Title: FRAIL-AF: Non Vitamin K Antagonist Anticoagulation in Frail Elderly Patients with AF
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Dr Linda Joosten

""My name is Linda Joosten. I'm a PhD student and a medical doctor from Utrecht University in the Netherlands. And yesterday, I presented at a hotline session at EC Congress about the FRAIL AF randomized Pragmatic trial.

Knowledge Gaps

So we already know that NOACs are preferred over VKAs in non-frail AF patients. But trial evidence is lacking in frail AF patients, and observational studies, they are suffering from confounding bias. So actually, we don't know whether frail AF patients should also receive a NOAC instead of a VKA. And it's even more questionable whether we should switch those frail AF patients from a VKA to a NOAC.

Study Design and Baseline Patient Characteristics

So the study design, it's a pragmatic randomized trial investigator initiated, and half of the patients who were randomized, they continued with care as usual, which is VKA with acenocoumarol or phenprocoumon and a targeted INR value between 2.0 and 3.0 and monitoring by the Dutch thrombosis services. And half of the patients, they switched from VKA treatments to NOAC treatments. So after randomization, we switched from VKA treatment to NOAC therapy.

NOACs Studied and Differences in Outcomes

We studied the group of NOACs as a whole compared to the group of VKA as a whole. So we didn't compare NOACs. The study was set up to compare one group to another group. We did, however, the posthoc analysis, subgroup analysis, where we looked at differences between NOACs because all four NOACs were prescribed in our trial, and

there we didn't see any difference. But I really have to note again that the study is empowered to see differences between NOACs. So it's really comparing the group of NOACs to the group of VKAs, so we can draw conclusions about which NOAC is best.

Key Results

The key results, they were very surprising and also unexpected. The FRAIL AF trial was set up as a superiority design with a hypothesis that switching from a VKA to a NOAC would lead to less bleeding. However, we saw the opposite. And that's also the reason why our independent data safety monitoring board decided to stop inclusion because we clearly saw that switching from a VKA to NOAC was contraindicated with a hazard ratio of 1.69 and a highly significant key value of 0.1. So the key message is that we shouldn't switch from a VKA to a NOAC because it leads to 69% more bleeding.

Take-Home Messages and Knowledge Gaps

So what are the main take-home messages? The first one is that FRAIL AF is a unique study. This is the first randomized NOAC trial in frail older patients. So we really have information beyond available evidence, evidence that cannot be subtracted from the four landmark NOAC trials. And yeah, so the second conclusion is that we should not switch from VKA treatment to NOAC treatment in frail older patients because this leads to 69% more bleeding. And the knowledge gaps. I think this study also gives us more questions because this is what we observe, but we don't know why we observe this. It could be that frail AF patients need lower doses of NOAC, for example. So maybe that's a good one to examine. The doses of NOACs in frail elderly patients. And another one is maybe the factor eleven inhibitors are a good idea for those frail patients. So I think that's for further research."