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Direct oral anticoagulants in real clinical practice: analysis of patient characteristics and prescribing patterns in a large teaching hospital

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Direct oral anticoagulants (DOACs) became rapidly accepted as an alternative to warfarin in the prevention of stroke in atrial fibrillation and prophylaxis of thromboembolic events. Their safety and efficacy have been well documented in several studies, however, as with any new drug, use in real-world population often reveals risk factors that may affect treatment outcomes. The aim of the study was to determine the prescribing patterns and analyse patient characteristics to identify incidence of selected factors (age, weight, comorbidities and interacting medication) that may affect DOAC safety and efficacy. We conducted a 12-months retrospective study of 504 patients who were initiated DOAC in a large university hospital. Basic demographics, indication for DOAC prescribing, renal functions, co-medication, comorbidities and prescribing service were collected from the hospital's electronic records. Rivaroxaban accounted for the majority of DOAC prescriptions (58.9%), and prophylaxis of deep venous thromboembolism was the main reason for initiation of DOACs (58.7%). We found significant variability in terms of age (16 – 96 years) and weight (34.5 – 184 kg). Chronic renal failure was present in 5.6% of patients. We identified 101 clinically relevant drug interactions of DOACs, mostly with selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors (31.7%) and nonsteroidal anti-inflammatory drugs (28.7%). Only three drug interactions were rated as contraindicated. Hypertension (48.6%), dyslipidaemia (33.1%), musculoskeletal disorders (21.0%) and diabetes mellitus (16.1%) were the most frequent comorbidities. Clinicians should be careful when prescribing DOACs to patients with comorbidities or co-medication that have the potential to increase risk of bleeding or decrease anticoagulant activity of DOACs.

1. Introduction

Introducing direct oral anticoagulants (DOACs) into clinical practice provided new therapeutic options in anticoagulation with numerous advantages over warfarin. DOACs rapidly became preferred by both clinicians and patients thanks to better convenience of the treatment: easy dosing schedule, rapid onset of action, predictable efficacy, no need of frequent INR controls and fewer interactions with co-medication or with food (Hale et al. 2016). Currently, there are three DOACs approved in the Czech Republic: dabigatran (DAB), apixaban (API) and rivaroxaban (RIV). They all are available for use in the following three indications: i) Prevention of venous thromboembolic events in adult patients who have undergone elective hip or knee replacement surgery [referred to as VTE]; ii) Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation [referred to as NVAF]; and iii) Treatment of deep vein thrombosis and pulmonary embolism, and prevention of their recurrence in adults [referred to as DVT/PE] (State Institute for Drug Control, 2017). Their safety and efficacy have been extensively studied and well documented in several clinical studies (Raschi et al. 2016). However, as with any new drug recently placed on the market, real-world patient data from everyday practice are required to reveal the risk factors that may potentially interfere with their safety and efficacy.

Since January 2016, a clinical pharmacy consultation service has been available in a Teaching Hospital in Pilsen. From the very beginning of its existence, DOACs were the most consulted drugs in terms of both safety and efficacy.

Given the broad range of the asked questions, we decided to provide an insight into prescribing patterns and to analyse characteristics of patients prescribed DOAC for the first time in our hospital. The aim of this study was to identify the incidence of selected factors, including age, weight, drug interactions and comorbidities that may influence the efficacy and safety of DOAC in a real world setting.

2. Investigations and results

2.1. Prescribing patterns

We retrospectively collected data on 504 patients who were initiated with DOACs in the hospital from December 2015 to November 2016. As detailed in Table 1, the majority of the patients received DOACs for DVT/PE (n=296; 58.7%). In NVAF patients (n=163), 76 of them switched from previous warfarin treatment and 71 were prescribed DOACs as a first-line anticoagulant treatment. In 16 patients starting DOACs, it was not clear whether they were on warfarin prior the DOAC initiation. Only 19 patients (3.8%) were prescribed DOACs after total hip or knee replacement surgery (VTE).

Finally, we identified 26 patients receiving DOACs beyond the approved indications. These clinical situations involved mainly posttraumatic primary prophylaxis of thrombotic events with current thrombosis not verified, or primary prophylaxis of thromboembolic events in patients with malignancy. RIV was the most frequently prescribed DOAC and accounted for more than a half of all newly prescribed DOACs during the study period (n=297; 58.9%).

Table 1: DOAC use by clinical indication

	API	RIV	DAB	Total
	n = 105 (20.9%)	n = 297 (58.9%)	n = 102 (20.2%)	n = 504 (100%)
Prevention of VTE in adults undergoing total hip or knee replacement surgery	**0**	**17**	**2**	**19 (3.8%)**
hip replacement	0	11	2	13
knee replacement	0	6	0	6
Prevention of stroke and systemic embolism in adult patients with NVAF	**35**	**69**	**59**	**163 (32.3%)**
DOAC initiated as first line anticoagulant in newly diagnosed NVAF	13	34	24	71
switch from warfarin to DOAC	18	32	26	76
data not available	4	3	9	16
Treatment of DVT and PE, and prevention of recurrent DVT and PE in adults	**66**	**197**	**33**	**296 (58.7%)**
DVT alone	45	152	18	215
pulmonary embolism (DVT not verified)	12	17	9	38
DVT along with PE	9	28	6	43
Other clinical diagnoses	**4**	**14**	**8**	**26 (5.2%)**

Abbreviations: API, apixaban; RIV, rivaroxaban; DAB, dabigatran; DOAC, direct oral anticoagulant; VTE, venous thromboembolic event; NVAF, nonvalvular atrial fibrillation; DVT, deep venous thromboembolism; PE, pulmonary embolism.

2.2. Study population characteristics

Characteristics of the whole study group are provided in Table 2. The mean age of the study patients was 59.6 years, ranging from 16 to 96 years. Nearly half of the study group comprised elderly patients aged 65 years or more (44.4%); one fifth (n=96) were ≥ 75 years old. Males accounted for the majority of the whole study group (58.5%), but gender proportions were different in each DOAC group.

All three DOAC groups were similar in terms of renal function (data available in 424 patients). Mean estimated glomerular filtration rate (eGFR) available within the last three months prior DOAC initiation was 77.4 mL/min, with a minimum of 24 mL/

Table 2: Study population characteristics

	API	RIV	DAB	Total
	n = 105	n = 297	n = 102	n = 504 (100%)
Gender				
Female	53 (50.5%)	120 (40.4%)	36 (35.3%)	209 (41.5%)
Male	52 (49.5%)	177 (59.6%)	66 (64.7%)	295 (58.5%)
Age (years)				
Mean age ± SD	62.4 ± 17.2	57.7 ± 16.4	62.3 ± 17	59.6 ± 16.8
Range	18 - 93	16 - 96	21 - 89	16 - 96
Elderly ≥ 65 years	57 (54.3%)	118 (39.7%)	49 (48.0%)	224 (44.4%)
Elderly ≥ 75 years	25 (23.8%)	41 (13.8%)	30 (29.4%)	96 (19%)
Renal function - eGFR (mL/min)	n = 92	n = 246	n = 86	n = 424
Mean eGFR ± SD	72 ± 24	81.8 ± 22.8	77 ± 18	77.4 ± 22.2
Range	24.0 - 133.2	25.2 - 130.2	27.6 - 110.4	24.0 - 133.2
eGFR 30 - 50 mL/min	14	17	3	34
eGFR 15 - 29 mL/min	1	3	1	5
Weight (kg)	n = 85	n = 219	n = 83	n = 387
Mean weight ± SD	88.6 ± 20.3	88.8 ± 20.2	85.1 ± 18.2	87.9 ± 19.8
Range	34.5 - 150	53.0 - 184.0	45.0 - 150.0	34.5 - 184.0
Comorbidities				
Hypertension	62	127	56	245 (48.6%)
Dyslipidemia	44	83	40	167 (33.1%)
Musculoskeletal disorders (various types)	26	62	18	106 (21.0%)
Diabetes mellitus type 2	20	45	16	81 (16.1%)
Heart failure	8	29	12	49 (9.7%)
Ischemic heart disease	15	20	11	46 (9.1%)
Previous GIT disorders with risk of bleeding	15	23	5	43 (8.5%)
Hepatic disorders	8	21	4	33 (6.5%)
Active malignancy	6	23	2	31 (6.2%)
Chronic renal failure	11	13	4	28 (5.6%)

	API	RIV	DAB	Total
Ischemic disease of lower limbs	5	19	1	25 (5.0%)
Bleeding episodes in history	4	14	5	23 (4.6%)
Previous cerebral ischemic event	6	10	7	23 (4.6%)
Psychiatric disorders	5	13	4	22 (4.4%)
Hypercoagulable state	4	12	2	18 (3.6%)
Vascular anomalies	2	7	3	12 (2.4%)
Epilepsy	2	5	1	8 (1.6%)
Collapse and/or fall in history	4	3	0	7 (1.4%)

Abbreviations: API, apixaban; RIV, rivaroxaban; DAB, dabigatran; SD, standard deviation; eGFR, estimated glomerular filtration rate; GIT gastrointestinal tract.

min. Chronic renal failure was documented in 28 patient records (5.6%).
Table 3 provides available data on prescribed doses of API, RIV and DAB within the approved indications according to renal functions. DOAC dose was not reduced in three NVAF patients with moderate renal failure (15 – 29 mL/min) treated with RIV. In one case, contraindication for DAB use in severe renal failure was not considered.

Table 3: DOAC doses according to indications and renal functions

		APIXABAN		RIVAROXABAN		DABIGATRAN	
	eGFR	SmPC	Our study	SmPC	Our study	SmPC	Our study
VTE	> 50 mL/min	5 mg	-	10 mg	10 mg (n=12) 15 mg (n=1) 20 mg (n=2)	220 mg	220 mg (n=2)
	30 - 50 mL/min	5 mg	-	10 mg	-	150 mg	-
	15 - 29 mL/min	Caution	-	Caution	-	Contraind.	-
NVAF	> 50 mL/min	10 mg	5 mg (n=9) 10 mg (n=17)	20 mg	10 mg (n=2) 15 mg (n=1) 20 mg (n=50)	300 mg	220 mg (n=18) 300 mg (n=26)
	30 - 50 mL/min	10 mg or 5 mg**	5 mg (n=4) 10 mg (n=3)	15 mg	10 mg (n=1) 15 mg (n=3) 20 mg (n=3)	300 mg or 220 mg**	220 mg (n=3)
	15 - 29 mL/min	5 mg	5 mg (n=1)	15 mg	15 mg (n=3)	Contraind.	220 mg (n=1)
DVT/PE	> 50 mL/min	20 mg*	5 mg (n=8) 10 mg (n=29) 20 mg (n=13)	30 mg*	30 mg (n=159)	300 mg	220 mg (n=2) 300 mg (n=30)
	30 - 50 mL/min	20 mg*	5 mg (n=2) 10 mg (n=1) 20 mg (n=2)	30 mg*	30 mg (n=5)	300 mg or 220 mg**	-
	15 - 29 mL/min	Caution	-	30 mg*	-	Contraind.	-

Abbreviations: eGFR, estimated glomerular filtration rate; VTE, venous thromboembolic event; NVAF, nonvalvular atrial fibrillation; DVT, deep venous thromboembolism; PE, pulmonary embolism; SmPC, summary of product characteristics; Caution, use with caution; Contraind., contraindicated. * denotes initial dose; ** denotes recommended dose in presence of additional bleeding risk factors

Data on total body weight was available in 387 patients and showed significant variability within the study group. Mean total body weight was 87.9 kg and weight extremes < 60 kg or > 110 kg were recorded in 66 patients (13.1%; 19 and 47 patients, respectively).
The most frequent chronic comorbidities (as recorded in patient records) included hypertension (48.6%), dyslipidaemia (33.1%), various musculoskeletal disorders (21.0%) and type 2 diabetes mellitus (16.1%).

2.3. Drug interactions with DOAC

Using SmPCs of the currently registered DOACs and Lexicomp drug interaction database (Lexicomp®), 101 potentially clinically relevant drug interactions were identified (Table 4) with a risk of increased (n = 96) or decreased (n = 5) effect of DOACs.
Half of these interactions (n=52, 51.5%) were inappropriate drug combinations with severity rating D, and 3 of them were rated as contraindicated combinations (RIV with itraconazole or with primidone). Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors (SSRI/SNRI) and nonsteroidal anti-inflammatory drugs (NSAID) accounted for the majority of all identified interactions (31.7% and 28.7%, respectively).

Table 4: Drug interactions with DOACs

DOAC	Interacting medication	Severity rating (Lexicomp)	Total count (n = 101)
API	clopidogrel	D	1
	ginkgo biloba	D	1
	NSAID (TPA, ibuprofen)	D	4
	NSAID (nimesulide)	C	2
	piracetam	C	2
	SSRI	C	11
RIV	itraconazole	X	1
	primidone	X	2
	clarithromycin	D	2
	clopidogrel	D	1
	ethinylestradiol+gestoden	D	1

DOAC	Interacting medication	Severity rating (Lexicomp)	Total count (n = 101)
	medroxyprogesterone	D	2
	verapamil	D	6
	NSAID (ASA, TPA, diclofenac, ketoprofen)	D	9
	NSAID (nimesulide, celecoxib)	C	4
	fluconazole	C	1
	verapamil	C	1
	SSRI	C	15
	piracetam	C	1
DAB	amiodarone	D	6
	propafenone	D	8
	carvedilol	D	2
	clarithromycin	D	1
	clopidogrel	D	1
	NSAID (ASA, ibuprofen)	D	7
	NSAID (nimesulide)	C	3
	SSRI/SNRI	C	6

Abbreviations: DOAC, direct oral anticoagulant; API, apixaban, RIV, rivaroxaban; DAB, dabigatran; NSAID, non-steroidal anti-inflammatory drugs; ASA, acetylsalicylic acid; TPA, tiaprofenic acid; SSRI, selective serotonine reuptake inhibitors; SNRI, serotonin-norepinephrine reuptake inhibitors.

2.4. Prescribing services

Analysis of prescribing services (Table 5) showed that internal medicine was the major prescriber (62.1%), followed by cardiology/cardiac surgery (15.9%), clinical pharmacology (12.9%) and orthopaedic surgery/traumatology (4.8%) and other specialisations.

Table 5: Prescribing services

	API	RIV	DAB	Total
	n = 105	n = 297	n = 102	n = 504 (100%)
Internal medicine	69	200	44	313 (62.1%)
Cardiology/Cardiac surgery	13	23	44	80 (15.9%)
Clinical pharmacology	17	44	4	65 (12.9%)
Orthopaedic surgery/ Traumatology	0	18	6	24 (4.8%)
Oncology/Hematooncology	1	6	1	8 (1.6%)
Neurology	2	1	3	6 (1.2%)
Clinical biochemistry	0	4	0	4 (0.8%)
Geriatric medicine/Long-term care	3	0	0	3 (0.6%)
Plastic surgery	0	1	0	1 (0.2%)

Abbreviations: API, apixaban; RIV, rivaroxaban; DAB, dabigatran.

3. Discussion

Our retrospective analysis of data on patients initiated DOAC identified several factors that may influence the safety and efficacy of the treatment.

We investigated the incidence of clinically relevant drug interactions with DOACs as these have been frequently discussed in our consultation service. Despite DOACs are generally considered to have a lower interaction potential than warfarin, evidence of serious sequelae caused by drug interaction has already been reported (Altena et al. 2014).

Focusing on clinically relevant DOAC-drug interactions, we identified 101 such combinations, involving mainly chronic medication (SSRI/SNRI, NSAID, antiarrhythmic agents). Most of them were rated as inappropriate drug combinations (Lexicomp rating D, 51.5%) or combinations requiring closer monitoring of patient (rating C, 45.4%). Only three of the interactions were rated as contraindicated (rating X).

SSRI/SNRI and NSAID were involved in the majority of identified interactions. Their antiplatelet properties provide the rationale for pharmacodynamic interactions leading to increased risk of bleeding. The combination is not recommended. If it cannot be avoided, patients should be monitored closely for symptoms of bleeding. For patients with increased risk of gastrointestinal bleeding, gastroprotection may be considered (Heidbuchel et al. 2015).

Pharmacokinetic interactions of DOACs include interference with their absorption, metabolism and excretion. It has been documented that apixaban, rivaroxaban, and dabigatran-etexilate (prodrug form of dabigatran) are substrates for the efflux transporter P-glycoprotein (P-gp). Moreover, rivaroxaban and apixaban are substrates for cytochrome P-450 3A4. Concomitant treatment with inducers or inhibitors of these proteins may lead to changes in DOAC plasma levels followed by either increased or decreased anticoagulant activity.

In 2015, the European Heart Rhythm Association updated their practical guide on DOAC use in NVAF patients providing recommendation for DOAC use and dose management in the most clinically relevant interactions (Heidbuchel et al. 2015). For example, strong inducers of P-gp/CYP 3A4 (rifampicin, carbamazepine, phenytoin, phenobarbital) should be avoided because of significant reduction of DOAC plasma levels. DOAC treatment failure after concomitant use with rifampicine (Altena et al. 2014) or phenytoin (Wiggins et al. 2016) has already been documented. Therefore, it is recommended to screen for potential drug interactions when initiating DOAC or adding a new medication to a patient already treated with DOAC to prevent bleeding events or anticoagulant treatment failure. Patients are also recommended to restrain particular foods and herbal products that may affect DOAC treatment. These include, but are not limited to, St John's Worth (*Hypericum perforatum*), grapefruit and any herbs with anticoagulant/antiplatelet properties (Nutescu et al. 2011).

It is of note, that despite NSAID accounted to nearly one-third of the all identified drug interactions (n = 29; 28.7%) this represents only 5.8% of patients of the whole study group. Such low incidence is in poor correlation with rather high incidence of musculoskeletal disorders identified in the records (21%). Previous studies (McKinley et al. 2004; Coleman et al. 2005; Kovacova and Durisova 2016) revealed that medication history in patient records are often incomplete and over-the-counter (OTC) drugs are frequently omitted. Further, NSAID belong to the most frequently used OTC drugs and patients consider them safe (Wawruch et al. 2008). Therefore, we presume that the actual consumption of NSAID, especially those freely available, could be far higher. In the study by Davidson et al. (2014) patients using rivaroxaban with NSAID had a 2.5-fold higher incidence of bleeding than those without NSAID. To minimize risk of bleeding events, patients with any painful conditions should be comprehensively educated and provided with suitable analgesic alternative (Burnett et al. 2016).

We found considerable age variability (16 - 96 years) in each DOAC subgroup. Similar age patterns were reported by others (Pattullo et al. 2016; Schuh et al. 2016) which indicates that prescribers accepted DOACs as adequate alternatives to warfarin even in very old patients. Several studies show that prescription rates of DOACs in the elderly have an increasing trend compared to warfarin numbers. Especially in NVAF they became swiftly preferred to warfarin (Xu et al. 2013; Olesen et al. 2015). One paediatric patient (aged 16) prescribed RIV was identified in the VTE group. Clinicians should be careful when prescribing DOACs for patients < 18 years, as neither safety nor efficacy studies in this population have been published.

Another significant variability was found in the weight range (34.5 – 184 kg) which was recorded in all DOAC groups. SmPCs of both RIV and API state that weight extremes do not require

dose adjustments. For API, weight under 60 kg is considered an increased risk of bleeding. Moreover, higher exposition is expected in women and patients over 65 years. In our study, we identified one patient with combination of all these risk factors (70-years old female, weight = 34.5 kg). She was prescribed API in reduced dose for DVT/PE.

Each of the DOACs undergoes at least partial renal elimination (API 25%; RIV 33%; DAB 80%) and adequate dose adjustment is therefore required in renal dysfunction. It is also important to follow-up progression of renal function decline in high risk patients (e.g. elderly, preexisting nephropathy). There is also a high risk of elevated plasma levels in patients with acute renal impairment.

Based on the available data on renal functions and the prescribed DOAC doses we conclude that prescribing patterns in our patients with moderate (30 – 50 mL/min) and severe (15 – 29 mL/min) renal impairment mostly complied with the dose reduction recommendations. Our findings are in contrast to results of Minhas et al. (2016) reporting high rates of missing dose reduction in renal dysfunction. In our patients, dose reduction was omitted in three NVAF patients with moderate renal impairment (30 – 50 mL/min) on rivaroxaban. We identified only one patient prescribed DAB for NVAF in eGFR under 30 ml/min (with reduced dose 2x110 mg). However, as revealed later, the eGFR value reflected only a transient decrease of her renal function with restoration within the following two months.

Several dose reductions were also recorded in normal renal functions (> 50 mL/min). Further analysis showed that the main 'non-renal' reasons were advanced age, interacting medication, previous bleeding events (with or without antithrombotic use) and malnutrition.

Surprisingly, chronic renal failure was listed in 28 records, but eGFR under 50 mL/min within the last three months was identified in 39 patients. The most probable explanation for such a discrepancy was omission of declining renal function from the list of diagnoses.

When initiating DOACs in impaired renal function, clinicians are advised to consider also several other factors that may potentiate the risk of bleeding, either *via* increasing of their plasma levels or *via* additional anticoagulant effects. These include, but are not limited to, another comorbidities and interacting co-medication.

Similar to other anticoagulant treatment, the risk of bleeding is the crucial safety issue for DOACs, as well. Clinical studies have primarily been focused on major GIT and intracranial bleeding and multiple mechanisms have been proposed (Vanassche et al. 2014). Therefore, we surveyed the records for incidence of comorbidities that may potentiate such risk. These involved GIT disorders with risk of bleeding (8.5%), previous bleeding events (4.6%), hepatic disorders (6.5%), active malignancy (6.2%), chronic renal impairment (5.6%) and risk of falls (1.4%). For example, in the patients with malignancies, DOACs seemed to be preferred in case of unstable INR or LMWH intolerance. Pros and cons should be carefully considered, as their use in this patient group is still questionable (Short and Connors 2014).

Treatment of DVT/PE and prevention of their recurrence was the most frequent indication for starting DOACs in our hospital (58.7%). Different results were obtained in other studies (Johnson et al. 2015; Pattullo et al. 2016) where NVAF was the most common indication for DOAC initiation (68.1% and 76.1%, respectively). We think the main reason for such a discrepancy arose from limitations for prescribing of DOACs in NVAF given by the national insurance system in the Czech Republic. Briefly, DOACs are covered by national insurance only after warfarin treatment failure or intolerance. Such insurance/coverage restrictions virtually made DOACs available as the second line anticoagulation in NVAF patients.

As revealed by the study of Johnson et al. (2015), a small portion (5.6%) of DOACs were prescribed in clinical situations beyond the approved indications. In our study, such cases accounted for 5.2% of all DOAC prescriptions.

Almost two-thirds (62.1%) of all the DOAC prescriptions were initiated by internal medicine specialists. This could be explained by the fact, that the hospital has three large departments of internal medicine providing both inpatient and outpatient care in several specialisations. As the internal medicine specialists were most frequently involved in management of DVT/PE patients, this also could be a reason for such high portion of DVT/PE.

RIV was the most frequently prescribed DOAC (58.9%) across all clinical situations, followed by API (20.9%) and DAB (20.2%). RIV was the leading DOAC also in some other studies (Johnson et al. 2015; Weitz et al. 2015; Khan et al. 2016), however, prescribing patterns differ substantially according to the type of health care facility and the market situation in the given country (Xu et al. 2013; Hale et al. 2016).

Some limitations of our study have to be addressed. Our results are based on pooled data on a significantly heterogeneous population in terms of the baseline characteristics, indication for DOACs, comorbidities and co-medication. That makes them rather generalised and comparison with studies focused on particularly defined subpopulation should be made carefully. On the other hand, the study was conducted in a large university hospital covering all specialities of potential DOAC prescribers from both outpatient and inpatient departments. Such design along with 12-month duration allowed us to investigate broad spectrum of clinical situations with DOACs initiation. Our results will contribute to the development of novel educational tools for patients and related health care professionals in our hospital.

In conclusion, direct oral anticoagulants provide new promising options in thromboembolic prophylaxis and treatment. Thanks to several advantages over warfarin, the increase in prescribing rates can be expected to continue. Therefore, understanding all risk factors that may possibly interfere with treatment outcomes is crucial. In our study, significant variability within patient characteristics and multiple drug interactions were revealed. Prospective, long term follow-ups are needed to evaluate the clinical impact of drug interactions as well as the relevance of the extremities in patient characteristics.

4. Experimental

4.1. Study design

We performed a 12-month retrospective analysis of prescribing patterns in a teaching hospital in Pilsen, a 1,729-bed academic hospital with more than 70,000 admissions and more than 1 million of ambulatory examinations annually.

From the hospital's electronic database, we identified patients who were prescribed API or RIV or DAB for the first time in the hospital during the analysed period. The analysis involved patients prescribed DOACs at hospital discharge (inpatients) as well as in ambulatory services of the hospital (outpatients).

4.2. Collected data

Following data were recorded: basic demographics (age, gender), indication for prescription of DOAC, prescribing service, renal function and weight within the last 3 months prior DOAC initiation, and comorbidities including those that may potentially interfere with DOAC treatment (risk of bleeding, risk of thromboembolic event).

Additionally, concomitant systemic medication was collected to evaluate potential drug interactions with DOACs. The drug interactions were analysed using Lexicomp Interaction database and clinically relevant drug interactions (risk rating C, D and X) were recorded.

4.3. Statistical analysis

The data were analysed using Microsoft Excel 2010 and IBM SPSS Statistics 23 for Windows.

Conflicts of interest: None declared.

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