Profile of Patients Anticoagulated over a period of One Year in the Respiratory unit of Federal Medical Centre, Owerri.

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ABSTRACT

Anticoagulation is indicated in several medical conditions including in the prevention and treatment of venous thromboembolism. Different anticoagulants are in use and may be taken through the oral or parenteral route.

We undertook a cross-sectional study of patients presenting or referred to the respiratory unit of the Federal Medical Centre, Owerri, who underwent anticoagulation between September 2018 to August 2019, to profile them based on their background demographics, medical/surgical characteristics, type and duration of anticoagulation used, complications and 30-day outcome.

A total of 106 patients were studied with an average age of 61.4 ± 17.8 years, age range of 18 – 98 years and a M:F ratio of 1.1:1. Majority (65.1%) of the patients were medical patients. Most (51.9%) of the patients were on low molecular weight heparin (LMWH) alone and the median treatment duration was 10 days. Two (1.9%) cases of nonfatal bleeding were recorded and the 30-day mortality rate was 21.7%. The choice of a LMWH either singly or in combination with a novel oral anticoagulant (NOAC) marginally predicted 30-day survival over the use of warfarin.

We conclude that anticoagulant therapy reduces mortality in the medical patient and the NOACs are a relatively safe option in achieving effective anticoagulation where facilities for routine monitoring do not readily exist.

Keywords: Anticoagulation, NOAC, survival.

INTRODUCTION

Anticoagulants are medications that prevent existing blood clots from expanding and the formation of newer ones by increasing the length of time it takes a blood clot to form. Different types of anticoagulants achieve this through different mechanisms of actions[1].

Various indications exist for anticoagulation and these include: Deep venous thrombosis (DVT), pulmonary embolism (PE), atrial fibrillation (AF) and

mechanical heart valves[2]. Ischaemic stroke, certain congenital heart diseases, artificial valve replacements, unstable angina, coronary artery bypass graft, angioplasty and stenting, carotid artery disease and peripheral artery disease also form indications for anticoagulation[2,3].

The main indications for anticoagulation include venous thromboembolism (VTE) prophylaxis in medical and surgical settings, VTE treatment, atrial fibrillation and valvular heart diseases. Incidence of VTE increases exponentially with age[3]. This could be partly explained by the fact that the prevalence of co-morbidities that contributes to VTE risk, such as malignancy or heart failure increases with age. Also, recovery of full mobility after an acute illness is much slower in the elderly compared to younger adults. Attempts have been made at defining among elderly medical inpatients higher risk subgroups being most likely to benefit from VTE prophylaxis. Independent risk factors have been identified including restriction of mobility, age ≥ 75 years, history of DVT or PE, chronic oedema of lower limbs, acute heart failure, paraparesis or paralysis of lower limb, infectious or rheumatic disease[3,4].

Historically, most patients who require parenteral anticoagulation received heparin whereas those requiring oral anticoagulants received warfarin (vitamin k antagonists - VKAs)[5]. Heparin is used in form of unfractionated and low molecular weight heparin. Warfarin, a racemic mixture of laevorotatory S- warfarin and laevorotatory R-warfarin, is the most clinically used oral anticoagulant. Warfarin acts by inhibiting the synthesis of Vitamin K-dependent clotting factors – factors II, VII, IX and X – and the anticoagulant proteins C and S. Physicians in developing countries face a lot of problems using warfarin. Anticoagulation, especially when using warfarin, requires good diagnostic facilities, appropriate monitoring tools and adequate anticoagulation management infrastructure (for routine monitoring of the INR and management of warfarin toxicity) which are not readily available in poor resource setting like ours, hence the need for newer agents which require little or no monitoring[6]. Also, the multiple food-drug and drug-drug interactions exhibited by warfarin and its narrow therapeutic margins limit its use in such resource-poor settings.

Newer agents used for anticoagulation include Factor Xa inhibitors, direct thrombin inhibitors (DTIs) and the fibrinolytics[7,8].

Oral anticoagulants – with VKAs or novel oral anticoagulants (NOACs) – is the mainstay of stroke prevention strategies in patients with non-valvular atrial fibrillation (NVAF). Supported by guidelines in the management of NVAF, the use of NOACs has increased markedly over the past five years since they were first licensed for this indication[9,10]. Since the introduction of NOACs, anticoagulant options have widened. VKAs such as warfarin, phenprocoumon and acenocoumarol have been used for stroke prevention in AF for many years[1]. Although highly effective the management of VKAs can be challenging and under pinned the need for alternatives[1].

The NOACs – apixaban, dabigatran, edoxaban and rivaroxaban – are increasingly prescribed in preference to VKAs because of their potential to improve the quality of care[9,10].

All NOACs have the following qualities:

- Offer effective stroke prevention with a good safety profile;
- Lack the requirement for routine coagulation monitoring or frequent dose adjustments;
- Have fixed–dose regimens, with rivaroxaban showing consistent dose-dependent plasma levels across a range of patient populations and pharmacodynamic parameters correlating with rivaroxaban plasma concentrations;
- Have a low risk of drug-drug or drug-food interactions.[11,12]

The following anticoagulants are approved in Europe for the prevention of stroke and systemic embolism in patients with NVAF and at least one additional risk factor for stroke:

a) VKAs: warfarin, phenoprocoumon and acenocoumarol[13,14,15].
b) Direct factor Xa inhibitors: apixaban[16], Edoxaban[17] and Rivaroxaban[18].
c) Direct thrombin inhibitor: Dabigatran[19,20,21].

Elderly patients and many immobilized patients represent a population at high risk of thromboembolism. Because risk of bleeding is high in the elderly, there is a general tendency among physicians to underuse anticoagulants in the elderly. With the introduction of these newer agents more patients could be managed with better outcome and little or no complications[1,4].

The direct thrombin inhibitors (DTIs) inhibit the intrinsic activity of thrombin. Unlike heparin, which also inhibits thrombin, the DTIs do not require a factor, and can inhibit thrombin directly[5,22,23]. Most DTIs are given as parenteral except for Dabigatran which is given orally. The DTIs are used as prophylaxis and treatment of VTE and acute coronary syndromes (ACS), and for the prophylaxis of thrombus formation in NVAF. Dabigatran, the only orally available DTI, is approved for the treatment of VTE in patients treated with concomitant parenteral anticoagulation for at least five days, and for the treatment of thrombus secondary to a NVAF.

Laboratory evaluations of the DTIs include measurement of thrombin time (TT) or ecarine clotting time (ECT). However, these tests are not widely available, thereby, limiting their applicability, particularly in the emergency setting. In the clinical setting, activated partial thromboplastin time (aPTT) can be used as a surrogate to monitor the effect of the DTIs[5,24].

The primary side effect of DTIs is haemorrhage, including gastro-intestinal and intracranial haemorrhage. The bleeding is dose-dependent and is more common in those over 75 years of age [5,25,26]. Until recently, no specific antidotes existed to counteract bleeding caused by the use of the NOACs. The American College of Cardiology Foundation and the American Heart Association recommend transfusion of packed red blood cells and Fresh Frozen Plasma (FFP). In addition, surgical interventions to control bleeding, if feasible, can be employed[5]. Idarucizumab has been approved as a reversal agent for bleeding caused by Dabigatran. It is a monoclonal antibody and is administered by the injectable route.[27] Andexanet alpha

is another reversal agent approved for bleeding from the factor Xa inhibitors apixaban and rivaroxaban.[28] Their cost and relative unavailability in resource-constrained settings limit their widespread use in those settings.

A 'user-friendly' score to assess one-year risk of major bleeding in a patient with AF was used. The 'HAS-BLED' score predicts the risk of bleeding based on a combination of risk factors (***h***ypertension, ***a***bnormal renal and liver function, ***s***troke, ***b***leeding, ***l***abile INR, ***e***lderly patients and use of alcohol and ***d***rugs)[29]. This bleeding risk schema is simple and easy to calculate, whereby a score of ≥ 3 indicates "high risk" and some caution and regular review of the patient is needed. Several studies have shown 'HAS-BLED' to have better predictive value than other published risk scores[29-31].

RATIONALE OF THE STUDY

This study was designed to assess the profile of patients who received anticoagulation over a one-year period. It looked at the demographic data of patients that were anticoagulated using the NOACs, the clinical consideration including diagnosis, co morbidities, complications and outcome following anticoagulation therapy. By considering the safety profile of the NOACS compared with warfarin and heparin in relation with monitoring and concern for complications especially moderate to severe bleeding among patients on anticoagulants, we hoped to make a case for the practice of routine anticoagulation in the right setting.

STUDY OBJECTIVE

The study aimed to investigate the profile of patients who received anticoagulants under our care over a one-year period, from September 2018 to August 2019.

METHOD

The study was a cross-sectional research work which assessed adults in the respiratory unit who received anticoagulation during a period of one year. They were either primarily seen in the unit or referred by other units for review within the period. The patients were recruited from all the medical wards, medical outpatients and intensive care unit (ICU). Also, the patients who were admitted in the surgical wards or orthopaedic wards and needed respiratory review were enlisted for the study. Patients were initially assessed for risk of bleeding using the `HAS BLED' score[29-31]and were then placed on anticoagulation therapy. For patients who were very sick, subcutaneous Enoxaparin at dosage of 40 mg daily was initially used for the first four days. Then Dabigatran 150mg twice daily was introduced on the 3rd or 4th day after which parenteral anticoagulant was withdrawn.

INCLUSION AND EXCLUSION CRITERIA

All consenting adults who were 18 years and above, admitted and non-ambulant for greater than 48 hours, including unconscious patients and had received any form of anticoagulation were included in the study. Also included were those who had atrial fibrillation. Exclusion criteria included patients who had any kind of bleeding problems – haemophiliacs, patients with peptic ulcer disease, intra cranial haemorrhage or abnormal platelet counts on laboratory investigation. Patients who were unwilling to participate were also excluded from the study.

DATA COLLECTION

The data were collected using a data sheet created for this purpose. Information obtained include patient's demographic data, clinical diagnosis and co-morbidities, risk factors/indications for anticoagulation, anticoagulant used, target monitoring, outcome and complications of anticoagulants. For our patients who required monitoring; INR, PT and PTTK were used when necessary. Recommended therapeutic ranges of INR are 2.0 – 3.0. Target INR was defined by the attainment of therapeutic ranges of oral anticoagulation in keeping with the guidelines. Patients were followed up weekly in the medical outpatient department for at least four weeks after discharge from the ward.

Desired outcome was defined by the attainment of prophylactic or therapeutic goals of oral anticoagulants for those who needed it. Other outcomes were in terms of patient survival during the period of study.

Ethical clearance was obtained from the Federal Medical Centre Owerri (FMCO) research and Ethics Committee (FMC/OW/HREC/1201).

RESULTS

A total of 106 patients were recruited over the study period, comprising 55 (51.9%) males and 51 (48.1%) females (M:F = 1.1:1). The mean (SD) age of the participants was 61.4 ± 17.8 years with an age range of 18 – 98 years. Patients who were older than 65 years of age made up 43 (40.6%) of the total number and only about a quarter (25.4%) of the patients were up to 50 years old. Medical patients made up 69 (65.1%) of the 106 patients (table 1).

The HAS-BLED score was significantly lower in the surgical patients compared to their medical counterparts (HAS-BLED score 0 – 1: 34 (91.9%) vs 37 (53.6%), p <0.001) (figure 1). No surgical patient had a HAS-BLED score of more than 2.

Fifty-five (51.9%) patients received Enoxaparin as the sole anticoagulant while 39 (36.8%) received it with Dabigatran, and 12 (11.3%) with Warfarin. The median (IQR) duration of treatment was 10 (5 – 30) days. There was a variable period between prescription of the anticoagulation and commencement, ranging from 0 – 15 days with a median (IQR) delay of 0 (0 – 2) day. The delay in commencing anticoagulation was evident when the anticoagulation prescribed was either a NOAC (median (IQR) delay of 1 (0 – 1.25) day) or LMWH alone (median (IQR) delay of 1 (0 – 2) day) compared to no delays between prescription and commencement of the VKA group of anticoagulants (p = 0.003) (table 2).

There were 2 (1.9%) non-fatal bleeds over the treatment period, both of which occurred in medical patients while on Dabigatran. None occurred with Warfarin treatment. The HAS-BLED score of the 2 patients with the bleeds was 3.

The 30-day mortality was 23 (21.7%). Of these, 22 (95.7%) were medical patients while 1 (4.3%) was a surgical patient (p <0.001). Nine (39.1%) of the deaths were of female patients as against 14 (60.9%) male patients (p = 0.330). Eleven (47.8%) of the deaths occurred in patients who were older than 65 years of age compared to 12 (52.2%) deaths in those younger than 65 years (p=0.556) (table 3).

The duration of treatment, type of anticoagulant, HAS-BLED score, a prior history of DVT/PE and the patient category were significantly associated with 30-day mortality. After adjusting for confounders by multiple logistic regression, longer durations of treatment were found to be significantly associated survival (OR for mortality = 0.66, 95% CI = 0.5 – 0.84; p=0.001). Also, the use of LMWH alone compared to LMWH *plus* warfarin (OR for mortality = 0.01, 95% CI = 0.00 – 0.25; p = 0.007), as well as LMWH *plus* dabigatran compared to LMWH *plus* warfarin (OR for mortality = 0.00, 95% CI = 0.00 – 0.12; p = 0.003) marginally, but significantly, predicted 30-day survival (table 4).

DISCUSSION

Anticoagulants are routinely used in medical practice in the management of patients. Indications are varied both in medical and surgical wards. Routine practice of anticoagulation has been known to prolong life and prevent morbidity and mortality in medical and surgical patients.

The demographic data showed more male preponderance with M: F ratio of 1.1:1. The age range is 18-98 years, with mean SD of 61.4 ± 17.8 years. Observation from the study shows a linear increase in number of patients that received anticoagulation as the age increases. This agrees with other studies which showed that anticoagulants are one of the most frequently prescribed medications in elderly patients. The reason is because the prevalence of medical conditions representing a risk for thromboembolic complications and requiring antithrombotic therapy increases with age [1].

Indications for use of anticoagulants are more in medical than in surgical patients probably because of prevailing more medical conditions and co-morbidities in the elderly. Reports show that 54% of hospital inpatients who had developed symptomatic VTE were general medical or non-surgical oncology inpatients[32,33]. This reflected in our study, as 65% of medical patients had indications for anticoagulation, while 35% were surgical patients. The clinical presentations were mainly Diabetes with complications. Untreated and poorly controlled diabetes is a common cause of hospital admission in our environment. Both acute and chronic complications eg diabetic coma and diabetic foot ulcers lead to limitation of movement, and many of these patients will require anticoagulation during this period. Other medical conditions include hypertension, CCF/AF and cerebrovascular accident (CVA). Many of the hypertensive patients have uncontrolled blood pressure which may predispose the patient to complications like CCF, stroke and various forms of cardiac arrhythmias. Independent risk factors, including restriction of mobility, age greater than seventy-five years, history of DVT or chronic oedema of lower limbs and acute heart failures in elderly patients are conditions requiring VTE prophylaxis[3,4]. Ischaemic CVA is common in our medical wards, many of which are associated with arrhythmias. Meta-analysis of randomized trials estimates the risk of DVT in hospitalized medical patients receiving no thrombo-prophylaxis to be as high as 20%[33,34]. Therefore, the use of anticoagulants in the

primary and secondary prevention of CVA and other medical patients is advocated. Fractures and other orthopaedic conditions are common cause of immobility and DVT. VTE is a significant cause of morbidity and mortality following major orthopaedic surgeries such as total hip arthroplasty (THA) and total knee arthroplasty (TKA)[35-36]. Previous studies have shown ten-fold increase in hospitalized patients after trauma, surgery or immobilized medical conditions [37].

Anticoagulant prophylaxis is, therefore, common practice in orthopaedic procedures since this reduces risk of thrombus formation, embolism and subsequent death from pulmonary embolism[35-36]. A good number – 15 (14.2%) – of our patients who had fractures received anticoagulation. Lower limb fractures are common causes of immobility and DVT; therefore, prophylactic anticoagulation is required to prevent embolism.

The HAS-BLED score is an effective means of predicting AF patients at increased risk of major bleeding during treatment with anticoagulants who will require closer monitoring [29-31]. Significant number of patients have low score <3. The score was significantly lower in surgical than medical patients (69 vs 37, p 0.002).

Two (1.9%) of our patients had non-fatal bleeds during the treatment period; and this was found among 2.9% of our medical patients that were on dabigatran. No bleeds occurred in patients on warfarin. The HAS-BLED score of these 2 patients were greater than three.

Majority of our patients (59.9%) received the low molecular weight heparin, enoxaparin as the sole anticoagulant. This is because in the acute and initial stage enoxaparin is started due to its prompt action and it does not require routine monitoring. Again, many of the patients were too sick to tolerate oral anticoagulant therapy; enoxaparin was then continued until their clinical conditions improve and they were able to take orally or, probably, their demise. Many of those patients who died had very short admission durations. Thirty-six percent of our patients received enoxaparin with dabigatran, while 11% received enoxaparin with warfarin.

Clinical and laboratory monitoring is a key issue in the management of patients on anticoagulants. Many centres have challenges in getting initial and subsequent results of PT and INR. When available, the cost and delay in getting the results make many physicians tilt to use of the new anticoagulants (NOACs), which is a major advantage of these groups because of their lack of requirement for routine coagulation monitoring. There has been argument for and against the use of NOACs because of their high cost. But the cost-effectiveness lies in prompt initiation of the NOACs without waiting for laboratory results. Considering the fact that time is money, then there lies justification in choosing the NOACs as it increases the chance of recovery and survival of the patient. Dabigatran was the most common available NOAC in the hospital pharmacy and open market and that was why most of our patients were placed on it. Most of our patients on admission did well while on Dabigatran. This is because during emergency and

acute stage, the caregivers will rally round to procure the drug. But once the patient is discharged home the story changes. We also observed that a one-week prescription was better than more than two weeks prescription. This is because the patient purchases his drugs through out of pocket expense and as such when prescription is given for a longer duration he finds it difficult to mobilize fund for the purchasing. Poverty remains an issue and a challenge to our health system. There is need to review the health insurance scheme in order to optimize its benefits.

We noticed a variable period of delay when the anticoagulants were prescribed. When enoxaparin and dabigatran were prescribed, there were longer delays in procurement of the drugs than when warfarin was prescribed. This variability period between prescription of the anticoagulants and commencement of the drug was significant especially when the anticoagulant was either a NOAC or LMWH compared with the VKA. This reflects the poor socio-economic status of the country.

The 30-day mortality rate was 23 (21.7%). These events were more significantly more common among the medical patients than their surgical counterparts but not among the different sexes. The reason for this may be attributed to the fact that most of the cases were medical patients whose conditions were quite critical on admission. These groups of patients had many complications and co-morbidities such as diabetes, hypertensive heart diseases and age-related problems. Longer duration of anticoagulation was an independent predictor of survival in this study.

In this study, patients with HAS-BLED risk scores of 2 or more had 185% greater odds of dying compared to patients with lower scores. This finding was no longer significant following adjustments for other confounders on logistic regression. Most of the factors considered in the scoring system (hypertension, abnormal renal and liver function, stroke, bleeding, labile INR, elderly patients and use of alcohol and drugs) are pointers to poor prognosis in medical and surgical patients[29-31].

We noticed a better survival outcome when LMWH alone or combined with dabigatran was used than when the anticoagulant employed was a combination of LMWH with warfarin. While the effect sizes of this study were modest at best, they do provide further evidence of the clinical utility, and possible survival benefits, of the NOACs and LMWH over warfarin-based therapies in the context of pulmonary embolism treatment.

CONCLUSION: The use of anticoagulants in medical practice is known to reduce morbidity and mortality. Routine monitoring of patients while using warfarin and heparin has been a huge challenge to physicians. The NOACs have widened the use of anticoagulants as they require little or no monitoring as well as guarantee patients' safety. We therefore advise use of the NOACs in clinical settings where laboratory monitoring poses a challenge.

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Authors contribution: The three authors were involved in the design of the study protocol.GCM, COUE and OFN drafted and wrote the manuscript.

Table 1. Baseline characteristics of patients

Characteristics	Frequency (%)
Gender	
Male	55 (51.9)
Female	51 (48.1)
Age (years) Mean (SD)	61.4 ± 17.8
Age group (years)	
≤35	10 (9.4)
36 – 50	17 (16.0)
51 – 65	36 (34.0)
>65	43 (40.6)
Patient category	
Medical	69 (65.1)
Surgical	37 (34.9)
Presentation (%)	
PE/DVT	15 (14.2)
CCF/AF	15 (14.2)
DM with complications	19 (17.9)
Stroke	10 (9.4)
Trauma	5 (4.7)
Fracture	15 (14.2)
Others	27 (25.5)
International Normalized Ratio (INR)	1.48 ± 0.37
HAS BLED risk score	
0	37 (34.9)
1	34 (32.1)
2	24 (22.6)
3+	11 (10.4)
Comorbidities (%)	
None	30 (28.3)
Hypertension	49 (46.2)
DM	36 (34.0)
Obesity	5 (4.7)
COPD	7 (6.6)
Others	23 (21.7)
Clinical findings	
Pulse rate (bpm)	
Systolic blood pressure (mmHg)	93.2 ± 17.3
Diastolic blood pressure (mmHg)	126.5 ± 23.0
	76.7 ± 14.4

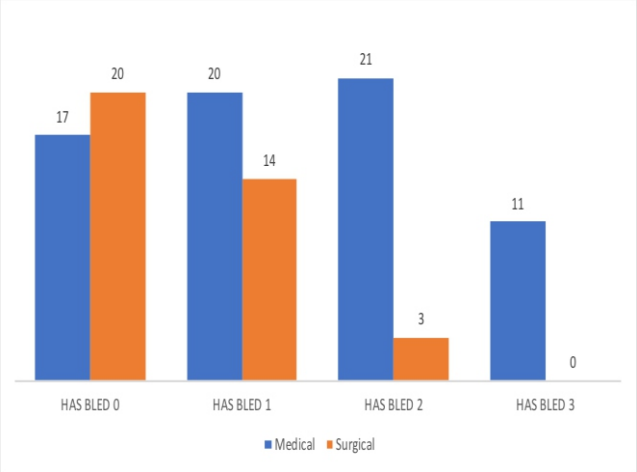

Fig. 1 Patient stratification by HAS -BLED score and type of patient

Table 2: Comparison of choice of anticoagulation used by duration of treatment and latency in commencing treatment

	Total (N=106)	Enoxaparin alone (n=55)	Warfarin + Enoxaparin (n = 12)	Dabigatran + Enoxaparin (n=39)	p-value [a,b]
Duration of treatment (days)‡	5 (3 – 9)	14 (2 – 18)	8 (3.25 – 17.25)	5 (3.75 – 7)	*<0.001*
Latency of commencement of anticoagulation (days)‡	0 (0 – 2)	1 (0 – 2)	0	1 (0 – 1.25)	*0.003*

‡Values are expressed as median (IQR).

[a]Kruskal-Wallis test. [b]Post-hoc testing of pairwise anticoagulant used showed no difference in duration of treatment between the three groups (adjusted Bonferroni p -value >0.05). There were, however, significant differences in the latency of treatment commencement between the VKAbased therapies and LMWH with or without the NOACs (adjusted Bonferroni p-value <0.05) but none between the LMWH alone and with the NOACs.

Table 3: Comparison of patient characteristics by 30-day outcome

Characteristic	**Survival (n=83)**	**Mortality (n=23)**	***p-value***
Age (years)§	60.6 ± 18.0	66.2 ± 16.3	*0.143*
Age group >65 years	34 (41.0)	11 (47.8)	*0.556*
Male (%)	41 (49.4)	14 (60.9)	*0.330*
Patient category			
Medical (%)	47 (56.6)	22 (95.7)	***0.001***
Previous anticoagulation (%)	10 (12.0)	4 (17.4)	*0.503*
History of cancer (%)	8 (9.6)	0 (0)	*0.196*
History of previous DVT/PE (%)	0 (0)	2 (8.7)	***0.007***
History of immobility (%)	45 (54.2)	15 (62.5)	*0.346*
History of Atrial fibrillation (%)	8 (9.6)	0 (0)	*0.196*
History of ischaemic CVA (%)	5 (6.0)	4 (17.4)	*0.100*
HAS-BLED score			***0.023***
0	35 (42.2)	2 (8.7)	
1	25 (30.1)	9 (39.1)	
2	16 (19.3)	8 (34.8)	
3+	7 (8.4)	4 (17.4)	
Pulse rate (bpm)§	92.9 ± 18.1	94.4 ± 14.2	*0.702*
Systolic BP (mmHg)§	124.6 ± 22.9	133.5 ± 22.7	*0.102*
Diastolic BP (mmHg)§	76.3 ± 14.4	78.3 ± 14.4	*0.558*
International Normalized Ratio (INR)	1.5 ± 0.4	1.4 ± 0.3	*0.649*
Type of anticoagulant (%)			
LMWH	42 (50.6)	13 (56.9)	***0.001***
VKA + LMWH	5 (6.0)	7 (30.4)	
NOAC + LMWH	36 (43.4)	3 (13.0)	
Duration of treatment (in days)‡	6 (3 – 9)	4 (3.25 – 6.5)	***<0.001***
Latency of treatment commencement (in days)‡	0 (0 – 1.75)	2 (0 – 2)	*0.675*

§Mean ± SD. ‡Median (IQR). [a]Enoxaparin. DVT: deep venous thrombosis; LMWH: low-molecular weight heparin; NOACs: Novel Oral Anticoagulants; PE: Pulmonary embolism; VKA: Vitamin K antagonist

Table 4: Multivariate analysis of predictors of 30-day mortality in patients on anticoagulants

Variable	AOR	95% CI	p-value
Duration of treatment (days)	0.68	0.54 – 0.86	0.001
VKA + LMWH vs LMWH	0.00	0.00 – 0.12	0.003
VKA + LMWH vs NOACs + LMWH	0.01	0.00 – 0.25	0.007
Medical vs Surgical patient	7.59	0.78 – 74.09	0.081
HASBLED risk score ≤2 vs >2	0.58	0.12 – 2.82	0.501
Previous DVT/PE	1.42×10^{12}	0.00 – ∞	0.999

AOR: Adjusted Odds Ratio; DVT: deep venous thrombosis; LMWH: low-molecular weight heparin; NOACs: Novel Oral Anticoagulants; PE: Pulmonary embolism; VKA: Vitamin K antagonist.

References

1. Robert- Ebadi E, Le Gal G, Righini M. Use of anticoagulants in elderly patients: practical recommendations. Clinical Interventions in Aging 2009; 4:165-177.
2. Anderson FA Jr, Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. Arch Intern Med. 1991;151 (5):933–938.
3. Stein PD, Hull RD, Kayali F, Ghali WA, Alshab AK, Olson RE. Venous thromboembolism according to age: the impact of an aging population. Arch Intern Med. 2004; 164(20):2260–
4. Weill-Engerer S, Meaume S, Lahlou A, et al. Risk factors for deep vein thrombosis in inpatients aged 65 and older: a case-control multicenter study. J Am Geriatr Soc. 2004; 52(8): 1299–1304.
5. Harter K, Levine M, Henderson SO. Anticoagulant Drug Therapy: A Review: West Journal of Emergency Medicine. 2015; 16(1): 11-17.
6. Anakwue RC, Ocheni S, Madu AJ. Utilization of Oral Anticoagulation in a Teaching Hospital in Nigeria. Annals of Medical and Sciences Research. 2014; 4(supple3): S286-S290.
7. Hirsh J, O'Donnell M, Eikelboom JW. Beyond unfractionated heparin and warfarin current and future advances. Circulation. 2007; 116:552–560.
8. Weitz JI, Eikelboom JW, Samama MM. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(suppl):e102s–51s.
9. Camm AJ, Lip GYH, De Caterina R et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J 2012;33:2719–2747.
10. January CT, Wann LS, Alpert JS et al. 2014 AHA/ACC/HRS Guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:e1–e76.
11. Eriksson BI, Quinlan DJ, Eikelboom JW. Novel oral Factor Xa and thrombin inhibitors in the management of thromboembolism. Annu Rev Med 2011;62:41–57.
12. Ruff CT, Giugliano RP, Braunwald E et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014;383:955–962.
13. Lip GYH, Tse HF, Lane DA. Atrial fibrillation. Lancet 2012;379:648–661.
14. Novartis Pharmaceuticals UK Ltd. Sinthrome® (Acenocoumarol BP) Summary of Product Characteristics. 2015. Available at: https://www.medicines.org.uk/emc/medicine/31675 [accessed 9 August 2016].
15. Mercury Pharma Group Ltd. Marevan® (Warfarin) Summary of Product Characteristics. 2014. Available at: https://www.medicines.org.uk/emc/medicine/21562 [accessed 19 January 2015].

16. Granger C.B., Alexander J.H., McMurray J.J. *et al.* Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981–92.
17. Giugliano RP, Ruff CT, Braunwald E et al. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2013;369:2093–2104.
18. Patel M.R., Mahaffey K.W., Garg J. *et al.* Rivaroxaban versus warfarin in non-valvular atrial fibrillation. N Engl J Med. 2011;36 5(10):883-91.
19. Connolly S.J., Ezekowitz M.D., Yusuf S. *et al.* Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009; 361(12):1139-51.
20. Connolly SJ, Ezekowitz MD, Yusuf S et al. Newly identified events in the RE-LY trial. N Engl J Med 2010; 363:1875–1876.
21. Connolly SJ, Wallentin L, Yusuf S. Additional events in the RE-LY trial. N Engl J Med 2014; 371: 1464–1465.
22. Ageno W, Gallus AS, Wittkowsky A, et al. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(suppl):e44S–e88S.
23. Yee DL, O'Brien SH, Young G. The pharmacokinetics and pharmacodynamics of anticoagulants in paediatric patients. Clin Pharmacokinet. 2013;52:967–80.
24. Ganetsky M, Babu KM, Salhanick SD, et al. Dabigatran: review of pharmacology and management of bleeding complications of this novel oral anticoagulant. J Med Toxicol. 2011;7:281–7.
25. Eikelboom JW, Wallentin L, Connolly SJ, et al. Risk of bleeding with two doses of dabigatran compared with warfarin in older and younger patients with atrial fibrillation: An analysis of the Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) Trial. Circulation. 2011; 123:2363–72.
26. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009; 361:1139–51.
27. Pollack Jr CV, Reilly PA, Eikelboom J et al. Idarucizumab for dabigatran reversal. NEJM. 2015; 373 (6): 511-520.
28. Siegal DM, Curnutte JT, Conolly SJ et al. Andexanet alfa for the reversal of factor Xa inhibitor activity. NEJM. 2015; 373 (25); 2413 – 2424.
29. Pisters R., Lane D.A., Nieuwlaat R. et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: The Euro Heart Survey. Chest 2010; 138 (5):1093–100.
30. Lip GYH, Banerjee A, Lagrenade I et al. Assessing the risk of bleeding in patients with atrial fibrillation: the Loire Valley Atrial Fibrillation project. Circ Arrhythm Electrophysiol 2012; 5:941–948.
31. Roldán V, Marín F, Fernández H et al. Predictive value of the HAS-BLED and ATRIA bleeding scores for the risk of serious bleeding in a 'real world' population with atrial fibrillation receiving anticoagulant therapy. Chest 2013; 143:179–184.
32. Goldhaber SZ, Dunn k, Mac Doughall RC. New onset of VTE among hospitalized patients at Brigham and Women's hospital is caused more often by prophylaxis failure than withholding treatment. Chest 2000; 118: 1680-4.
33. Nwagha TU, Onwunakwe HE. Understanding the RECORDS3 Trial and its impact on anticoagulation practice in poor resource countries. Nigerian Journal of Clinical Practice 2016; 19:695-9.
34. Mismetti P, Laporte-Simitsidis S, Tardy B, Cucherat M, Buchuler A, Julillard-Delsart D et al. Prevention of Venous thromboembolism in Internal Medicine with unfractionated or LMW Heparins: A meta-analysis of randomized clinical trials. Thrombo Haemost; 2000 83:14-9.
35. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwel CW et al. Prevention of VTE: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004; 126 3 supple: 3388-4008.
36. Russel RD, Hotchkiss WR, Knight JR, Huo MH. The efficacy and safety of Rivaroxaban for venous thromboembolism prophylaxis after total hip and total knee arthroplasty. Thrombosis 2013; 2013:762310.37. Prophylaxis of Venous Thromboembolism. A National Clinical Guideline; 2002. Available from http://www.sign.ac.uk/pdf/sign62.pdf. (last assessed)