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Atrial Fibrillation Management in Acute Stroke Patients in Türkiye: Real-life Data from the NöroTek Study

Türkiye'de İnme Hastalarında Atrial Fibrilasyonun Yönetimi: NöroTek Çalışması Gerçek Hayat Verileri

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Abstract

Objective: Atrial fibrillation (AF) is the most common directly preventable cause of ischemic stroke. There is no dependable neurology-based data on the spectrum of stroke caused by AF in Türkiye. Within the scope of NöroTek-Türkiye (TR), hospital-based data on acute stroke patients with AF were collected to contribute to the creation of acute-stroke algorithms.

Materials and Methods: On May 10, 2018 (World Stroke Awareness Day), 1,790 patients hospitalized at 87 neurology units in 30 health regions were prospectively evaluated. A total of 929 patients [859 acute ischemic stroke, 70 transient ischemic attack (TIA)] from this study were included in this analysis.

Results: The rate of AF in patients hospitalized for ischemic stroke/TIA was 29.8%, of which 65% were known before stroke, 5% were paroxysmal, and 30% were diagnosed after hospital admission. The proportion of patients with AF who received "effective" treatment [international normalization ratio ≥2.0 warfarin or non-vitamin K antagonist oral anticoagulants (NOACs) at a guideline dose] was 25.3%, and, either no medication or only antiplatelet was used in 42.5% of the cases. The low dose rate was 50% in 42 patients who had a stroke while taking NOACs. Anticoagulant was prescribed to the patient at discharge at a rate of 94.6%; low molecular weight or unfractionated heparin was prescribed in 28.1%, warfarin in 32.5%, and NOACs in 31%. The dose was in the low category in 22% of the cases discharged with NOACs, and half of the cases, who received NOACs at admission, were discharged with the same drug.

Conclusion: NöroTek[TR] revealed the high but expected frequency of AF in acute stroke in Türkiye, as well as the aspects that could be improved in the management of secondary prophylaxis. AF is found in approximately one-third of hospitalized acute stroke cases in Türkiye. Effective anticoagulant therapy was not used in three-quarters of acute stroke cases with known AF. In AF, heparin, warfarin, and NOACs are planned at a similar frequency (one-third) within the scope of stroke secondary prophylaxis, and the prescribed NOAC dose is subtherapeutic in a quarter of the cases. Non-medical and medical education appears necessary to prevent stroke caused by AF.

Keywords: Acute stroke, transient ischemic attack, anticoagulant, relapse, therapeutic dose, Holter monitoring

Öz

Amaç: Atrial fibrilasyon (AF) iskemik inmenin doğrudan önlenebilir en sık nedendir. Ülkemizde AF nedenli inme spektrumuna dair nöroloji kaynaklı geniş ölçekte bir veri bulunmamaktadır. NöroTek-Türkiye (TR) kapsamında akut inme algoritmalarının oluşturulmasına katkı yapması beklenen AF tespit edilen akut inme hastalarına dair hastane verisi toplanmıştır.

Gereç ve Yöntem: 10 Mayıs 2018 Dünya İnme Farkındalık Günü'nde 30 sağlık bölgesine yer alan 87 nöroloji biriminde yatmakta olan 1.790 hasta prospektif olarak değerlendirilmiştir. Çalışmada yer alan toplam 929 hasta [859 akut iskemik inme, 70 geçici iskemik atak (GİA)] bu analize dahil edilmiştir.

Bulgular: İskemik inme/GİA sebebiyle ile interne edilmiş hastalarda AF oranı %29,8 olup bunların %65'i bilinmekte olan, %5'i paroksismal ve %30'u yeni tanıdır. AF tanısı ile gelen hastalarda "etkin" tedavi [internasyonel normalizasyon oranı ≥2,0 varfarin veya rehber dozunda non-vitamin K antagonist oral antikoagülan (NOAK)] alanların oranı %25,3 olup, %42,5 olguda ya hiç ilaç kullanılmamakta ya da sadece antiplatelet kullanılmaktaydı. Düşük doz kullanım oranı 42 NOAK alırken inme geçirmiş olguda %50 idi. Taburcu edilirken antikoagülan %94,6 (düşük molekül ağırlıklı veya non-fraksiyone heparin %28,1; varfarin %32,5 ve NOAK %31) hastaya reçete edilmişti. NOAK ile taburcu edilen olguların %22'sinde doz düşük kategoride olup gelişte NOAK almakta olan olguların yarısı aynı ilaçla taburcu edilmiştir.

Sonuç: NöroTek^{TR} ülkemizde AF'nin akut inmedeki sıklığı yanı sıra sekonder proflaksi perspektifinde yönetiminin geliştirilebilecek yönlerini ortaya koydu. Türkiye'de hastanede yatan akut inme olgularının yaklaşık üçte birinde AF saptanmıştır. AF'si bilinen akut inme olgularının dörtte üçünde etkin antikoagülan tedavi kullanılmamaktaydı. AF'de inme sekonder proflaksisi kapsamında heparin, varfarin ve NOAK planlaması benzer sıklıkta (üçte bir) olup reçete edilen NOAK dozu dörtte bir olguda subterapötiktir. AF'ye bağlı inmenin önlenebilmesi non-medikal ve medikal eğitim gerekli görünmektedir.

Anahtar Kelimeler: Akut inme, geçici iskemik atak, antikoagülan, nüks, terapötik doz, Holter monitörizasyon

Introduction

Atrial fibrillation (AF) is among the most common directly preventable causes of ischemic stroke (1). In Türkiye, there is no large-scale neurology-based data on medical practices to prevent stroke in patients with AF. In hospital-based cases, the frequency of AF in patients with acute ischemic stroke (AIS) has been reported to be around 20% (2,3). The frequency of AF in patients with AIS is variable in prospective case-control studies. The frequency was 24% (4) in Ankara ACROSS, in which 787 patients from three hospitals were included, 12.4% (5) in E-KIP, in which 1,136 patients from 11 hospitals were included, and 18.8% in Türk-MST (6), in which 3,100 patients from 40 centers were analyzed. In NöroTek-Türkiye data collected in a single day from 87 centers, the frequency of AF in 929 patients with AIS or transient ischemic attack (TIA) was found to be 29.8% (7). In this analysis, strategies for the prevention of stroke in AF using drugs in the NöroTek study were investigated.

Materials and Methods

Patients

On May 10, 2018 (World Stroke Awareness Day), 1,790 patients hospitalized in 87 centers representing 30 healthcare regions in Türkiye were included in the study. Of these, 929 patients with AIS (n = 859) and TIA (n = 70) were analyzed within the scope of this research. Although the methods and plans of the NöroTek study are briefly summarized here, its details have also been published previously (7,8). NöroTek, a point prevalence study, was approved as a "clinical study for the consortium" by the Non-Interventional Ethics Committee of Hacettepe University Faculty of Medicine (date: 27/3/2018, no: 18/331). Consent forms received from patients regarding data sharing and the permissions obtained from the managers of the participating centers and the completed data forms were stored in the participating centers.

The data collected for the first day of the NöroTek study related to demographic characteristics, vascular risk factors, previous hospitalization(s), symptoms, in-hospital and imaging timing metrics, and detailed metrics and outcomes of stroke treatments administered, such as intravenous tissue plasminogen activator and/or mechanical thrombectomy. Data collected at discharge included duration of hospital stay, discharge route, modified Rankin scale score (9), and mortality. In addition, investigations for etiology, metrics, examinations and practices regarding prevention and treatment, and complications during the hospital stay were noted (7).

Questions regarding medical prophylaxis in AF within the scope of NöroTek were as follows: first day (i) presence of AF; (ii) if AF was present, the drugs used [aspirin, other antiplatelet drugs, warfarin, and non-vitamin K antagonist oral anticoagulant (NOAC)]; and (iii) international normalization ratio (INR) level at admission in those using warfarin and the name of the drug and the dose for those using NOAC. Questions about AF on the day of discharge were the following: (iv) type of AF; (v) name and dose of prophylactic agents used at the time of discharge [heparin, low molecular weight heparin (LMWH), warfarin, NOAC, other]; and (vi) reason for this in patients not given anticoagulants.

Definitions of AF were as follows: (i) known AF: patients with a previously known diagnosis of AF and AF detected on the admission electrocardiogram (ECG); (ii) newly diagnosed AF: patients who were not previously known to have AF, but in whom AF was documented by the time of discharge; (iii) paroxysmal AF: patients who were previously diagnosed as having AF, but AF could not be detected on their admission ECG or bedside monitoring during their hospital stay.

Statistical Analysis

All values were given as numbers and percentages. The normal distribution of the data was examined using visual histogram analysis or Shapiro–Wilk tests. According to this result, differences between groups were evaluated using a Student's t-test, Mann–Whitney U test, chi-square or Fisher's exact test. The statistical significance level was set as $P < 0.05$. All calculations were performed using SPSS version 22.0 software.

Results

Of the 929 patients with AIS (n = 859) and TIA (n = 70) analyzed within the scope of the study, 179 (19.3%) had known AF, 85 (9.2%) had newly diagnosed AF, and 13 (1.4%) had AF; AF,

including paroxysmal AF, was detected in a total of 277 (29.8%) patients. The numbers of patients with AF provided by the centers are given in additional Supplementary 1.

Of 179 patients with known AF, 52 (29.1%) were not using any medication. The number of patients using aspirin was 23 (12.8%), and one patient was using clopidogrel. The total rate of patients using antiplatelet agents was 13.4%, while 55 (30.7%) patients were using warfarin; INR monitoring was not performed on two of these patients. While the INR level was subtherapeutic in 40 (72.7%) patients and supratherapeutic in one patient, it was noted that the INR level was in the therapeutic range in 12 (6.7% and 21.8% of those using warfarin) patients. Dabigatran was used in 10 (5.6%) patients, and it was determined that a standard dose was used in two patients and a low dose was used in seven patients, while the dose used in one patient was not known. Apixaban was used in eight patients, and in five patients, the dose was standard. In three patients, low doses were used. Rivaroxaban was used in 23 patients, with standard doses used in 13 and low doses in 10 patients. Edoxaban was used in one patient, at a low dose, and LMWH was used in three patients. While it was determined that low doses of LMWH were used for bridging in two of these patients, the dose was standard in one patient. In two patients, the name of the drug could not be determined. To summarize, it was determined that only 18.4% of the patients used therapeutically effective anticoagulant agents. Drug use rates in the therapeutic range were determined as 13 (57%) for rivaroxaban, 12 (22%) for warfarin, five (63%) for apixaban, two (20%) for dabigatran, and one (33%) for LMWH.

No information could be obtained regarding antiplatelet and anticoagulant drugs administered in the hospital in eight patients. The rate of patients discharged with LMWH was 27.1% and the rate of patients discharged with heparin was 1.1%. Warfarin was given in 90 (32.5%) and NOACs in 86 (31%) patients. While an antiplatelet drug was given in eight patients, no medication was given for secondary stroke prevention in seven patients. The reasons for this were reported as hemorrhagic transformation in three patients, massive infarction in two patients, decompressive hemicraniectomy in one patient, and esophageal varicose vein in one patient. No difference was detected between the groups, either in terms of group size or in pairwise comparisons ($P > 0.05$). Dabigatran was the preferred NOAC in 25 (29.1%) patients, apixaban in 28 (32.6%), rivaroxaban in 31 (36.1%), and edoxaban in two (2.3%). The prescribing of low doses was detected in eight (32%) patients receiving dabigatran, four (14.3%) patients receiving apixaban, six (19.4%) patients receiving rivaroxaban, and one (50%) patient receiving apixaban. In the NOAC group, a total of 19 patients (22.1%) were given low-dose medication (Table 1).

No medication change was made in 37 (67.3%) of the 55 patients who were using warfarin at admission. Eleven patients were discharged with LMWH, while seven patients were switched to NOACs (two had dabigatran, three had apixaban, and two had rivaroxaban). The INR level at admission was low (70.3%) in 26 patients whose medication was not changed; NOAC administration was started in four of the 12 patients (33%) whose INR level was at a therapeutic level.

Of the patients with known AF who had a stroke while using dabigatran, six (60%) continued to use dabigatran, while two of them were switched to LMWH, one to warfarin, and one to rivaroxaban. In five (83.3%) patients who continued with dabigatran, the dabigatran dose used at admission was low (2 x 110 mg/d). Warfarin and rivaroxaban were started in two patients who received adequate doses of dabigatran.

Half of the eight patients who had an AIS/TIA while receiving apixaban were discharged with apixaban. Two of them (50%) were using low doses of medication (1x5 and 1x2.5 mg/d). While two of these patients were switched to dabigatran, one continued using LMWH and another continued using rivaroxaban. Moreover, LMWH and dabigatran were continued in two patients who had a stroke while receiving standard-dose apixaban.

Of the 10 (43.5%) patients who had a stroke under rivaroxaban and were discharged with rivaroxaban, seven were using low-dose medication and two were using it irregularly. While a patient using a standard dose of rivaroxaban continued using it, the other drugs given in this group were LMWH (n = 5), no drug (n = 2), dabigatran (n = 3), apixaban (n = 1), and aspirin-clopidogrel combination (n = 1).

The patient who had a stroke under low-dose edoxaban, was discharged with a low dose (30 mg/d).

As a result, 15 of the 21 patients (71.4%) who were discharged with the same NOAC they were using before the stroke had either low doses or irregular use. In 17 patients (corresponding to 17.5% of the patients using OAC and NOAC) the drug dose was sufficient, and they were switched to another agent. Of the four patients using warfarin, one was switched to dabigatran, two to apixaban, and one to rivaroxaban. Of the two patients using dabigatran, one was switched to warfarin and one to rivaroxaban. Of the two patients using apixaban, one was switched to dabigatran

Table 1. Anticoagulant/antiplatelet treatments decided at the hospital for patients with atrial fibrillation

AF	Known	Newly diagnosed	Paroxysmal	Total (%)
n	179	85	13	277
Heparin	1 (0.6%)	2 (2.4%)	0 (0%)	3 (1.1%)
LMWH	43 (24%)	30 (35.3%)	2 (15.4%)	75 (27.1%)
Warfarin	62 (34.6%)	27 (31.8%)	1 (7.7%)	90 (32.5%)
NOAC	61 (34.1%)	24 (28.2%)	1 (7.7%)	86 (31%)
Antiaggregant	5 (2.8%)	2 (2.4%)	1 (7.7%)	8 (2.9%)
No drug	4 (2.2%)	0 (0%)	3 (23.1%)	7 (2.5%)
No data	3 (1.7%)	0 (0%)	5 (38.5%)	8 (2.9%)

AF: Atrial fibrillation, LMWH: Low molecular weight heparin, NOAC: Non-vitamin K antagonist oral anticoagulants

and one to LMWH. Of the nine patients using rivaroxaban, five switched to LMWH, three to dabigatran, and one to apixaban. In 61 patients, the INR level or NOAC dose was low, and a total of 53 (87%) of them continued using the same drug. In 37 of the 40 patients receiving warfarin, nine of the 10 patients receiving rivaroxaban, five of the seven patients receiving dabigatran, and two of the four patients receiving apixaban, the low-dose agent was increased to the effective dose. In eight patients in this group, changes in medication were made.

Discussion

It has been five years since the NöroTek study data were collected. However, the data should be regarded as up-to-date given that the interim period included the extraordinary conditions of the pandemic. That said, it is important to identify and correct the medical strategies used to prevent stroke in patients with AF, the frequency of which is predicted to increase significantly with the aging of the population in Türkiye, wherein life has almost completely normalized for around one year (10,11). At this point, the NöroTek data still represent an important source and comparison tool.

According to the findings of the NöroTek study, 42.5% of patients with AF who were hospitalized due to AIS in 2018 were either not using medication or only using an antiplatelet agent. The rate of standard-dose and effective anticoagulant usage was only 18.4%. As expected, this is a much higher rate compared to case studies including patients with AF without stroke from Türkiye (12,13,14). Clearly, the use of anticoagulants in an inappropriate dosage and order is a risk factor for stroke, stroke recurrence, and general mortality (15,16,17,18). In cases including patients who had AIS while using anticoagulants, the rate of detection of etiological mechanisms other than AF was 20%–24%, the rate of cardioembolism despite adequate anticoagulant treatment was 44%, and the rate of cardioembolism under inadequate anticoagulant treatment was 32% (2,19). Although etiological classification was not possible in NöroTek, it could be concluded that the share of inadequate anticoagulant use in stroke etiology was much higher compared to cases in Western countries (19). However, this is a finding that indicates a higher rate of the preventable stroke due to AF is higher in Türkiye. In other words, a reduction in the stroke rate can be achieved by increasing patient compliance through medical, socioeconomic, and, importantly, reimbursement regulations (20).

In cases of cardioembolic stroke recurrence attributed to inadequate dose and frequency of NOAC or subtherapeutic warfarin use, optimization of the dose is a more logical solution than switching agents. In cardioembolism that develops under effective oral anticoagulant, changing the agent does not appear to have a significant advantage over continuing with the same agent. Of course, stroke etiologies that cannot be prevented with anticoagulants must be adequately and appropriately excluded in both groups of patients. However, adding antiplatelets to oral anticoagulant therapy in cardioembolism is not considered a rational practice (19,21). In light of this information, the NöroTek study provided important information about strategies to prevent recurrence of cardioembolism due to AF after AIS in Türkiye. It will be necessary to compare all of the strategies with the data to allow them to be updated.

First, many patients with AIS with AF (27.1%) are discharged with LMWH, although this is not standard procedure (22). It is likely that the rules set by the reimbursement system in Türkiye play a decisive role here (20).

Second, although it was administered for secondary prophylaxis and on discharge from the hospital, the NOAC dose was observed to be at a subtherapeutic level in 22.1% of the patients. It is not possible to reveal the reasons for this within the scope of the NöroTek study, but unnoted hemorrhagic transformation, concomitant use of antiplatelet drugs, detection of microbleeds on magnetic resonance imaging, uncontrolled hypertension, low creatinine clearance, low body mass index, and advanced age may have played a role (15,23,24). It should also be noted that in the NöroTek study, no significant difference was found among NOACs in terms of low dose preference. On the other hand, in large-scale cardiology studies conducted in Türkiye, such as NOAC-TR (51%), RAMSES (30.4%), NOAC-TURC (47.6%), and ROTA (22.2%), NOAC dosing and patient compliance were reported to be similar and at a low level (14,25,26,27). This should be noted as a problem that needs to be resolved, albeit that there have been improvements over time (14,28).

Third, in 70% of the patients who had a stroke while using warfarin, the INR level was subtherapeutic, and these patients continued using warfarin following improved compliance and dosage. Approximately one-third of the remaining patients were switched to NOACs and two-thirds to LMWH. In Türkiye, the time of stay within the therapeutic range among patients using warfarin is only 50% (20). Of course, it is rational to expect the risk of stroke to increase as this period decreases. In addition, in patients who had a stroke while using OACs or NOACs, if the dose was low, the main strategy (87%) appeared to be to continue with the same agent while increasing the dose to the optimal amount. To a lesser extent, another NOAC, LMWH, or warfarin was preferred. In addition, 17.5% of patients receiving OACs and NOACs were switched to another agent while the drug dose was sufficient. This is an approach that is encountered in practice but is not sufficiently supported by scientific data (19,21).

It can be argued that the point prevalence or "flash mob research" (FMR) method was first applied in neurology in the NöroTek study. In these studies, a basic question that generally has a clear answer or the frequency of a practice or strategy is determined in a large number of patients (often on a national scale) (29,30). We have discussed the pros and cons of this method previously (7,8). In brief, FMR is a method of study with high accuracy that produces data on the extent of the problem rather than causes and solutions and pursues simple but important answers (31).

Conclusion

As a result, NöroTek revealed the frequency of AF in patients with AIS/TIA in Türkiye, as well as the aspects that could be improved in its management from the perspective of secondary prophylaxis. Here, AF was detected in approximately one-third of hospitalized patients with AIS/TIA in Türkiye. Effective anticoagulant treatment was not used in three quarters of the patients with known AF. The selection of heparin, warfarin, and NOACs within the scope of secondary prophylaxis of stroke in AF was similar in frequency (one in three), and the prescribed NOAC dose was subtherapeutic in one in four of the patients. Non-

medical and medical education appears to be necessary to prevent stroke due to AF.

Ethics

Ethics Committee Approval: Non-Interventional Ethics Committee of Hacettepe University Faculty of Medicine (date: 27/3/2018, no: 18/331).

Informed Consent: The authors have stated that they obtained signed consent for data sharing from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: All authors, Concept: M.A.T., E.M.A., A.Ö.Ö., Design: M.A.T., E.M.A., A.Ö.Ö., Data Collection or Processing: All authors, Analysis and Interpretation: M.A.T., E.M.A., A.Ö.Ö., Literature Search: M.A.T., Writing: M.A.T.

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References

1. Freedman B, Potpara TS, Lip GY. Stroke prevention in atrial fibrillation. Lancet 2016;388:806-817.
2. Dinç Y, Bakar M, Hakyemez B. Causes of ischemic stroke in patients with atrial fibrillation. Turk J Neurol 2020;26:311-315.
3. Kumral E, Özkaya B, Vardarli E, et al. Ege stroke data bank: an analysis of 2000 patients with stroke. Turk J Neurol 1997;3:3-12.
4. Erkent İ, Topçuoğlu MA, Sorgun MH, et al. The role of education level and gender from the perspective of preventable stroke: Ankara ACROSS subgroup analysis. Turk J Cereb Vasc Dis 2020;26:236-242.
5. Kunt R, Cinar BP, Yüksel B, et al. Clinical-epidemiological and radiological characteristics of stroke patients: a multicentre study. Int J Clin Pract 2021:e14963.
6. Özdemir G, Özkan S, Uzuner N, Özdemir O, Gücüyener D. Major risk factors for cerebrovascular disease in Turkey: Turkish multi centric stroke trial results. Turk J Cereb Vasc Dis 2000;6:31-35.
7. Topcuoglu MA, Arsava EM, Özdemir AÖ, et al. In hospital neurovascular disease management in Turkey: rationale, hypothesis, methods, and descriptive characteristics (NöroTek: Turkey Neurology One-Day Study). Turk J Cereb Vasc Dis 2021;27:217-242.
8. Topçuoğlu MA, Özdemir AÖ, Aykaç Ö, et al. Gastrostomy in hospitalized patients with acute stroke: "NöroTek" Turkey Point Prevalence Study Subgroup Analysis. Turk J Neurol 2022;28:134-141.
9. Rankin J. Cerebral vascular accidents in patients over the age of 60. II. Prognosis. Scott Med J 1957;2:200-215.
10. Topçuoğlu MA. Stroke epidemiology and near future projection in Turkey: analysis of Turkey data from the Global Burden of Disease Study. Turk J Neurol 2022;28:200-211.
11. Topçuoğlu MA. Acute stroke agenda in Turkey: 2023. Turk J Cereb Vasc Dis 2023;29:1-5.
12. Kocabaş U, Ergin I, Yavuz V, et al. Prevalence and associated factors of inappropriate dosing of direct oral anticoagulants in patients with atrial fibrillation: the ANATOLIA-AF study. Cardiovasc Drugs Ther 2022.
13. Sayin BY, Al Mahmeed W, Ragy HI, et al. Middle east treatment strategies and clinical outcomes in patients with atrial fibrillation: one-year follow-up data from Garfield-AF study. Adv Ther 2021;38:2391-2405.
14. Kocabaş U, Ergin I, Yavuz V, et al. Real-world evaluation of anticoagulant treatment patterns in patients with atrial fibrillation: data from multicenter ROTA study. Turk Kardiyol Dern Ars 2023;51:88-96.
15. Caso V, de Groot JR, Sanmartin Fernandez M, et al. Outcomes and drivers of inappropriate dosing of non-vitamin K antagonist oral anticoagulants (NOACs) in patients with atrial fibrillation: a systematic review and meta-analysis. Heart 2023;109:178-185.
16. Liu X, Huang M, Ye C, Xiao X, Yan C. Effect of non-recommended doses versus recommended doses of direct oral anticoagulants in atrial fibrillation patients: a meta-analysis. Clin Cardiol 2021;44:472-480.
17. Zhang XL, Zhang XW, Wang TY, et al. Off-label under- and overdosing of direct oral anticoagulants in patients with atrial fibrillation: a meta-analysis. Circ Cardiovasc Qual Outcomes 2021;14:e007971.
18. Shantsila A, Lip GYH, Lane DA. Contemporary management of atrial fibrillation in primary and secondary care in the UK: the prospective long-term AF-GEN-UK registry. Europace 2023;25:308-317.
19. Polymeris AA, Meinel TR, Oehler H, et al. Aetiology, secondary prevention strategies and outcomes of ischaemic stroke despite oral anticoagulant therapy in patients with atrial fibrillation. J Neurol Neurosurg Psychiatry 2022;93:588-598.
20. Topcuoglu MA, Arsava EM. Time in therapeutic range among warfarin users in Turkey: are there enough data to set definitive criteria for reimbursement? Turk Kardiyol Dern Ars 2021;49:254-256.
21. Acar B, Akpınar ÇK, Alioglu Z, et al. Use of NOAC in clinical practice of stroke: Expert Opinion of the Turkish Society of Cerebrovascular Diseases. Turk J Cereb Vasc Dis 2020;26:190-235.
22. Ye Y, Zhou W, Cheng W, Liu Y, Chang R. Short-term and long-term safety and efficacy of treatment of acute ischemic stroke with low-molecular-weight heparin: meta-analysis of 19 randomized controlled trials. World Neurosurg 2020;141:26-41.
23. Gustafson WL, Saunders J, Vazquez SR, Jones AE, Witt DM. Real-world study of direct oral anticoagulant dosing patterns in patients with atrial fibrillation. Pharm Pract (Granada) 2019;17:1709.
24. Montrasio G, Reiner MF, Wiencierz A, et al. Prevalence and risk of inappropriate dosing of direct oral anticoagulants in two Swiss atrial fibrillation registries. Vascul Pharmacol 2022;147:107120.
25. Altay S, Yıldırımtürk Ö, Çakmak HA, et al. New oral anticoagulants-TURKey (NOAC-TURK): Multicenter cross-sectional study. Anatol J Cardiol 2017;17:353-361.
26. Başaran Ö, Dogan V, Beton O, et al. Suboptimal use of non-vitamin K antagonist oral anticoagulants: results from the RAMSES study. Medicine (Baltimore) 2016;95:e4672.
27. Emren SV, Şenöz O, Bilgin M, et al. Drug adherence in patients with nonvalvular atrial fibrillation taking non-vitamin k antagonist oral anticoagulants in Turkey: NOAC-TR. Clin Appl Thromb Hemost 2018;24:525-531.
28. Ertaş F, Kaya H, Kaya Z, et al. Epidemiology of atrial fibrillation in Turkey: preliminary results of the multicenter AFTER study. Turk Kardiyol Dern Ars 2013;41:99-104.
29. Alsma J, van Saase JLCM, Nanayakkara PWB, et al. The power of flash mob research: conducting a nationwide observational clinical study on capillary refill time in a single day. Chest 2017;151:1106-1113.
30. Crabtree A, Kavanagh E, Chamberlain C, et al. Right needle, right patient, right time? A national flash-mob audit of thromboprophylaxis in palliative care. Thromb Res 2023;223:95-101.
31. Moons P. Flash mob studies: a novel method to accelerate the research process. Eur J Cardiovasc Nurs 2021;20:175-178.

Supplementary 1 Link: http://glns.co/wmgcp