



Impact of FFR_{CT} on 1-Year Outcomes: Lessons from the ADVANCE Registry

Manesh Patel on behalf of the ADVANCE investigators

**BL Nørgaard, TA Fairbairn, K Nieman, T Akasaka, DS Berman, GL Raff,
LM Hurwitz Koweek, G Pontone, T Kawasaki, NPR Sand, JM Jensen, T Amano,
M Poon, KA Øvrehus, J Sonck, MG Rabbat, S Mullen, B De Bruyne, C Rogers,
H Matsuo, JJ Bax, J Leipsic**

Disclosures

Research Grants:

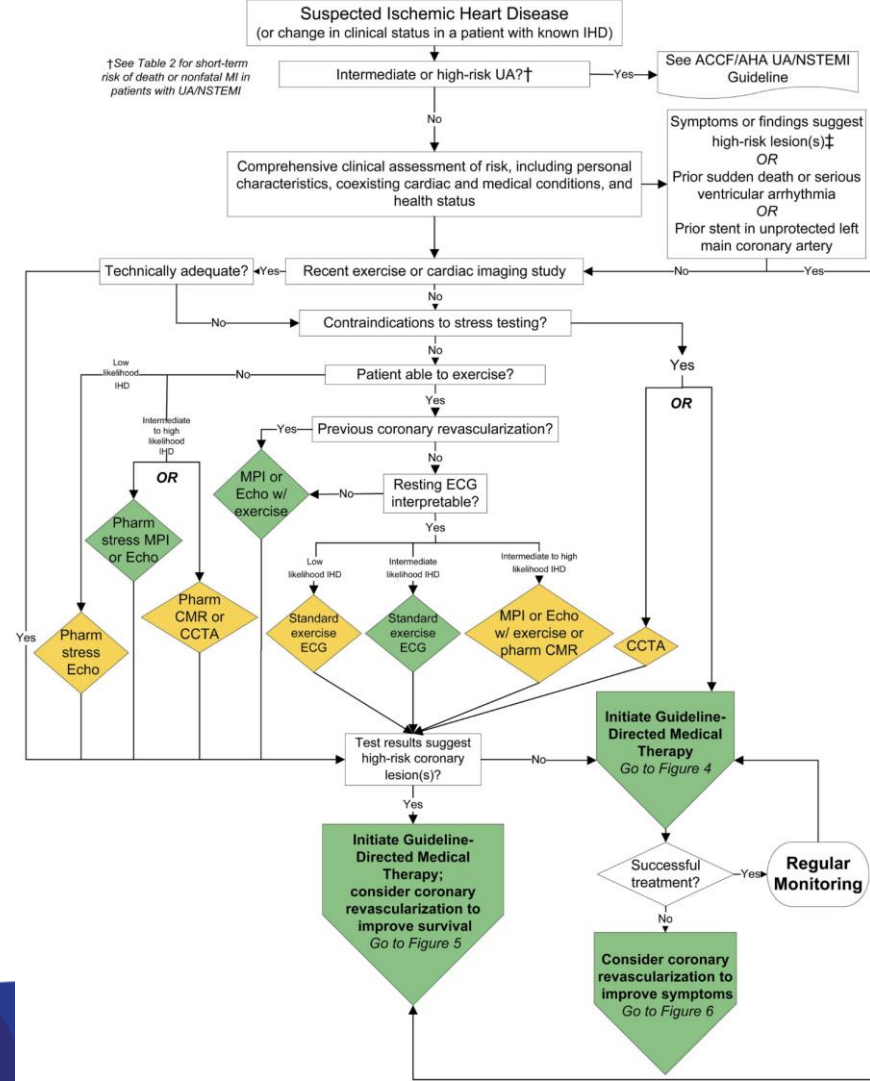
HeartFlow, Bayer, Janssen,
Phillips, Medtronic,
AstraZeneca, NIH

Advisory Board:

Bayer, Janssen, Amgen

Background: Evaluation of Suspected Ischemic Coronary Artery Disease

Guidelines recommendations:
Based on pre-test likelihood of disease, ability to exercise, test characteristics, and ability to discriminate downstream risk



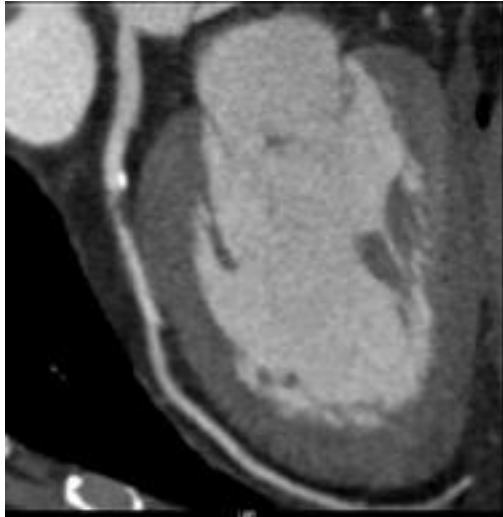
Coronary CT Angiography (CCTA) for Assessment of Chest Pain

- Increasingly used as primary diagnostic strategy for assessment of chest pain
- High sensitivity but modest specificity
- Randomized trials compared to functional testing
- Associated with high rates of follow-on invasive coronary angiography (ICA) showing non-obstructive coronary disease and increased rates of revascularization
- Cannot alone guide revascularization owing to the lack of functional information

Imaging in Coronary Artery Disease — Hope of Combining Anatomy and Function

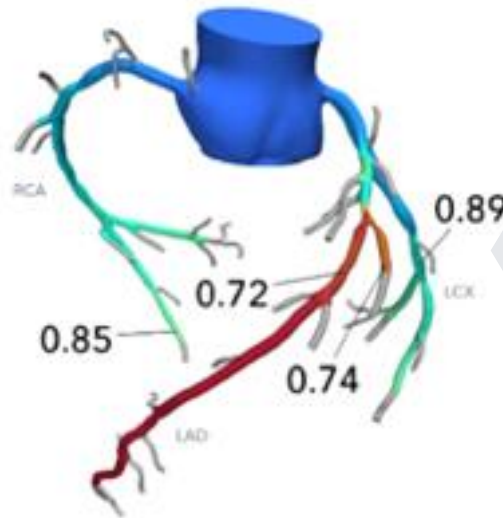
Anatomical
Testing

Coronary CT Angiography



Anatomical
and Functional

FFR_{CT}

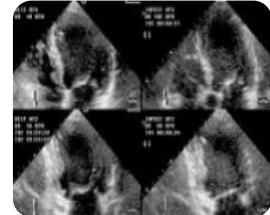


Functional
Testing

Treadmill ECG



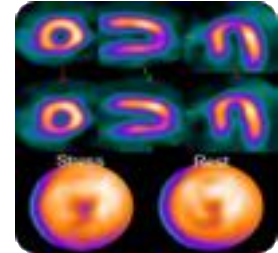
Stress Echo



Stress MRI



SPECT

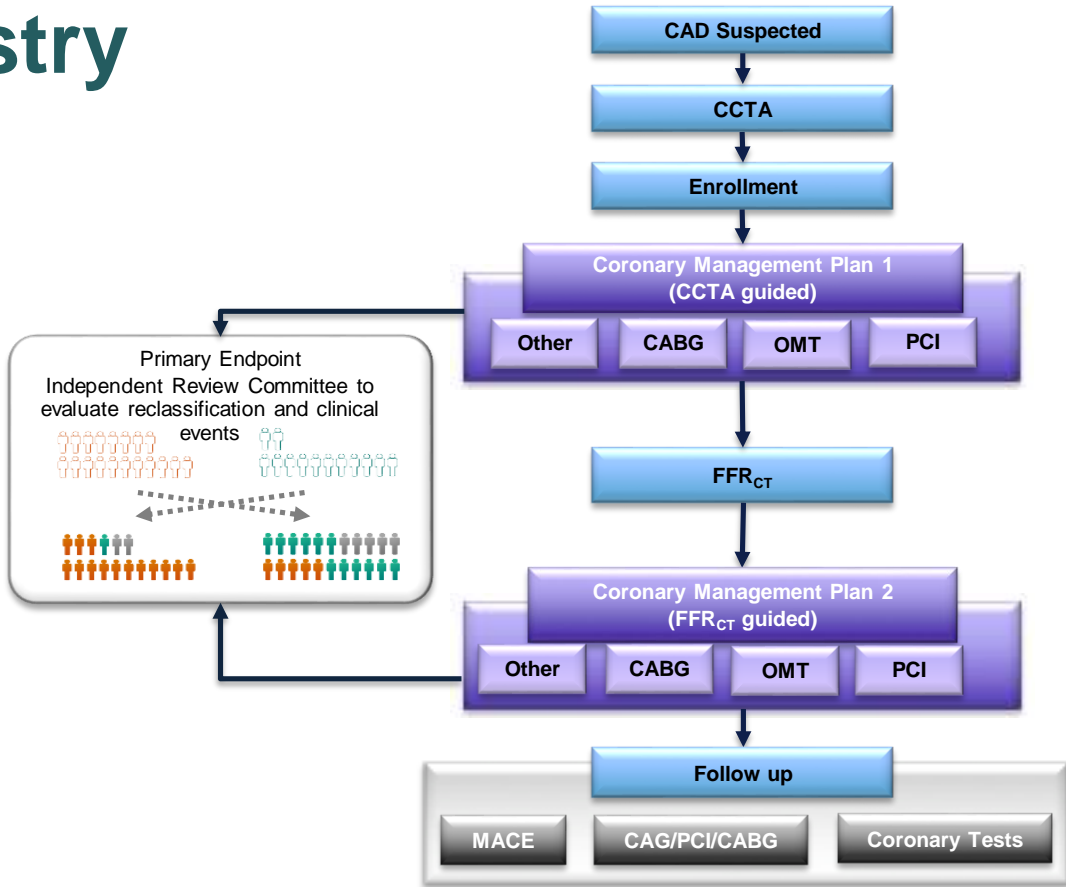


ADVANCE Registry

Objectives

- Understand the use of fractional flow reserve derived from CTA (FFR_{CT}) in real-world practice
- Determine the incremental information provided by FFR_{CT} in patients with atherosclerosis
- Understand downstream procedures and outcomes

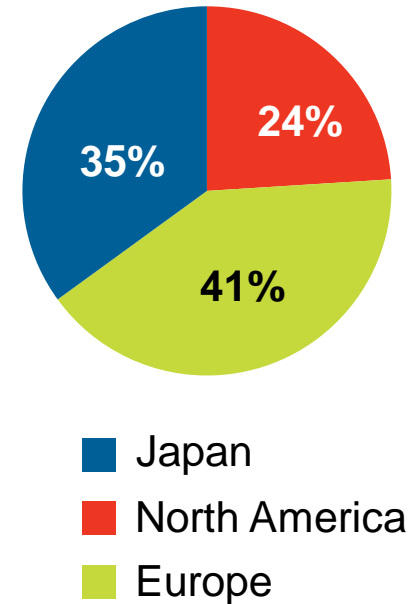
J Cardiovasc Comput Tomogr 2017;11:62-7.



ADVANCE Registry: Methods

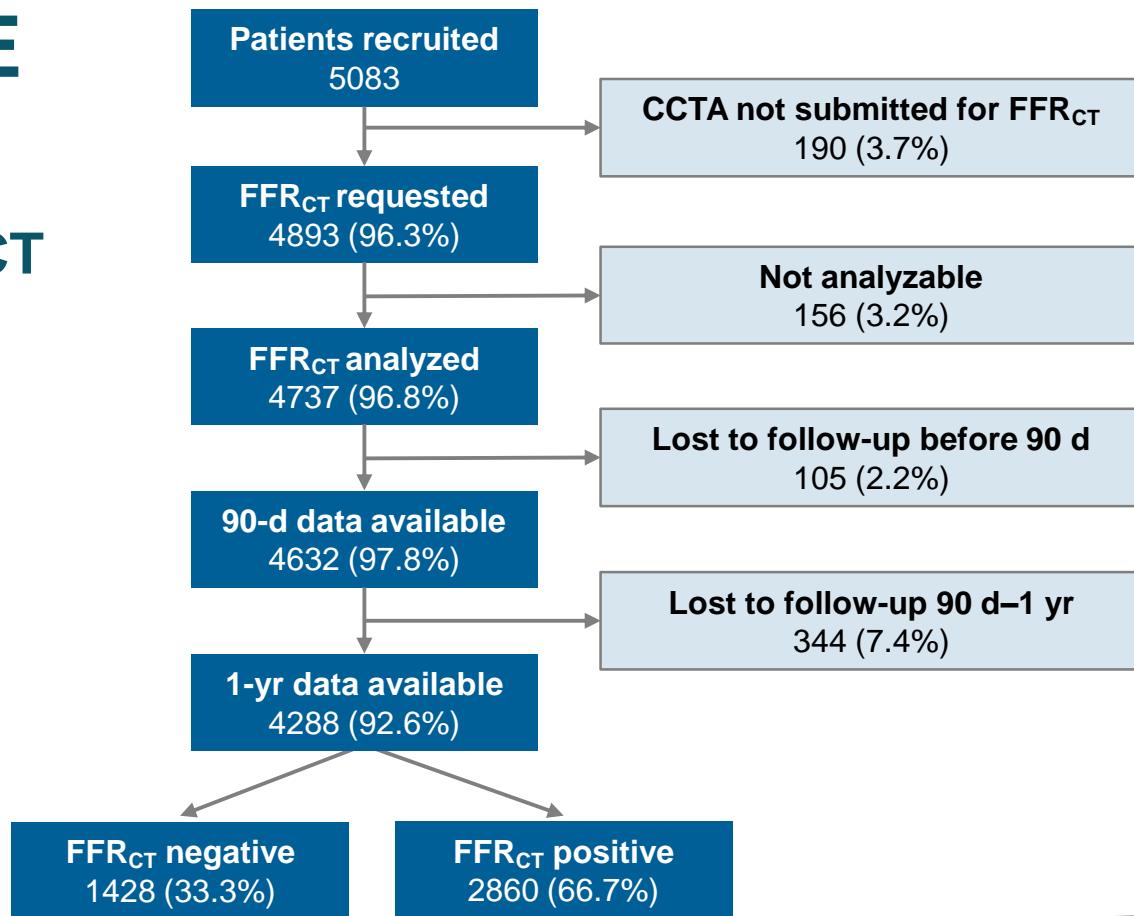
5083 patients undergoing CCTA with clinically suspected coronary artery disease were prospectively enrolled at 38 sites in Europe, North America, and Japan between July 2015–October 2017

- Event adjudication performed by independent Clinical Events Committee
 - MACE: Death, Myocardial Infarction (MI), or unplanned hospitalization for Acute Coronary Syndrome (ACS) leading to revascularization
- Primary endpoint:
 - 66.9% reclassification rate using a post-FFR_{CT} management plan vs. a post-CCTA management plan
- 90-day outcomes:
 - Post-FFR_{CT} treatment recommendation was associated with fewer ICAs without obstructive disease and improved prediction of revascularization
 - FFR_{CT} helped discriminate patients at lower risk of adverse events



ADVANCE 1-Year Results

ADVANCE Patients with FFR_{CT}



Patient Demographics by Outcomes at 1 Year

Demographic	Patients with FFR _{CT} (N=4737)	Patients with FFR _{CT} and No 1-year Follow-up (N=418)	Patients with MACE at 1-year Follow-up (N=55)	Patients with No MACE and 1-year Follow-up (N=4264)
Age	66.0 (59–73)	66.52 (59–75)	69.02 (62–75.5)	65.93 (59–73)
Male	66.2%	63.64%	72.73%	66.32%
Angina type				
None	24.57%	23.92%	20.00%	24.70%
Typical	21.64%	20.81%	23.64%	21.69%
Dyspnea	9.96%	8.61%	21.82%	9.94%
Atypical	36.46%	39.71%	23.64%	36.30%
Non-cardiac pain	6.27%	4.78%	7.27%	6.40%
Unknown	1.10%	2.15%	3.64%	0.96%

CCTA=coronary computed tomography angiography; FFR_{CT}=fractional flow reserve derived from CCTA; MACE=major adverse cardiac events.

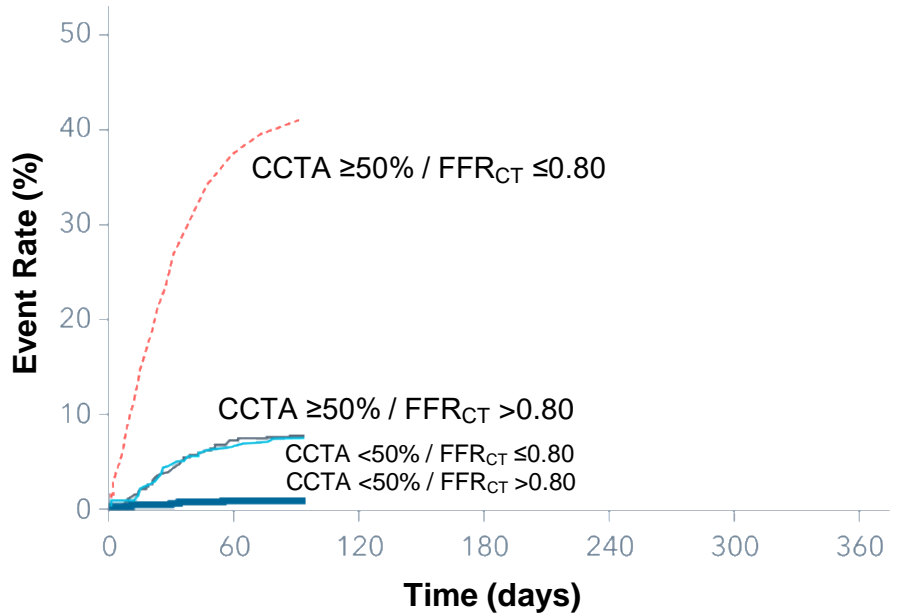
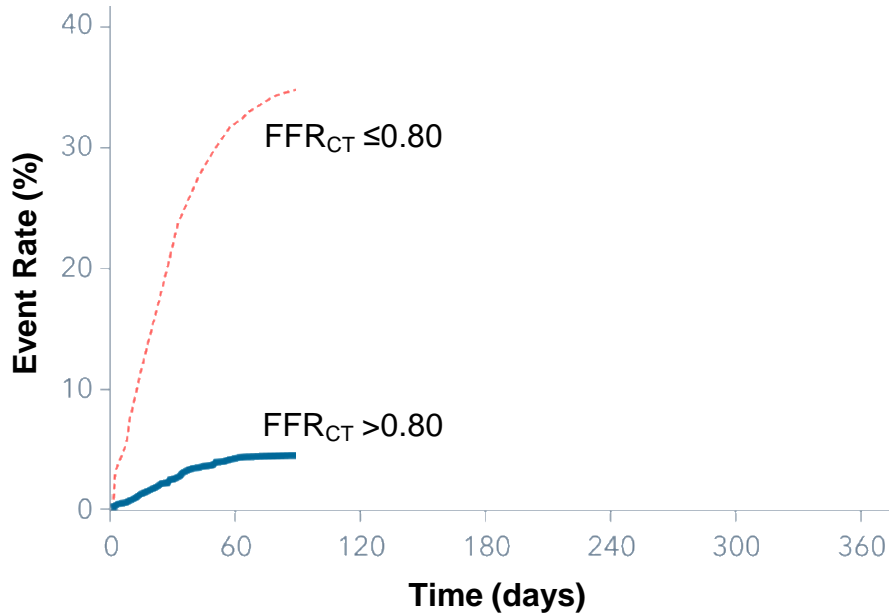
Patient Demographics by Outcomes at 1 Year

(continued)

Demographic	Patients with FFR _{CT} (N=4737)	Patients with FFR _{CT} and No 1-year Follow-up (N=418)	Patients with MACE at 1-year Follow-up (N=55)	Patients with No MACE and 1-year Follow-up (N=4264)
Diabetes	21.89%	22.97%	32.73%	21.65%
Hypertension	59.85%	59.57%	58.18%	59.90%
Smoking status	16.82%	19.86%	14.55%	16.56%
CCTA findings				
<50%	1324 (27.95%)	139 (33.25%)	8 (14.55%)	1177 (27.6%)
>50%	3409 (71.97%)	279 (66.75%)	46 (83.64%)	3084 (72.33%)
CCTA not evaluable	4 (0.08%)	0 (0.00%)	1 (1.82%)	3 (0.07%)
>0.80 FFR _{CT}	1592 (33.61%)	158 (37.80%)	12 (21.82%)	1422 (33.35%)
(≤0.8) FFR _{CT}	3145 (66.39%)	260 (62.20%)	43 (78.18%)	2842 (66.65%)

CCTA=coronary computed tomography angiography; FFR_{CT}=fractional flow reserve derived from CCTA; MACE=major adverse cardiac events.

ADVANCE 1-Year Results: Revascularization as a Function of FFR_{CT} and Anatomic Stenosis



Low Rate of MACE at 1 Year

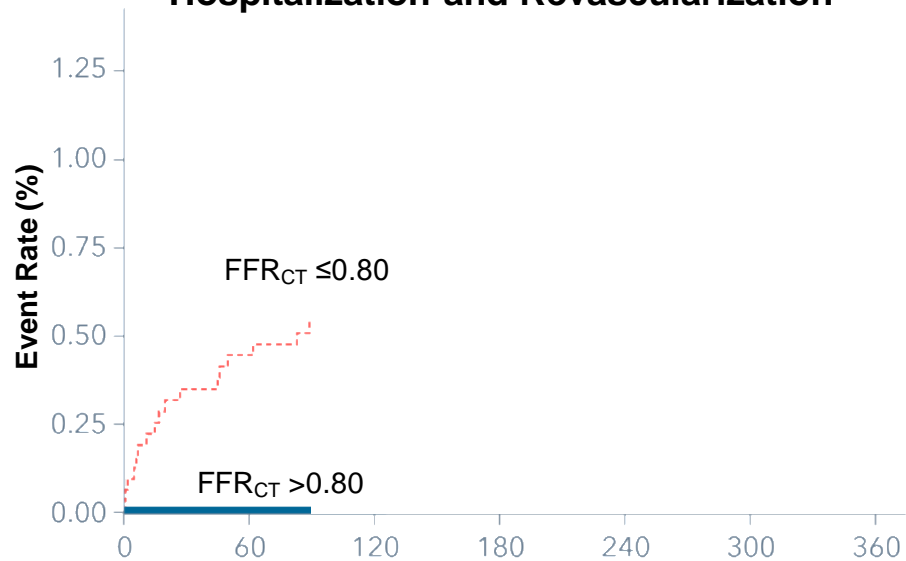
Type of Event		1-Year (N)
Mortality		35
CV mortality		15
MI		12*
ACS leading to unplanned hospitalization and revascularization		8
Revascularization	90-day (N)	From 90-day to 1-Year (N)
PCI	1026	185
CABG	150	28

ACS=acute coronary syndrome; CABG=coronary artery bypass grafting; CV=cardiovascular; MI=myocardial infarction; PCI=percutaneous coronary intervention.*Note the total MACE events are based on time to event.

There was one MI event (13 total in follow-up) that occurred in a patient after an ACS with unplanned hospitalization leading to revascularization.

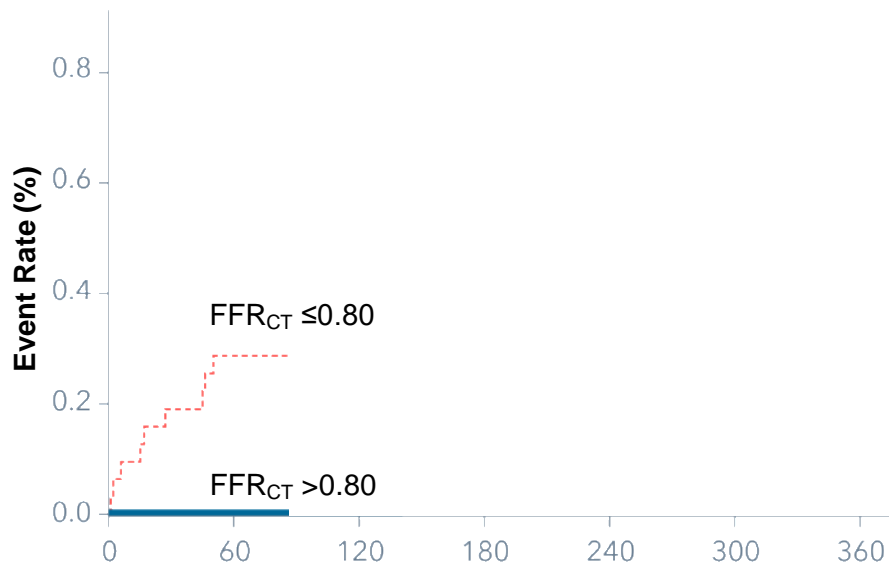
Clinical Outcomes through 1 Year: Clinical Events Stratified by FFR_{CT} (n=4737)

All-cause Death, MI, ACS Leading to Unplanned Hospitalization and Revascularization



FFR _{CT} Value	Number at risk						
≤ 0.80	3145	3127	3116	3106	3089	3082	3074
> 0.80	1592	1587	1583	1576	1570	1566	1558

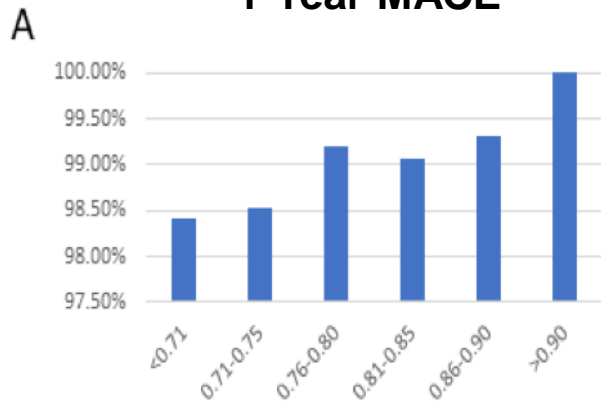
Cardiovascular Death or MI



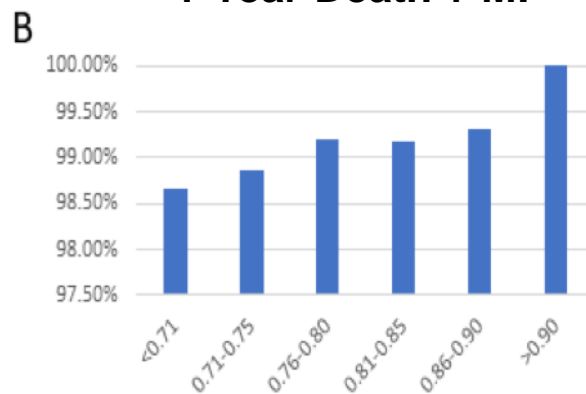
	Number at risk						
	3145	3131	3120	3111	3093	3086	3079
	1592	1587	1583	1576	1571	1568	1560

Clinical Outcomes through 1 Year: Stratified by FFR_{CT} (n=4737)

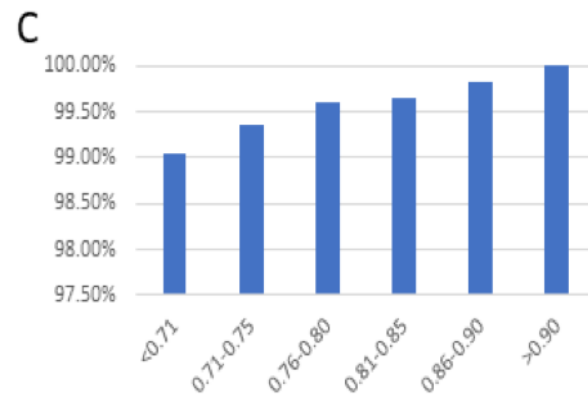
**Event Free Survival
1-Year MACE**



**Event Free Survival
1-Year Death + MI**



**Event Free Survival
1-Year CV Death + MI**



Distribution of event-free survival by categorical FFR_{CT} values for: **(A)** MACE, **(B)** Death and MI, **(C)** Cardiovascular death and MI.

Limitations

- This observational registry does not allow for treatment conclusions as patients were not randomized after imaging and clinical decisions were made at the sites of care based on test results
- Limitations of international real-world registry:
 - Cannot exclude the inclusion bias
 - Sites that routinely perform CCTA
 - 1-year patients lost to follow-up
- This analysis is a patient level analysis and not a lesion level analysis

Summary

In an international, real-world registry population ~ 5000 patients:

- 1) Overall all patients had low rates of MACE at 1 year
- 2) Major Adverse Cardiovascular Events were progressively higher at lower FFR_{CT} values
- 3) The vast majority of patients with $FFR_{CT} > 0.80$ had initial conservative (non-invasive) management and lower rates of revascularization at 1 year
- 4) Patients with $FFR_{CT} > 0.80$ trended towards lower rates of MACE and had significantly lower rates of CV death or MI

Implications for Clinical Practice

- The ADVANCE Registry shows the use of FFR_{CT} as a complement to CCTA in current real-world clinical practice.
- Overall rates of MACE in patients undergoing CCTA are low and highlight the need for ongoing efforts to refine the pre-test evaluation and risk assessment in clinical practice.
 - Focus of ongoing Randomized PRECISE Trial.
- Lower rates of revascularization and clinical events in patients with $\text{FFR}_{\text{CT}} > 0.80$ who were managed conservatively provide reassurance regarding this clinical strategy.

Thank You

ADVANCE Investigators

Bernard de Bruyne, Bjarne Nørgaard, Jesper Jensen, Gianluca Pontone, Kazushige Kadota, Tomohiro Sakamoto, Junya Shite, Mitsuyasu Terashima, Hiroshi Ito, Tomohiro Kawasaki, Hitoshi Matsuo, Yoshihiro Morino, Takashi Akasaka, Hiromasa Otake, Nobuhiro Tanaka, Tetsuya Amano, Shunichi Yoda, Gilbert Raff, Mark Rabbat, Subha Raman, Guilherme Attizzani, John Lesser, Enrico Martin, Markus Scherer, Lynne Koweeck, Manesh Patel, Moneal Shah, Mark Ibrahim, Juan Plana, Daniel Berman, Michael Poon, Tjebbe Galema, Niels Peter Sand, Bram Roosens, Timothy Fairbairn, Ian Purcell, Francesca Pugliese, Jeroen Bax, Kristian Ovrehus, Jonathon Leipsic

All the patient partners who agreed to participate



ORIGINAL RESEARCH

One-Year Impact on Medical Practice and Clinical Outcomes of FFR_{CT}: The ADVANCE Registry

Manesh R. Patel, MD,^a Bjarne Linde Nørgaard, MD, PhD,^b Timothy A. Fairbairn, MB ChB, PhD,^c Koen Nieman, MD, PhD,^d Takashi Akasaka, MD,^e Daniel S. Berman, MD,^f Gilbert L. Raff, MD,^g Lynne M. Hurwitz Koweeck, MD,^h Gianluca Pontone, MD, PhD,^h Tomohiro Kawasaki, MD,ⁱ Niels Peter Rønnow Sand, MD, PhD,^j Jesper M. Jensen, MD, PhD,^h Tetsuya Amano, MD,^k Michael Poon, MD,^l Kristian A. Øvrehus, MD, PhD,^l Jeroen Sonck, MD,^m Mark G. Rabbat, MD,ⁿ Sarah Mullen, MBT,^o Bernard De Bruyne, MD, PhD,^p Campbell Rogers, MD,^o Hitoshi Matsuo, MD, PhD,^q Jeroen J. Bax, MD, PhD,^r Jonathon Leipsic, MD^s

ABSTRACT

BACKGROUND Guidelines for management of chest pain using non-invasive imaging pathways are based on short-to-intermediate term outcomes.

OBJECTIVES One-year data from the international ADVANCE Registry of patients undergoing coronary computed tomography angiography (CCTA) was used to evaluate the relationship of fractional flow reserve derived from CTA (FFR_{CT}) with downstream care and clinical outcomes.

METHODS Patients (n=5083) evaluated for clinically suspected coronary artery disease (CAD) and in whom atherosclerosis was identified by CCTA were prospectively enrolled at 38 international sites from July 15, 2015–October 20, 2017. Demographics, symptom status, CCTA and FFR_{CT} findings and resultant site-based treatment plans, and clinical outcomes through 1 year were recorded and adjudicated by a blinded core laboratory. Major adverse cardiac events (MACE), death, myocardial infarction (MI), and acute coronary syndrome leading to urgent revascularization were captured.

RESULTS At 1 year, 449 patients did not have follow-up data. Revascularization occurred in 1208 (38.4%) with FFR_{CT} ≤0.80 and in 89 (5.6%) with an FFR_{CT} >0.80 (RR 6.87, CI 5.59–8.45; p<0.001). MACE occurred in 55 patients, 43 events occurred in patients with an FFR_{CT} ≤0.80 and 12 in those with an FFR_{CT} >0.80 (RR 1.81, CI 0.96–3.43; P=0.06). Time to first all-cause death or MI occurred in 38 (1.2%) patients with FFR_{CT} ≤0.80 compared with 10 (0.6%) patients with FFR_{CT} >0.80 (RR 1.92, CI 0.96–3.85; P=0.06). Time to first cardiovascular death or MI occurred more in patients with FFR_{CT} ≤0.80 compared with FFR_{CT} >0.80 (25 [0.8%] vs. 3 [0.2%]; RR 4.22, CI 1.28–13.95; P=0.01).

CONCLUSIONS The 1-year outcomes from the ADVANCE FFR_{CT} registry show low rates of events in all patients, with less revascularization and a trend towards lower MACE and significantly lower cardiovascular death or MI in patients with a negative FFR_{CT} compared with patients with abnormal FFR_{CT} values. (J Am Coll Cardiol Img 2019)
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