trial fibrillation (AF) is one of the most common diseases and is increasing worldwide. The detection of arrhythmia, including atrial fibrillation, has become earlier and easier than before as a result of new emerging devices. Several types of anticoagulation drugs for preventing the severe complications of AF can be used. The clinician can also select from an increasing number of invasive therapies to intervene in pulmonary veins, which are known to be the cause of AF. However, it is still not easy to prevent arrhythmia-associated adverse events in persons at high risk or patients with the diseases in terms of life-long management.

The risk for AF is thought to be multifactorial and polygenic, which is also the case for other common diseases. Due to genetic analysis, it is becoming possible to use polygenic predictors to identify individuals at risk.1 In the meantime, it has been reported that genetic and lifestyle factors were independently associated with susceptibility to coronary artery disease.2 It is not yet clear if genetic and lifestyle factors are independently associated also with susceptibility to AF.

It is known that some lifestyles, for example, excessive alcohol consumption, are associated with the incidence of atrial fibrillation and adverse atrial remodeling. Recently, Voskoboinik, et al reported that abstinence from alcohol reduced the recurrence of AF in a randomized control study in drinkers.3 The report clearly showed the decisive importance of lifestyle on AF.

On the other hand, even if someone recognizes the importance of lifestyle modification, it tends to be difficult for them to change their lifestyle, especially in persons/patients with asymptomatic arrhythmia. Moreover, the other issue of lifestyle modification is how to monitor and evaluate their lifestyle. Although body weight reduction might be a current possible marker candidate, there is no single reliable surrogate or causative marker with which to predict the risk for AF or drug/lifestyle treatment to prevent AF.

Homocysteine levels increase if homocysteine/methionine metabolism is impaired. If persons/patients want to maintain normal metabolism, appropriate levels of vitamins B6, B12, and folic acid, which are essential factors in the folic acid pathway, are required. Ethanol intake and malnutrition of folic acid pathway associated nutrients can lead to inhibition of the critical points of the pathway at multiple sites. The molecular mechanisms that contribute to the elevated plasma homocysteine levels in AF remain unclear. Therefore, it is important to determine whether homocysteine-lowering therapy with vitamins B6 and B12, folic acid supplementation, or alcohol abstinence could prevent new-onset AF and AF recurrence.

It would also be quite important to determine whether differences in homocysteine levels between individuals depends on lifestyle or genetic factors. If it does not largely depend on genetic factors, we should focus on lifestyle management in high homocysteine individuals. Some articles have reported on the relation between alcohol intake and homocysteine. Kamat, et al reviewed the possible mechanisms of alcohol-induced toxicity related to homocysteine.5 Acetaldehyde, which is derived from ethanol, reduces methionine production by inhibiting conversion from homocysteine to methionine. A possible mechanism is that alcohol exposure results in hyperhomocysteinemia. This mechanism is one of the therapeutic targets of lifestyle modification in hyperhomocysteinemia in AF.

The blood homocysteine level itself seems to control the epigenetic regulation of genes. Drinking ethanol and a
Figure. Relationship between atrial fibrillation and blood homocysteine level. Hyperhomocysteinemia is associated with new atrial fibrillation (AF) and recurrence. The homocysteine level reflects the severity of AF. Alcohol intake increases blood homocysteine levels. Moreover, ethanol and its metabolite result in inhibition of epigenetic modification that affects protein production. Ethanol itself and hypomethionine appeared in hyperhomocysteine, accelerate abnormal epigenetic modification (hypomethylation of DNA). In the step, a shortage of substance (methionine) and ethanol-inhibited methionine processing and the enzymatic activity of DNA methyltransferases were crucial mechanisms.

Disclosure
Conflicts of interest: The authors declare that they do not have any conflicts of interest related to this study.

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