Prognostic value of selective myocardial perfusion imaging after coronary CTA

A multicentre cohort study

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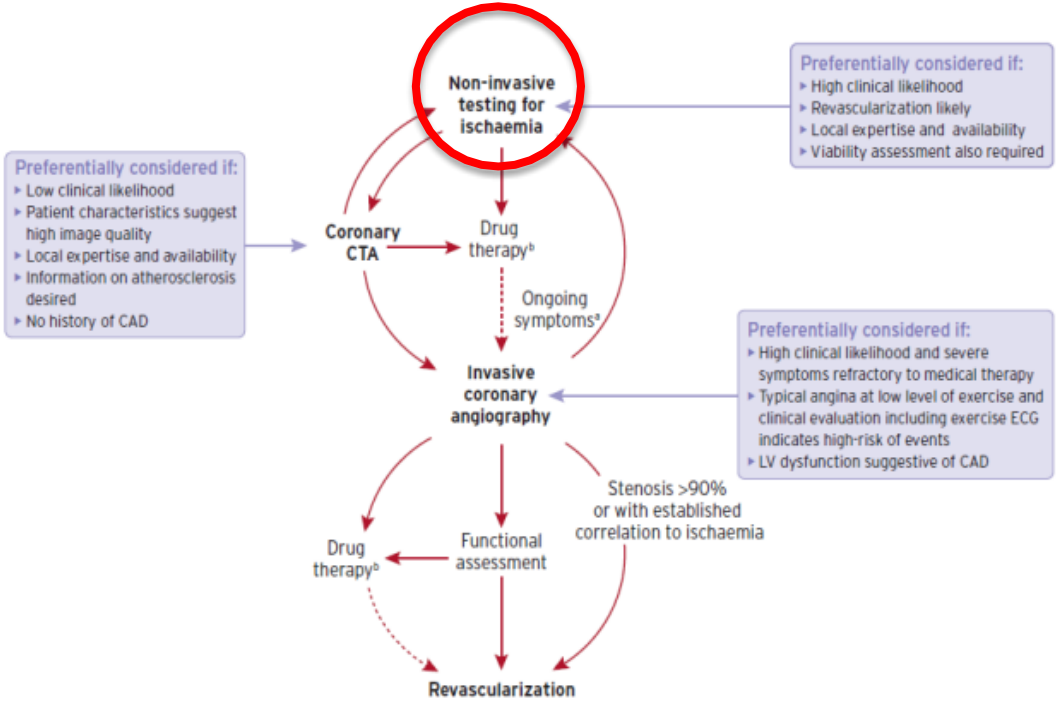
- Declaration of interest: None

Introduction

Myocardial perfusion imaging (MPI) is recommended as first-line diagnostic test in stable coronary artery disease (CAD) in patients with moderate-to-high pre-test probability



2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019

Introduction

Myocardial perfusion imaging (MPI) is recommended as first-line diagnostic test in stable coronary artery disease (CAD) in patients with moderate-to-high pre-test probability

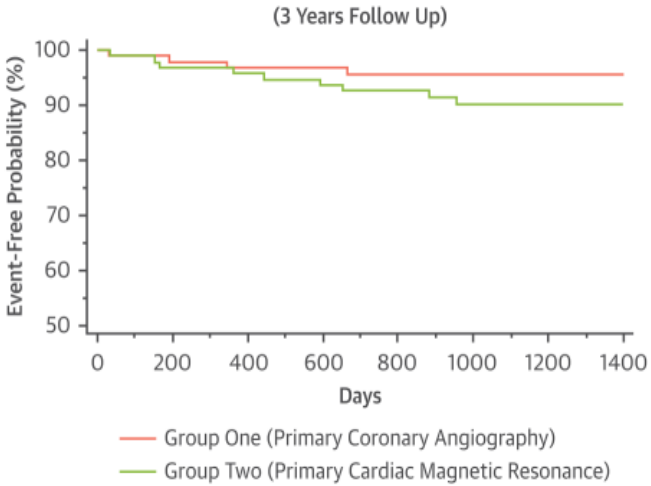
Diagnostic performance of CMR, SPECT, and PET myocardial perfusion imaging

	No. of studies	Sensitivity (%)	Specificity (%)
Patient level			
CMR	7	87(73–94)	87(82–90)
SPECT	8	72(52–86)	79(71–85)
Vessel level			
CMR	12	85(75–92)	89(85–93)
SPECT	9	64(47–77)	89(86–91)
PET	4	83(68–92)	89(85–91)

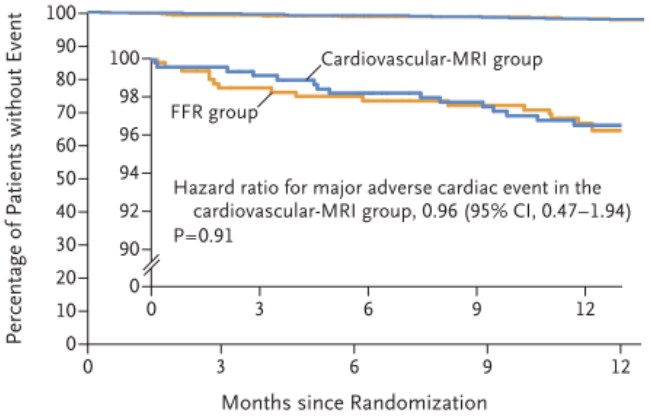
Yang K et al. A meta-analysis. Int J Cardiol. 2019

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019

Randomized studies have showed similarly prognosis when patients are evaluated with magnetic resonance (MR) or invasive coronary angiography (ICA) as first-line test

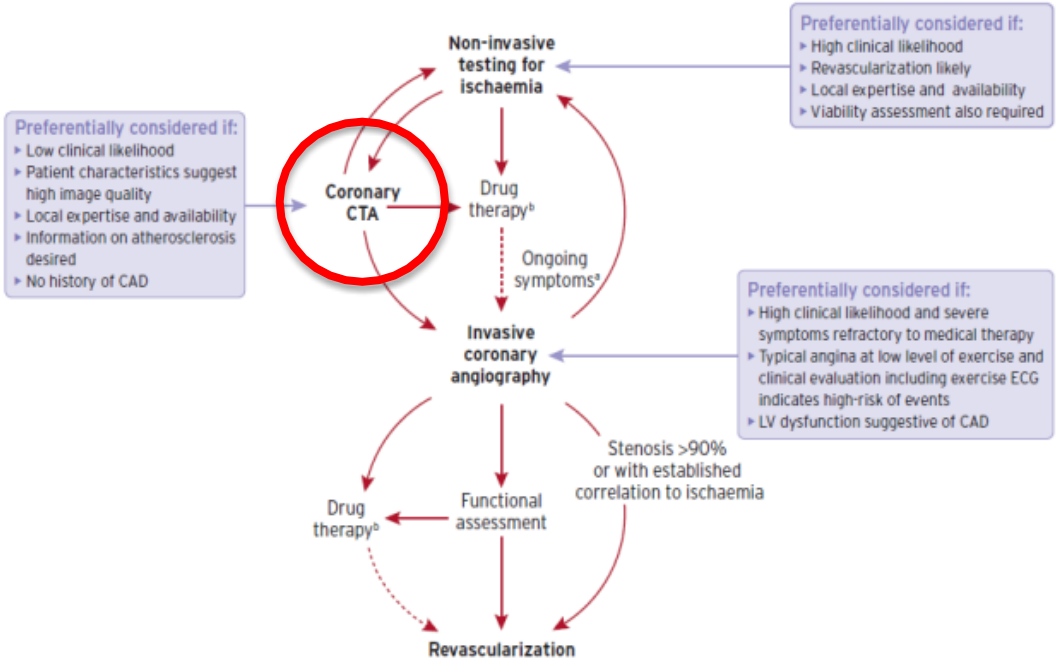


Buckert Det al, JACC Cardiovasc Imaging. 2018



Nagel E et al, N Engl J Med. 2019

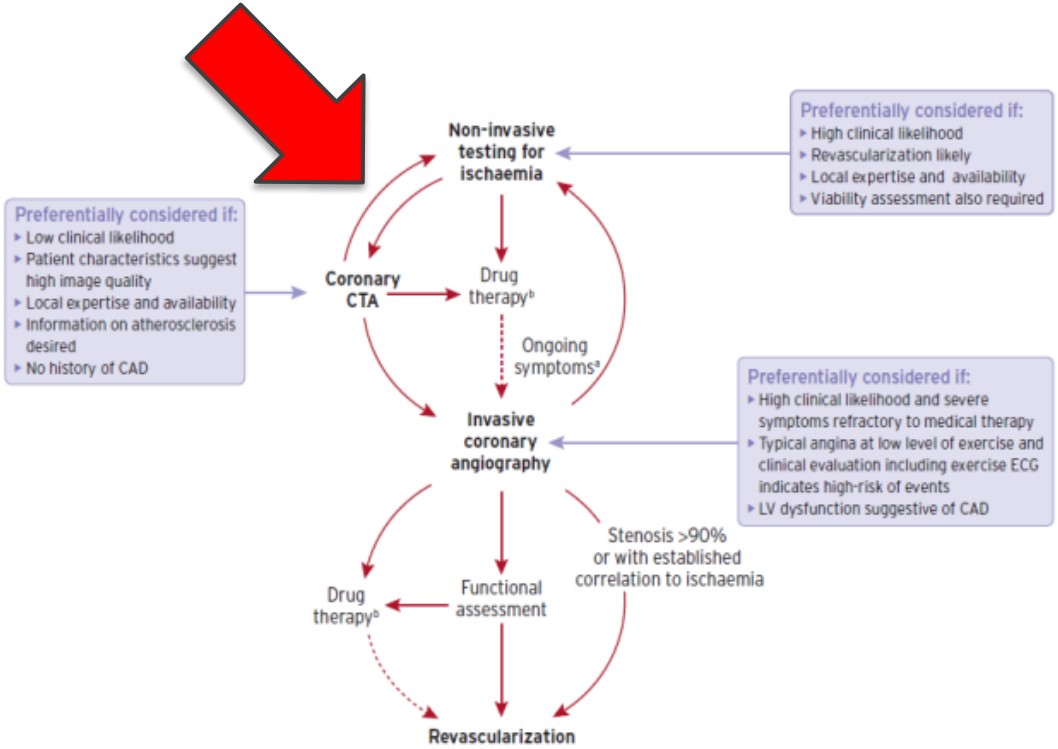
Coronary computed tomography angiogram (CTA) is also recommended as first-line diagnostic test in stable CAD in patients with low-to-moderate pre-test probability



2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019

Coronary computed tomography angiogram (CTA) is also recommended as first-line diagnostic test in stable CAD in patients with low-to-moderate pre-test probability

Due to moderate positive predictive value of coronary CTA, selective MPI is recommended after coronary CTA
- to avoid unnecessary ICA
- to potential guide revascularization



2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019

Use of diagnostic imaging tests in the initial diagnostic management of symptomatic patients with suspected coronary artery disease

Recommendations	Class[a]	Level[b]
Non-invasive functional imaging for myocardial ischaemia[c] or coronary CTA is recommended as the initial test to diagnose CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.[4,5,55,73,78–80]	I	B
It is recommended that selection of the initial non-invasive diagnostic test is done based on the clinical likelihood of CAD and other patient characteristics that influence test performance,[d] local expertise, and the availability of tests.	I	C
Functional imaging for myocardial ischaemia is recommended if coronary CTA has shown CAD of uncertain functional significance or is not diagnostic.[4,55,73]	I	B
Invasive coronary angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood, severe symptoms refractory to medical therapy or typical angina at a low level of exercise, and clinical evaluation that indicates high event risk. Invasive functional assessment must be available and used to evaluate stenoses before revascularization, unless very high grade (>90% diameter stenosis).[71,72,74]	I	B
Invasive coronary angiography with the availability of invasive functional evaluation should be considered for confirmation of the diagnosis of CAD in patients with an uncertain diagnosis on non-invasive testing.[71,72]	IIa	B
Coronary CTA should be considered as an alternative to invasive angiography if another non-invasive test is equivocal or non-diagnostic.	IIa	C
Coronary CTA is not recommended when extensive coronary calcification, irregular heart rate, significant obesity, inability to cooperate with breath-hold commands, or any other conditions make obtaining good image quality unlikely.	III	C
Coronary calcium detection by CT is not recommended to identify individuals with obstructive CAD.	III	C

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2019

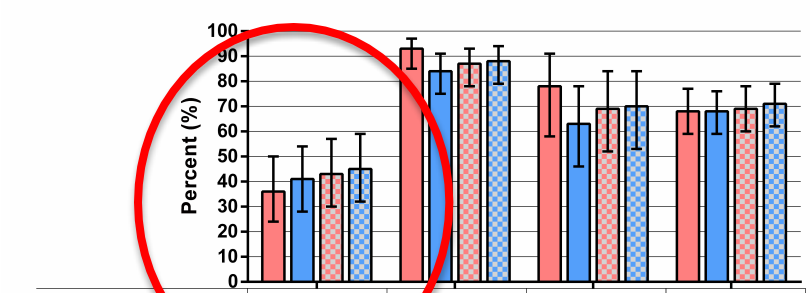
Diagnostic accuracy of selective MPI after coronary CTA

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2018) 19, 369–377
doi:10.1093/ehjci/jex342

Diagnosing coronary artery disease after a positive coronary computed tomography angiography: the Dan-NICAD open label, parallel, head to head, randomized controlled diagnostic accuracy trial of cardiovascular magnetic resonance and myocardial perfusion scintigraphy

L. Nissen[1]*, S. Winther[2], J. Westra[2], J.A. Ejlersen[3], C. Isaksen[4], A. Rossi[5], N.R. Holm[2], G. Urbonaviciene[6], L.C. Gormsen[7], L.H. Madsen[1], E.H. Christiansen[2], M. Maeng[2], L.L. Knudsen[1], L. Frost[6], L. Brix[4], H.E. Bøtker[2], S.E. Petersen[5], and M. Bøttcher[1]

Patients with obstructive CAD by coronary CTA were randomized 1:1 to CMR or MPS and subsequent ICA with FFR analysis
N=292



	Sensitivity	Specificity	PPV	NPV
MPS	36% (24-50)	93% (85-97)	78% (58-91)	68% (59-77)
CMR	41% (28-54)	84% (75-91)	63% (46-78)	68% (59-76)
Prior knowledge MPS	43% (30-57)	87% (78-93)	69% (52-84)	69% (60-78)
Prior knowledge CMR	45% (32-59)	88% (79-94)	70% (53-84)	71% (62-79)

Diagnostic accuracy of selective MPI after coronary CTA

Patients with obstructive CAD by coronary CTA underwent FFRct, MPS and ICA with FFR analysis. N=143

Prospective Comparison of FFR Derived From Coronary CT Angiography With SPECT Perfusion Imaging in Stable Coronary Artery Disease

The ReASSESS Study

Niels Peter Rønnow Sand, MD,[a,b] Karsten Tange Veien, MD,[c] Søren Steen Nielsen, MD,[d] Bjarne Linde Nørgaard, MD,[e] Pia Larsen, PhD,[f] Allan Johansen, MD,[g] Søren Hess, MD,[h] Lone Deibjerg, MD,[i] Majed Husain, MD,[a] Anders Junker, MD,[c] Kristian Korsgaard Thomsen, MD,[a] Allan Rohold, MD,[b] Lisette Okkels Jensen, MD[c]

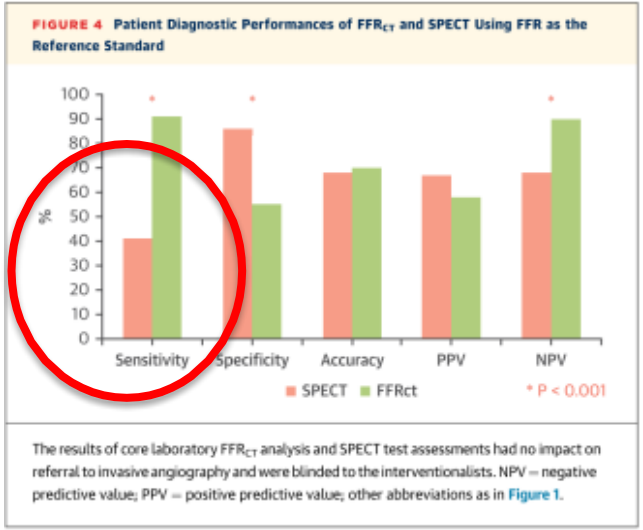


FIGURE 4 Patient Diagnostic Performances of FFR_{CT} and SPECT Using FFR as the Reference Standard

The results of core laboratory FFR_{CT} analysis and SPECT test assessments had no impact on referral to invasive angiography and were blinded to the interventionalists. NPV = negative predictive value; PPV = positive predictive value; other abbreviations as in Figure 1.

No large studies have investigated the prognostic value of selective MPI after coronary CTA

Objective

To investigate the prognosis for patients completing coronary CTA with stratification for post-CTA diagnostic work-up.

This was performed by comparing 4 groups of patients:

A) No CAD → deferral after CTA

B) CAD → medically treated after CTA

C) CAD → referral to MPI after CTA

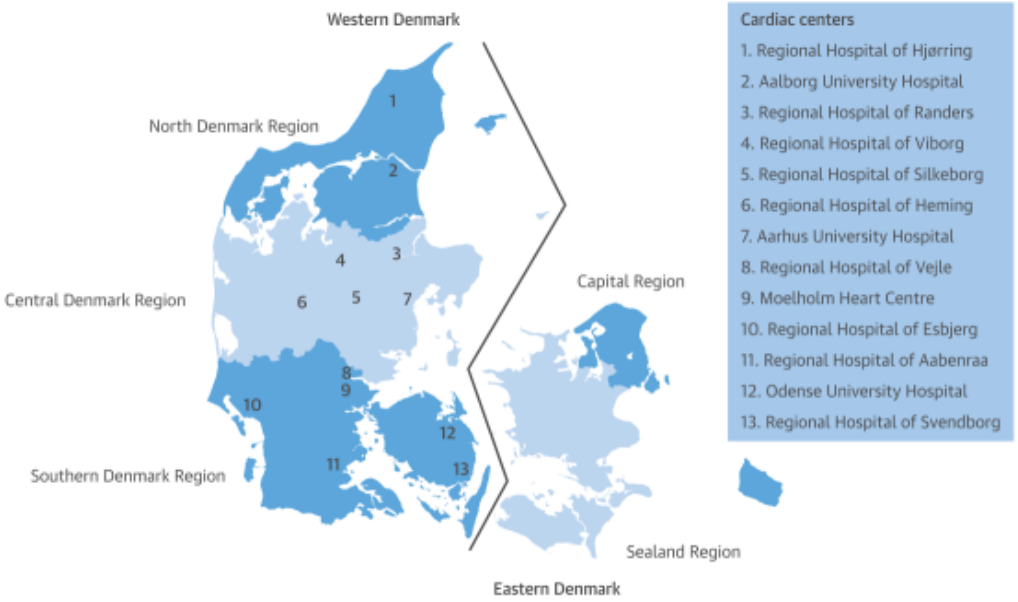
D) CAD → referral to ICA after CTA

Study design

This cohort study was conducted using a regional Danish population-based clinical quality database, The Western Denmark Heart Registry.

We identified all patients who underwent first-time coronary CTA from 2008 to 2017 at all hospitals in the Western part of Denmark .

The Danish national healthcare service is publicly financed and allows for linkage of all administrative healthcare registries.

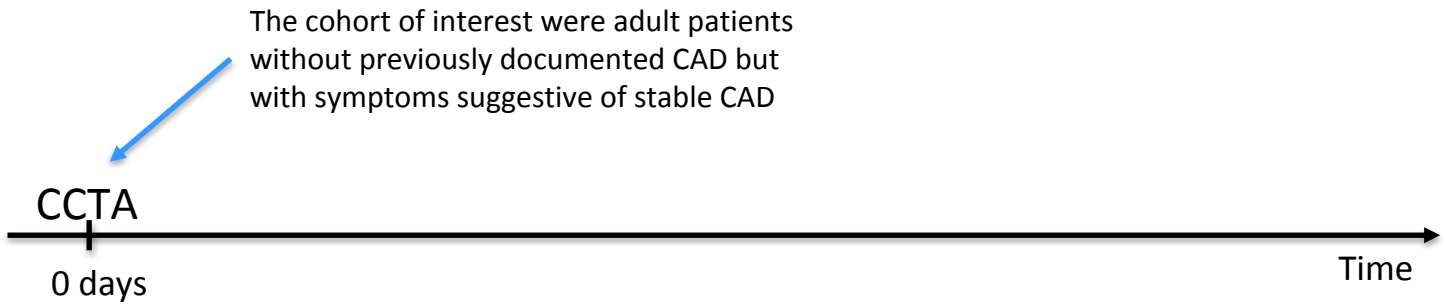


Uptake area 3.3 million; 55% of the total Danish population

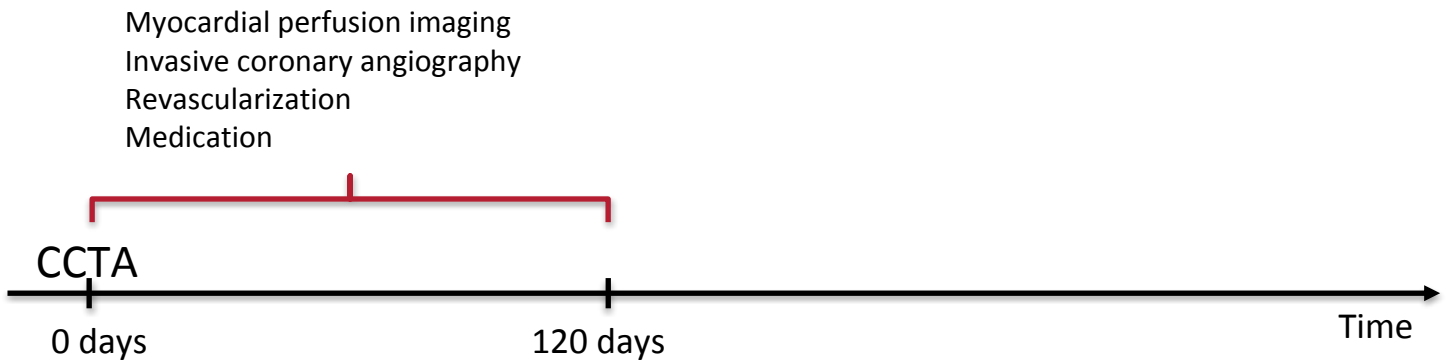
Schmidt M et al, The Western Denmark Heart Registry: Its Influence on Cardiovascular Patient Care. J Am Coll Cardiol. 2018

Study design

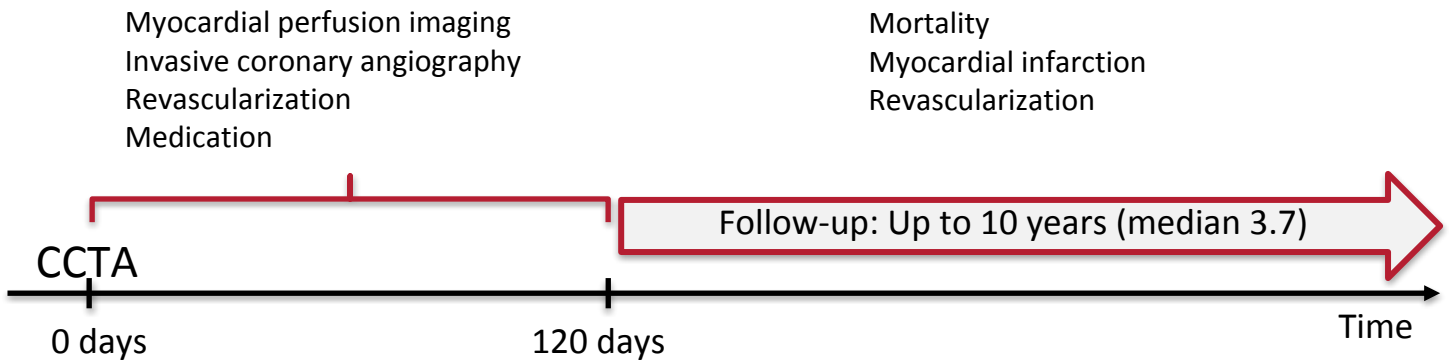
Study design



Study design



Study design



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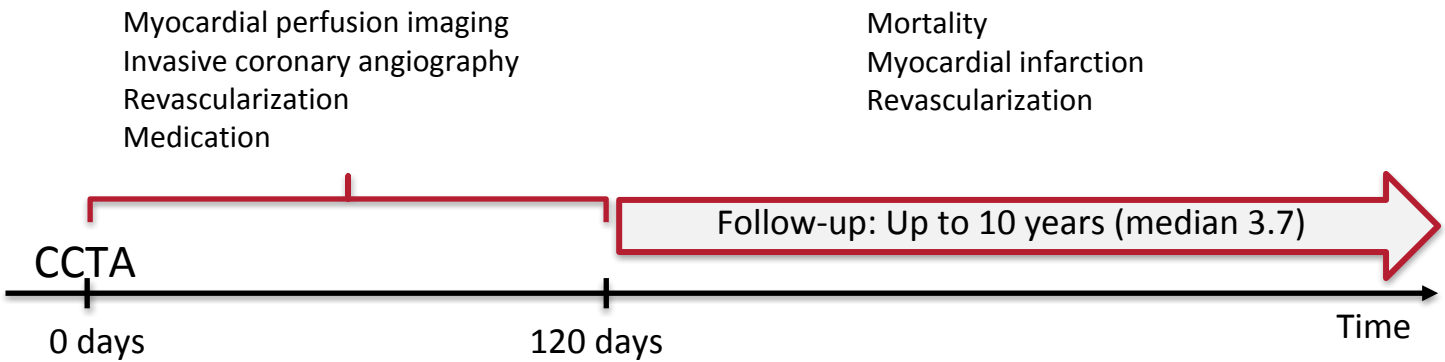


Time-to-event analysis

1) Unadjusted analysis

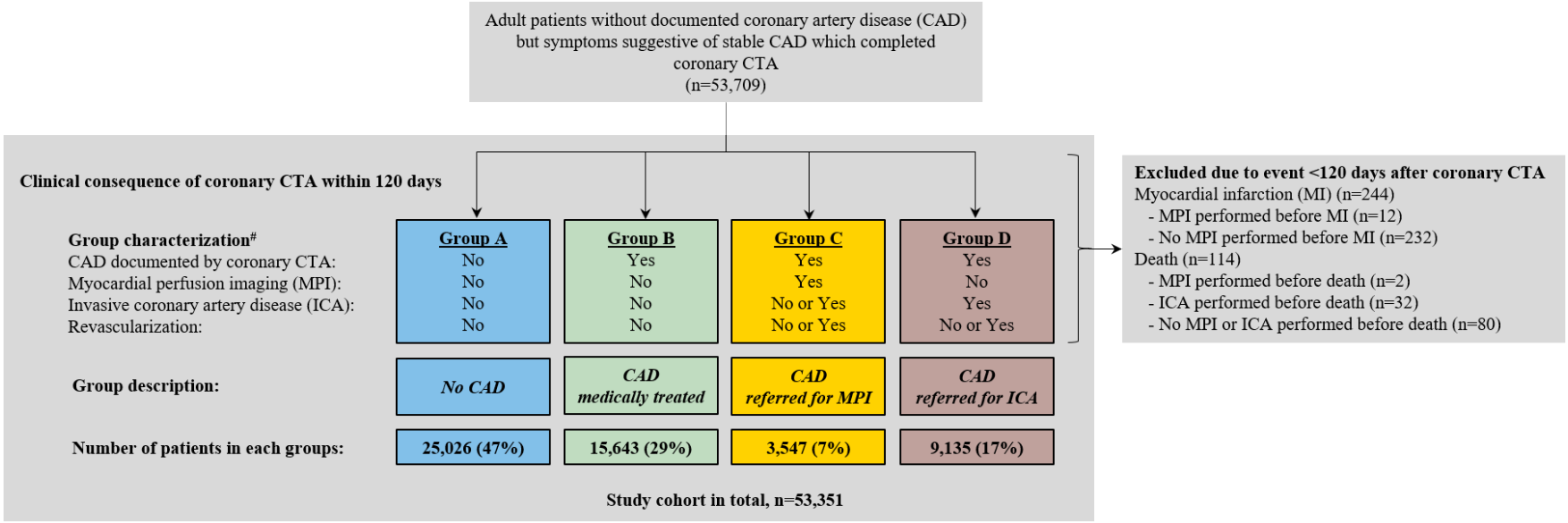
2) Adjusted analysis including:
   - Baseline characteristic
   - Post test use of lipid and blood pressure lowering medicine

3) Stratified analysis according to disease severity at the coronary CTA

The Western Denmark Heart Registry of Coronary Computed Tomography Angiogram

Adult patients without documented coronary artery disease (CAD) but symptoms suggestive of stable CAD which completed coronary CTA
(n=53,709)

The Western Denmark Heart Registry of Coronary Computed Tomography Angiogram

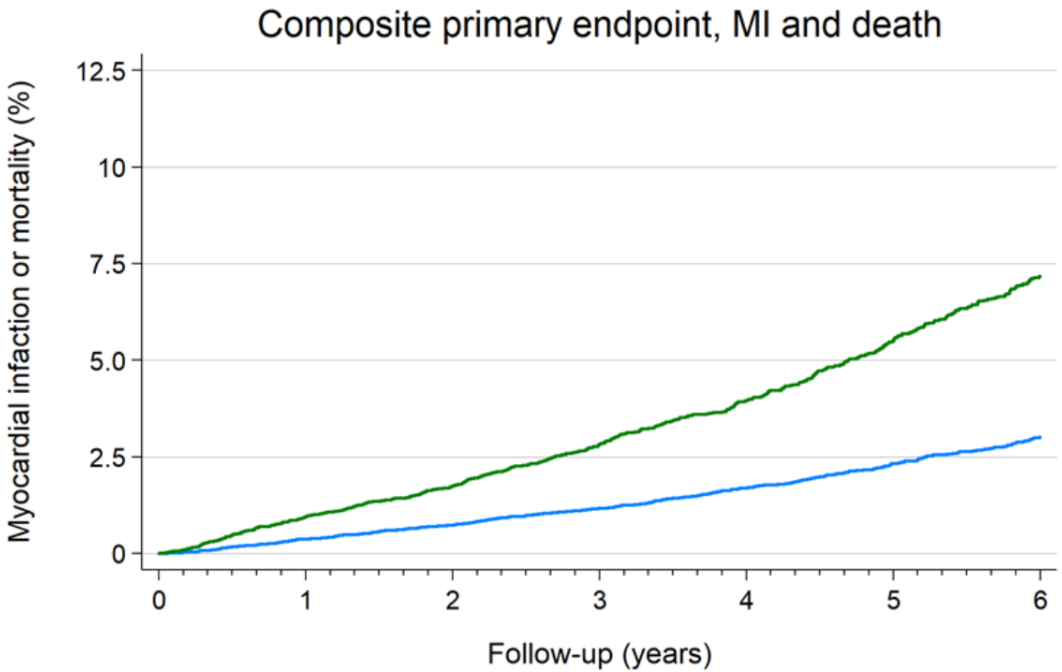


Patient demographics

Groups	Total	No CAD	CAD medically treated	CAD referred for MPI	CAD referred for ICA
	All patients				
Number of patients	53351 (100 %)	25026 (46.9 %)	15665 (29.4 %)	3547 (6.7 %)	9113 (17.1 %)
Characteristic					
Sex, male	24402 (45.7 %)	9535 (38.1 %)	7731 (49.3 %)	1782 (50.2 %)	5354 (58.8 %)
Age (years)	57.4 ±11.3	52.7 ±10.9	61.1 ±9.8	60.3 ±10.6	62.9 ±9.5
- <50	13775 (25.8 %)	10151 (40.6 %)	2108 (13.5 %)	599 (16.9 %)	917 (10.1 %)
- 50- <60	16565 (31.1 %)	8368 (33.4 %)	4859 (31.0 %)	1021 (28.8 %)	2317 (25.4 %)
- 60 - <70	15851 (29.7 %)	5143 (20.6 %)	5752 (36.7 %)	1298 (36.6 %)	3658 (40.1 %)
- ≥70	7160 (13.4 %)	1364 (5.4 %)	2946 (18.8 %)	629 (17.8 %)	2221 (24.4 %)
Body Mass Index (kg/m²) [b]	26.7 ±4.4	26.5 ±4.5	26.9 ±4.4	26.9 ±4.4	27.0 ±4.3
Smoking					
- Never	20573 (38.6 %)	10829 (43.3 %)	5587 (35.9 %)	1274 (35.9 %)	2883 (31.6 %)
- Former	17338 (32.5 %)	7036 (28.1 %)	5550 (35.4 %)	1294 (36.5 %)	3458 (38.0 %)
- Active	11160 (20.9 %)	4958 (19.8 %)	3335 (21.3 %)	699 (19.7 %)	2168 (23.8 %)
- Missing	4280 (8.0 %)	2203 (8.8 %)	1193 (7.6 %)	280 (7.9 %)	604 (6.6 %)
Symptoms					
- Typical chest pain	5105 (9.6 %)	1589 (6.4 %)	1215 (7.8 %)	412 (11.6 %)	1889 (20.7 %)
- Atypical chest pain	20702 (38.8 %)	9400 (37.6 %)	6173 (39.4 %)	1660 (46.8 %)	3469 (38.1 %)
- Non-specific chest pain	13816 (25.9 %)	7444 (29.8 %)	4204 (26.8 %)	729 (20.6 %)	1439 (15.8 %)
- Dyspnea	3181 (6.0 %)	1101 (4.4 %)	1091 (7.0 %)	299 (8.4 %)	690 (7.6 %)
- Missing	10547 (19.8 %)	5492 (22.0 %)	2982 (19.0 %)	447 (12.6 %)	1626 (17.8 %)
Pre-test probability risk scor[c]	9% [5-18]	6% [3-11]	12% [7-20]	13% [7-24]	17% [9-32]

Baseline coronary CTA

Groups	Total	No CAD	CAD medically treated	CAD referred for MPI	CAD referred for ICA
	All patients				
Number of patients	53351 (100 %)	25026 (46.9 %)	15665 (29.4 %)	3547 (6.7 %)	9113 (17.1 %)
Coronary artery calcium score and computed tomography angiogram					
CACS	0 [0-83]	0 [0-0]	30 [6-99]	63 [0-266]	278 [65-709]
- 0	23350 (43.8 %)	20171 (80.6 %)	1501 (9.6 %)	903 (25.5 %)	775 (8.5 %)
- 1-99	12299 (23.1 %)	0 (0.0 %)	9676 (61.8 %)	935 (26.4 %)	1688 (18.5 %)
- 100-399	6013 (11.3 %)	0 (0.0 %)	2881 (18.4 %)	775 (21.9 %)	2357 (25.9 %)
- ≥400	4797 (9.0 %)	0 (0.0 %)	816 (5.2 %)	601 (16.9 %)	3380 (37.1 %)
- Missing	6892 (12.9 %)	4855 (19.4 %)	791 (5.1 %)	333 (9.4 %)	913 (10.0 %)
Disease severity by CTA:					
- No CAD	26001 (48.9 %)	25026 (100.0 %)	0 (0.0 %)	568 (16.2 %)	407 (4.5 %)
- Non obstruktiv CAD	15789 (29.7 %)	0 (0.0 %)	13884 (89.0 %)	917 (26.2 %)	988 (10.9 %)
- CACS but no CTA performed	3329 (6.3 %)	0 (0.0 %)	564 (3.6 %)	459 (13.1 %)	2306 (25.4 %)
- 1 vessel disease	5658 (10.6 %)	0 (0.0 %)	930 (6.0 %)	1249 (35.7 %)	3479 (38.4 %)
- 2 vessel disease	1746 (3.3 %)	0 (0.0 %)	150 (1.0 %)	255 (7.3 %)	1341 (14.8 %)
- 3 vessel disease	675 (1.3 %)	0 (0.0 %)	79 (0.5 %)	53 (1.5 %)	543 (6.0 %)



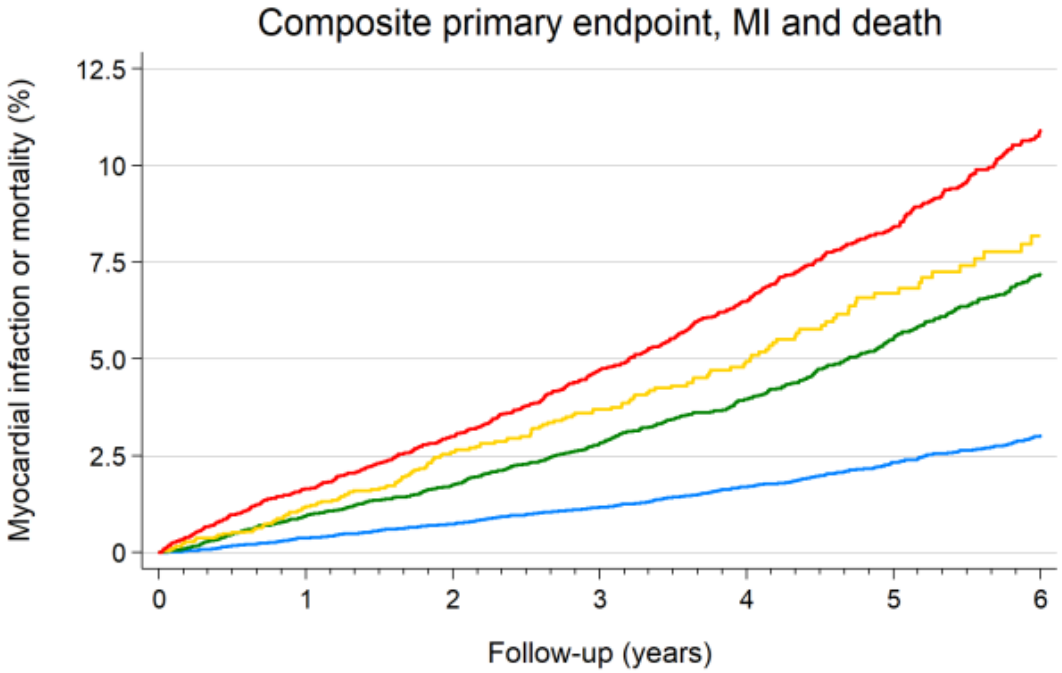
Annual events rates

1.2% (CI: 1.2-1.2)

0.5% (CI: 0.5-0.5)

Clinical consequence of coronary CTA

CAD medically treated (n = 15,665)
No CAD (n = 25,026)



Annual events rates

1.9% (CI: 1.8-2.1)

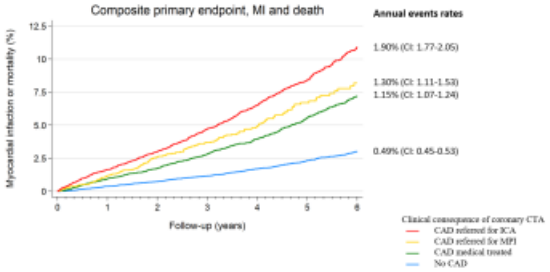
1.3% (CI: 1.1-1.5)

1.2% (CI: 1.1-1.2)

0.5% (CI: 0.5-0.5)

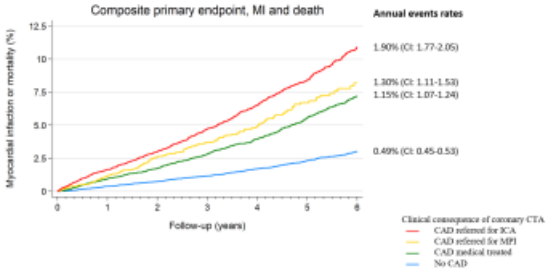
Clinical consequence of coronary CTA

- CAD referred for ICA (n = 9,113)
- CAD referred for MPI (n = 3,547)
- CAD medically treated (n = 15,665)
- No CAD (n = 25,026)



	No CAD	CAD medically treated	CAD referred for MPI	CAD referred for ICA
Hazard ratios, unadjusted	Ref.	2.4 (2.1-2.7)	2.8 (2.4-3.4)	3.9 (3.5-4.3)
Hazard ratios, adjusted #	Ref.	1.4 (1.2-1.6)	1.7 (1.4-2.0)	1.9 (1.7-2.2)

Hazard ratios are adjusted for age, gender, smoking status and comorbidity at baseline together with post-test use of antihypertensive and lipid-lowering therapy.



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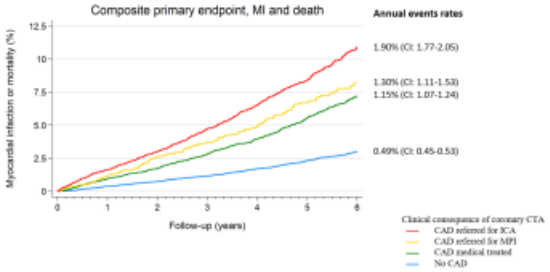
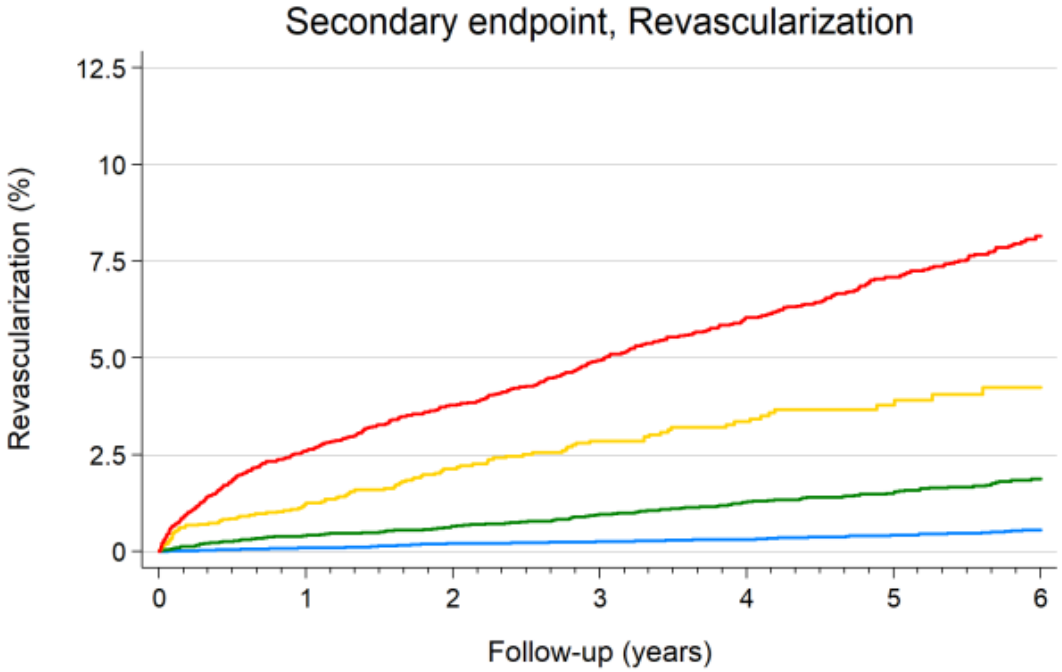


	No CAD	CAD medically treated	CAD referred for MPI	CAD referred for ICA
Hazard ratios, unadjusted	Ref.	2.4 (2.1-2.7)	2.8 (2.4-3.4)	3.9 (3.5-4.3)
Hazard ratios, adjusted [#]	Ref.	1.4 (1.2-1.6)	1.7 (1.4-2.0)	1.9 (1.7-2.2)

[#] Hazard ratios are adjusted for age, gender, smoking status and comorbidity at baseline together with post-test use of antihypertensive and lipid-lowering therapy.



Annual events rates

1.6% (CI: 1.5-1.7)

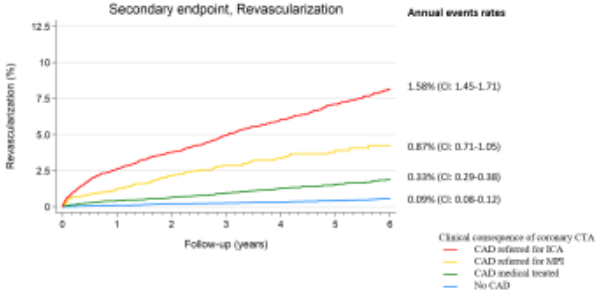
0.9% (CI: 0.7-1.1)

0.3% (CI: 0.3-0.4)

0.1% (CI: 0.1-0.1)

Clinical consequence of coronary CTA

- CAD referred for ICA (n = 9,113)
- CAD referred for MPI (n = 3,547)
- CAD medically treated (n = 15,665)
- No CAD (n = 25,026)



	No CAD	CAD medically treated	CAD referred for MPI	CAD referred for ICA
Hazard ratios, unadjusted	Ref.	3.45 (2.70-4.43)	8.90 (6.73-11.77)	16.63 (13.39-20.65)
Hazard ratios, adjusted #	Ref.	2.50 (1.93-3.23)	6.13 (4.58-8.21)	9.18 (7.16-11.78)

Hazard ratios are adjusted for age, gender, smoking status and comorbidity at baseline together with post-test use of antihypertensive and lipid-lowering therapy.

Objective

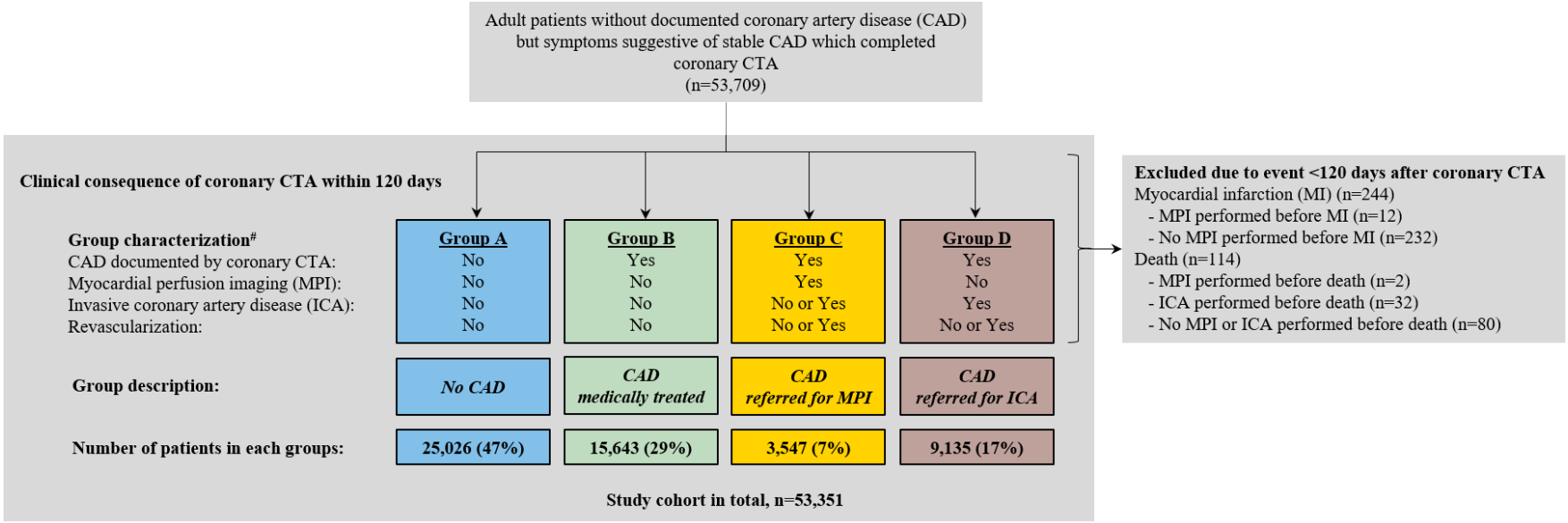
To investigate the prognosis for patients completing coronary CTA with stratification for post-CTA diagnostic work-up.

This was performed by comparing 4 groups of patients:

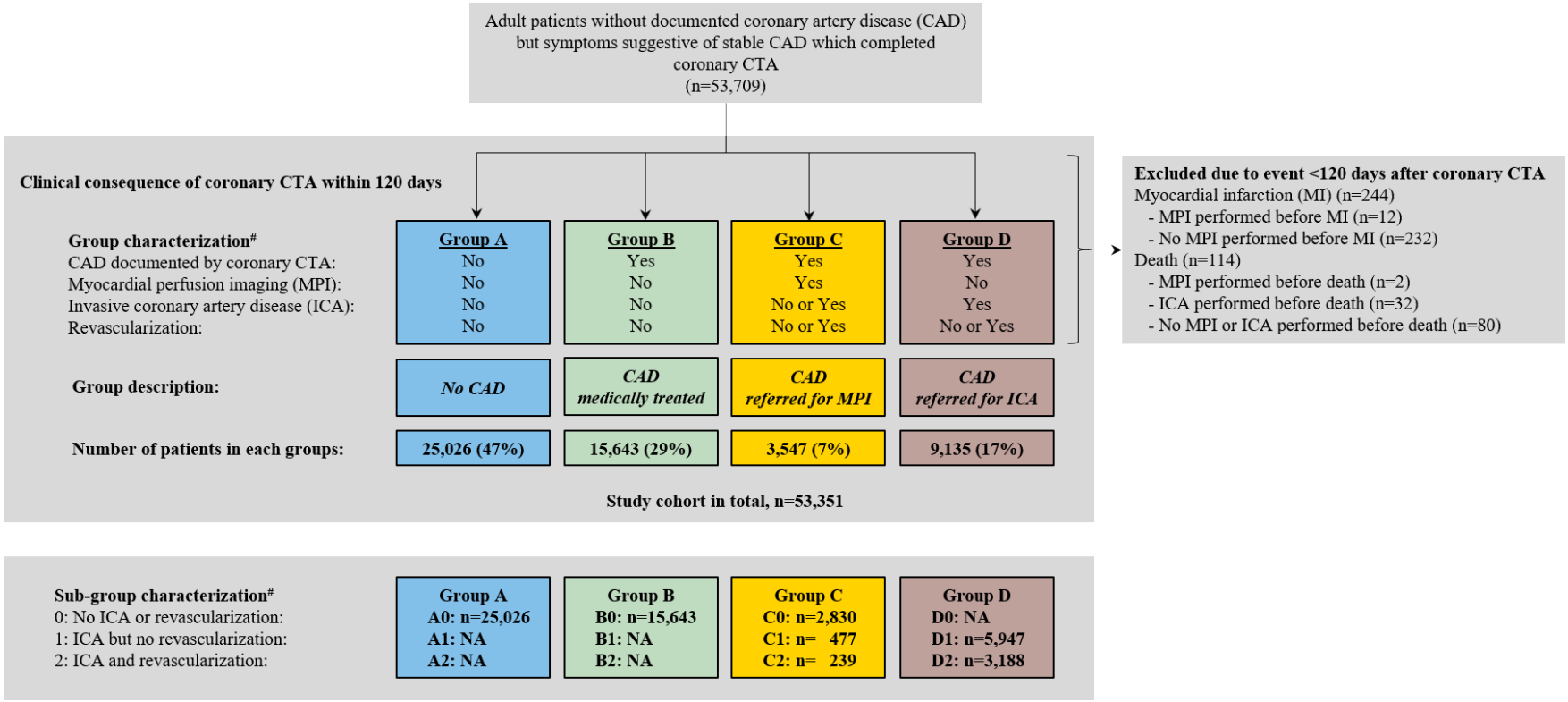
A) No CAD at CTA and were deferral
B) CAD at CTA and were medically treated
C) CAD at CTA and referral to MPI
D) CAD at CTA and referral to ICA

The secondary aim was to investigate the prognosis of the subgroup completing MPI after CTA who did not undergo ICA.

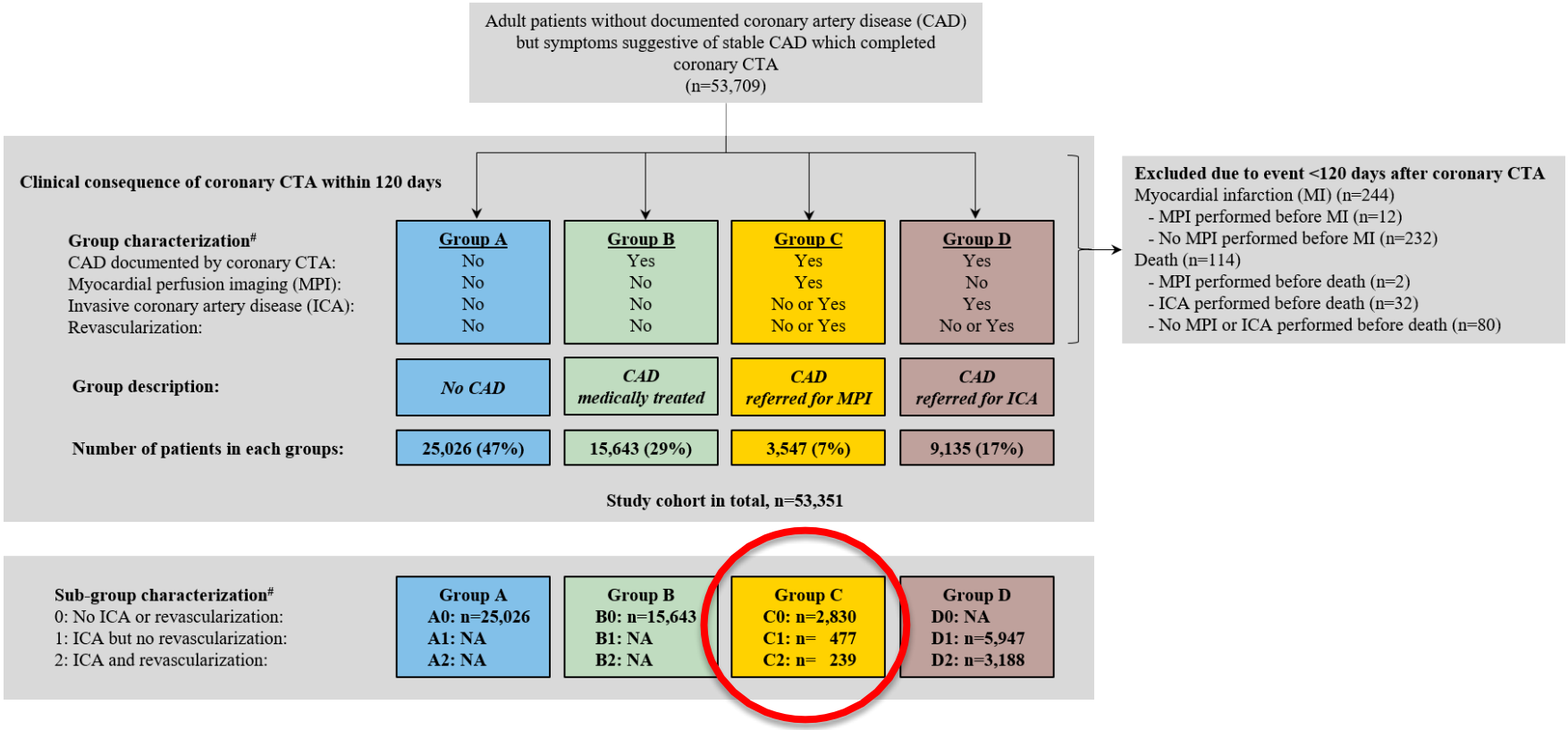
The Western Denmark Heart Registry of Coronary Computed Tomography Angiogram

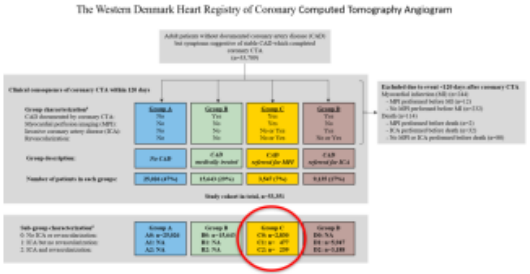


The Western Denmark Heart Registry of Coronary Computed Tomography Angiogram



The Western Denmark Heart Registry of Coronary Computed Tomography Angiogram

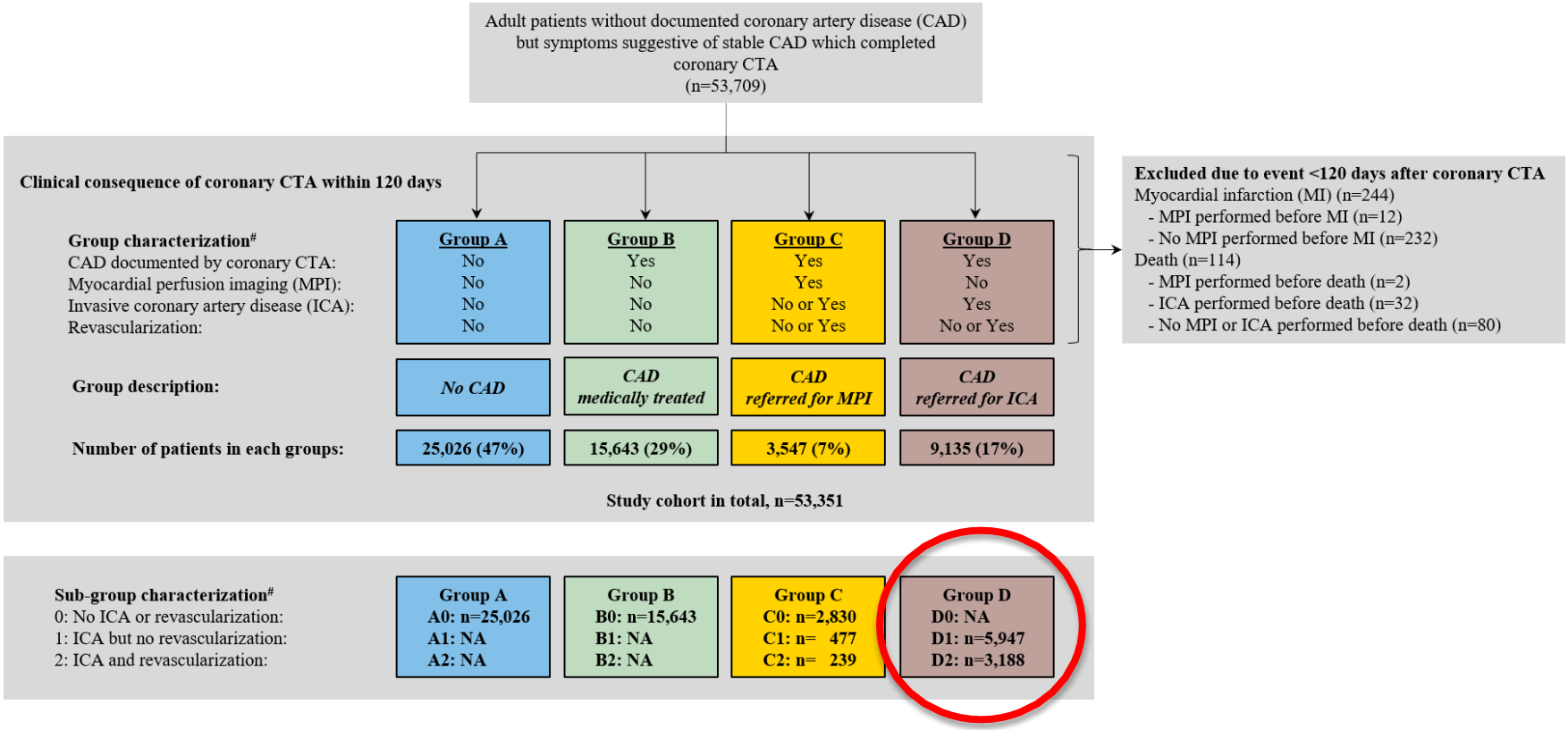


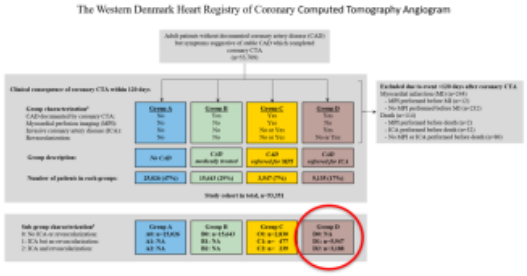


CAD referred for MPI

- No ICA or revascularization: **n = 2,830 (80 %)**
- ICA but no revascularization: **n = 477 (13 %)**
- ICA and revascularization: **n = 239 (7 %)**

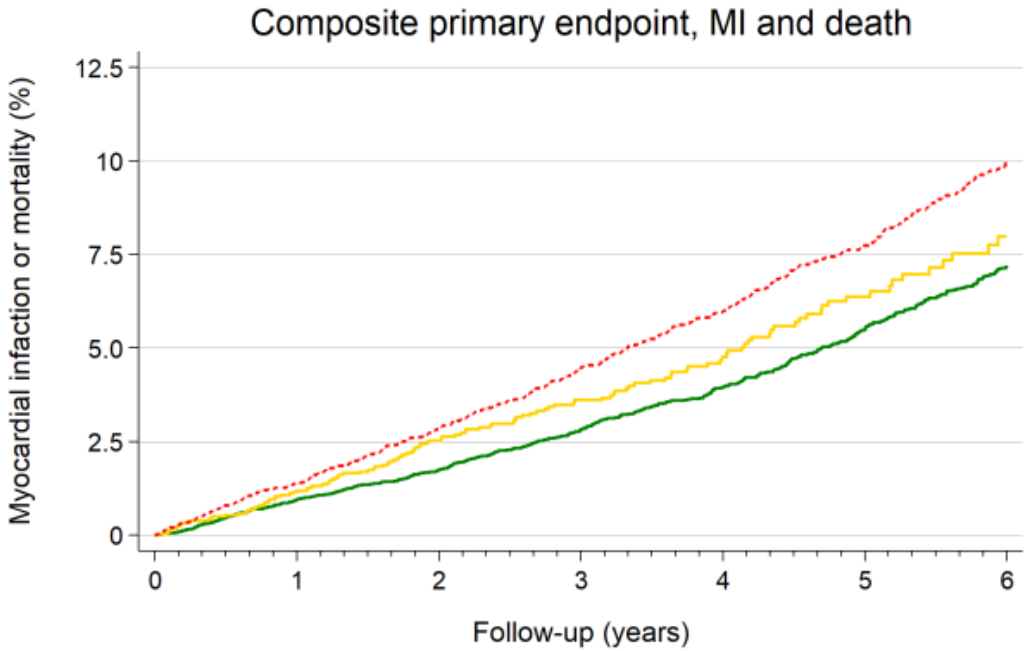
The Western Denmark Heart Registry of Coronary Computed Tomography Angiogram



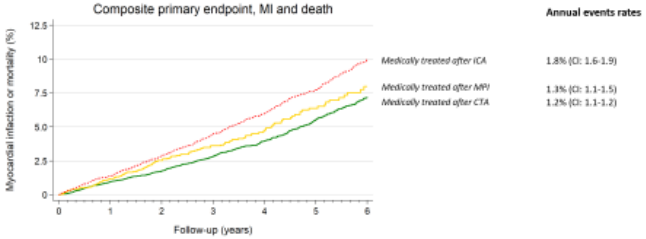


CAD referred for ICA

- No ICA or revascularization: **n = NA**
- ICA but no revascularization: **n = 5.947 (65 %)**
- ICA and revascularization: **n = 3.188 (35 %)**

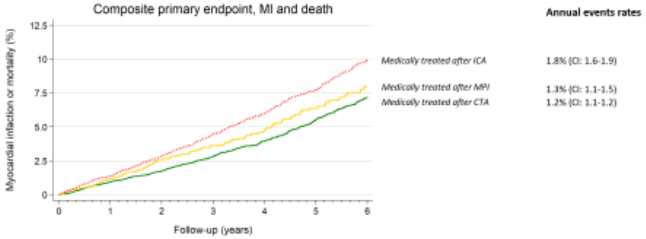


	Annual events rates
Medically treated after ICA	1.8% (CI: 1.6-1.9)
Medically treated after MPI	1.3% (CI: 1.1-1.5)
Medically treated after CTA	1.2% (CI: 1.1-1.2)



	Medically treated after CTA	Medically treated after MPI	Medically treated after ICA
Hazard ratios, unadjusted	0.9 (0.7-1.1)	Ref	1.3 (1.1-1.6)
Hazard ratios, adjusted #	0.8 (0.7-1.0)	Ref	1.1 (0.9-1.3)

Hazard ratios are adjusted for age, gender, smoking status and comorbidity at baseline together with post-test use of antihypertensive and lipid-lowering therapy.



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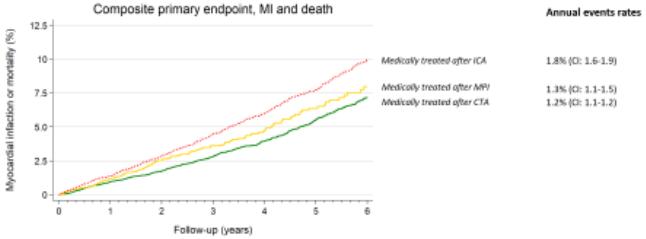

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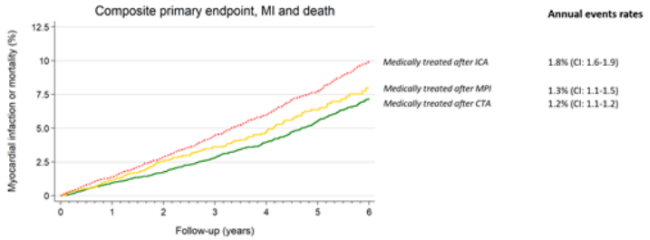
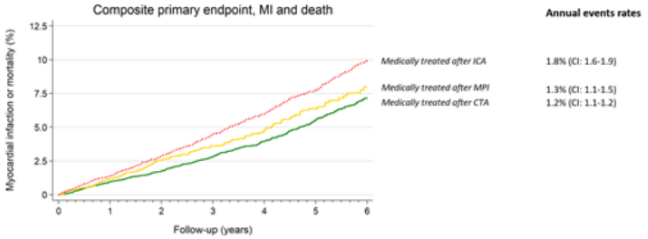
Stratified analysis of coronary disease severity according to the baseline coronary CTA



Hazard ratios, adjusted #	Medically treated after CTA	Medically treated after MPI	Medically treated after ICA
All patients	0.81 (0.67-0.98)	Ref	1.08 (0.89-1.33)
Coronary artery calcium score <400	0.97 (0.76-1.25)	Ref	1.13 (0.85-1.50)
Coronary artery calcium score ≥400	0.83 (0.59-1.18)	Ref	0.68 (0.49-0.94)
No or non-obstructive CAD at coronary CTA	0.80 (0.60-1.06)	Ref	1.25 (0.91-1.71)
1-vessel disease at coronary CTA	1.62 (1.04-2.51)	Ref	1.39 (0.92-2.08)
2-or 3-vessel disease at coronary CTA	1.08 (0.56-2.07)	Ref	0.79 (0.44-1.44)

Hazard ratios are adjusted for age, gender, smoking status and comorbidity at baseline together with post-test use of antihypertensive and lipid-lowering therapy.



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Limitations

Referral/selection bias might have impacted the results due to the retrospective design.

The extent of perfusion defects on MPI were not available.

The external validity in unknown, due to these data reflect referral practice after CTA over the last 10 year in Denmark

Conclusion

Using real-world data of patients who underwent coronary CTA, we demonstrated low long-term event rates (<2% annual event) for revascularization and for combined death and myocardial infarction regardless of post-CTA diagnostic work-up.

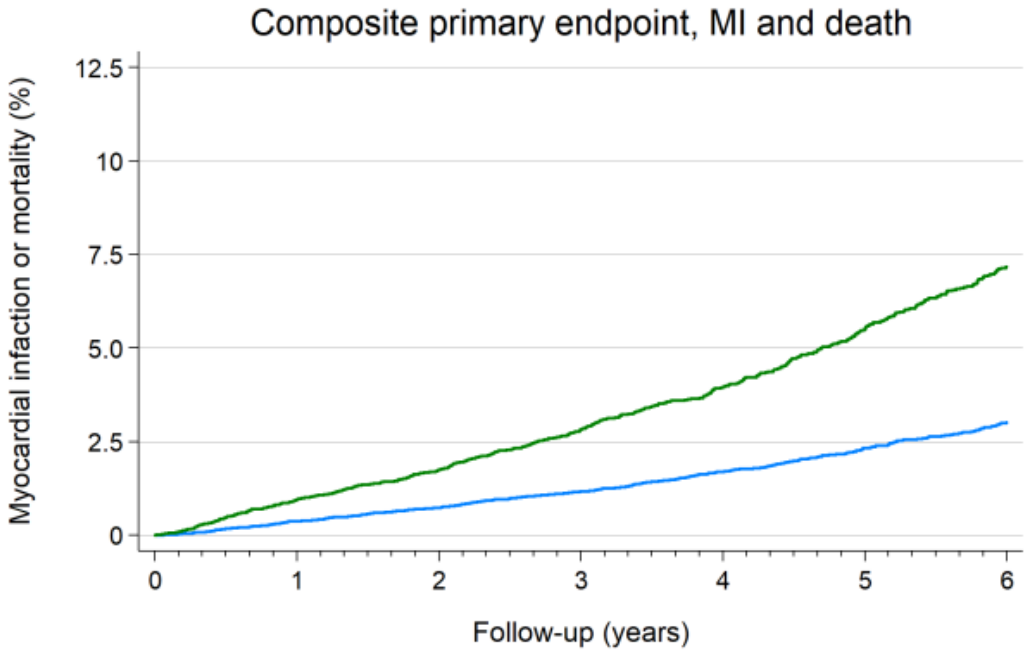
This study confirms the overall effectiveness (80% were medically treated after MPI) and safety (low event rates) of a diagnostic strategy with selective MPI after coronary CTA.
This indicates that MPI can be used to safely defer patient from ICA.

Nonetheless, selective ICA seem to be a better strategy in patients with high disease burden.

Thanks to

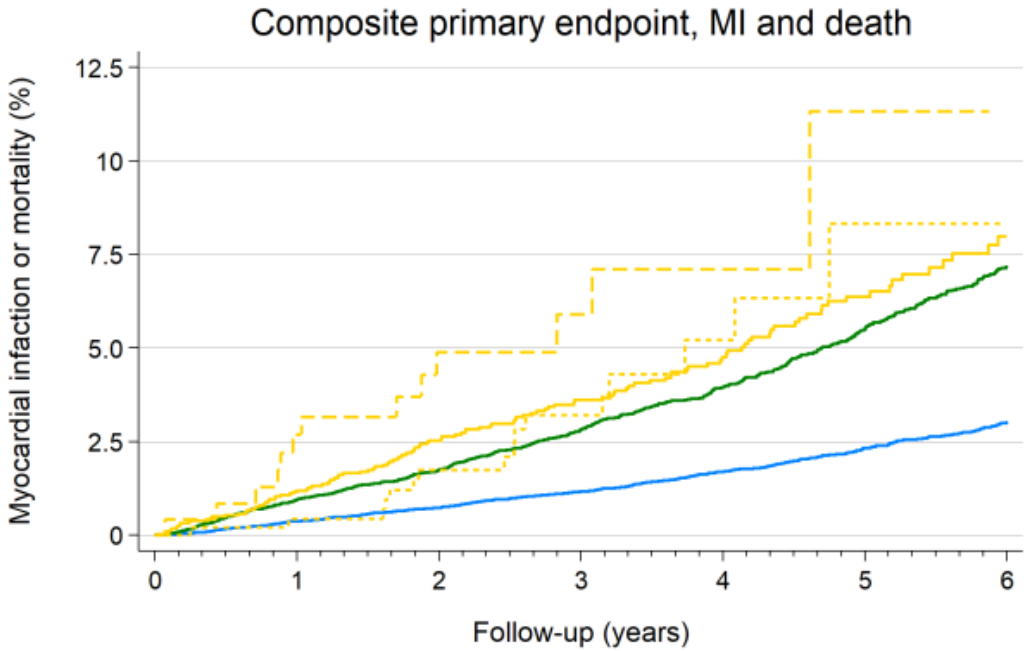
Ina Trolle Andersen, MSc, PhD, Lars Christian Gormsen, MD, PhD, Flemming Hald Steffensen, MD, PhD, Lene Hüche Nielsen, MD, PhD, Erik Lerkevang Grove, MD, PhD, Axel Cosmus Pyndt Diederichsen, Grazina Urbonaviciene, MD, PhD, Jess Lambrechtsen, MD, PhD, Tomas Zaremba, MD, PhD, Frank-Peter Elpert, MD, PhD, Majed Husain, MD, M.Sc., Marek Wojciech Zelechowski, MD, Hans Erik Bøtker, MD, DMSc, and Morten Bøttcher, MD, PhDon behalf of The Western Denmark Cardiac CT Study Group

Supplementum

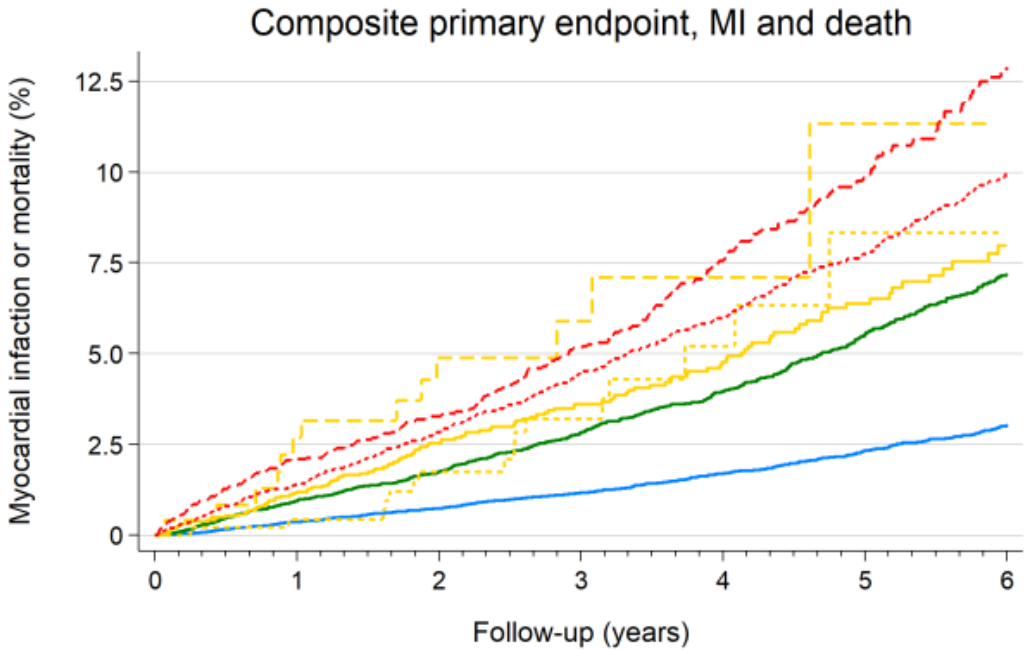


Annual events rates

CAD medically treated	1.15% (CI: 1.07-1.24)
No CAD	0.49% (CI: 0.45-0.53)



	Annual events rates
MPI: ICA and revascularization	2.07% (CI: 1.20-3.55)
MPI: ICA but no revascularization	1.16% (CI: 0.71-1.89)
MPI: No ICA and no revascularization	1.28% (CI: 1.08-1.52)
CAD medically treated	1.15% (CI: 1.07-1.24)
No CAD	0.49% (CI: 0.45-0.53)



	Annual events rates
ICA: Revascularization	2.20% (CI: 1.95-2.48)
MPI: ICA and revascularization	2.07% (CI: 1.20-3.55)
ICA: No revascularization	1.76% (CI: 1.60-1.93)
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Stratified analysis of MPI modality

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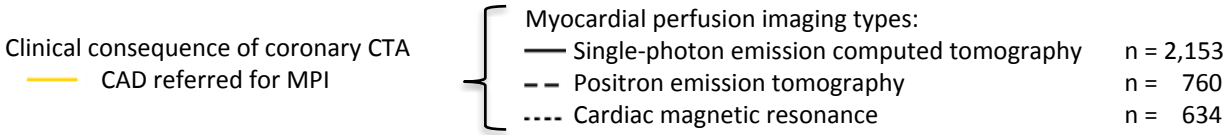
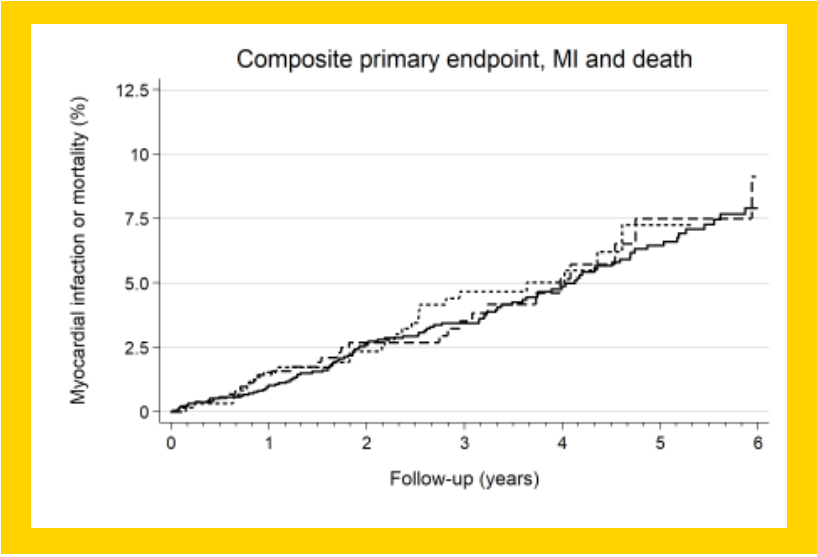


Stratified analysis of MPI modality

Clinical consequence of coronary CTA
CAD referred for MPI

Myocardial perfusion imaging types:
Single-photon emission computed tomography n = 2,153
Positron emission tomography n = 760
Cardiac magnetic resonance n = 634



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