gastrointestinal bleeding differs by age.

Although all these studies contribute to confirm the link between antithrombotics and the risk of bleeding, additional investigation are needed in the setting of the general population. Indeed, the real incidence of presentation to the Emergency Department due to any bleeding in the real-life is still lacking.

Clinical utility of the results of the present study

The present study provides a real-life picture of the impact of minor and major bleeding events presented to the ED and confirms that bleeding events are relatively frequent and need observation and admission as far as supraventricular arrhythmias to the Emergency Department [21]. Our study confirms previous reported data in terms of overall mortality, mortality in special subset as patients with intracranial haemorrage, use of reversal treatment including reversal factor, factor replacement, transfusion or fresh frozen plasma. Moreover, the present study adds to the body of evidence that relatively low mortality rate, except for intra cranial bleeding, affects patients with bleeding event beyond comorbidities and

older age;. In addition, it suggests that bleeding patients, especially those who were given antiplatelets or anticoagulants, were more likely to undergo prolonged in-hospital stay, and to need reversal treatment or transfusion, at least. However, the present study suggests that physicians on duty in the Emergency Department should be comfortable managing bleeding patients also when taking antithrombotics.

Limitations and Strengths

The present study has some limitations. Our study is limited to patients of a single country with relatively few cases and may not be representative of other dissimilar settings. We included patients with any bleeding events and not just those events considered to be major (28). However, the study was designed to estimate case fatality rates in those who suffered a minor or major bleeding event. A relatively small number of patients with ongoing direct oral anticoagulants treatment. Eventually, we are aware of the imprecision in the estimation of the population-based real incidence of bleeding events because we did not know how many patients received anticoagulants in the same territory of the study.

Strengths are represented by the large series of consecutive participants; the hard endpoint represented by in-hospital mortality; the multicenter design of the study, the prospective design, and the large catchment area with 3 million inhabitants involved.

Conclusions

Out of one-hundred and fifty-thousand visits to the Emergency Department, less than 2% claims any bleeding events, during three-month survey in a catchment area of 2 million inhabitants. Major bleeding account for one in four. Patients with on-going antithrombotics were more likely to receive reversal treatment or transfusion. Overall, in-hospital death was low and account for 1.2%. Major bleeding was more likely to predict primary and secondary endpoints; age was more likely to predict the composite of death or admission; warfarin was more likely to predict the composite of reversal treatment or blood transfusion. One in four patients needed prolonged in-hospital stay.

Conflicts of Interest

The Authors declare no potential conflicts of interest. Departmental sources supported the work.

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