Russian Journal of Cardiology 2023;28(S2):5307
doi:10.15829/1560-4071-2023-5307
https://russjcardiol.elpub.ru

LITERATURE REVIEWS
ISSN 1560-4071 (print)
ISSN 2618-7620 (online)
ISSN 2782-2257 (online)

Comparing the efficacy and safety of direct oral anticoagulants with vitamin K antagonist in patients with atrial fibrillation and chronic kidney disease stages IV and V: systematic review and meta-analysis

Skorodumova E. G.[1], Suvorov A. Yu.[2], Enginoev S. T.[3,4], Kercheva M. A.[5], Grebenyuk M. A.[2]

Aim. This study aims to compare efficacy and safety of direct oral anticoagulants (DOAC) with vitamin K antagonist (VKA) in patients with atrial fibrillation (AF) and chronic kidney disease (CKD) stages IV and V.

Material and methods. We systematically searched the PubMed, Google Scholar, Web of Science databases from 1990 to 2022 and included all published studies that compared DOACs with VKA in patients with atrial fibrillation and chronic kidney disease stages IV and V. To search the articles, we used the PICO strategy: Patient, Intervention, Comparison, Outcome of Interest. Data extraction was undertaken by five independent researches, and then a meta-analysis was performed.

Results. Out of all, 6 studies were included in the meta-analysis: 3 randomized controlled trials (n=353) and 3 retrospective analyses (n=37470). The efficacy of DOACs was comparable with VKA. In terms of safety, DOACs and VKA also showed no statistical differences: hemorrhagic stroke, major/minor/gastrointestinal bleeding, general mortality.

Conclusion. In terms of efficacy and safety, the indicators of DOACs and VKA were generally comparable.

Keywords: vitamin K antagonist, direct oral anticoagulants, rivaroxaban, terminal renal failure, atrial fibrillation, chronic kidney disease.

Relationships and Activities: none.

[1]I. I. Dzhanelidze Research Institute for Emergency Medicine, St. Petersburg, Russia; [2]I. M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation, Moscow, Russia; [3]Federal Center for Cardiovascular Surgery of the Ministry of Health of the Russian Federation, Astrakhan, Russia; [4]Astrakhan State Medical University of the Ministry of Health of the Russian Federation, Astrakhan, Russia; [5]Research Institute of Cardiology, Tomsk Scientific Center, Siberian Branch of the Russian Academy of Medical Sciences, Tomsk, Russia.

Skorodumova E. G.* ORCID: 0000-0002-4961-5570, Suvorov A. Yu. ORCID: 0000-0002-2224-0019, Enginoev S. T. ORCID: 0000-0002-8376-3104, Kercheva M. A. ORCID: 0000-0003-1444-1037, Grebenyuk M. A. ORCID: none.

*Corresponding author: lisavetta91@mail.ru

Received: 06.12.2022
Revision Received: 31.01.2023
Accepted: 12.02.2023

For citation: Skorodumova E. G., Suvorov A. Yu., Enginoev S. T., Kercheva M. A., Grebenyuk M. A. Comparing the efficacy and safety of direct oral anticoagulants with vitamin K antagonist in patients with atrial fibrillation and chronic kidney disease stages IV and V: systematic review and meta-analysis. *Russian Journal of Cardiology*. 2023;28(2S):5307. doi:10.15829/1560-4071-2023-5307. EDN AGORXI

Chronic kidney disease (CKD) is complicated by atrial fibrillation (AF) in every fourth patient [1]. In case of combination of these two pathologies, the risk of thromboembolic complications increases against the background of equally high risk of bleedings [2]. Decrease in glomerular filtration rate (GFR) is an independent predictor of ischemic stroke/systemic embolism and bleeding [3], whereas anticoagulant treatment of patients with AF is a foundation of the prevention of thromboembolic complications. This makes it important to search the most effective and safe anticoagulant therapy in patients with CKD stages IV-V. Before the advent of alternative anticoagulants with different renal excretion, safety and efficacy parameters, vitamin K antagonist (VKA) served as the drug of choice in patients with AF [4]. However, a number of the clinical trials such as ROCKET [5], ARISTOTLE [6], RE-LY [7],

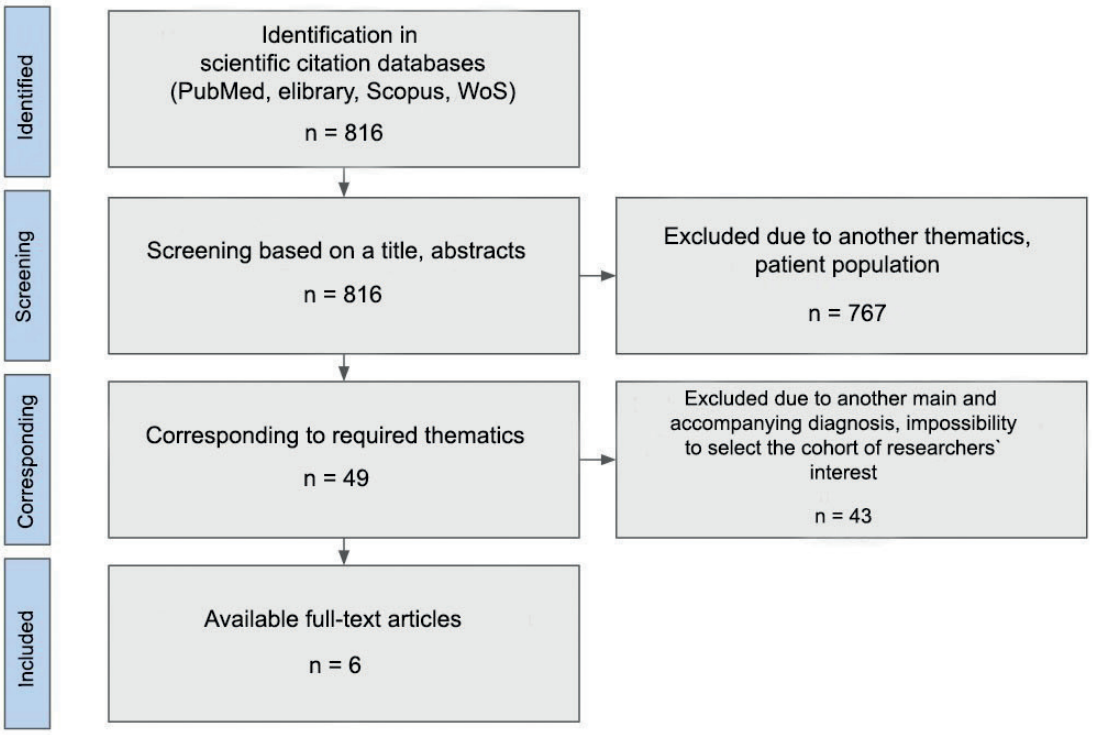

Figure 1. PRISMA-diagram of the selection.

showed the advantage or comparability of direct oral anticoagulants (DOACs) compared to VKA in patients with CKD stages I-III [3]. Meanwhile, patients with CKD stages IV-V were mainly excluded from these studies because of high risks of lethal outcome and development of complications including bleedings [8, 9]. Besides, taking of VKA is associated with calcification of vessels that additionally worsens the course of the disease, being a motivation to search an alternative therapy [10]. The modern position of experts regarding to the prescription of anticoagulants and choice of a certain drug in patients with CKD stages IV-V is that the use of DOACs in patients with CKD stage IV (creatinine clearance 15 — <30 ml/min) can be considered as to use with "caution" in reduced doses taking into account the clearance in these patients; in patients with CKD stage V (creatinine clearance <15 ml/min) as well as in patients who receive renal replacement therapy with hemodialysis, the prescription of these drugs is not approved [10] because the results of the observational studies cast doubt on the benefit of DOACs in this group of patients, while randomized controlled trials (RCT) were not carried out [11].

The paucity of the data on the use of DOACs in patients with CKD stages IV-V, on the one hand, and acceptability of their use in patients with GFR 15-30 ml/min/1,73 m^2 [9] against the background of more effective and safe use of this group of drugs in patients with CKD stages I-III, on the other hand, make the conduction of the studies on their comparison with warfarin relevant. Our meta-analysis was aimed to compare efficacy and safety of DOACs and VKA in patients with AF and CKD stages IV-V.

Material and methods

Systematic review and meta-analysis were performed in accordance with international recommendations (PRISMA)[1] (Figure 1). PICO strategy was used for the search of the studies:

- Patient — patients older than 18 years with AF and CKD stages IV-V;
- Intervention — the use of DOACs;
- Comparison — the use of VKA;
- Outcomes — the number of the endpoints: ischemic stroke, major hemorrhages, minor hemorrhages, gastrointestinal hemorrhages, total mortality.

The data sources. Literature search was conducted in the following databases: PubMed, Google Scholar, Web of Science from 1990 to 2022 for all studies where it was used terminology such as "kidney renal failure" or "terminal kidney failure", or

[1] R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/.

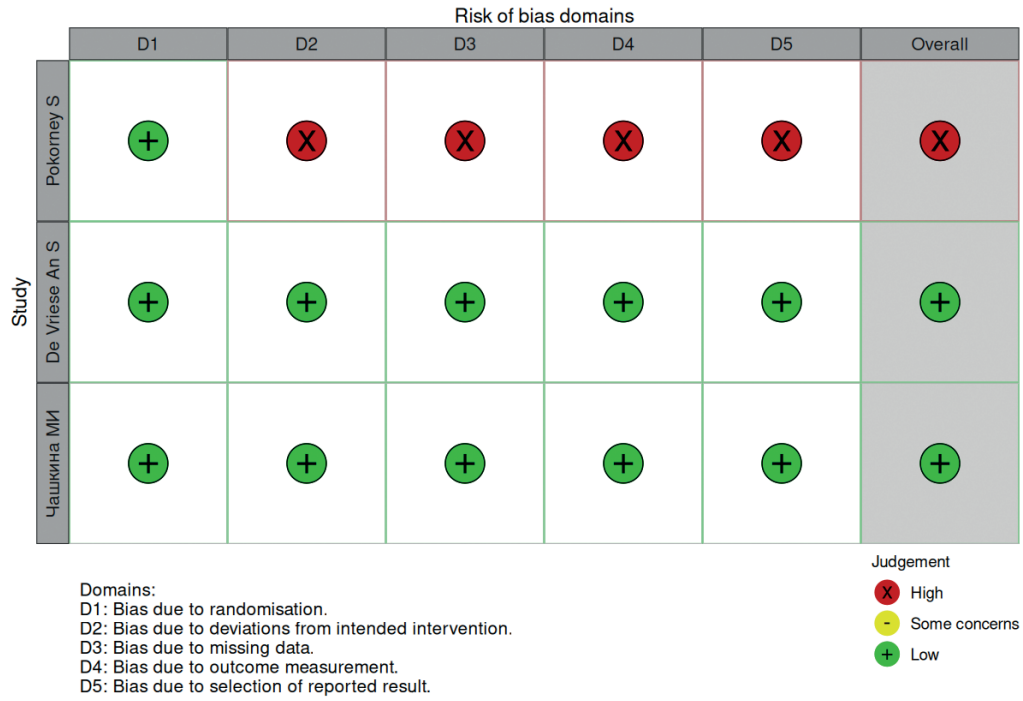

Figure 2. RCT traffic light plot.

"terminal chronic kidney disease", or "end-stage chronic kidney disease", or "Hemodialysis Patients", or "chronic kidney disease";

• and "Atrial fibrillation" (AF);

• and "NOAC" (new oral anticoagulants) or "DOAC";

• and "warfarin" or "Vitamin K antagonist" in the title or abstract.

The selection of the studies. All studies comparing DOACs and VKA in individuals with CKD IV-V stages and AF were included into our study. The Figure 1 showed the PRISMA-diagram of the selection.

The exclusion criteria:

• The studies which did not inform on clinical outcomes;

• The articles in which not the whole group had AF;

• The articles in which patients had GFR >29 ml/min/1,73 m^2.

The data extraction and quality assessment. Five reviewers independently of each other extracted the data including the details of the publications, criteria of inclusion/exclusion, demographic data of patients, sample size and results obtained. Systematic errors of publications were estimated using a funnel plot. Plot asymmetry indicated a systematic error of publication.

The data analysis. The present meta-analysis included 6 studies which documented efficacy and safety of DOACs in patients with AF and CKD stages IV-V. Three of them were RCTs, and the other 3 — large non-randomized retrospective cohort trials (non-RRCTs). All the studies contained a subgroup of patients who received VKA as well as a subgroup received one or several DOACs. Thus, the subgroup received VKA was chosen as reference; the subgroups received DOACs were main within the framework of this meta-analysis.

The investigated criteria of efficacy and safety included the following endpoints: total mortality for the time period of the study conduction, systemic arterial embolisms, newly emerged ischemic stroke, hemorrhagic stroke, major and minor hemorrhages, and when it was possible, gastrointestinal bleedings were selected separately.

The analytical data processing and meta-analysis were performed using R v.4.2 with connection of meta, metafor, dmetar libraries.

To estimate the different types of potential bias, traffic light plots were used separately for RCTs (RoB) and non-RRCTs (ROBINS-I).

Due to retrospective character of a half of the studies, odds ratio (OR) was used to estimate weighted effect size.

Due to significant differences in the sizes of the studies, different time period of their conduction, different types of the study designs (RCT/non-RRCT) as well as the differences in the goals stated in the research, we used the random effects model as the main model for the meta-analysis conduction.

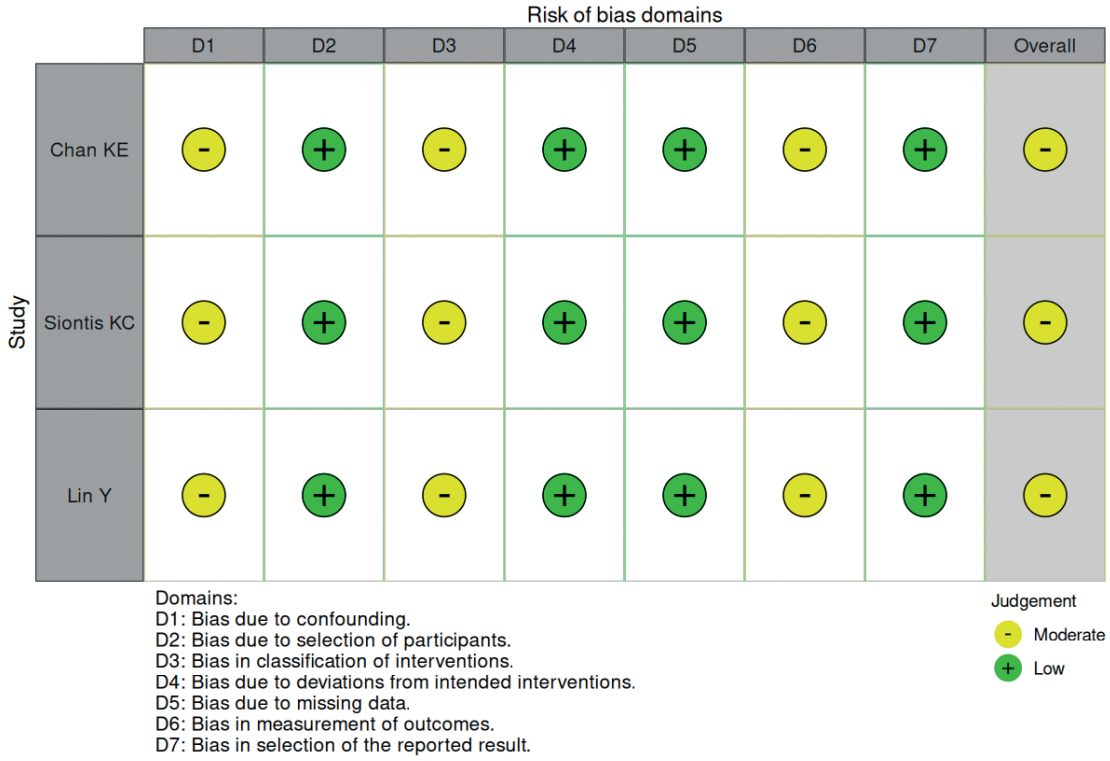

Figure 3. Non-RRCT traffic light plot.

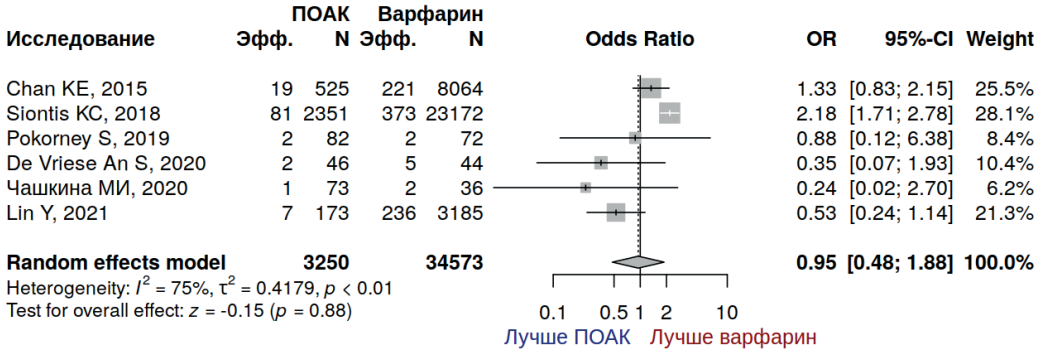

Figure 4. Forest plot for comparison of the effect regarding to the ischemic stroke prevention.
Abbreviation: ПОАК — прямые пероральные антикоагулянты (DOAC — direct oral anticoagulants).

Heterogeneity was estimated by the reverse dispersion method; to estimate dispersion of distributional effects in the random effects model (τ^2), restricted maximum-likelihood method (restricted maximum-likelihood estimator (REML)) was used. The estimation of heterogeneity was conducted by calculating Q-statistics and its significance, and I^2-Higgins and Thompson statistics.

Sensitivity analysis was carried out according to the principle *leave-one-out* with estimation of the impact of the exclusion of each study on the weighted effect and heterogeneity.

The potential publication bias was conducted visually using the funnel plots, and also when calculating the Peters test (at the same time, the results of this test are doubtful taking into account the small number of studies).

To make possible subgroups we considered the type of the study and the type of the anticoagulant used as well as their combination. Because of small number of the studies included into the meta-analysis, the results of the subgroup analysis are generally hypothesis-forming in nature; the results of the traditionally used Q-test (Omnibus test) and its significance are also

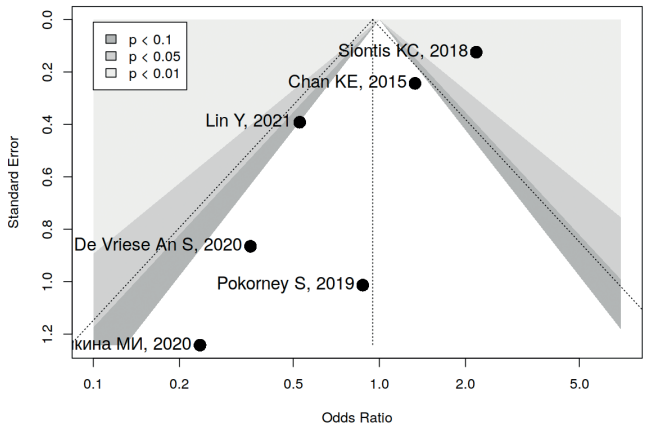

Figure 5. Funnel plot for comparison of a publication bias.

questionable, which is a limitation of this study [12, 13]. In the subgroup analysis, a common across all the studies without recalculation across the subgroups was used; such an approach is recommended for this type of analysis under condition of small number of studies in meta-analysis [13, 14].

Due to the significant above-mentioned differences in the studies as well as their small number in the meta-analysis, it was decided to refrain from conducting a network meta-analysis (this contradicts the basic postulate of transitivity of included studies according to the Cochrane recommendations[2] until the greater number of analogous studies appears).

Results

The quality assessment of the studies included into the meta-analysis

The 6 studies included into the meta-analysis contain the information on 34573 patients.

Among 3 RCTs one study was conducted in Russian Federation. The Pokorney S[3] study was stopped because of the lack of funding but its results are partly available. Other RCTs are conducted in accordance with protocols and included small size samples. Thus, the probability of bias at different stages of the conduction of these studies is assessed as quite low. Below, the RCT traffic light plot is given (Figure 2). The three included cohort studies declared the endpoint evaluation and consideration of safety

[2] Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from https://www.training.cochrane.org/handbook.

[3] Pokorney S. RENal hemodialysis patients ALlocated apixaban versus warfarin in Atrial Fibrillation — RENAL-AF Poster in AHA-2019 Some information about research in https://clinicaltrials.gov/ct2/show/results/NCT02942407.

Table 1

Clinical characteristics of patients

Author and link to the study	Type of study	Year of study	Number of included patients	DOAC drug	Mean age, years	Women, %	CHA_2DS_2-VASc mean point	Stroke %	Embolisms, %	HF, %	AH, %	DM, %
Chan K [15]	non-RRCT	2015	VKA — 8064 D — 281 R — 244	dabigatran, rivaroxaban	VKA — 70,6 D — 68,4 R — 66,9	VKA — 38,8 D — 26,9 R — 39,5	VKA — 2,4 D — 2,3 R — 2,2	VKA — 12,7 D — 12,5 R — 16,0	VKA — 12 D — 11,2 R — 14,6	VKA — 20,8 D — 14,6 R — 14,1	No data	VKA — 67,9 D — 70,4 R — 67,8
De Vriese A [16]	RCT	2020	VKA — 44 R — 46	rivaroxaban	VKA — 80,3 R — 79,9	VKA — 43,3 R — 23,9	VKA — 4,8 R — 4,7	VKA — 36,4 R — 32,6	No data	VKA — 20,5 R — 37,0	No data	VKA — 45,5 R — 45,5
Lin Y [8]	non-RRCT	2021	VKA — 3185 R — 173	rivaroxaban	VKA — 69 R — 75	VKA — 49 R — 45	VKA — 3,7 R — 4,0	VKA — 13 R — 19	No data	VKA — 37 R — 33	No data	VKA — 51 R — 41
Siontis K [4]	non-RRCT	2018	VKA — 23172 A — 2351	apixaban	VKA — 68,9 A — 68,1	VKA — 54,3 A — 54,1	VKA — 5,24 A — 5,27	No data	No data	VKA — 77,5 A — 79,5	VKA — 99,6 A — 99,6	VKA — 74,9 A — 75,4
Pokorney S[3]	RCT	2019	VKA — 72 A — 82	apixaban	No data	VKA — 30,5 A — 41,5	No data	No data	No data	No data	No data	No data
Chashkina M [8]	RCT	2020	VKA — 36 R — 73	rivaroxaban	VKA — 78 R — 77	VKA — 61 R — 56	VKA — 4,7 R — 4,6	VKA — 36 R — 10	VKA — 28 R — 8,2	VKA — 44 R — 56	VKA — 96 R — 98	VKA — 44 R — 37

Abbreviations: A — apixaban, VKA — vitamin K antagonist, AH — arterial hypertension, D — dabigatran, non-RRCT — non-randomized cohort retrospective trial, DOAC — direct oral anticoagulants, R — rivaroxaban, RCT — randomized controlled trial, DM — diabetes mellitus, HF — heart failure.

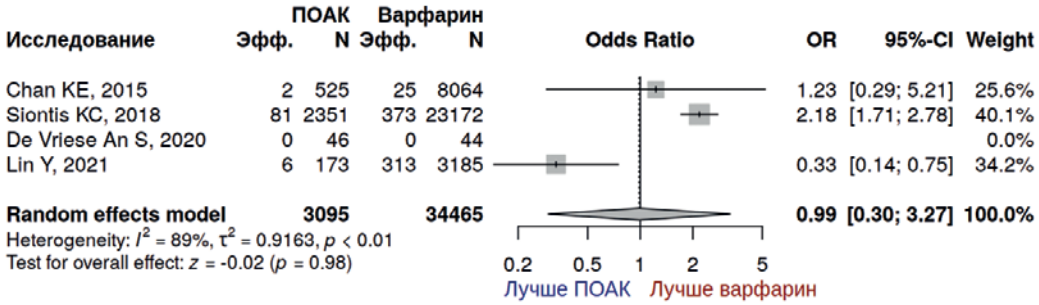

Figure 6. Forest plot for comparison of the effect regarding to systemic embolism prevention.
Abbreviation: ПОАК — прямые пероральные антикоагулянты (DOAC — direct oral anticoagulants).

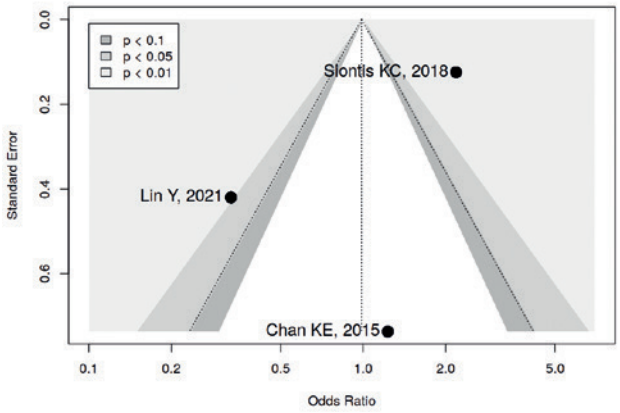

Figure 7. Funnel plot for comparison of a publication bias.

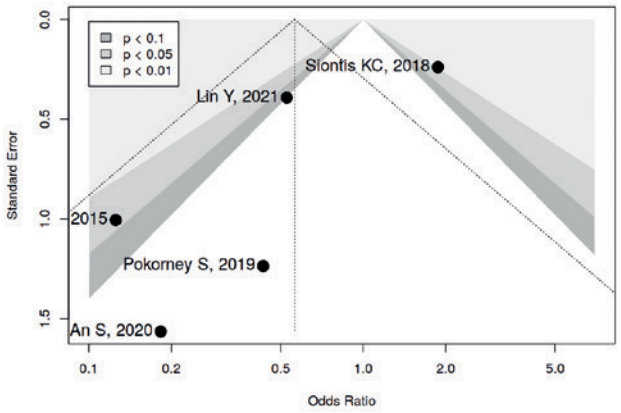

Figure 9. Funnel plot for comparison of a publication bias.

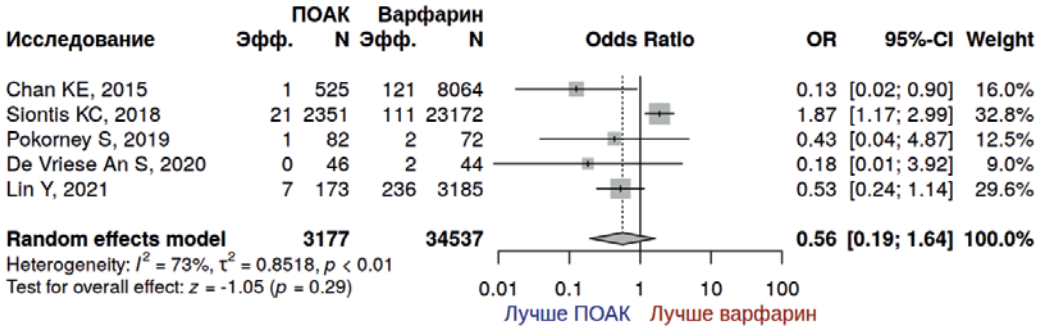

Figure 8. Forest plot for evaluation of odds of the hemorrhagic stroke development in patients.
Abbreviation: ПОАК — прямые пероральные антикоагулянты (DOAC — direct oral anticoagulants).

and efficacy criteria in different ways. The aims of these studies were also a little bit different that can potentially lead to confounding when estimating a weighted effect. In general, the authors of the meta-analysis assess all non-RRCTs as having these of those sources of bias up to moderate (Figure 3).

The clinical characteristics of patients

The clinical characteristics of patients are presented in Table 1.

The studies included 34573 patients who received VKA therapy, 281 — dabigatran, 2433 — apixaban and 536 — rivaroxaban therapy. In general, the groups were comparable in the main demographic parameters.

The quality assessment of efficacy

The main purpose of taking anticoagulants in patients with AF is the prevention of thrombotic and thromboembolic complications. Among the efficacy

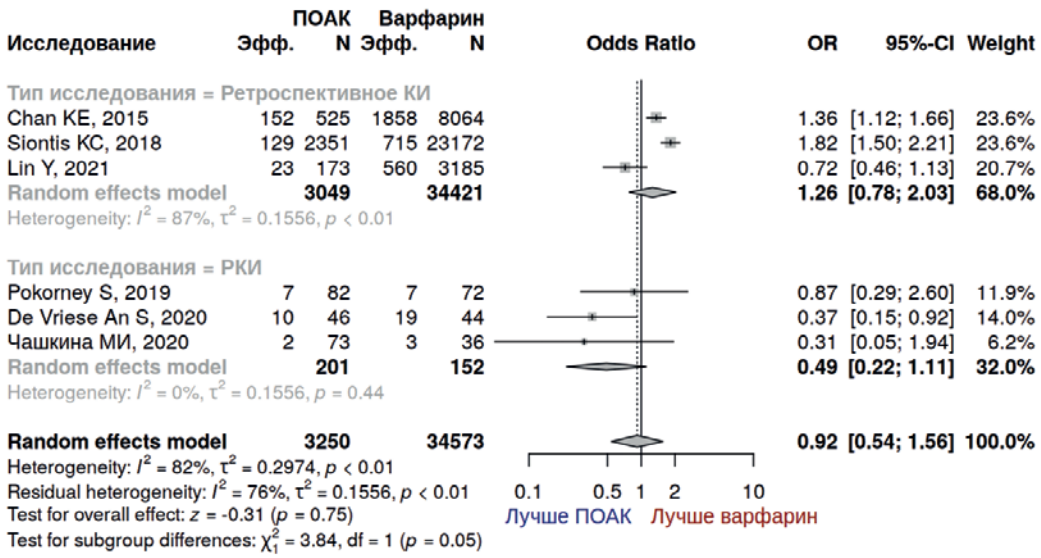

Figure 10. Forest plot for assessment of safety regarding to major hemorrhage depending on the type of the study.
Abbreviations: ПОАК — прямые пероральные антикоагулянты (DOAC — direct oral anticoagulants), РКИ — рандомизированные контролируемые исследования (RCT — randomized controlled trials).

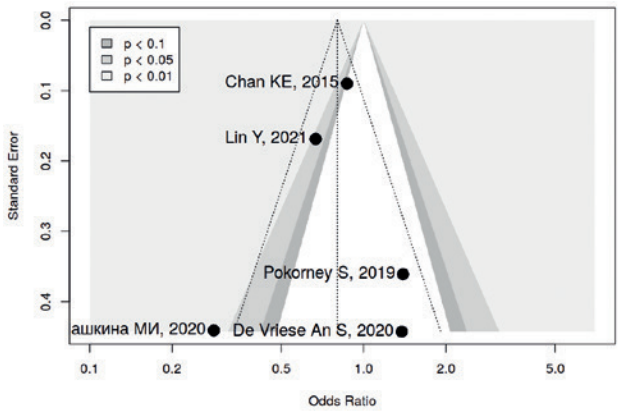

Figure 11. Funnel plot for comparison of a publication bias.

criteria newly occurred ischemic stroke and systemic arterial embolisms were evaluated.

Ischemic stroke

Regarding to ischemic stroke, DOACs were generally comparable with VKA, OR =0,95 (0,48; 1,88), p=0,88 (Figure 4). The only study where VKA had more beneficial effect was the study of Siontis KC, et al. [4]. Visually, on the funnel plot, the RCT results are more displaced to the side of the DOAC advantage, however, 2 large non-RRCTs balance their influence. The Peters test results also speak rather about the absence of a publication bias (Figure 5).

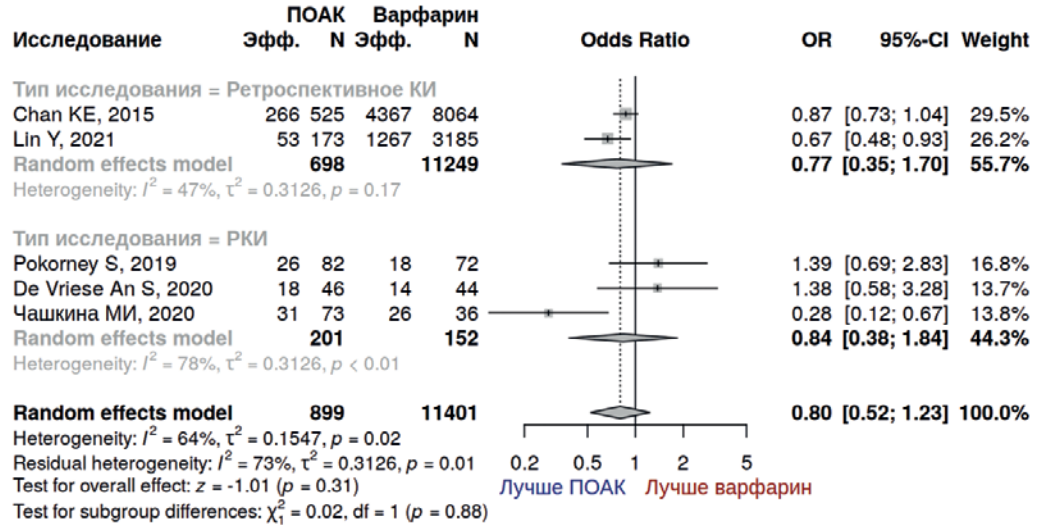

Figure 12. Forest plot for assessment of safety regarding to minor hemorrhage depending on the type of the study.
Abbreviations: ПОАК — прямые пероральные антикоагулянты (DOAC — direct oral anticoagulants), РКИ — рандомизированные контролируемые исследования (RCT — randomized controlled trials).

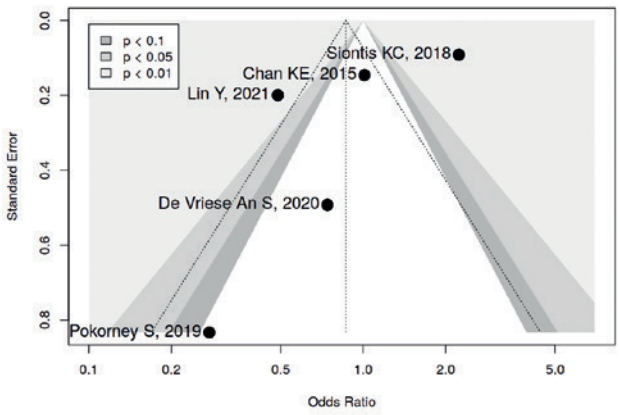

Figure 13. Funnel plot for comparison of a publication bias.

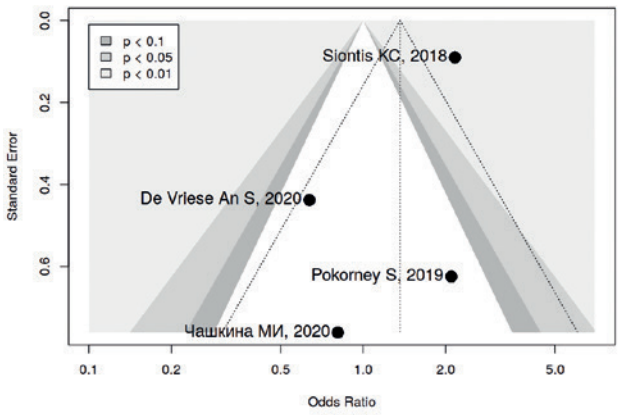

Figure 15. Funnel plot for comparison of a publication bias.

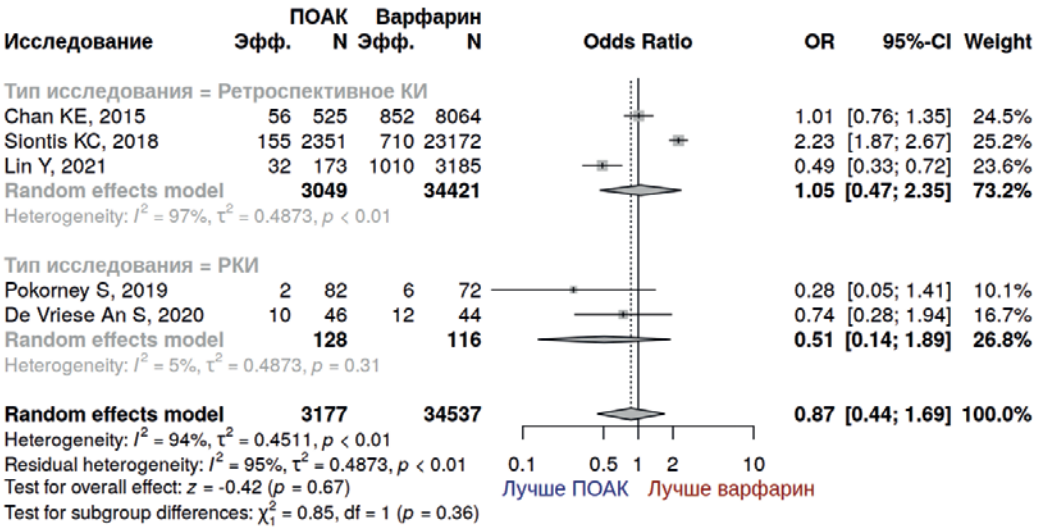

Figure 14. Forest plot for assessment of safety regarding to gastrointestinal bleeding depending on the type of the study.
Abbreviations: ПОАК — прямые пероральные антикоагулянты (DOAC — direct oral anticoagulants), РКИ — рандомизированные контролируемые исследования (RCT — randomized controlled trials).

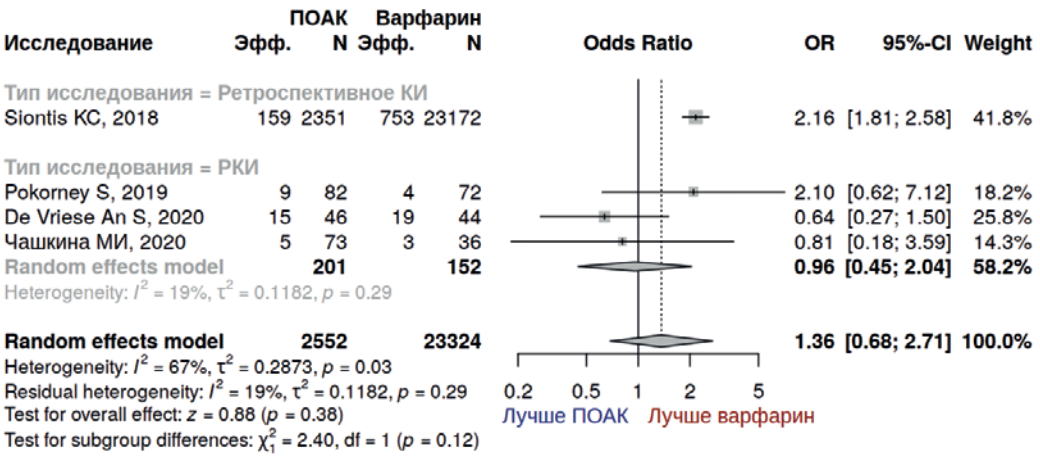

Figure 16. Forest plot for assessment of safety regarding to total mortality depending on the type of the study.
Abbreviations: ПОАК — прямые пероральные антикоагулянты (DOAC — direct oral anticoagulants), РКИ — рандомизированные контролируемые исследования (RCT — randomized controlled trials).

Systemic embolisms

The information on systemic embolisms were available in 4 studies where the effect was multidirectional. Of these 4 studies only one was RCT (De Vriese AS, et al. [16]), in which, however, the achievement of the endpoint was not noted. A weighted effect indicates an equivalent efficiency of DOACs and VKA, OR =0,99 (0,30; 3,27), p=0,98 (Figure 6). To estimate a potential publication bias with 3 studies, only funnel plot was used; the studies are placed relatively symmetrically, and there is no foundation to talk about signs of an obvious bias (Figure 7).

Assessment of safety criteria

Among the safety criteria, we evaluated both those that are directly related to the use of anticoagulants in the form of hemorrhagic complications and indirectly — in the form of total mortality. Certainly, patients with CKD stages IV-V can develop coagulopathy of this or that degree apart from anticoagulant-induced, and, taking into account the burden associated with cardiac rhythm disturbance, the mortality is induced by well-known causes.

Hemorrhagic stroke

The information on such a formidable complication as hemorrhagic stroke was available in 5 studies. The study of Slontis KC, et al. [4] noted the advantage of VKA, and as for the other studies, the endpoint was shifted to the side of the advantage of DOACs that was significant only in the study of Chan KE, et al. [15]. A weight effect showed significant advantage of neither DOACs or VKA, OR =0,56 (0,19; 1,64), p=0,29 (Figure 8). Visually, the larger studies with an insignificant error are grouped near the weight effect, while the small RCTs are shifted to the left. The Peters test demonstrates a low likelihood of publication bias (Figure 9).

Major hemorrhages

The large non-RRCTs of Chan KE, et al. [15] and Siontis KC, et al. [4] demonstrate the advantage of VKA over DOACs, and as for the other studies which all are RCTs, DOACs are more benefit, moreover, in the RCT of De Vriese AS, et al. [16], DOACs are significantly more benefit than VKA. The weighted effect shows an obvious advantage of neither DOACs or VKA, OR =0,92 (0,54; 1,56), p=0,75 (Figure 10). The Peters test results show low likelihood of publication bias but visually, it can be noted that the results are concentrated at the side where DOACs have an advantage in the effect (Figure 11).

Minor hemorrhages

The interpretation of this endpoint was somewhat different from the study to study. It was possible to conduct the analysis of this complication for 5 studies. In general, in comparison of DOACs to VKA, the results of the studies demonstrate multidirectional character, and the weighted effect indicates an advantage of neither DOACs or VKA, OR =0,80 (0,52; 1,23), p=0,31 (Figure 12). The visual analysis and Peters test results indicate the low likelihood of publication bias (Figure 13).

Gastrointestinal bleedings

The results of 5 studies were available to estimate the endpoint in the form of gastrointestinal bleedings. The comparison of safety of DOACs with VKA revealed no any advantages, OR =0,87 (0,44; 1,69), p=0,65 (Figure 14). Visual assessment demonstrates a certain tendency to the displacement to the side of the DOACs advantage, however, the Peters test results are not significant (Figure 15).

Total mortality

The total mortality results were available for all RCTs and 1 non-RRCTs. In general, an advantage of neither VKA or DOACs was noted, OR =1,36 (0,68; 2,71), p=0,38 (Figure 16).

Discussion

As far as we know, this is the first meta-analysis which investigates the efficacy and safety profiles of DOACs compared to VKA in patients with AF and CKD stages IV-V. Unlike other meta-analyses [15, 17] which included patients with different CKD stages or patients who received renal replacement therapy with hemodialysis, we focused precisely on patients with CKD stages IV-V and AF who are not presented separately in the previous studies and, in detailed analysis of the included studies, we notice that they involved patients not only with AF but also with deep vein thrombosis and pulmonary thromboembolism.

Our meta-analysis is a comprehensive review of the current data of six clinical trials for the use of DOACs and VKA in patients with AF and CKD stages IV-V regarding their safety and efficacy as well as separate analysis of DOAC drugs in the subgroups. It included 3 RCTs (one of them was carried out by Russian authors) and 3 retrospective studies. This systematic review included 37823 patients with AF and CKD stages IV-V, 3250 (8,6%) of which took DOACs and 34573 (91,4%) took VKA. The result showed that DOACs were as effective as warfarin in prevention of stroke and systemic embolism and safe regarding to hemorrhagic stroke, major, minor and gastrointestinal hemorrhages, and lethal outcomes.

The results of a previously published meta-analysis [17] comparing DOACs with VKA in patients with AF who received renal replacement therapy with hemodialysis showed that DOACs were as effective as VKA in prevention of stroke and safe regarding to the development of hemorrhagic stroke,

major and gastrointestinal hemorrhages. However, DOACs were associated with higher frequency of systemic embolism, minor hemorrhages and lethal outcomes compared to VKA.

One of the main advantages of DOACs over VKA is the absence of the need in laboratory control. But for some patient cohorts including patients on hemodialysis, it can be important to determine either actual concentration of DOACs (quantitatively), or the effect of DOACs (qualitatively). None of the included studies evaluated the level or effect of DOACs that may reflect the real situation with DOAC monitoring.

The study limitations. Our systematic review included small number of the studies and patients, and the lesser part of them is RCT. Consequently, it is difficult to come to definitive conclusions because of the limited data. In particular, the data of observational studies should be interpreted carefully because even in consistent cohorts, probably, there is a high degree of systematic selection error in distribution of patients using one of methods. Besides, the different DOAC drugs in different doses were used. In addition, the included studies had heterogeneous criteria of inclusion/exclusion and different determinations of each outcome and duration of follow-up. Like in other meta-analyses, endpoint determination can vary depending on the results of the safety and efficacy investigation. Some studies do not give a clear determination of the subtypes of stroke, systemic embolism and subtypes of hemorrhage (major or minor). And also, the etiology of bleeding, especially cerebral hemorrhage, is not specified.

Conclusion

According to the conducted systematic review and meta-analysis in patients with AF and CKD stages IV-V: there was no statistically significant superiority of DOACs or VKA in efficacy regarding to decrease in the risk of stroke or systemic embolism. As for safety in this category of patients, neither DOACs or VKA had a superiority regarding to hemorrhagic stroke, major hemorrhages, minor hemorrhages, gastrointestinal bleedings and total mortality. Thus, DOACs and VKA were comparable in efficacy and safety.

Relationships and Activities: none.

References

1. Soliman EZ, Prineas RJ, Go AS, et al. Chronic Renal Insufficiency Cohort (CRIC) Study Group. Chronic kidney disease and prevalent atrial fibrillation: the Chronic Renal Insufficiency Cohort (CRIC). Am Heart J. 2010;159:1102-7. doi:10.1016/j.ahj.2010.03.027.
2. Hwang HS, Park M-W, Yoon HE, et al. Clinical Significance of Chronic Kidney Disease and Atrial Fibrillation on Morbidity and Mortality in Patients with Acute Myocardial Infarction. American Journal of Nephrology. 2014;40(4):345-52. doi:10.1159/000368422.
3. Hindricks G, Potpara T, Dagres N, et al. Corrigendum to: 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC, European Heart Journal. 2021;42(40):4194. doi:10.1093/eurheartj/ehab648.
4. Siontis KC, Zhang X, Eckard A, et al. Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States. Circulation. 2018;138(15):1519-29. doi:10.1161/CIRCULATIONAHA.118.035418.
5. Fox KA, Piccini JP, Wojdyla D, et al. Prevention of stroke and systemic embolism with rivaroxaban compared with warfarin in patients with non-valvular atrial fibrillation and moderate renal impairment. Eur Heart J. 2011;32(19):2387-94. doi:10.1093/eurheartj/ehr342.
6. Granger CB, Alexander JH, McMurray JJV, et al. for the ARISTOTLE committees and investigators. ARISTOTLE primary results. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981-92. doi:10.1056/NEJMoa1107039.
7. Connolly SJ, Ezekowitz MD, Yusuf S, et al. RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361(12):1139-51. doi:10.1056/NEJMoa0905561.
8. Lin Y-C, Chen B-L, Shih C-M, et al. Effectiveness and safety of rivaroxaban versus warfarin in Taiwanese patients with end-stage renal disease and nonvalvular atrial fibrillation: A real-world nationwide cohort study. PLoS ONE. 2021;16(4):e0249940. doi:10.1371/journal.pone.0249940.
9. Chashkina MI, Andreev DA, Kozlovskaya NL, et al. Safety performance of rivaroxaban versus warfarin in patients with atrial fibrillation and advanced chronic kidney disease. Kardiologiia. 2020;60(11):94-100.
10. Steffel J, Collins R, Matthias A, et al. European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation. EP Europace. 2021;23(10):1612-76. doi:10.1093/europace/euab065.
11. Reinecke H, Engelbertz C, Schäbitz WR. Preventing stroke in patients with chronic kidney disease and atrial fibrillation: benefit and risks of old and new oral anticoagulants. Stroke. 2013;44(10):2935-41. doi:10.1161/STROKEAHA.113.001701.
12. Dettori JR, Norvell DC, Chapman JR. Fixed-Effect vs Random-Effects Models for Meta-Analysis: 3 Points to Consider. Global Spine J. 2022;12(7):1624-6. doi:10.1177/21925682221110527.
13. Peters JL, Sutton AJ, Jones DR, et al. Comparison of two methods to detect publication bias in meta-analysis. JAMA. 2006;295(6):676-80. doi:10.1001/jama.295.6.676.
14. Borenstein M, Higgins JP. Meta-analysis and subgroups. Prev Sci. 2013;14(2):134-43. doi:10.1007/s11121-013-0377-7.
15. Chan KE, Edelman ER, Wenger JB, et al. Dabigatran and Rivaroxaban Use in Atrial Fibrillation Patients on Hemodialysis. Circulation. 2015;131(11);972-9. doi:10.1161/CIRCULATIONAHA.114.014113.
16. De Vriese AS, Caluwé R, Pyfferoen L, et al. Multicenter Randomized Controlled Trial of Vitamin K Antagonist Replacement by Rivaroxaban with or without Vitamin K2 in Hemodialysis Patients with Atrial Fibrillation: the Valkyrie Study. Journal of the American Society of Nephrology. 2020 Jan;31(1):186-96. doi:10.1681/ASN.2019060579.
17. Elfar S, Elzeiny SM, Ismail H, et al. Direct Oral Anticoagulants vs. Warfarin in Hemodialysis Patients With Atrial Fibrillation: A Systematic Review and Meta-Analysis. Front Cardiovasc Med. 2022;9:847286. doi:10.3389/fcvm.2022.847286.