Stopping NOACs for Ablation of Atrial Fibrillation May Cause Asymptomatic Brain Lesions by MRI

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VIENNA, AUSTRIA — Perhaps it can be settled now: stopping new oral anticoagulants (NOACs) prior to ablation procedures for atrial fibrillation (AF) is not only unnecessary, it's probably bad for the brain and should be avoided.

A prospective study of 410 consecutive patients[1], with the rare feature of routine cerebral MRI both before and after standard pulmonary-vein isolation (PVI) for AF, showed a high rate of new, asymptomatic, and perhaps reversible brain lesions in patients who stopped NOACs before the procedure. But there were fewer such lesions in patients who instead maintained oral anticoagulation with vitamin-K antagonists (VKA) during the procedure.

By now, the field has gained confidence with experience and accumulating clinical trial insights to keep patients on the NOAC or VKA they are already taking even as heparin is initiated for the ablation procedure itself. The new MRI experience hints at the magnitude of the potential hazard of withdrawing oral anticoagulation for the procedure.

Per contemporary practice, the patients who stayed on their prescribed VKA therapy throughout the procedure showed a 9.6% rate of asymptomatic, mostly small cerebral lesions at postprocedure MRI. Those who had previously been prescribed a NOAC but went off the drug one day before the procedure, also per standard practice at the time, showed a 17.3% rate of such brain lesions (P=0.049).

The rate for uninterrupted VKA is consistent with "older numbers" in the pre-NOAC era, when the rate was "around 12%," Dr Michael Derndorfer (Elisabethinen University Teaching Hospital, Linz, Austria) told **theheart.org**|Medscape Cardiology. He reported the new findings here at the European Heart Rhythm Association (EHRA) EUROPACE-CARDIOSTIM 2017 sessions.

Dr Michael Derndorfer

When they were referred for AF ablation, the patients were already on dabigatran (*Praxada*, Boehringer Ingelheim), apixaban (*Eliquis*, Bristol-Myers Squibb/Pfizer), or rivaroxaban (*Xarelto*, Bayer/Johnson & Johnson), or the VKAs phenprocoumon or acenocoumarol, both derivatives of coumarin. Edoxaban (*Savaysa/Lixiana*, Daiichi Sankyo) wasn't available in Austria at the time, Derndorfer said when interviewed.

The findings do not say that VKAs should be preferred over NOACs prior to AF ablation, he emphasized. Rather, they underscore the importance of uninterrupted oral anticoagulation throughout the procedure, whether with VKAs or NOACs. "It was the discontinuation, why we had so many more," he said, calling the rate of asymptomatic cerebral lesions in the NOAC group "astonishingly" high.

In an interview, Dr Josep Brugada Terradellas (University of Barcelona, Spain) seemed to agree. The cohort was treated at a time when it was standard practice to interrupt NOACs for the ablation procedure, "but now we are not discontinuing them. So the impressive 17% [rate of] new events localized to the brain has probably dramatically decreased."

Experience with the NOACs had been fairly limited in AF patients referred for ablation, so they were stopped before the procedure out of caution. "We were more cautious [about] preventing bleeding than in preventing stroke, because the rate of stroke is very low," Terradellas said, referring to clinical stroke. Asymptomatic cerebral events like those documented here were not on the radar. "If you don't look for them, you don't see them." As it turned out, with experience, he said, "now we know there is no big danger for bleeding, so we can keep the patient on the NOACs."

The current MRI findings, according to Derndorfer, go further to suggest that any interruption in oral anticoagulation could be a bad idea. There's no evidence that the asymptomatic lesions have a long-term effect, he said when interviewed, but "some suggest they could mean cognitive decline in the future."

Currently at his center, patients are routinely imaged before and after AF ablation but are no longer followed long-term with MRI. Long-term follow-up imaging had previously shown them that the asymptomatic lesions, at least those of about 5 mm in size, are no longer visible by MRI after 3 months. Those that had been larger than 1 cm persisted but remained asymptomatic, as best as they could determine.

Clinically there were few differences between patients who had been prescribed VKAs or NOACs; about two-thirds had paroxysmal AF and one-third persistent AF, less than one-third were women, and the duration of AF and history of hypertension, stroke, transient ischemic attack, and diabetes was about the same in both groups.

Baseline and Procedural Features, Interrupted NOACs and Uninterrupted VKA, in Patients Referred to AF Ablation

Parameter	On NOACs, n=96	On VKA, n=314	*P*
Baseline			
LVEF (%)	60.8	56.9	<0.0001
Left atrial diameter (mm)	41.5	39.7	0.01
$CHADS_2$	0.96	0.68	0.006
CHA_2DS_2-VASc	1.63	1.19	0.003
Procedural			
Achieved ACT (sec)	301.3	345.1	<0.0001
Procedure time (min)	179.5	171.9	0.523
Ablation time (min)	37.1	45.3	0.001

VKA=vitamin-K antagonist
ACT=activated clotting time

However, patients in the interrupted NOAC group had higher stroke risk as gauged by $CHADS_2$ and CHA_2DS_2-VASc scores. And although procedural heparin was titrated to an activated clotting time (ACT) of 300 to 400 in everyone, per recommendations, the mean achieved ACT was significantly lower in the interrupted-NOAC group.

Indeed, apparent predictors of the new asymptomatic cerebral lesions included larger left atrial diameter, higher stroke risk scores, and perhaps a lower achieved ACT during the procedure, according to Derndorfer.

"This is a very unreproducible study, because they [performed] MRI of the brain before and after ablation in every patient," Terradellas said. "That's something you usually can do onlyif you do a research project. It's so complex and costly that you can not do that for every patient."

But it's "confirmatory," he said. This study was an unusual demonstration of the potential consequences of interrupted oral anticoagulation, but clinical practice has moved on: NOACs are no longer interrupted for ablation procedures, he said. Ongoing randomized trials are now looking at the issue, and "we are expecting them to show that you should not stop the NOACS."

Derndorfer declared no relevant financial relationships. Terradellas has previously disclosed relationships with Boehringer Ingelheim, the Sorin Group, Daiichi Sankyo, Sanofi, Medtronic, and Boston Scientific.

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References

Derndorfer M, Martinek M, Sigmund E, et al. Novel oral anticoagulants vs warfarin to prevent asymptomatic cerebral lesions during ablation of atrial fibrillation. *Europace* 2017; 19 (Suppl 3), iii30. Abstract P247, available here.

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