# [Non-vitamin K antagonist oral anticoagulants in adults with a Fontan circulation: are they safe?](https://www.ncbi.nlm.nih.gov/pubmed/31245011)

Yang H, Veldtman GR, Bouma BJ, Budts W, Niwa K, Meijboom F, Scognamiglio G, Egbe AC, Schwerzmann M, Broberg C, Morissens M, Buber J, Tsai S, Polyzois I, Post MC, Greutmann M, Van Dijk A, Mulder BJ, Aboulhosn J.

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**Take Home Points:**

* The 2014 PACES/HRS gave NOACS a class III recommendation for use in Fontan patients with atrial arrhythmias – this was based on a lack of data rather than reported adverse events.
* This is the first study providing prospective safety data for the use of NOACS in Fontan patients.
* They showed comparable safety and efficacy to VKA’s with an annual rate of 2.9% respectively for thromboembolism and major bleeding.
* Since the mean follow-up in this study was only 1.4 years, longer follow-up data is needed.



***Commentary from Dr. Blanche Cupido (Cape Town, South Africa), section editor of ACHD Journal Watch:*** Patients with Fontan circuits are at risk of both thromboembolism and bleeding. Previous recommendations included the use of aspirin or Vitamin K antagonists. The data supporting its use is scanty and derived largely form observational studies. Furthermore, both poor INR control with limited time in therapeutic range as well as aspirin resistance, reduced the efficacies of both these treatment strategies. In the treatment of non-valvular AF, Non- vitamin K antagonist oral anticoagulants (NOACS) have been shown to be as efficacious as vitamin K antagonists (VKA’s) in reducing thromboembolic events with fewer intracranial bleeds and drug interactions as well as obliterating the need for INR monitoring. In Fontan patients with atrial arrythmias, NOACS currently have a class III recommendation by the PACES/HRS 2014 guideline. This recommendation was based on the lack of adequate available data and not on a documented safety hazard. Therefore, despite this recommendation, NOACS have been used increasingly in this population.

This study focused on the safety and efficacy of NOAC use in Fontan patients with prior atrial arrhythmia. Patients enrolled in the NOTE registry (NOACS for thromboembolic prevention in patients with CHD). The NOTE registry is a worldwide ongoing prospective registry in ACHD patients on NOACS for the prevention of thromboembolism. Recruitment commenced in April 2014 (35 centers in 10 countries including Europe, North America, the Middle East and east Asia). Consecutive patients with Fontan circulation were identified. Patients were followed up at 6 months, 1 year and 2 years.

Primary endpoints were thromboembolism (ischemic CVA, TIA, systemic or pulmonary embolism, intra-cardiac embolism) and major bleeding (defined as bleeding requiring hospitalizations / interventions/the transfusion of 2 or more units of packed cells or a haemoglobin drop > 20 g/L and/or fatal bleeding or bleeding occurring in one of the following critical sites: intracranial, intraspinal, intraocular, pericardial, intra-articular or intra-muscular with compartment syndrome. Minor bleeding was a secondary endpoint.

A total of 74 Fontan patients were identified from a total of 513 ACHD patients on NOACS. The indications for NOACS were atrial arrhythmias (n=52), primary prevention (n=12) and secondary prevention (n=10). The CHA2DS2VASc score was >1 in 66% (n=49) and only 2 patients had high HAS-BLED scores.

During the mean follow-up of 1.4 years (102.4 patient years), 3 thromboembolic events (pulmonary emboli, 1 ischemic cerebrovascular event –) and 3 major bleeds (2 menorrhagia, 1 major GIT bleed)occurred in 5 patients with AP Fontans and one patient with TCPC - annual rate 2,9%, 95% CI 0.7-7.6%, respectively. Minor bleeding occurred in 15 patients (annual rate 15.8%, 95% CI 9.1-25.2%).

Figure 1A below shows the Kaplan-Meier curves of survival free from thromboembolism, major bleeding and minor bleeding.



Two patients died during follow-up – 1 heart failure and 1 cancer death.

Prior to NOAC initiation, 50% (n=37) were on VKA’s, 26% (n=19) were taking aspirin and 24% (n=18) had no antithrombotic treatment. In the subgroup who started NOACS de-novo for primary prevention (i.e. no prior VKA or aspirin use), no thromboembolic events of major bleeding occurred.



Figure 1B above depicts the event free survival of those patients on VKA’s in the 3 years prior to changing to NOACS. In this group, over a 3.5year period, the annual event rate was 6.2% for thromboembolism (95% CI 1.9% to 14.4%) and 0% for major bleeding.

A total of 14 patients stopped NOAC therapy to recommence VKA’s. Reasons included: thromboembolism (n=3), bleeding (n=4), side-effects (n=2), pregnancy (n=2), patient refusal (n=2), Fontan conversion (n=1).