Health Services Research

Shorter Hospital Stay and Fewer Hospitalizations in Patients With Visible Hematuria on Direct Oral Anticoagulants Compared to on Vitamin K Antagonists

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OBJECTIVE To investigate the influence of type of anticoagulation − direct oral anticoagulants (DOAC) vs vitamin K antagonists (VKA) − on length of hospital stay (LOS) and hospitalization rates in patients with visible hematuria, as visible hematuria in anticoagulated patients can be distressing, difficult to control and even life-threatening.

METHODS This retrospective cohort study was conducted at the emergency department (ED) of a tertiary university hospital in Switzerland. All patients admitted with visible hematuria from January 1, 2013 to December 31, 2016 were included. We compared the primary clinical outcome parameters (hospitalization rate and LOS) as well as secondary outcomes (ICU admission, ED LOS, and in-hospital mortality) in patients with visible hematuria on either DOAC therapy, VKA therapy or no anticoagulants.

RESULTS We included 811 (100%) patients with visible hematuria; 53 (6.5%) patients were on DOAC, compared to 85 (10.5%) on VKA and 673 (83.0%) patients without any anticoagulation. In confounder-adjusted multivariable testing, there were fewer hospitalizations (odds ratio: 2.2, 95% confidence interval [CI]: 1.1-4.9, $P = .028$) and shorter LOS (geometric mean ratio: 2.2, 95% CI: 1.3-4.0, $P = .006$) on DOAC than on VKA. The secondary outcomes were not significantly associated with the anticoagulation groups. No differences were found between the DOAC and no-anticoagulant groups for any outcome.

CONCLUSION Visible hematuria in patients on DOAC therapy is associated with shorter hospital stays and fewer hospitalizations compared to VKA. UROLOGY 00: 1−8, 2019. © 2019 Elsevier Inc.

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Hematuria is responsible for up to a third of emergency urological referrals, and up to two-thirds of admitted patients with hematuria are reported to be on anticoagulation.[1-3] Visible hematuria can be difficult to control and life-threatening, particularly in anticoagulated patients.[4,5] A recent large retrospective cohort study from Canada included older adults and demonstrated higher rates of hematuria-related complications with than without antithrombotic medications.[5] Furthermore, hematuria can be distressing for the patient and consequently might lead to poor compliance with the anticoagulant therapy, an increased risk of stroke and even death.[6−8]

The most recent review on visible hematuria and oral anticoagulant medication suggested that there is an increased risk of potentially life-threatening major hematuria in patients on therapy with direct oral anticoagulants (DOACs).[4] However, this conclusion was based on the pooled analysis of only 33 DOAC patients in more than

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175,000 patients on antithrombotic therapy. Although there have been extensive studies on the classical vitamin K antagonist (VKA) warfarin, little is known about visible hematuria in patients on the new DOACs. This is an important omission, as current guidelines on anticoagulant treatment in venous thromboembolism and atrial fibrillation support the use of DOACs rather than VKA, so that the prevalence of DOACs in emergency admissions has rapidly increased.[9-11]

The present study therefore investigated the length of hospital stay (LOS) and hospital admission rate as primary outcomes in visible hematuria patients on DOACs − in comparison to patients on (1) VKA and (2) without any anticoagulant medication. The secondary outcomes were in-hospital mortality, length of emergency department (ED) stay, and admissions to the intensive care unit (ICU).

METHODS

Study Design and Setting

This retrospective cohort study was set in the adult ED of Bern University Hospital (Inselspital), Switzerland, a self-contained, interdisciplinary department treating patients aged 18 years and older.

Inclusion Criteria

All patients were included who were admitted from January 1, 2013 to December 31, 2016 to our ED with a diagnosis of visible hematuria.

Exclusion Criteria

The following exclusion criteria were used:

- No signs of visible hematuria, eg, micro hematuria,
- Visible hematuria in the history, but not current,
- Elective, clinical control after emergency consultation,
- Nonspecified hematuria or insufficient information for inclusion ie, missing diagnosis.

For the sake of legibility, the expression "visible hematuria" is replaced throughout by "hematuria".

Study Outcomes

The primary outcomes were hospitalization rate and length of stay (LOS), defined as time in hospital. Secondary outcomes were ICU admission, length of ED stay (defined as time in ED) as well as in-hospital mortality.

Data Collection and Extraction

A full text search in the medical database of the ED (E.care, Turnhout, Belgium) was performed for the keywords "hematuria" (and spelling variants) from January 1, 2013 to December 31, 2016. The patient histories and diagnoses were analyzed in full text to test the eligibility criteria and to determine study inclusion.

Patient characteristics (age, gender), characteristics of patient ED interaction (admission type and triage category) and investigated study outcomes were extracted from the medical database. Triage in our ED is made by registered nurses using the Swiss triage scale.[12] Furthermore, laboratory results from the ED evaluation were collected (ie, creatinine, international normalized ratio [INR], hemoglobin [Hb], and platelets).

The following medical data were extracted manually from the full text ED records: indication for oral anticoagulation, additional therapy with platelet aggregation inhibitors, type of platelet aggregation inhibitor therapy, abdominal trauma, current abdominal pain, pre-existing structural urological conditions (nephrostomy, ileum conduit, and permanent bladder catheter), and previous (<7 d) invasive urological intervention (eg, recent bladder, renal or prostate surgery). To classify the comorbidity of the included patients, the Charlson Comorbidity Index was determined,[13] with full-text analysis of the diagnosis (including diabetes mellitus, liver disease, malignancy, AIDS, chronic kidney disease, chronic heart failure, COPD, peripheral vascular disease, dementia, peptic ulcer disease, connective tissue disease, cerebrovascular disease, hemiplegia, infarction as well as age). Additionally, the characteristics of hematuria were described, including recurrent bleeding, dysuria, associated urogenital infection, pre-existing urological tumor (including bladder, prostate, or renal malignancy), start of hematuria, urine blood clot, bladder tamponade, urinary retention, treatment (observational, lavage catheter, or emergency operation), and blood transfusion.

The definition of a "major hematuria" is inconsistent in the urological literature.[4] In order to give an impression of the extent and severity of hematuria, 2 definitions of severe hematuria used in the literature are presented in this manuscript: (1) "major hematuria" defined by the presence of bladder tamponade or placement of a lavage catheter, (2) "relevant hematuria" defined by the need of hospital admission or the need of blood transfusion.

Exposure

In order to determine anticoagulation status on arrival, the identified full text records were manually screened for VKA medications − "acenocoumarol", "phenprocoumon", or "warfarin" − as well as DOAC medication − "apixaban", "dabigatran", "edoxaban", or "rivaroxaban". The included patients with hematuria were grouped by anticoagulant status (DOAC, VKA, and no anticoagulation).

Data Analysis

All statistical analyses were performed in Stata 13.1 (StataCorp, The College Station, TX) and statistical significance was defined as a P <.05. For descriptive analysis, proportion was accompanied by the total number in the category and continuous variables as medians with interquartile range (IQR). DOAC patients were compared to VKA patients or to patients without anticoagulant medication, with respect to different variables, using the Mann Whitney U or Fisher's exact tests, as applicable.

Potential confounders for multivariable modeling were identified by univariable testing. All identified confounders (with at least very weak evidence, defined as P <.2,[14] for an univariable association with type of anticoagulation using Kruskal Wallis respectively Fisher's exact tests,) were included in the multivariable model. Multivariable associations between study outcomes and the type of anticoagulation were analyzed by models of linear regression (continuous outcomes) or logistic regression (binary outcomes; odds ratios as a measure of strength of association), including potential cofounders. In order to allow multivariable linear regression, non-normally distributed data were log transformed. We therefore present the exponentiated coefficients of the regression analysis, as these correspond to the geometric mean (GM) ratio of the nonlog transformed values.

To test the robustness of our primary findings, we conducted sensitivity analysis, which varied the included variables in our

multivariable model by (1) including all potential confounders, (2) removing covariables that showed less than weak evidence ($P > .1$) to obtain the final model (backward selection), and (3) excluding all patients without anticoagulation in the final multivariable model.

The mechanisms of hematuria may be different for patients with trauma or urogenital infection compared to patients with chronic conditions or with hematuria of unknown mechanism. Subgroup analysis excluding trauma and urogenital infections was therefore performed.

Ethics

The need for informed consent was waived by the ethics committee of Canton Bern, Switzerland, as the patient data were anonymous and part of routine patient care. The study is registered with the responsible ethics committee under the number 073/2015.

RESULTS

Baseline Characteristics

The key word database search of all 131,229 patients admitted over the 4 years study period identified 3,229 ED admissions. Full text screening of the medical reports excluded 2,418 ED admissions, mostly due to missing signs of hematuria (n = 1,762) (eg, diagnosis of micro hematuria) or solely historical hematuria (n = 576). Finally, 811 (100%) patients could be included in the primary analysis. No included patient had more than one consultation in the study period with hematuria. Fifty-three (53, 6.5%) patients were on DOAC therapy (47 [88.7%] rivaroxaban, 5 [9.4%] apixaban, 1 (1.9%) dabigatran) and 85 (10.5%) on VKA therapy (82 [96.5%] phenprocoumon, 2 [2.4%] acenocoumarol, 1 [1.2%] warfarin). The median INR 2.4 (IQR 1.8-3.2) was in the therapeutic range in the VKA group.

Platelet-aggregation-inhibitor therapy was documented in 157 patients (19.5%). The predominant type of platelet-aggregation-inhibitor therapy was acetylsalicylate acid in all groups (for overview of all baseline characteristics, see Table 1).

Relevant hematuria was found significantly more often ($P = .011$) in anticoagulated patients (DOAC: 52.8%, VKA: 64.7%) than in patients without anticoagulation (no anticoagulation: 34.5%; for overview of all hematuria characteristics).

Identification of Potential Confounders

All potential confounders except for urolithiasis ($P = .942$), abdominal pain ($P = .295$), and therapy with platelet aggregation inhibitors ($P = .650$) showed at least very weak evidence ($P < .2$) for a difference between the three study groups and were therefore included in the multivariable model. The associations of all potential confounders with the type of anticoagulant are shown in Table 2.

Association of Clinical Outcomes and Type of Anticoagulant

In univariable analysis, the primary outcomes of hospitalization rate and length of hospitalization did not exhibit a significant association with the type of anticoagulant (VKA vs DOAC) ($P = .166$ and $P = .071$, respectively). There was a small number of deaths in all study groups without significant difference in mortality between the groups ($P = .456$). In-hospital mortality was therefore removed from the multivariable analysis. All univariable associations of the clinical outcomes with the type of anticoagulant are shown in Table 3.

After adjustment for associations with the identified confounders in the multivariable analysis, positive associations were identified between hospitalization rate (odds ratio [OR] 2.3; 95% confidence interval [CI]: 1.1, 4.9; $P = .027$) and LOS (GM 2.2 [95% CI: 1.3, 4.0], $P = .006$) and the type of anticoagulant (VKA compared to DOAC) (Table 4). The number of urological interventions performed, were not significantly different in both groups (DOAC 13 [46.4%] vs 21 [38.2%], $P = .275$).

The most common reasons for hematuria reported in hospitalized patients in the DOAC and VKA group were unspecific OAK-related bleeding (DOAC 5 [17.9%] vs VKA 19 [34.5%]), neoplasm (DOAC 9 [32.1%] vs 9 16.4%]), and infection (DOAC 3 [10.7%] vs 12 [21.8%]) without significant difference between the groups ($P = .306$).

No significant associations ($P = .977$ and $P = .998$) were found between the primary outcomes and the group with no anticoagulation compared to DOAC.

The secondary outcomes did not exhibit any significant association with the anticoagulation groups in confounder-adjusted multivariable analysis.

Sensitivity Analysis

Analysis of sensitivity in confounder-adjusted multivariable analysis showed that the significant positive associations between hospitalization and LOS and the type of anticoagulant (VKA compared to DOAC) were robust (presented as Supplementary Table 1-3)

Confounder-adjusted Multivariable Subgroup Analysis After Exclusion of Trauma and Urogenital Infections

After exclusion of all patients with a documented urogenital infection or trauma, there remained a subgroup including 43 patients with DOAC, 64 patients with VKA anticoagulation, and 370 patients with no anticoagulation. Restriction of the analysis to these patients enhanced the previously identified positive associations between hospitalization rate (OR 2.8 [95%: CI 1.2, 6.6], $P = .017$) and LOS (GM 2.7 [95% CI: 1.4; 5.3], $P = .004$) and the type of anticoagulant (VKA compared to DOAC) (Supplementary Table 4).

DISCUSSION

In confounder-adjusted multivariable testing, our study found fewer hospital admissions as well as shorter LOS in hematuria patients seen in the ED on DOAC than on VKA. The length of stay in ED, ICU admissions as well as in-hospital mortality – the secondary outcomes – did not differ significantly between the DOAC and VKA groups.

Primary Outcomes: Hospitalization Rate and LOS

In confounder-adjusted multivariable modeling, our study identified a nearly three-fold increase in the odds for hospitalization and a similar increase in LOS for patients on VKA therapy compared to patients on DOAC. As in-hospital patient treatment is a relevant cost-factor compared to outpatient medicine, these findings may not only be of benefit for the treatment of the individual patient but can also contribute to a reduction in the financial burden on the healthcare system from bleeding complications.

Table 1. Baseline and hematuria characteristics of the study cohort according to type of anticoagulant

Characteristics	DOAC	VKA	*P**	No Anticoagulant Therapy	*P**
Patient data					
N	53 (100.0)	85 (100.0)	—	673 (100.0)	—
Age (years)	77 (65-85)	73 (66-80)	.175	52 (33-71)	<.001
Admission					
Walk-in	24 (45.3)	43 (50.6)		471 (70.0)	
GP referral	7 (13.2)	17 (20.0)		62 (9.2)	
Out-patient	7 (13.2)	14 (16.5)		41 (6.1)	
Secondary transfer	15 (28.3)	11 (12.9)	.159	99 (14.7)	.002
Triage category	3 (2-3)	3 (2-3)	.673	3 (3-3)	<.001
Indication for anticoagulant therapy					
Atrial fibrillation	18 (33.3)	35 (40.7)		—	—
Thromboembolic event	18 (33.3)	22 (25.6)		—	—
Mechanic heart-valve	1 (1.9)	17 (19.8)		—	—
Post-surgery	1 (1.9)	0 (0)		—	—
Other	10 (18.6)	6 (7.0)		—	—
Not documented or unknown	6 (11.1)	6 (7)	.003	—	—
Additional platelet-aggregation-inhibitor therapy[#]					
Acetylsalicylate acid	10 (18.9)	12 (14.0)		110 (16.3)	
Clopidogrel	2 (3.8)	3 (3.5)		20 (3.0)	
Prasugrel	0 (0.0)	0 (0.0)		1 (0.2)	
Ticagrelor	0 (0.0)	0 (0.0)		1 (0.2)	
None	41 (77.4)	71 (83.5)	.621	541 (80.2)	.741
Laboratory data					
Creatinine (μmol/L)[+]	100 (85-125)	99 (80-137)	.823	82 (68-107)	.002
INR[+]	1.1 (0.9-1.3)	2.4 (1.8-3.2)	<.001	0.9 (0.9-0.9)	<.001
Hemoglobin (g/L)[+]	121 (103-139)	123 (106-143)	.302	133 (120-145)	.002
Platelets (G/l)	226 (190-280)	214 (159-291)	.425	233 (190-286)	.661
Hematuria characteristics					
Recurrent bleeding	20 (37.7)	25 (29.4)	.353	145 (21.6)	.010
Visible hematuria start [d][+]	1 (0-3)	1 (0-4)	.656	0 (0-1)	.053
Blood clot	6 (11.3)	20 (23.5)	.116	131 (19.5)	.200
Tamponade	6 (11.3)	9 (10.6)	1.000	78 (11.6)	1.000
Urinary retention	7 (13.2)	12 (14.1)	1.000	104 (15.5)	.843
Relevant hematuria	28 (52.8)	55 (64.7)	.211	232 (34.5)	.011
Major hematuria	17 (32.1)	25 (29.4)	.849	150 (22.3)	0.126
Dysuria	6 (11.3)	25 (29.4)	.020	291 (43.2)	<.001
Treatment					
Observational (wait & see)	36 (67.9)	63 (74.1)		537 (79.8)	
Lavage catheter	16 (30.2)	20 (23.5)		127 (18.9)	
Surgical (emergency operation)	1 (1.9)	2 (2.4)	.747	9 (1.3)	.089

DOAC, direct oral anticoagulant; N, number; VKA, Vitamin K antagonists.
Median (interquartile range) or number (percentage) as appropriate.
* Mann Whitney U or Fisher's exact test of the comparison between group of columns left of p value with DOAC group as applicable.
[#] Any patient may be on more than one medication.
[+] Missing values in percent (DOAC, VKA, no anticoagulation): Creatinine (9.4%, 9.4%, 24.7%); INR (9.4%, 9.4%, 28.7%); Hemoglobin (7.6%, 10.6%, 24.1%), Visible hematuria start (11.3%, 15.3%, 8.0%).

The findings were (1) robust in subgroup analysis performed to exclude the influence of the potential differences in mechanism of hematuria in trauma and urological infections (Supplementary Table 4) and (2) could also be confirmed in multiple sensitivity analyses with variations in the multivariable modeling (Supplementary Table 1-3). In addition, we did not find a difference in urological procedures between both groups nor in the definitive cause of hematuria that may explain this finding.

One of the reasons contributing to the presented finding may be that DOAC have shorter half-lives than VKA and that stopping DOAC therapy is known to be sufficient in most bleeding situations.[15] In contrast to this, bleeding events on VKA therapy frequently warrant reversal of anticoagulant therapy.[15] In contrast to this, VKA therapy must be restarted carefully, often in an in-hospital setting.

This finding in hematuria patients is consistent with the shorter LOS and fewer hospital admissions that had also been demonstrated in our ED population for other bleeding complications (epistaxis patients) on DOAC compared to VKA.[16] Other factors that may influence the risk of bleeding risk in patients on anticoagulant drugs include problems with medication compliance, variations in individual anticoagulant effect or acute variations in renal function that may lead to nontherapeutic DOAC concentrations. Unfortunately, measurement of DOAC concentrations is not part of routine ED evaluation and the time point of the last intake of DOAC is often

Table 2. Potential confounders of the association type of anticoagulant and length of hospital stay/hospitalization

	DOAC	VKA	P*	No Anticoagulant Therapy	P+
Gender (female)	11 (20.8)	22 (25.9)	.543	251 (37.3)	.008
Therapy with platelet aggregation inhibitors	12 (22.6)	14 (16.5)	.380	132 (19.6)	.650
Abdominal trauma	1 (1.9)	1 (1.2)	1.000	49 (7.3)	.028
Abdominal pain	22 (41.5)	33 (38.8)	.858	317 (45.1)	.295
Charlson Comorbidity Index	6 (4-10)	5 (3-7)	.019	2 (0-5)	<.001
Pre-existing structural urogenital condition	18 (34.0)	18 (21.2)	.113	94 (14.0)	.001
Urolithiasis	4 (7.6)	8 (9.3)	.767	65 (9.7)	.942
Previous urological intervention	4 (7.6)	1 (1.2)	.072	31 (4.6)	.150
Urogenital tumor	39 (73.6)	14 (26.4)	.298	76 (11.3)	.003
Urogenital infection	9 (17.0)	20 (23.5)	.398	258 (38.3)	<.001

DOAC, direct oral anticoagulant; N, number; VKA, Vitamin K antagonists.
Median (interquartile range) or number (percentage) as appropriate.
* Mann Whitney U or Fisher's exact test of the group comparison: DOAC vs VKA.
+ Kruskal Wallis test or Fisher's exact test of the group comparison: all groups.

Table 3. Univariable outcome analysis of patients according to type of anticoagulant

Outcomes	DOAC	VKA	P*	No Anticoagulant Therapy	P*
Primary					
Hospitalization rate	28 (52.8)	55 (64.7)	.211	232 (34.5)	.011
Length of hospital stay, days	1.0 (0.2-4.0)	3.0 (0.2-7.0)	.071	1.0 (0.1-3.0)	.002
Secondary					
Admission ICU	4 (7.6)	9 (10.6)	.766	28 (4.2)	.283
Length of ED stay, min	251 (198-316)	267 (198-371)	.495	206 (142-306)	.004
In-hospital death	1 (1.9)	0 (0.0)	.384	7 (1.0)	.456

DOAC, direct oral anticoagulant; ED, emergency department; ICU, intermediate care unit; VKA, Vitamin K antagonists.
Median (interquartile range) or number (percentage) as appropriate.
* Mann-Whitney U or Fisher's exact test of the comparison between group of columns left of *P* value and DOAC group as applicable.

unknown. Therefore, we cannot exclude that a suboptimal compliance with DOAC therapy contributes to the results of our study. As compliance is a known major issue with many medications and skipping only one dose plays no role in VKA compared to DOAC, further research is needed on the inclusion of DOAC level measurements in clinical routine practice.[17] In contrast to this, INR measurements are part of routine evaluation and confirmed therapeutic VKA levels in the majority of our patients.

The combination of DOAC or VKA and inhibitors of platelet aggregation has been previously found to increase the risk of hematuria-related complications, including hospital admissions.[5] This association could not be replicated in our population as in our specific hematuria bleeding population, platelet aggregation inhibitor therapy did not turn out to be a significant confounder. Additional research on the combination of antithrombotic and DOAC medication in hematuria patients is warranted. Furthermore, future research could investigate the possibility of identifying patients with preconditions that are more vulnerable to hematuria with different types of anticoagulant.

In the comparison of DOAC with patients without anticoagulant medication, in univariable testing, we could demonstrate a significant difference between DOAC and no anticoagulation. In contrast to the comparison of DOAC and VKA, in multivariable testing, controlled for confounders identified in our investigation, the comparison of DOAC with patients without anticoagulant medication failed to demonstrate any significant difference for hospitalization or LOS.

This finding is inconsistent with the higher odds of hospitalization found by Wallis et al[5] for every anticoagulant medication. Older investigations — dating back to 1994 — found no association between anticoagulant use and hematuria but did not include the newer DOAC medications.[18] The reason for this finding cannot be conclusively clarified with our retrospective study. To investigate, if there might be additional confounders not included in our study or if the faster and easier procedure of stopping and restarting DOAC therapy compared to VKA contributes to this finding, further prospective research is necessary.

Secondary Outcomes: In-hospital Mortality, ICU Admission and Length of ED Stay

In the light of our main findings of increased LOS and hospitalization in VKA compared to DOAC patients, it is reassuring that (1) no patient died during ED care and only very few patients died in hospital — without any difference between the investigated groups, (2) no difference in ICU admission was found and (3) there were no significant difference in the length of ED stay for different anticoagulation status — probably because the ED treatment was similar.[15] This supports the evidence that implementation of local emergency guidelines is crucial for the management of anticoagulant bleeding.[15,19]

Table 4. Uni- and multivariable analysis for the (A) primary outcomes hospitalization and length of hospital stay and (B) secondary outcomes length of ED stay and ICU admission and DOAC vs VKA or DOAC vs no anticoagulation.

A) Hospitalization	Odds Ratio (95% CI)	*P*
Univariable		
DOAC vs VKA	1.64 (0.81, 3.29)	.167
DOAC vs no anticoagulation	0.47 (0.27, 0.82)	.008
Multivariable		
Group		
DOAC	1.0 (base)	
VKA	2.33 (1.10, 4.94)	.028
No anticoagulation	0.99 (0.53, 1.86)	.977
Gender [being female]	0.54 (0.37, 0.79)	.002
Abdominal trauma	2.87 (1.54, 5.32)	.001
Charlson Comorbidity Index [per point]	1.22 (1.16, 1.29)	<.001
Structural urogenital condition	0.68 (0.44, 1.06)	.087
Previous urological intervention	0.89 (0.43, 1.89)	.771
Urogenital infection	0.61 (0.41, 0.90)	.013
Length of Hospital Stay (log transformed)	**GM Ratio (95% CI)***	***P***
Univariable		
DOAC vs VKA	1.77 (0.95, 3.31)	.071
DOAC vs no anticoagulation	0.49 (0.28, 0.82)	.007
Multivariable		
Group		
DOAC	1.0 (base)	
VKA	2.24 (1.26, 4.00)	.006
No anticoagulation	1.00 (0.61, 1.64)	.998
Gender [being female]	0.67 (0.51, 0.88)	.005
Abdominal trauma	3.20 (0.38, 0.63)	<.001
Charlson Comorbidity Index [per point]	1.20 (1.15, 1.25)	<.001
Structural urogenital condition	0.68 (0.48, 0.96)	.025
Previous urological intervention	0.49 (0.39, 1.24)	.219
Urogenital infection	0.67 (0.50, 0.89)	.006
B) Length of ED Stay (log transformed)	**GM Ratio (95% CI)***	***P***
Univariable		
DOAC vs VKA	1.05 (0.89, 1.23)	.599
DOAC vs no anticoagulation	0.81 (0.68, 0.94)	.007
Multivariable		
Group		
DOAC	1.0 (base)	
VKA	1.07 (0.88, 1.29)	.486
No anticoagulation	0.9 (0.76, 1.06)	.194
Gender [being female]	0.89 (0.82, 0.98)	.014
Abdominal trauma	1.07 (0.91, 1.26)	.390
Charlson Comorbidity Index [per point]	1.03 (1.01, 1.04)	<.001
Structural urogenital condition	0.87 (0.78, 0.97)	.011
Previous urological intervention	0.85 (0.7, 1.02)	.084
Urogenital infection	0.87 (0.8, 0.96)	.005
ICU Admission	**Odds Ratio (95% CI)**	***P***
Univariable		
DOAC vs VKA	1.45 (0.42, 4.97)	.554
DOAC vs no anticoagulation	0.53 (0.18, 1.58)	.255
Multivariable		
Group		
DOAC	1.0 (base)	
VKA	1.74 (0.49, 6.24)	.394
No Anticoagulation	0.53 (0.16, 1.77)	.301
Gender [being female]	1.27 (0.57, 2.82)	.562
Abdominal trauma	16.20 (6.86, 38.27)	<.001

Continued

Table 4. Continued

ICU Admission	Odds Ratio (95% CI)	*P*
Charlson Comorbidity Index [per point]	1.10 (0.98, 1.23)	.108
Structural urogenital condition	1.39 (0.59, 3.29)	.449
Previous urological intervention[#]	—	—
Urogenital infection	0.67 (0.15, 1.23)	.114

CI, confidence interval; DOAC, direct oral anticoagulant; ED, emergency department; GM, geometric mean; ICU, intensive care unit.
* All coefficients are expressed as exponentials to correspond to the GM ratio.
[#] Predicts failure perfectly and was dropped from the analysis together with 36 non used consultations

Emergency physicians should know about the pros and cons of the different anticoagulant medications in order to counsel the patient and his/her treating physician as anticoagulation is frequent in ED patients.

Limitations

As our investigation is limited to ED admissions of one single center, the transferability to other patient populations remains unknown and warrants further investigations.

Documentation bias cannot be completely excluded in any retrospective investigation, despite careful review of all included data. Because this is a retrospective study, missing data cannot be completely avoided despite great efforts to guarantee the completeness of the data extraction and to keep the number of missing values as low as possible. Nevertheless, these biases can be assumed to be equally distributed between all patients groups and are therefore most likely not to compromise the conclusion of this study.

The distribution of the difference DOACs, with rivaroxaban being the DOAC with the highest prevalence in our data, reflects the DOAC distribution in our population.[10] The general prevalence of patients on anticoagulation is also mirrored in group size of anticoagulation vs no-anticoagulation group.

Further prospective multicenter investigations are recommended. These should include more patients on different DOACs. DOAC levels should be measured, to evaluate the influence of possible medication interactions[20] or medication compliance as well as the timing of last medication intake.

CONCLUSION

Visible hematuria is associated with a lower risk of hospitalization together with shorter LOS in patients on DOAC compared to patients on VKA therapy. This finding may help the clinician to select anticoagulant therapy for patients at risk for hematuria.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.06.004.

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