Turk Kardiyol Dern Ars 2019;47(1):4-9 doi: 10.5543/tkda.2018.82830

ORIGINAL ARTICLE

Safety of radial coronary angiography with uninterrupted direct-acting oral anticoagulant treatment

Oral antikoagülan tedavi kesilmeden yapılan radyal arter yoluyla koroner anjioyografi güvenliği

Tuğba Kemaloğlu Öz, M.D.,[1] Tayfun Gürol, M.D.,[1] Nedim Umutay Sarıgül, M.D.,[2] Utku Aslan, M.D.,[1] Maryam Kobegenova, M.D.,[1] Alper Aydın, M.D.,[1] Özer Soylu, M.D.,[1] Bahadır Dağdeviren, M.D.[1]

[1]Department of Cardiology, Bahçeşehir University Faculty of Medicine, İstanbul, Turkey

[2]Department of Cardiology, Kardio Bremen, Bremen, Germany

ABSTRACT

Objective: It is not known whether direct-acting oral anticoagulants (DOACs), such as dabigatran, apixaban, and rivaroxaban increase the risk of bleeding complications during or after coronary catheterization. The aim of this study was to investigate the safety of uninterrupted DOAC treatment during diagnostic radial coronary angiography (CAG).

Methods: This study included 160 patients who underwent diagnostic radial cardiac catheterization. The 60 patients in the group who were using a DOAC (apixaban, rivaroxaban, or dabigatran) were enrolled in a Group A. Post-procedure results from patients in Group A were compared with those of an age- and sex-matched control group (Group B) that included 100 patients who underwent radial CAG who did not use a DOAC.

Results: There was no significant difference in the procedure and compression times, creatinine level, or presence of hypertension, diabetes mellitus, smoking, alcohol use, vascular disease, or congestive heart failure between the 2 groups. During the 1 -month follow-up period, only 1 radial occlusion was registered in the control group (Group B). There was no case of a large hematoma (>5 cm or extending to the forearm), dissection, fistula, perforation, or compartment syndrome. Hematomas smaller than 5 cm were seen in 2 patients (1 in each group). No thrombotic events were observed during follow-up examinations.

Conclusion: Performing radial CAG with uninterrupted DOAC treatment appears to carry no risk of increased early or short-term complications. The simple, uninterrupted DOAC strategy is comfortable, easy, and safe.

ÖZET

Amaç: Dabigatran, apiksaban ve rivaroksabandan oluşan direkt etkili oral antikoagülanların (DOAK) koroner anjiyografi (KAG) sırasında ve sonrasında kanama riskini artırıp artırmadığı bilinmemektedir. Bu çalışmada DOAK tedavisine ara verilmeden yapılan KAG'nin güvenli olup olmadığı araştırıldı.

Yöntemler: Çalışmamıza radyal arter yoluyla KAG yapılması kararlaştırılan toplam 160 hasta dahil edildi. Bu hastaların 60'ı DOAK (apiksaban, rivaroksaban ya da dabigatran) tedavisi almakta olup Grup A olarak adlandırıldı. Grup A'nin işlem sırasında ve sonrasındaki sonuçları yaş ve cinsiyet olarak eşleştirilmiş DOAK kullanmayan 100 hastadan oluşan kontrol grubuyla (Grup B) karşılaştırıldı.

Bulgular: İşlem ve baskı süresi, kreatinin seviyesi, cinsiyet, hipertansiyon, diyabet, sigara ve/veya alkol kullanımı, damar hastalığı, kalp yetersizliği açısından iki grup arasında anlamlı fark saptanmadı. Bir aylık takip süresi boyunca, sadece kontrol grubundaki (Grup B) bir hastada radyal arter tıkanıklığı tespit edildi. Geniş hematom (>5 cm ya da ön kola uzanan hematom), diseksiyon, fistül, perforasyon ya da kompartman sendromuna rastlanmadı; 5 cm'den küçük hematom toplam iki hastada gözlendi (her iki gruptan birer hasta). İşlem sırasında ve takip süresince trombotik olay yaşanmadı.

Sonuç: Direkt etkili oral antikoagülanlar tedavisine ara verilmeden radyal arter yoluyla yapılan KAG erken ya da kısa dönemde komplikasyon riskini artırmamaktadır. Basitçe uygulanan aralıksız DOAK tedavi stratejisi konforlu, kolay ve güvenlidir.

Received: December 15, 2017 *Accepted:* September 06, 2018

Correspondence: Dr. Tuğba Kemaloğlu Öz. Bahçeşehir Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, İstanbul, Turkey.
Tel: +90 216 - 579 81 95 e-mail: tugbakemalogluoz@gmail.com

Chronic oral anticoagulation therapy with direct-acting oral anticoagulants (DOACs), such as dabigatran, apixaban, and rivaroxaban, is widely used in patients with non-valvular atrial fibrillation (AF). DOACs have a high efficacy/safety ratio and predictable effects, without the need for routine monitoring interventions.[1] It is not known whether DOACs increase the risk of bleeding during or after coronary catheterization. The European Heart Rhythm Association guideline suggests that DOACs should be temporarily discontinued for elective interventions,[1] but there are no data about the use of DOACs with diagnostic coronary angiography (CAG). It is common practice to interrupt DOAC therapy before either radial or femoral CAG. However, parenteral anticoagulants are necessary to prevent thrombosis in the radial artery.[2,3] The use of parenteral anticoagulants during radial CAG is associated with low rates of bleeding complications.[4–6] The greatest advantage of this approach is fewer access-site complications. Since the radial artery is small and superficial, it is easily compressible, and bleeding complications are extremely rare.[7–9] Data about uninterrupted treatment with DOACs during cardiac catheterization are lacking. The aim of this pilot study was to investigate the safety of uninterrupted DOAC treatment during diagnostic radial CAG.

METHODS

Study population

This was an observational, single-center, prospective study that included 160 patients who underwent diagnostic radial cardiac catheterization between January 2012 and January 2017. A total of 60 patients who were at least 18 years of age, who had AF (paroxysmal, persistent, or permanent) not caused by a prosthetic valve or moderate or severe mitral stenosis (nonvalvular AF) and who were using one of the standard dose DOACs (rivaroxaban 20 mg once daily, apixaban 5 mg twice daily, or dabigatran 150 mg twice daily) were enrolled in Group A. Post-procedure results from the patients in Group A were compared with those of a control group (Group B) that included 100 age- and sex-matched patients who underwent radial CAG and did not use a DOAC. Every patient had a normal Allen test. The study protocol was approved by the institutional review board and written, informed consent was obtained from all patients before the CAG procedure.

Abbreviations:

AF	*Atrial fibrillation*
CAG	*Coronary angiography*
DOAC	*Direct-acting oral anticoagulant*
IAC	*Interrupted anticoagulation*
RAO	*Radial artery occlusion*
UAC	*Uninterrupted anticoagulation*
OAC	*Oral anticoagulation*

Patients with a prior coronary artery bypass graft, anemia with a hemoglobin concentration of less than 10 g/dL, known bleeding diathesis, a clinically significant gastrointestinal bleeding history, a creatinine level greater than 1.2 mg/dL, or a contraindication for radial access were excluded from the study.

Procedures

All of the procedures were performed in a single cardiology unit by 4 independent expert interventional cardiologists. Patients in both groups received the standard anticoagulant therapy of an intra-arterial bolus of 5000 IU of unfractionated heparin during cardiac catheterization. Allen testing was done to assess hand perfusion. The radial artery was punctured with a 21-G needle and a 0.021-inch guidewire (Cordis Corp., Miami, FL, USA) was inserted. A 5-F or 6-F sheath was used, and the angiograms were performed using TIG 5-F (Terumo Medical Corp., Somerset, NJ, USA), Judkins left 3.5-F or Judkins right 4-F (Cordis Corp., Miami, FL, USA; Johnson & Johnson, New Brunswick, NJ, USA) catheters. The right radial artery was the preferred vascular approach, but in 3 patients, the left side was used for vascular reasons. There were no cases of crossover to femoral artery access.

A total of 5000 units of sodium heparin with 200 μg nitroglycerine was given to each patient (both A and B groups) via the radial artery before the procedure was initiated. The introductory catheter was exchanged for a 0.035-inch x 180-cm guidewire (Biocath, Sao Paulo, Brazil). After the procedure, an elastic compressor bandage was used for at least 2 hours for hemostasis. The patients were allowed to be ambulatory immediately following the procedure.

An examination was performed by clinical visit at discharge, and all of the patients were contacted by telephone within 24 hours after catheterization to identify any complications. A follow-up examination was performed 1 month after the procedure. Complications of the procedure, such as radial occlusion, dissection, fistula, perforation, small (≤5 cm) or large hematoma (>5 cm or extending to the forearm), or compartment syndrome, were assessed at the follow-up visit.

Statistical analysis

SPSS Statistics for Windows, Version 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Numeric variables were expressed as mean±SD. Mean, SD, and percentage were used in the descriptive analysis of the data. Differences in categorical variables between groups were tested using an independent samples t-test and the Mann-Whitney U test, as appropriate. Categorical variables were compared via a chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

The baseline characteristics of the patients are summarized in Table 1. A total of 160 patients (38.7% women) were included in the study. Of the 60 patients in Group A (46% women) who were anticoagulated with DOACs at the time of the procedure, 73.3 % (44 patients) were using rivaroxaban, 15% (9 patients) were using apixaban, and 11.6% (7 patients) were using dabigatran. The use of antiplatelet drugs and dual antiplatelet therapy was statistically significantly more frequent in Group B than in group A. There were no significant differences between the groups with regard to the procedure and compression times or creatinine level between the 2 groups. Furthermore, there were no significant differences in age, gender, the prevalence of hypertension, diabetes mellitus, smoking, alcohol use, vascular disease, or congestive heart failure between the 2 groups.

There were very few complications. None of the patients in Group A, all of whom used a DOAC due to nonvalvular AF, had complications during the CAG, nor did the control patients in Group B. During the 1-month follow-up period, only 1 radial occlusion was observed, which was in a patient in the control group. There were no cases of a large hematoma (>5 cm or extending to the forearm), dissection, fistula, perforation, or compartment syndrome. Hematomas smaller than 5 cm were seen in 2 patients (1 in each group). No thrombotic events were observed during follow-up examinations.

DISCUSSION

This prospective study demonstrated the safety and feasibility of radial CAG in patients with uninterrupted DOAC treatment. Although the patients in Group A, who received DOAC therapy, were consid-

Table 1. Baseline demographic and procedural characteristics of the patients

Variable	Group A			Group B			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Age in years			68.6±11.2			67.1±12.3	0.879
Women	28	46.7		34	34		0.111
Diabetes mellitus	17	28.3		29	29		0.845
Hypertension	47	78.3		77	77		0.845
Smoking	29	48.3		54	54		0.48
Alcohol use	4	6.7		9	9		0.60
Vascular disease	4	6.7		5	5		0.658
Congestive heart failure	3	5		11	11		0.19
Acetylsalicylic acid	2	3.3		61	61		0.001
Clopidogrel	9	15		34	34		0.009
Dual antiplatelet therapy	2	3.3		24	24		0.001
Previous radial catheterization	14	23.3		27	27		0.607
Creatinine (mg/dL)			0.98±0.21			0.96±0.20	0.721
Procedure time (min)			24.4±7.8			22.7±6.7	0.138
Compression time (min)			128±12			126±14	0.311

P values of <0.05 were considered significant. SD: Standard deviation.

ered at high risk for bleeding, they did not have more early or late hemorrhagic or thromboembolic complications than the patients in the control group.

DOACs are gaining in popularity for use in different areas of cardiology, including for coronary interventions. Current data and guidelines for AF treatment do not recommend the uninterrupted use of DOAC therapy during elective procedures. According to the European Heart Rhythm Association guideline, DOACs should be discontinued at least 24 hours before patients are taken to the catheter laboratory, and the DOAC's effects should have disappeared before the procedure.[1] There is no clear suggestion about the need for bridging therapy before CAG or the time of interruption of DOAC use. The safety and efficacy of bridging therapy has been investigated in patients receiving other anticoagulants who underwent CAG, pacemaker implantation, AF ablation, and general surgery.[10–14] No advantages of bridging therapy were demonstrated in any of these studies, and the therapy was associated with prolonged hospitalization, an increased risk of bleeding, thromboembolism, and sub-therapeutic anticoagulation. In addition, a parenteral approach is not comfortable for patients.[12,15–18] Without bridging therapy, patients may be at risk of thromboembolic complications. More recent data suggest that uninterrupted anticoagulation therapy may be preferable to bridging treatment.[19] A recent study found that even AF of less than 48 hours duration can significantly increase the risk for thromboembolism.[20] To date, there are no data available to recommend maintaining or interrupting DOAC before radial CAG. In the present study, patients were protected from thromboembolic complications as a result of continuous DOAC treatment.

Fewer bleeding complications and improved patient comfort make the radial approach attractive for patients receiving DOACs who undergo CAG.[17,21,22] A meta-analysis demonstrated that radial CAG had a 73% reduction in major bleeding complications compared with CAG using the femoral route.[8] In the RIVAL (Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes) trial, the incidence of major vascular complications was 1.4% in patients when the radial approach was used, as compared to 3.7% in patients where femoral access was used.[5] In our study, only the radial route was used and despite continuous DOAC treatment, there were no significant differences in bleeding complications.

The incidence of radial artery occlusion (RAO) after radial CAG has been reported to be 1% to 10%.[23] Intraprocedural administration of anticoagulants decreases RAO.[2,24,25] Additionally, Pancholy et al.[26] demonstrated that patients receiving only warfarin treatment who underwent radial CAG without parenteral anticoagulation had a higher incidence of RAO. In the present study, intra-artery heparin was given to patients in both groups because of the efficacy of this parenteral anticoagulant in preventing arterial occlusion. RAO and bleeding complications were similar between the 2 groups.

Karjalainen et al.[27] retrospectively analyzed cases of patients on warfarin therapy referred for percutaneous intervention. They compared interrupted anticoagulation (IAC) versus uninterrupted anticoagulation (UAC) treatment. Although the femoral route was used in the majority of patients in both groups (78% in the UAC group and 80% in the IAC group), percutaneous coronary intervention was determined to be safe with UAC. Additionally, Gallego-Sánchez et al.[28] evaluated the safety of transradial diagnostic cardiac catheterization in patients under acenocoumarol (oral anticoagulant [OAC]) therapy. Their results support an uninterrupted OAC regimen during radial catheterization, as in our study. However, the bleeding complications that were a main concern were rare in the present study. Hematomas smaller than 5 cm were seen 2 patients (1 in each group). Serious bleeding complications, including life-threatening hemorrhage or larger hematomas (>5 cm) did not occur in either group. Similarly, no other serious complications of the access site, including dissection, fistula, perforation, or compartment syndrome, were seen.

Limitations

Our study has several limitations. Firstly, this is a single-center study and the sample size was limited because the study consisted of a very special group that underwent diagnostic radial cardiac catheterization during uninterrupted DOAC treatment and the patients in the control group used antiplatelet drugs statistically significantly more frequently than the patients in Group A. Additionally, although the patients in Group A were heterogeneous in terms of drug

type, the number of patients who were using different DOACs was insufficient to compare them with each other. Despite these limitations, the study's results may provide a new and comfortable option to both patients and interventionalists.

Conclusion

Performing radial CAG with uninterrupted DOAC treatment appears to carry no increased risk of early- or short-term complications. According to the results of our pilot study, the simple uninterrupted DOAC strategy seems to be comfortable, easy, and safe. This research may lead to more extensive, comprehensive studies.

Peer-review: Externally peer-reviewed.

Conflict-of-interest: None.

Authorship contributions: Concept: T.K.Ö., T.G., N.U.S., U.A., M.K., A.A., Ö.S., B.D.; Design: T.K.Ö., T.G., N.U.S., U.A., M.K., A.A., Ö.S., B.D.; Supervision: T.K.Ö., B.D.; Materials: T.K.Ö., T.G., N.U.S., U.A., M.K., A.A., Ö.S., B.D.; Data: T.K.Ö.; Analysis: T.K.Ö., T.G., N.U.S., U.A., M.K., A.A., Ö.S., B.D.; Literature search: T.K.Ö., T.G., N.U.S., U.A., M.K., A.A., Ö.S., B.D.; Writing: T.K.Ö.; Critical revision: T.K.Ö., T.G., N.U.S., U.A., M.K., A.A., Ö.S., B.D.

REFERENCES

1. Heidbuchel H, Verhamme P, Alings M, Antz M, Diener HC, Hacke W, et al. Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation. Europace 2015;17:1467–507. [CrossRef]
2. Spaulding J, Lefèvre T, Funk F, Thèbault B, Chauveau M, Ben Hamda K, et al. Left radial approach for coronary angiography: results of a prospective study. Cathet Cardiovasc Diagn 1996;39:365–70. [CrossRef]
3. Pancholy SB. Comparison of the effect of intra-arterial versus intravenous heparin on radial artery occlusion after transradial catheterization. Am J Cardiol 2009;104:1083–5. [CrossRef]
4. Hetherington SL, Adam Z, Morley R, De Belder MA, Hall JA, Muir DF, et al. Primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction: changing patterns of vascular access, radial versus femoral artery. Heart 2009;95:1612–8. [CrossRef]
5. Jolly SS, Yusuf S, Cairns J, Niemelä K, Xavier D, Widimsky P, et al; RIVAL trial group. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised parallel group, multicentre trial. Lancet 2011;377:1409–20. [CrossRef]
6. Hamon H, Mehta S, Steg PG, Faxon D, Kerkar P, Rupprecht HJ, et al. Impact of transradial and transfemoral coronary interventions on bleeding and net adverse clinical events in acute coronary syndromes. EuroIntervention 2011;7:91–7. [CrossRef]
7. Rao SV, Ou FS, Wang TY, Roe MT, Brindis R, Rumsfeld JS, et al. Trends in the prevalence and outcomes of radial and femoral approaches to percutaneous coronary intervention: a report from the National Cardiovascular Data Registry. JACC Cardiovasc Interv 2008;1:379–86. [CrossRef]
8. Jolly SS, Amlani S, Hamon M, Yusuf S, Mehta SR. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. Am Heart J 2009;157:132–40. [CrossRef]
9. Agostoni P, Biondi-Zoccai GG, de Benedictis ML, Rigattieri S, Turri M, Anselmi M, et al. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures; Systematic overview and meta-analysis of randomized trials. J Am Coll Cardiol 2004;44:349–56. [CrossRef]
10. Tolosana J, Berne P, Mont L, Heras M, Berruezo A, Monteagudo J, et al. Preparation for pacemaker or implantable cardiac defibrillator implants in patients with high risk of thrombo-embolic events: Oral anticoagulation or bridging with intravenous heparin? A prospective randomized trial. Eur Heart J 2009;30:1880–4. [CrossRef]
11. Wazni OM, Beheiry S, Fahmy T, Barrett C, Hao S, Patel D, et al. Atrial fibrillation ablation in patients with therapeutic international normalized ratio: Comparison of strategies of anticoagulation management in the periprocedural period. Circulation 2007;116:2531–4. [CrossRef]
12. Jamula E, Douketis J, Schulman S. Perioperative anticoagulation in patients having implantation of a cardiac pacemaker or defibrillator: A systematic review and practical management guide. J Thromb Haemost 2008;6:1615–21. [CrossRef]
13. Annala A, Karjalainen P, Porela P, Nyman K, Ylitalo A, Airaksinen K. Safety of diagnostic coronary angiography during uninterrupted therapeutic warfarin treatment. Am J Cardiol 2008;102:386–90. [CrossRef]
14. Karadağ B, İkitimur B, Öngen Z. Perioperative management in patients receiving newer oral anticoagulant and antiaggregant agents. Turk Kardiyol Dern Ars 2012;40:548–51. [CrossRef]
15. Wang T, Robinson L, Ou F, Roe M, Ohman E, Gibler W, et al. Dis-syndrome previously on warfarin anticoagulation: Physician practice in the CRUSADE registry. Am Heart J 2008;155:361–8. [CrossRef]
16. El-Jack S, Ruygrok P, Webster MW, Stewart JT, Bass NM, Armstrong GP, et al. Effectiveness of manual pressure hemostasis following transfemoral coronary angiography in patients on therapeutic warfarin anticoagulation. Am J Cardiol 2006;97:485–8. [CrossRef]
17. Lev-Ran O, Kramer A, Gurevitch J, Shapira I, Mohr R. Low-molecular-weight heparin for prosthetic heart valves: Treatment failure. Ann Thorac Surg 2000;69:264–5. [CrossRef]
18. Spandorfer JM, Lynch S, Weitz HH, Fertel S, Merli GJ. Use of

enoxaparin for the chronically anticoagulated patient before and after procedures. Am J Cardiol 1999;84:478–80. [CrossRef]

19. Garg A, Khunger M, Seicean S, Chung MK, Tchou PJ. Incidence of thromboembolic complications within 30 days of electrical cardioversion performed within 48 hours of atrial fibrillation onset. JACC Clin Electrophysiol 2016;2:487–94. [CrossRef]
20. Bonnet-Zamponi D, Aumont MC, Comets E, Bruhat C, Chauveheid MP, Duval X, et al. Heparin bridging therapy and bleeding events in octogenarian inpatients with atrial fibrillation starting anticoagulation: results of an ancillary study. J Am Geriatr Soc 2011;59:2174–8. [CrossRef]
21. Douketis JD, Spyropoulos AC, Kaatz S, Becker RC, Caprini JA, Dunn AS, et al; BRIDGE Investigators. Perioperative bridging anticoagulation in patients with atrial fibrillation. N Engl J Med 2015;373:823–33. [CrossRef]
22. Lip GY, Huber K, Andreotti F, Arnesen H, Airaksinen JK, Cuisset T, et al; Consensus Document of European Society of Cardiology Working Group on Thrombosis. Antithrombotic management of atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing coronary stenting: executive summary--a Consensus Document of the European Society of Cardiology Working Group on Thrombosis, endorsed by the European Heart Rhythm Association (EHRA) and the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2010;31:1311–8. [CrossRef]
23. Kotowycz MA, Dzavík V. Radial artery patency after transradial catheterization. Circ Cardiovasc Interv 2012;5:127–33.
24. Feray H, Izgi C, Citiner D, Men EE, Saltan Y, Baltay A, et al. Effectiveness of enoxaparin for prevention of radial artery occlusion after transradial cardiac catheterization. J Thromb Thrombolysis 2010;29:322–5. [CrossRef]
25. Plante S, Cantor WJ, Goldman L, Miner S, Quesnelle A, Ganapathy A, et al. Comparison of bivalirudin versus heparin on radial artery occlusion after transradial catheterization. Catheter Cardiovasc Interv 2010;76:654–8. [CrossRef]
26. Pancholy SB, Ahmed I, Bertrand OF, Patel T. Frequency of radial artery occlusion after transradial access in patients receiving warfarin therapy and undergoing coronary angiography. Am J Cardiol 2014;113:211–4. [CrossRef]
27. Karjalainen PP, Vikman S, Niemelä M, Porela P, Ylitalo A, Vaittinen MA, et al. Safety of percutaneous coronary intervention during uninterrupted oral anticoagulant treatment. European Heart Journal 2008; 29:1001–10. [CrossRef]
28. Gallego-Sánchez G, Gallardo-López A, Córdoba-Soriano JG, Gutiérrez-Díez A, Melehi D, Barrionuevo-Sánchez MI, et al. Safety of transradial diagnostic cardiac catheterization in patients under oral anticoagulant therapy. J Cardiol 2017;69:561–4. [CrossRef]

Keywords: Anticoagulants; apixaban; coronary angiography; dabigatran; radial artery; rivaroxaban.

Anahtar sözcükler: Antikoagülanlar; apiksaban; koroner anjiyografi; dabigatran; radyal arter; rivaroksaban.