Korean Circ J. 2018 May;48(5):433-434
https://doi.org/10.4070/kcj.2018.0081
pISSN 1738-5520·eISSN 1738-5555

kcj
Korean Circulation Journal

Editorial

Oral Anticoagulants for Atrial Fibrillation Patients with Active Cancer

Do Young Kim, MD, and Hong Euy Lim, MD, PhD

Division of Cardiac Electrophysiology, Korea University Cardiovascular Center, Korea University Guro Hospital, Seoul, Korea

▸ See the article "Effect of Non-vitamin K Antagonist Oral Anticoagulants in Atrial Fibrillation Patients with Newly Diagnosed Cancer" in volume 48 on page 406.

Received: Mar 6, 2018
Accepted: Mar 21, 2018

Correspondence to
Hong Euy Lim, MD, PhD
Division of Cardiac Electrophysiology, Korea University Cardiovascular Center, Korea University Guro Hospital, 148, Gurodong-ro, Guro-gu, Seoul 08308, Korea.
E-mail: hongeuy@korea.ac.kr
hongeuy1046@gmail.com

ORCID iDs
Do Young Kim
https://orcid.org/0000-0002-5601-9427
Hong Euy Lim
https://orcid.org/0000-0001-8102-8352

Conflict of Interest
The authors have no financial conflicts of interest.

Author Contributions
Writing - original draft: Kim DY, Lim HE; Writing - review & editing: Lim HE.

Cancer patients are at elevated risk of both thrombotic and bleeding complications.[1] Furthermore, they are likely to have atrial fibrillation (AF) and the risk of AF is already increased in cancer patients before diagnosis of malignancy.[1)2)] The association between cancer and AF could be explained by common risk factors such as old age, obesity, inflammation, and metabolic disorders.[1)] In this regard, proper management for prevention of thromboembolic event is clinically important in AF patients with active cancer. Despite a hypercoagulable state associated with AF as well as cancer, optimal oral anticoagulants (OACs) therapy remains challenging because of drug interaction between OAC and chemotherapy agents and changes in nutritional and metabolic status related to nausea, vomiting, anorexia, and weight loss.[3)4)] As a result, only limited AF patients with cancer could achieve adequate time in therapeutic range (TTR) of warfarin therapy.[4)] Non-vitamin K oral anticoagulants (NOACs) emerge as an attractive OAC treatment option for those patients because of no or minimal drug-drug interaction and fixed dose without requiring frequent international normalized ratio (INR) monitoring,[3)5)] but evidence regarding NOACs for AF patients with active cancer is limited because major randomized clinical trials (RCTs) of NOACs for AF patients excluded patients with active cancer. As a large RCT regarding NOACs versus warfarin in AF patients with active cancer is absent, retrospective comparative study using observational data offers the opportunity to address this undetermined issue in a timely manner.

In a recent article in *Korean Circulation Journal*, Kim et al.[6)] investigated the efficacy and safety of NOACs among patients with AF and newly diagnosed cancer. In their retrospective and propensity score matched study, Kim et al.[6)] reported the incidence of stroke/systemic embolism (SE), all-cause mortality, and major bleeding event were significantly lower in NOACs treated group as compared to those with warfarin. In addition, these results were not affected by different type or reduced dosage of NOACs. Although 71.9% patients of NOACs group had reduced dose of NOACs and half of them were taking unapproved low dose of NOACs, the efficacy end point in the NOACs group was comparable with that of well controlled warfarin group with optimal INR and the bleeding risk was significantly lower in the NOACs group as compared with warfarin treated patients who achieved the time in TTR of ≥60%. However, only one-fifth patients of the warfarin treated group achieved TTR

The contents of the report are the author's own views and do not necessarily reflect the views of the *Korean Circulation Journal*.

of ≥60% and this result reflects difficulty of maintaining stable INR range in the warfarin treated group, maybe because of metabolic interactions with chemotherapy agents and antibiotics, chemotherapy-induced pancytopenia, dehydration due to poor oral intake, and the frequent need for surgical or invasive procedures. Unfortunately, Kim et al.[6] did not report data regarding medications including chemotherapy agents and type of active cancer, and all of which makes the net benefit of NOACs therapy versus warfarin uncertain. Moreover, this limitation raises another questions as to whether reduced dosed NOACs suffice in the setting of active cancer and AF because many chemotherapy agents have significant interaction with the CYP3A4 enzyme which can alter the drug level of NOACs and chemotherapy may lead to higher bleeding risk as well.[7] Although the authors themselves acknowledge the obvious limitation that is the retrospective design, this study has limited applicability to AF patients with active cancer, who often receive chemotherapy or repeated undergo invasive procedures.

In conclusion, the decisions regarding whether or not to initiate OAC therapy and which OAC to choose are complex. Optimal maintaining TTR in warfarin therapy is very challenging and the use of NOACs can be a good alternative option for AF patients with active cancer. Since evidence supporting the use of NOACs in cancer patients for any indication is extremely limited,[3][8] further large prospective studies regarding safety and pharmacokinetics of NOACs in AF patients with active cancer will be needed and decision making on initiation and dosing of NOACs for those patients should be made on individualized approach.

REFERENCES

1. Farmakis D, Parissis J, Filippatos G. Insights into onco-cardiology: atrial fibrillation in cancer. *J Am Coll Cardiol* 2014;63:945-53.
PUBMED | CROSSREF
2. Conen D, Wong JA, Sandhu RK, et al. Risk of malignant cancer among women with new-onset atrial fibrillation. *JAMA Cardiol* 2016;1:389-96.
PUBMED | CROSSREF
3. Lee AY, Peterson EA. Treatment of cancer-associated thrombosis. *Blood* 2013;122:2310-7.
PUBMED | CROSSREF
4. Lee YJ, Park JK, Uhm JS, et al. Bleeding risk and major adverse events in patients with cancer on oral anticoagulation therapy. *Int J Cardiol* 2016;203:372-8.
PUBMED | CROSSREF
5. Senoo K, Lane D, Lip GY. Stroke and bleeding risk in atrial fibrillation. *Korean Circ J* 2014;44:281-90.
PUBMED | CROSSREF
6. Kim K, Lee YJ, Kim TH, et al. Effect of non-vitamin K antagonist oral anticoagulants in atrial fibrillation patients with newly diagnosed cancer. *Korean Circ J* 2018;48:406-17.
CROSSREF
7. Short NJ, Connors JM. New oral anticoagulants and the cancer patient. *Oncologist* 2014;19:82-93.
PUBMED | CROSSREF
8. Hendrie PC, Garcia DA. Are new oral anticoagulants ready for use in patients with cancer? *J Natl Compr Canc Netw* 2013;11:1446-9.
PUBMED | CROSSREF

https://doi.org/10.4070/kcj.2018.0081