# Comparison between Direct Oral Anticoagulation (DOAC) Interruption and DOAC Continuation in Patients Undergoing Elective Invasive Coronary Angiography or Percutaneous Coronary Intervention

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment started |
| **Health condition type** | Coronary artery disorders |
| **Study type** | Interventional research applied for the first time in human subjects |

## Summary

### ID

NL-OMON51007

**Source**
ToetsingOnline

**Brief title**
SLIM 2 study

### Condition

- Coronary artery disorders

**Synonym**
Chronic Coronary Syndrome Coronary Artery Disease

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Zuyderland
**Source(s) of monetary or material Support:** Zuyderland

## Intervention

- Other intervention

**Keyword:** Continuation, DOAC, Interruption, NOAC

**Explanation**

N.a.

## Outcome measures

**Primary outcome**

Primary endpoint<br />
In hospital major bleeding, BARC bleeding definition 3 or 5.

**Secondary outcome**

Secondary endpoints<br />
• 30 days follow-up<br />
- Major bleeding, BARC bleeding definition 3 or 5.<br />
- Major adverse cardiac and cerebrovascular events (MACCE): composite of death,<br />
myocardial infarction, revascularisation and stroke (haemorrhagic or ischemic)<br />
- NACE: the composite of MACE and major or minor bleeding.<br />
- Myocardial infarction<br />
- Stroke<br />
- Minor bleeding, BARC bleeding definition 1-2.

# Study description

**Background summary**

Patients with atrial fibrillation (AF) often have coexisting coronary artery disease (CAD). The prevalence of CAD in patients with AF ranges from 17 to 46.5%. An estimated 5 to 15% of all AF patients will require coronary stenting and therefore will receive antiplatelet therapy in addition to Vitamin K Antagonists (VKA) or Direct Oral Anticoagulants (DOAC) (2). In patients using

VKA it is recommended to defer elective coronary angiography until INR is <1.8 when femoral artery access is used, or <2.2 when radial artery access is used (3). However, in a meta-analysis conducted by Kowalewski et al., no significant differences of periprocedural bleeding risk between interrupted or uninterrupted VKA use (4). In addition, DOACs are more commonly used in preventing thromboembolic complications in patients with AF, thereby substituting VKA use. This shift in antiocoagulant use, opposes a challenge in managing ischemic and bleeding complications in invasive coronary angiograqphy (ICA) and percutaneous coronary interventions (PCI).

Patients using DOAC and undergoing ICA or PCI may have an increased risk of bleeding complications. Therefore, it is recommended to discontinue DOAC at least 12 to 48 hours in advance of ICA or PCI, depending on renal function and the particular DOAC regimen (5). In order to reduce bleeding risk, it is preferred to use radial access instead of femoral access. Multiple studies show a higher risk of bleeding complications when femoral access is used (6-8). In contrast to periprocedural VKA use, only limited articles are available regarding uninterrupted use of DOAC during ICA or PCI. In 2019 Chongprasertpon et al. found no significant differences between interrupted and uninterrupted DOAC in elective ICA or PCI (1). However, an important limitation of this study is the limited amount of participants and the fact that no significant bleedings were found in both groups of 49 patients.

To our knowledge, no large population studies have focused on periprocedural continuation of DOAC therapy in patients diagnosed with chronic coronary syndrome (CCS) and undergoing elective ICA or PCI. Clinical decisions on DOAC use must therefore be based on clinical trials in which substantial numbers of patients with acute coronary syndrome (ACS) were included. Radial artery access is preferred along with intraprocedural unfractionated heparin either at a standard dose (70-100 U/kg) or, in those with uninterrupted VKA, at a lower dose of 30-50 U/kg (5). The ESC guidelines for the management of ACS in patients presenting with NSTEMI (2020) state that UFH at a dose of 60 IU/kg should be administered in patients with DOAC usage (9). Pre-treatment with aspirin 75-100 mg daily is recommended, and clopidogrel (300-600 mg loading dose if not on long-term maintenance therapy) is recommended in preference to prasugrel or ticagrelor (5).

In addition, a recent report from the National Cardiovascular Data Registry (NCDR) Acute Coronary Treatment and Intervention Outcomes Network Registry (ACTION-registry) which included more than 26.000 patients showed that DOAC therapy was not associated with an increased risk of in-hospital bleeding. However, no information was given concerning periprocedural DOAC use in this study (6).

In clinical practice, it is commonly seen that patients or physicians forget to temporarily discontinue DOAC therapy, prior to an elective procedure. This forms a practical problem in daily care, assumingly raising both costs and time

needed in preparation for an elective procedure. In this prospective study, we aim to examine the safety of DOAC continuation in patients who undergo ICA or PCI in both elective and emergency procedures.

## Study objective

The aim of our study is to study the safety of continued DOAC use during ICA or CAG in elective procedures, by comparing the risk of in-hospital and 30-day bleeding complications between continued and interrupted DOAC use.

## Study design

Eligible patients will be randomized to DOAC continuation or interruption at the moment when ICA or PCI is planned. After randomisation the patient will be instructed either to continue DOAC use as usual or to stop DOAC 24 hours in advance of the procedure. Treatment will be assigned on the basis of a 1:1 ratio.

Interruption of pre-procedural DOAC use is mainly based on expert opinion (15). Clearance of DOACs is predominantly renal. Therefore, timing of DOAC interruption depends on renal clearance of a patient. Clearance must be measured at least 3 months prior to the procedure. Figure 2 shows an overview of DOAC interruption, varying for each DOAC and creatinine clearance.

Stopping DOAC 24 hours prior to the procedure implies that there must be at least 24 hours between intake of the last dose of DOAC and start of the procedure.

## Intervention

Group 2 (intervention): DOAC continuation
In group 2, all patients will continue to use their specific DOAC as usual. This means that no adjustments of DOAC use will be made before and after ICA or PCI. After the procedure patients will continue to use DOAC from the next planned dose.

## Study burden and risks

Based on earlier research on VKAs, no significant bleeding complications were seen comparing bleeding rates in patiënts with uninterrupted versus interrupted VKA use. Furthermore Chongpraserton et al. showed no significant bleedingcomplications in a population of 98 patients on DOAC, undergoing elective ICA or PCI. Half of this population continued DOAC use and the other group shortly interrupted DOAC periprocedural.

Based on these findings, no risk differences are expected between the two

groups. If any difference in risk will be present, this must be only a small risk, based on the low number of bleedingcomplications that were seen in earlier studies.

# Contacts

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# Trial sites

## Trial sites in the Netherlands

Isala
Target size: 100

Rijnstate
Target size: 100

Amsterdam UMC
Target size: 150

Maastricht Universitair Medisch Centrum +
Target size: 300

St. Antonius Ziekenhuis
Target size: 300

Zuyderland
Target size: 670

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

o Patients aged between 18-85 years using DOAC and undergoing elective ICA or PCI.
o Written informed consent

### Exclusion criteria

- Patients initially presenting with Acute Coronary Syndrome (STEMI, NSTEMI, UA)
- Patients <18 or >85 years old
- Calculated CLCR <30 mL/min
- Patients simultaneously participating in another clinical trial
- History or condition associated with increased bleeding risk, as listed below:
o Major surgical procedure within 30 days before the procedure
o Known inaccessible radial artery during previous procedure
o History of GI bleeding in the previous 6 months
o History of intracranial, intraocular, spinal, or atraumatic intra-articular bleeding
o Chronic bleeding disorder
o Known intracranial neoplasm, arteriovenous malformation, or aneurysm
o Known anemia with last measured haemoglobin value <6 mmol/L [9.67 g/dL]
o Current pregnancy or breast-feeding
o Known significant liver disease (e.g., acute clinical hepatitis, chronic active hepatitis, cirrhosis), or ALT >3 x the ULN

## Study design

### Design

| | |
|---|---|
| Study phase: | N/A |
| Study type: | Interventional research applied for the first time in human subjects |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Other type of control |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment started |
| Start date (anticipated): | 08-09-2022 |
| Enrollment: | 1270 |
| Duration: | 1 months (per patient) |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | N.a. |

### IPD sharing statement

**Plan to share IPD:** Yes

**Plan description**
N.a.

## Ethics review

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|---|---|
| Approved WMO Date: | 30-08-2021 |
| Application type: | First submission |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 20-04-2023 |
| Application type: | Amendment |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |

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| Approved WMO Date: | 22-04-2024 |
| Application type: | Amendment |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 14-05-2024 |
| Application type: | Amendment |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 20-12-2024 |
| Application type: | Amendment |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 31-03-2025 |
| Application type: | Amendment |
| Review commission: | METC Atrium-Orbis-Zuyd (beëindigt) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| CCMO | NL77708.096.21 |
| Research portal | NL-007596 |