Diagnostic Performance of Photon Counting Computed Tomography in High-Risk Patients With Acute Coronary Syndrome Without ST-segment Elevation

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Primary objective: - To study the diagnostic accuracy of PCCT (± CT-derived fractional flow reserve [FFRct]) as compared to the reference standard ICA (± FFRinv) in the NSTE-ACS population referred to the UMCG. Secondary objectives: - To study the…

Ethical review	Approved WMO
Status	Pending
Health condition type	Coronary artery disorders
Study type	Observational non invasive

Summary

ID

NL-OMON57442

Source
ToetsingOnline

Brief title
PCCT in NSTE-ACS patients

Condition

- Coronary artery disorders

Synonym
coronary artery disease, myocardial infarction, NSTE-ACS

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Siemens,Siemens in het kader van de PUSH grant en innovatiefonds van de afdeling Cardiologie.

Intervention

Keyword: coronary angiography, coronary CT angiography, NSTE-ACS, photon-counting CT

Outcome measures

Primary outcome

The diagnostic accuracy of PCCT (±FFRct) for the diagnosis of (hemodynamically)

obstructive CAD compared to the reference standard, ICA (±FFRinv).

Secondary outcome

- Percentage (%) of NSTE-ACS patients approached to participate in the study

that receive PCCT and ICA within the predefined time frame;

- Agreement of revascularization decision and strategy based on PCCT (±FFRct)

as compared to ICA (±FFRinv);

- Radiation exposure (mSv), volume of contrast (ml), complication rate (%) for

PCCT and ICA;

- Agreement of PCCT in assessing plaque volume (total and by plaque component),

and high-risk features as compared to IVUS and/or OCT.

Study description

Background summary

Each year >20 million patients in Europe and North America present with (suspected) acute coronary syndrome (ACS). ACS patients are differentiated into two groups according to ST-segment elevation on electrocardiography, namely ST-elevation myocardial infarction (STEMI) and non-ST-elevation ACS (NSTE-ACS). There has been a continuous increase in the occurrence of NSTE-ACS over the past few decades, also confirmed by data from the Dutch Heart Registry. Importantly, compared to STEMI patients, NSTE-ACS patients are older, have more

co-morbidity and carry worse long-term prognosis, resulting in a growing burden for the healthcare system. Underlying coronary pathology in these patients ranges from structurally normal epicardial vessels to non-obstructive atherosclerotic plaques and extensive obstructive coronary artery disease (CAD).

Based on initial risk stratification, most NSTE-ACS patients have an indication for invasive coronary angiography (ICA) <24-hours after presentation. In case of significant obstructive CAD amenable to revascularization, either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is performed. Importantly, ICA is costly and due to its invasive nature, associated with a low risk of detrimental complications. Moreover, only ~50% of patients undergo (direct) revascularization.

According to recent UMCG data of NSTE-ACS patients referred for ICA, merely 56% of the patients were revascularized during the ICA procedure. Thus, in a large group of NSTE-ACS patients, who turn out to have no indication for coronary intervention or the intervention is not technically feasible, the ICA may be considered unnecessary. Moreover, in the Netherlands, the ICA is often performed twice, first in the regional hospital (non-interventional center), and in case of relevant findings the patient is referred for a second ICA procedure to an interventional center. There, PCI is performed, often preceded by an additional invasive fractional flow reserve (FFRinv) measurement, to assess the hemodynamical significance of lesions. In addition to being patient-unfriendly, this approach wastes hospital and emergency-service resources (length of hospital stay, transfer of patients between hospitals). Concluding, there is an urgent clinical need for a non-invasive alternative to ICA, to pre-select patients for invasive management in order to prevent unnecessary (dual) ICA.

In the last decades, computed tomography (CT) has undergone remarkable improvements in hardware and software technology, with increase in temporal and spatial resolution at even reduced radiation exposure. Nowadays, coronary CT angiography (CTA) is very accurate in ruling out obstructive CAD. Coronary CTA recently received a class I indication for evaluation in stable chest pain. Furthermore, coronary CTA is an alternative to ICA to exclude obstructive CAD in acute patients with low-intermediate risk, normal or inconclusive cardiac troponins, and/or ECG without ischemic changes.

Our study aims to extend the indication of coronary CTA to the high-risk NSTE-ACS patient cohort. These high-risk NSTE-ACS patients generally have more extensive CAD. This has so far limited the application of coronary CTA in this patient group, as coronary CTA is more often non-conclusive in case of more extensive CAD, with overestimation of stenosis degree, and low specificity in case of stents and/or severe calcifications (due to blooming artefacts). Photon counting CT (PCCT) technology has recently entered the clinical imaging realm. This novel modality has a better spatial resolution and soft-tissue contrast, and reduces image noise and artefacts. Consequently, it has better image quality and diagnostic accuracy at a similar radiation dose compared to conventional coronary CTA. Initial results show reduction in blooming and better visualization of the coronary lumen (with less overestimation of

stenosis). PCCT may also have an important additional value in patients with coronary stents. Another important improvement of PCCT is the potential for characterization of atherosclerotic plaques. The composition and extent of coronary plaques was shown to have important prognostic value. The gold standard for (vulnerable) plaque characterization is invasive coronary imaging (intravascular ultrasound [IVUS] or optical coherence tomography [OCT]). PPCT was shown to outperform conventional coronary CTA for plaque evaluation due to improved spatial resolution.

Study objective

Primary objective:
- To study the diagnostic accuracy of PCCT (± CT-derived fractional flow reserve [FFRct]) as compared to the reference standard ICA (± FFRinv) in the NSTE-ACS population referred to the UMCG.

Secondary objectives:
- To study the agreement of revascularization decision and strategy based on PCCT (±FFRct) as compared to ICA (±FFRinv);
- To study the practical feasibility of performing PCCT in NSTE-ACS patients;
- To compare safety parameters between PCCT and ICA: radiation exposure, amount of contrast used, complication rate;
- To assess the preliminary cost effectiveness of PCCT in NSTE-ACS patients;
- To study the accuracy of coronary plaque evaluation with PCCT as compared to invasive IVUS and/or OCT.

Study design

Prospective single-center study.

All consented NSTE-ACS patients will undergo PCCT, followed by ICA. The patient flow is a reflection of the current situation in our region (HartNet Noord Nederland). The PCCT will be performed within 20-hours after presentation in order to comply with the 24-hour time-window recommended for ICA. All efforts will be made not to delay the ICA in comparison to the patients not participating in the study. If the PCCT scan cannot be performed within the 20-hour time window, or there are clinical reasons why ICA should be performed expeditiously, the PCCT scan will be cancelled and the patient will undergo ICA without further delay.

The PCCT will be performed with a first-generation dual-source PCCT scanner (NAEOTOM Alpha; Siemens Healthineers). First, a CT scan without intravenous contrast will be performed for calcium scoring (unless prior in case of revascularization). Next, a CT angiography of the coronary arteries will be performed with intravenous contrast, after administration of beta-blockers (if indicated) and nitroglycerin. A high-density contrast medium followed by

isotonic saline will be injected with personalized concentration and flow rate. Depending on the scanning protocol used, automatically determined best systolic, best diastolic, and/or multiphase data will be reconstructed with a section thickness of 0.2-0.4 mm.

All main vessels and first degree side-branches (>2mm diameter) will be assessed. Both the operator performing ICA as well as the investigator assessing PCCT images will be blinded for the findings of the other modality. FFRct and FFRinv will be calculated or measured, respectively, for every stenosis of 30-90%. Siemens FFRct software will be used for the analysis. In grafts/grafted vessels FFRct is not validated and thus will not be measured. The determination of significant stenosis in these patients would be based on anatomical assessment (i.e. PCCT and ICA). Hereby the possible results of the analysis of PCCT scans and ICA:

- Non-significant stenosis/ non-obstructive CAD: This refers to a stenosis of less than 30%, or a stenosis between 30% and 90% without reduced FFRinv or FFRct value (if performed).
- Significant stenosis/ obstructive CAD:
- Coronary CTA/ ICA only (in case of already revascularized vessel i.e. after CABG or PCI): Stenosis of 70% or more, or a stenosis of 50% in the left main.
- Coronary CTA/ICA and FFRct / FFRinv: Stenosis between 30% and 90% with an FFR value below 0.80.
- Highly significant stenosis/ obstructive CAD: For stenosis of more than 90%, the FFRct/FFRiv analyses are not performed.
- Chronic Total Occlusion (CTO): This is classified and assessed separately.

The revascularization decision based on PCCT±FFRct will be compared to ICA±FFRinv. There are five potential test results:
- no coronary pathology
- non-significant CAD/ non-obstructive CAD; revascularization is not indicated
- significant CAD/ obstructive CAD; PCI is indicated and feasible
- significant CAD/ obstructive CAD; CABG is indicated and feasible
- significant CAD/ obstructive CAD; revascularization is not feasible

The diagnostic accuracy of stenosis detection with PCCT±FFRct will be compared against the reference standard i.e. ICA±FFRinv.

Follow-up will be performed according to the post-ACS protocol of the HartNet network; all major cardiovascular adverse events (MACE: composite outcome of all-cause mortality, myocardial infarction, stroke, and unplanned revascularization) during 1-year will be collected.

Study burden and risks

The benefits of this research endeavor are multifaceted. By reducing the need for invasive procedures in the future for a significant proportion of patients

with NSTE-ACS, PCCT holds the promise of minimizing patient discomfort, reducing healthcare costs, and mitigating the risk of procedural complications. Moreover, the integration of FFRct enhances the diagnostic accuracy of PCCT, thereby facilitating more precise identification of patients who truly necessitate revascularization. This not only optimizes resource allocation but also ensures that interventions are directed towards those who stand to derive the greatest clinical benefit.

However, the pursuit of these benefits is not without inherent risks. The risks associated with the non-invasive imaging techniques are minimal and related to contrast, and radiation exposure. The incidence of side effects due to contrast is rare and the side effects are almost exclusively mild. Potential side effects of iodine contrast include flushing, and (mild) skin rash. Patients with impaired renal function are at risk of contrast induced nephrotoxicity, however eGFR<30ml/min is an exclusion criterium for study participation. Additionally, the radiation dose associated with the newest ultrafast low-dose PCCT scan is maximally about 13mSv. For comparison, the average radiation exposure from a nuclear scan in cardiology is about 9 mSv, and annual background radiation is approximately 2.5 mSv. This means the radiation dose corresponds to 4-5 times the annual background radiation. While the radiation theoretically carries a slightly increased risk of developing cancer 15-20 years later, this risk is very small and decreases with increasing age, especially above 60 years. Therefore, this additional radiation exposure for this study is relatively low and outweighs the potential benefits.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients with high-risk NSTE-ACS (Acute Coronary Syndrome without ST-segment Elevation), defined as:
- acute chest pain,
- ECG without ST-elevation,
- high sensitivity troponin (hsTn) elevation (3x above the limit, rise and fall) or no/low hsTn + history of CABG (Coronary Artery Bypass Grafting) and/or PCI (Percutaneous Coronary Intervention),
- planned ICA (Invasive Coronary Angiography) within 24-hours after diagnosis (during office hours).

Exclusion criteria

- low risk and very high risk NSTE-ACS (Acute Coronary Syndrome without ST-segment Elevation),
- severe kidney dysfunction (eGFR <30 ml/min*1,73m2),
- known iodine contrast allergy
- individuals with implanted medical devices, such as pacemakers or implantable cardioverter defibrillators, and mechanical valves
- inability to provide informed consent,
- pregnancy,
- ICA (Invasive Coronary Angiography) performed in a non-interventional center,
- limited diagnostic workup and/or direct conservative treatment (e.g. due to comorbidities)

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2025
Enrollment:	206
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	23-04-2025
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL87144.042.24