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Apixaban Prescription Suitability at Hospitals Saudi Arabia

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Abstract
Studies conducted in Saudi Arabia have shown that most hospitalized NVAF patients were given the recommended dosage of apixaban and rivaroxaban. To increase the dosage appropriateness for hospitalized patients with nonvalvular atrial fibrillation (NVAF), healthcare providers should become knowledgeable about the latest recommendations for nonvitamin K-antagonist oral anticoagulants.
Aim of the study: The aim of this study was to examine Apixaban prescribing practices and identify instances of improper use.
Methodology: At Hospitals Saudi Arabia, descriptive statistics from a retrospective cross-sectional study were performed on 220 patients who were prescribed Apixaban.
Results: The findings verify that as the renal function test's normal rate rises or falls, the recommended dosage falls. This indicates that physicians are prescribing the right amount of apixaban.
Conclusion: The majority of apixaban prescriptions were written for patients based on approved dosages after pharmacist and physician verification.
Keywords: Apixaban, Prescription and Suitability.

Introduction

Apixaban is a selective oral direct reversible inhibitor of coagulation factor Xa (FXa) that has been approved for use in treating pulmonary embolism (PE) and deep vein thrombosis (DVT), reducing the risk of recurrent PE and DVT following initial therapy, and providing thromboprophylaxis in patients who have had elective hip or knee replacement surgery. Patients with nonvalvular atrial fibrillation can also be treated with apixaban. Apixaban can be eliminated in a number of ways, such as via metabolism, intestinal excretion, and renal clearance (Wang, X. et al., 2016).

Direct oral anticoagulants, or DOACs, have been the subject of substantial randomized clinical investigations involving patients with nonvalvular atrial fibrillation. DOACs were demonstrated to be either noninferior or superior to warfarin in terms of effectiveness end goals, with comparable or lower rates of bleeding, especially cerebral hemorrhage. Information regarding the type of DOAC utilized, dosage, and adoption rate is scarce, nevertheless. Previous studies on adoption rates showed that DOAC use increased while warfarin use decreased (Wong, S. L. et al., 2018).

Since DOACs have a shorter half-life and are therefore associated with a quicker onset of action, strict adherence is likely to be a significant factor in the clinical practice of DOAC efficacy in patients with atrial fibrillation. However, in practice, adherence is still challenging. Few large-scale real-world studies on DOAC adherence have been reported, and there have been concerns raised regarding the potential impact of low adherence on DOAC efficacy. Problems with DOAC dosage schedules, renal function, and drug interactions can all lead to suboptimal DOAC use (Perreault, S. et al. 2020).

Thromboprophylaxis after hip or knee replacement surgery, prevention of recurrent deep vein thrombosis and pulmonary embolism, treatment of deep vein thrombosis or pulmonary embolism, and reduction of stroke risk in

non-valvular atrial fibrillation are among the thromboembolic disorders for which apixaban, an oral direct factor Xa inhibitor, has been approved for clinical use (Lip et al., 2018).

Apixaban's oral bioavailability is around 50%. In a clinical context, bioavailability is not much impacted by food. Oral dosages up to 10 mg are dose-proportionately increased following apixaban administration. With a half-life of roughly 12 hours, apixaban is quickly absorbed and reaches its peak concentration 3–4 hours after oral administration. Apixaban can be eliminated through metabolism, biliary excretion, and direct intestinal excretion, among other routes. Renal excretion accounts for around 27% of the total clearance of apixaban. Apixaban can be taken at a set dosage without the need for therapeutic drug monitoring because of its consistent pharmacokinetics across a wide range of users and its low number of clinically significant interactions with the majority of widely prescribed drugs. Plasma levels and the pharmacodynamic impact of apixaban are closely connected (Byon et al., 2019).

Patients who are at risk of stroke or venous thromboembolism (VTE) are increasingly being treated in clinical settings using direct oral anticoagulants (DOACs). Long-term users benefit from these drugs' quick anticoagulation onset, stable anticoagulation profile (which allows the prescription of specific doses), and absence of need for routine monitoring. Acute ventricular fibrillation (VTE) can be prevented and treated with the selective factor Xa inhibitor apixaban. In patients with nonvalvular atrial fibrillation, it is also authorized to prevent stroke. It works quickly and produces consistent coagulation results, just like many other DOACs. Apixaban has a strong safety record and is equally effective at preventing stroke and VTE as vitamin K antagonists, according to a number of randomized controlled trials, such as ARISTOTLE and AMPLIFY(Hurst et al., 2017).

To prevent overdose and bleeding or thromboembolic events that could result in strokes, direct oral anticoagulants (DOACs) must be taken as prescribed. The range of anticoagulant alternatives available for the treatment of venous thromboembolism (VTE) and atrial fibrillation (AF) has increased with the development of DOACs. Significant research shown that they have a better safety profile and fewer severe bleeding events than vitamin K antagonists (VKAs) when used to treat VTE in both acute and long-term settings. Compared to VKAs, fewer cases of hemorrhagic strokes and cerebral hemorrhages were reported in AF patients (Moudallel et al., 2018).

Literature review

32 intensive care unit (ICU) patients with severe COVID-19 respiratory illness who were treated with apixaban for atrial fibrillation (AFib), venous thromboembolism (VTE), catheter-induced thrombosis, and COVID-19-induced coagulopathy were included in this single-center, retrospective cohort study. The purpose of this study was to describe the safety and effectiveness results of a group of COVID-19 patients in the intensive care unit (ICU) who were using apixaban as a therapeutic dose for a severe respiratory condition. According to the study's findings, apixaban seems to be safe and helpful for critically ill intensive care unit patients with severe COVID-19 illness (Wenzler et al., 2020).

In a prospective, open, multi-center study with blinded outcome assessment, Kirchhof et al. (2018) evaluated vitamin K antagonists (VKA, international normative ratio 2-3) against continuous apixaban (5 mg b.i.d.) in patients with atrial fibrillation who were at risk of stroke. According to the study's findings, atrial fibrillation ablation patients who are at risk for stroke can safely and effectively utilize continuous apixaban to reduce their risk of bleeding, stroke, and cognitive decline (Kirchhof et al., 2018).

Apixaban and rivaroxaban were not part of the randomized controlled studies that included patients with upper extremity deep vein thrombosis (UE-DVT), despite being licensed for the treatment of venous thromboembolism (VTE). The safety and efficacy of rivaroxaban and apixaban in the management of acute UE-DVT were assessed by an investigation. According to the findings, treating UE-DVT with rivaroxaban or apixaban seemed to be just as safe and successful as using LMWH/warfarin (Houghton et al., 2020).

Significant of study

Studies conducted in Saudi Arabia have shown that most hospitalized NVAF patients were given the recommended dosage of apixaban and rivaroxaban. To enhance dosage appropriateness in hospitalized patients with nonvalvular atrial fibrillation (NVAF), healthcare providers should become knowledgeable with the latest recommendations for non-vitamin K-antagonist oral anticoagulants (Alshibani, 2023). The aim of this study was to examine Apixaban prescribing practices and identify instances of improper use.

Objectives

1- Examine how Apixaban is prescribed.
2- Verify that doctors are administering the appropriate dosage of Apixaban.
3- List the most often used Apixaban indications.

Questions

1- What are the Apixaban prescribing patterns?
2- Do physicians recommend the right dosage of Apixaban?

3- Which Apixaban indications are most frequently used?

Study Design

Descriptive statistics of a retrospective cross-sectional study.

Study area and target population

Patients who received Apixaban at Hospitals Saudi Arabiaduring the period of five years ranging from 2017-2022.

Sample size

220 Patients who received Apixaban at Hospitals Saudi Arabia.

Tools and Procedures

Data Collection Sheet

Inclusion criteria:

1- All patients aged 18 years and over.
2- who received Apixaban from January 2017 to December 2022.

Exclusion criteria:

1- Any patient received Apixaban outside the time range from January 2017 to December 2022.

Methodology

This chapter discusses the research design, approach, setting, participants ofthe study, data gathering, validation process and ethical considerations, as well as data analysis.

Research Design:

Cross-sectional quantitative descriptive study design.

Population, sample and sampling technique:

The population of the research are Hospitalized patients with NVAF who received the recommended dose of apixaban and rivaroxaban.

The study focuses on a sample of Hospitalized patients with NVAF who received the recommended dose of apixaban and rivaroxaban and meet our inclusion/exclusion criteria. The sample size was found that 197 participants.

Results

Table(1) demographic data:

Variable	Category	Frequency	Percent
Gender	Male	95	48.2
	Female	102	51.8
Age	Minimum=17 Maximum=96 Mean=62.2183, STD=18.07		

1-Gender

From the above table we conclude that (51.8%)of the sample study are females ,and (48.2%) of the sample study are males

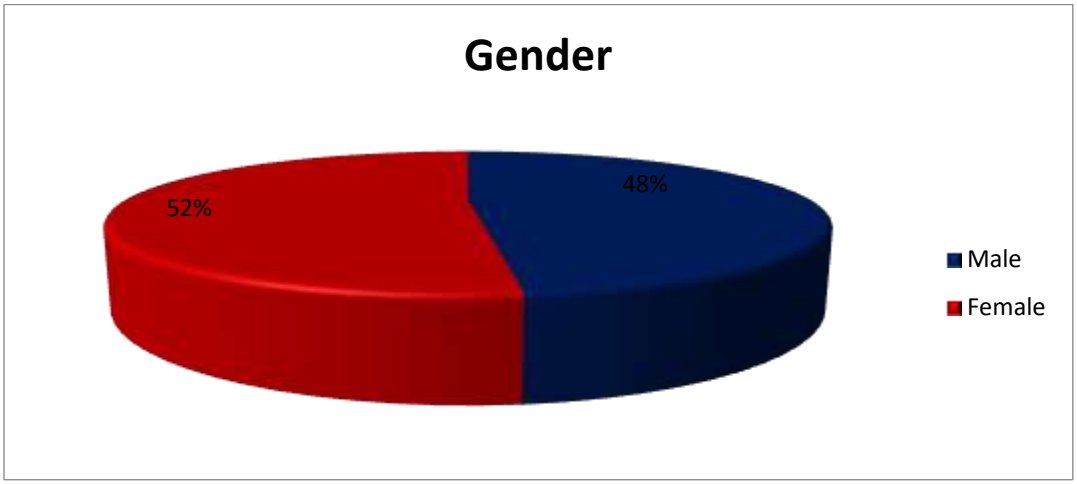

Figure 1. gender.

2-Age

The age of the sample study is ranged between 17 and 96 years old with mean ages (62.2183) and standard deviation (18.07)

Identify the most common indications for Apixaban.

Table (2) Apixaban Indication:

Apixaban Indication	Frequency	Percent
Arterial Embolism	2	1.0
Atrial Fibrillation	62	31.4
Cardioembolic Stroke	7	3.6
COVID-19 Positive	46	23.4
DVT prophylaxis	2	1
DVT treatment	23	11.7
Heparin-induced thrombocytopenia	2	1
Hepatic vein thrombosis (HVT)	1	0.5
Inferior vena cava (IVC) thrombosis	1	0.5
No clear indication	10	5.1
Portal Veins Thrombus	2	1
Pulmonary Embolism	9	4.6
Suspected COVID-19	5	2.5
Thrombocytopenia	1	0.5
VTE prophylaxis in orthopedic surgery	24	12.2
Total	**197**	**100.0**

From the above table we conclude that (31.4%) of the sample study take Apixaban Indication to Atrial Fibrillation , (23.4 %) of the sample study take Apixaban Indication to COVID-19 Positive,(12.2%) of the sample study take Apixaban Indication to VTE prophylaxis in orthopedic surgery, and (11.7%) of the sample study take Apixaban Indication to DVT treatment

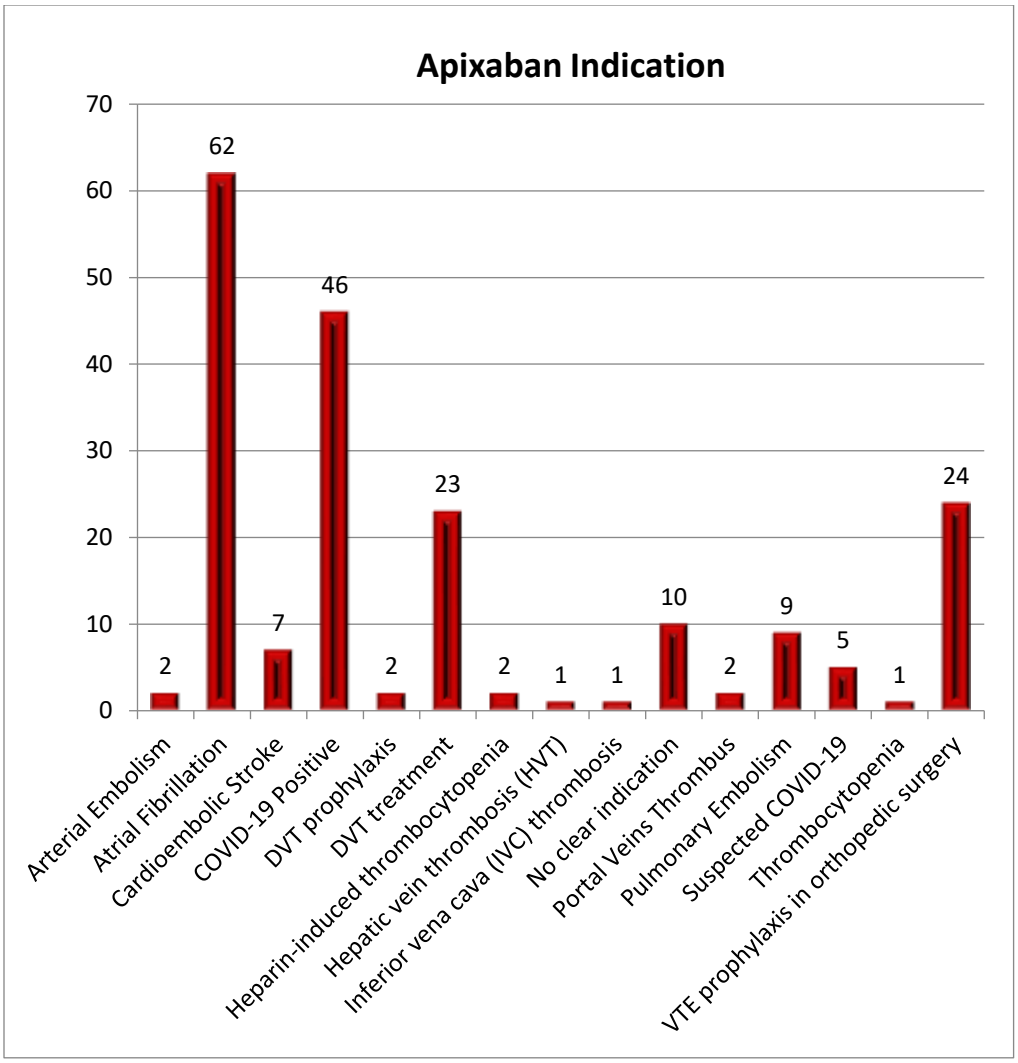

Figure 2.Apixaban Indication.

Explore prescribing patterns of Apixaban.

Table(3) Dose:

Dose	Frequency	Percent
2.5 mg	93	47.2
5 mg	81	41.1
5 mg / 2.5 mg	2	1.0
10 mg	3	1.5
10 mg / 5 mg	18	9.1
Total	**197**	**100.0**

From the above table we conclude that (47.2%) of the sample study their Dose of Apixaban is 2.5 mg , (41.1%) of the sample study their Dose of Apixaban is 5 mg, (9.1%) of the sample study their Dose of Apixaban is 10 mg / 5 mg , (1.5%) of the sample study their Dose of Apixaban is10 mg, and (1.0%) of the sample study their Dose of Apixaban is 5 mg / 2.5 mg

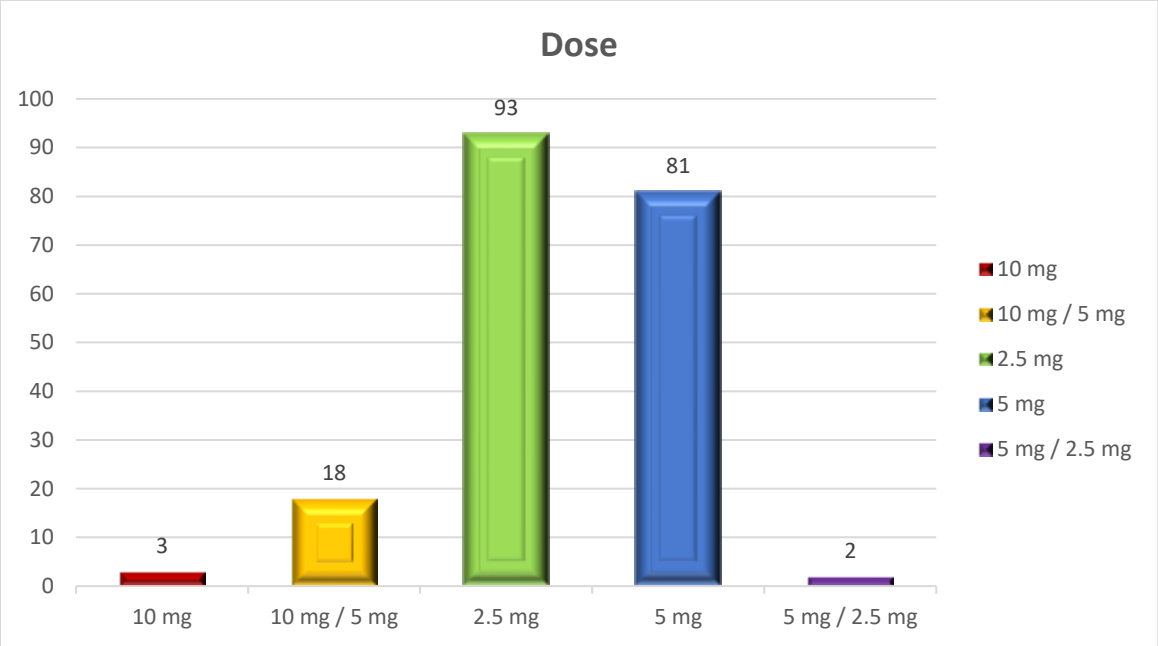

Figure 3. Dose.

Table (4) Frequency times:

Frequency times	Frequency	Percent
Once daily	14	7.1
Twice daily	183	92.9
Total	**197**	**100.0**

From the above table we conclude that (92.9%) of the sample study take Doseof Apixaban Twice daily , and (7.1 %) of the sample study take Dose of Apixaban Once daily

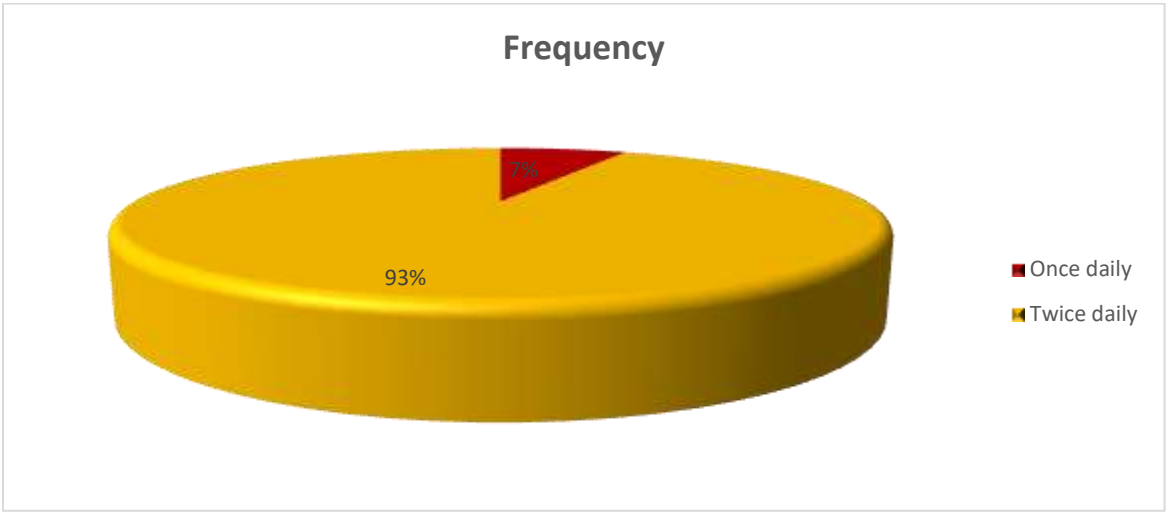

Figure 3. Frequency.

Determine if doctors prescribe the appropriate dose of Apixaban.

1-For Serum Creatinine (SCr) (umol/L) we found the Dose of Apixaban was distributed as the following table (5):

		Serum Creatinine			
		Mean	STD	Max	Min
Dose	2.5 mg	131.73	125.623	801	41
	5 mg	121.28	92.053	588	47
	5 mg / 2.5 mg	200.50	53.033	238	163
	10 mg	85.00	38.626	127	51
	10 mg / 5 mg	83.35	90.241	426	36

The above table illustrates the Dose of Apixaban according to Serum Creatinine where Normal Range of Serum Creatinine is (50 - 115) , and from the table we found that the dose of 2.5 mg , 5 mg is recommended to when Serum Creatinine is more than 115 and less than 50

so, the results confirm that With an increase or decrease from the normal rate, the specified dose decreases This means that doctors prescribe the appropriate dose of apixaban

table (6)Creatinine Clearance:

		Creatinine Clearance			
		Mean	STD	Max	Min
Dose	2.5 mg	68.49	31.873	145	4
	5 mg	68.95	32.591	135	7
	5 mg / 2.5 mg	34.00	12.728	43	25
	10 mg	84.00	43.555	132	47
	10 mg / 5 mg	99.88	33.213	153	9

The above table illustrates the Dose of Apixaban according to Creatinine Clearance where Normal Range of Serum Creatinine is 1.73 m, and from the table we found the dose of 2.5 mg , 5 mg is recommended to Creatinine Clearance more than 1.73 and less than 1.73

so, the results confirm that With an increase or decrease from the normal rate, the specified dose decreases This means that doctors prescribe the appropriate dose of apixaban

Discussion

Patients with nonvalvular atrial fibrillation (NVAF) can prevent stroke and systemic embolism by using apixaban, a direct oral anticoagulant (DOAC). The only requirement for renal dose adjustments for other DOACs is creatinine clearance. However, apixaban necessitates more intricate dosage adjustments, which could lead to errors while giving it (Gibson, C. M. et al. 2018).

According to prescribing dosage guide for apixaban which prescribed in this table (7):

Disease	Dose in normal kidney	Dose in abnormal kidney and age ≥80
Covid 19	2.5mg	2.5mg
Stroke & systemic embolization	5mg	2.5mg
Deep veinous thrombosis & pulmonary embolization	10mg for 7 days Then 5mg	
Hip replacement & knee replacement	2.5mg	2.5mg
Atrial fibrillation	5mg	2.5mg
prophylaxis in orthopedic surgery	2.5mg	2.5mg

We discovered that the findings support the idea that the recommended dosage falls when the kidney function test's normal rate rises or falls. This indicates that physicians are prescribing the right amount of apixaban.

Based on apixaban prescribing patterns, we discovered that the doses of apixaban were 10 mg, 5 mg, and 2.5 mg. These doses were prescribed based on the severity of the patient's condition; for example, we discovered that doctors prescribed 10 mg and 5 mg for pulmonary embolization and deep veinous thrombosis because these conditions are critical.

The usual dosage was 5 mg; if the patient was older than 80 years or had an abnormal renal function test, the dosage was reduced.

Our study's findings were supported by a 2018 study by Gibson, C. M. et al., which discovered that 87.0% of apixaban prescriptions were dosed in compliance with the approved labeling. This suggests that hospitalized patients continue to follow the more complex apixaban dosage guidelines. The providers identified the most pertinent orders. The number of orders at the permitted dose rose as a result of pharmacist evaluation, even if it was still quite modest. These findings are consistent with other research that found that between 77% and 86% of apixaban orders adhered to the package insert's recommendations (Gibson, C. M. et al. 2018).

Conclusion

The majority of apixaban prescriptions were written for patients based on approved dosages after pharmacist and physician verification.

References

1. Byon, W., Garonzik, S., Boyd, R. A., & Frost, C. E. (2019). Apixaban: A clinical pharmacokinetic and Pharmacodynamic Review. *Clinical Pharmacokinetics*, *58*(10), 1265–1279. https://doi.org/10.1007/s40262-019-00775-z
2. Lip, G. Y. H., Banerjee, A., Boriani, G., Chiang, C. en, Fargo, R., Freedman, B., Lane, D. A., Ruff, C. T., Turakhia, M., Werring, D., Patel, S., &Moores, L. (2018). Antithrombotic therapy for Atrial Fibrillation. *Chest*, *154*(5), 1121–1201. https://doi.org/10.1016/j.chest.2018.07.040
3. Hurst, K., O'Callaghan, J. M., & Handa, A. (2017). Quick reference guide to apixaban. *Vascular Health and Risk Management*, *Volume 13*, 263–267. https://doi.org/10.2147/vhrm.s121944
4. Moudallel, S., Steurbaut, S., Cornu, P., & Dupont, A. (2018). Appropriateness of DOAC prescribing before and during hospital admission and analysis of determinants for inappropriate prescribing. *Frontiers in Pharmacology*, *9*. https://doi.org/10.3389/fphar.2018.01220
5. Wenzler, E., Engineer, M. H., Yaqoob, M., & Benken, S. T. (2020). Safety and efficacy of apixaban for therapeutic anticoagulation in critically ill ICU patients with severe COVID-19 respiratory disease. *TH Open*, *04*(04). https://doi.org/10.1055/s-0040-1720962
6. Kirchhof, P., Haeusler, K. G., Blank, B., De Bono, J., Callans, D., Elvan, A., Fetsch, T., Van Gelder, I. C., Gentlesk, P., Grimaldi, M., Hansen, J., Hindricks, G., Al-Khalidi, H. R., Massaro, T., Mont, L., Nielsen, J. C., Nölker, G., Piccini, J. P., De Potter, T., … Di Biase, L. (2018). Apixaban in patients at risk of stroke undergoing atrial fibrillation ablation. *European Heart Journal*, *39*(32), 2942–2955. https://doi.org/10.1093/eurheartj/ehy176
7. Houghton, D. E., Casanegra, A. I., Peterson, L. G., Cochuyt, J., Hodge, D. O., Vlazny, D., McBane, R. D., Froehling, D., &Wysokinski, W. E. (2020). Treatment of upper extremity deep vein thrombosis with apixaban and rivaroxaban. *American Journal of Hematology*, *95*(7), 817–823. https://doi.org/10.1002/ajh.25820
8. Alshibani, M. (2023). Appropriateness of rivaroxaban and apixaban dosing in hospitalized patients with a newly diagnosed nonvalvular atrial fibrillation at a single Tertiary Hospital. *Medicine*, *102*(36). https://doi.org/10.1097/md.0000000000035058
9. Wong, S. L., Marshall, L. Z., & Lawson, K. A. (2018). Direct oral anticoagulant prescription trends, switching patterns, and adherence in Texas Medicaid. *The American journal of managed care*, *24*(8 Spec No.), SP309–SP314.
10. Perreault, S., de Denus, S., White-Guay, B., Côté, R., Schnitzer, M. E., Dubé, M. P., ... & Tardif, J. C. (2020). Oral anticoagulant prescription trends, profile use, and determinants of adherence in patients with atrial fibrillation. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *40*(1), 40-54.
11. Wang, X., Tirucherai, G., Marbury, T. C., Wang, J., Chang, M., Zhang, D., ... & Frost, C. (2016). Pharmacokinetics, pharmacodynamics, and safety of apixaban in subjects with end-stage renal disease on hemodialysis. *The journal of clinical Pharmacology*, *56*(5), 628-636.
12. Gibson, C. M., Smith, C. B., Davis, S., & Scalese, M. J. (2018). Assessment of apixaban prescribing patterns for nonvalvular atrial fibrillation in hospitalized patients. *Annals of Pharmacotherapy*, *52*(1), 54-59.