Enhanced Screening Methods …

TNO innovation for life

Dedicated to innovation in aerospace

Age Limitations Commercial Air Transport Pilots

… in Part 3: Screening of Cardiovascular Risks in Asymptomatic Pilots (Deliverable No. 3)

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- *Cardiological and Aviation Medicine Practice, Maennedorf, Switzerland*

Pilots' age limits workshop

EASA European Aviation Safety Agency

Cologne, 18-19 March 2019

Disclosures: No conflicts of interest

Content Part 3

When the initial screening reveals an elevated or high CVD risk (e.g., >10% PROCAM risk score) or has a clinically determined higher risk of CVD, the pilot concerned should be referred to a cardiologist with aeromedical expertise for enhanced risk assessment in order to identify and substantiate the CVD risk and to advise on fitness for pilot duties and risk factor modification (individual prevention).

Although the majority of cases of referral to cardiological expertise will concern coronary pathology (e.g., stenosis, plaques), it is emphasized that a cardiological examination is also indicated in cases of conduction abnormalities, arrhythmias, heart muscle disease, and valvular heart disease and aortopathy.


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2018 ESC Pocket Guidelines
Committee for Practice Guidelines
SYNCOPE
2018 ESC Pocket Guidelines
Committee for Practice Guidelines
4th Universal MI
Universal Definition of Myocardial Infarction
ESC
European Society of Cardiology
2018 ESC Pocket Guidelines
Committee for Practice Guidelines
HYPERTENSION
ESC/ESH Guidelines for the Management of Arterial Hypertension
ESC
European Society of Cardiology
ESH
European Society of Hypertension
2018 ESC Pocket Guidelines
Committee for Practice Guidelines
MYOCARDIAL REVASCULARIZATION
ESC/EACTS Guidelines on Myocardial Revascularization
CVD DURING PREGNANCY
Guidelines for the Management of Cardiovascular Diseases during Pregnancy
ESC
European Society of Cardiology

4.1 CT Coronary Artery Calcium Score (CACS)

The determination of the coronary artery calcium by computed tomography, often called calcium scoring, is widely used. Its prognostic value has been well established by many publications (Baber et al., 2015; Budoff et al., 2013; Detrano et al., 2008). The CACS is a non-contrast, cardiac-gated CT that can be done in 10-15 minutes, with about 0.5 to 1 mSv of radiation (Einstein, 2015).

The Agatston method uses the weighted sum of lesions with a density above 130 HU, multiplying the area of calcium by a factor related to maximum plaque attenuation. Standardized categories for the calcium score have been developed with scores of 0 indicating the absence of calcified plaque, 1 to 10 minimal plaque, 11 to 100 mild plaque, 101 to 400 moderate plaque, and >400 severe plaque. Risk categories associated with the coronary calcium scores and their associations with the 10-year and annual coronary event rates are presented in Table 4.

Table 4 Interpretation of Calcium scores- Summary of CAC absolute event rates

CAC Score (CACS)	Risk	10-Year Event Rate % (Hecht, 2015) *n*=14,856	Annual Event Rate % (Rozanski et al., 2007) *n*=1,153
CACS = 0	Very low	1.1-1.7	0.45
CACS = 1-100	Low risk	2.3-5.9	1.11
CACS = 101-400	Intermediate risk	12.8-16.4	1.14
CACS > 400	High risk	22.5-28.6	3.00
CACS >1000	Very High	37.0	4.01

In the Heinz Nixdorf Recall Study, 4,487 subjects without CHD were followed for 5 years (Erbel et al., 2010). The prevalence of low (<100), intermediate (100-399), and high (≥400) CAC scores was 72.9%, 16.8%, and 10.3%, respectively.

A coronary calcium score of 100, at a population level, is an established clinical threshold above which the probability of obstructive disease and coronary events becomes moderately elevated, with event rates exceeding 1%/year (Greenland et al., 2010; Hecht, 2015). In conformity with this clinical threshold it is recommended that a CACS >100 should result in aircrew being temporarily grounded pending further investigation.

CACS is a strong predictor at population level but is in some cases a poor discriminator at individual level and if performed in isolation may not predict risk on an individual basis, mainly because CACS is not sensitive to identify non-calcified plaques (e.g., Parsons et al., 2017) and it is known that a large number of vulnerable plaques are predominantly non-calcified (Hausleiter et al., 2006).

European Heart Journal (2016) 37, 2315–2381
doi:10.1093/eurheartj/ehw106

JOINT ESC GUIDELINES

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Recommendations for imaging methods

Recommendations	Class[a]	Level[b]	Ref[c]
Coronary artery calcium scoring may be considered as a risk modifier in CV risk assessment.	IIb	B	120–125
Atherosclerotic plaque detection			
recommended.			

ABI = ankle–brachial index; CV = cardiovascular; IMT = intima–media thickness.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Principles of cardiac imaging

- Anatomic versus Functional Imaging
- The Ischemic Cascade
- Regulation of Myocardial Blood Flow
- Concept of Pre-test Probability

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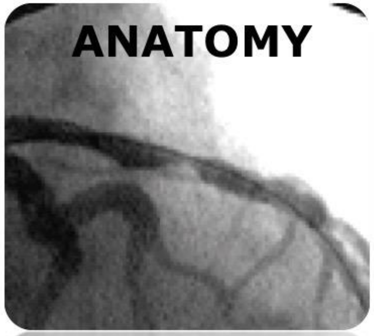
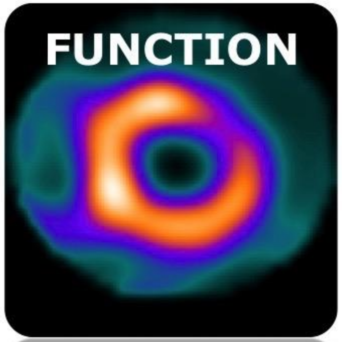
Vice-President, European Association of Cardiovascular Imaging (EACVI)
European Society of Cardiology

Validation steps of cardiac imaging

- Diagnostic accuracy
- Prognostic value
- Impact on patient treatment/outcomes
- Cost-effectiveness

Principles of Imaging –
Anatomical versus functional imaging





INV	• Invasive coronary angiography • IVUS/OCT	• Fractional flow reserve
NON-INV	• CT coronary angiography	• (Stress ECG) • Myocardial perfusion SPECT/PET • Stress echocardiography • Stress CMR

Coronary anatomical and functional tests often disagree i.e. they are not interchangeable

→Complementarity of coronary anatomy and function

Noninvasive CAD Imaging - Overview

ANATOMICAL

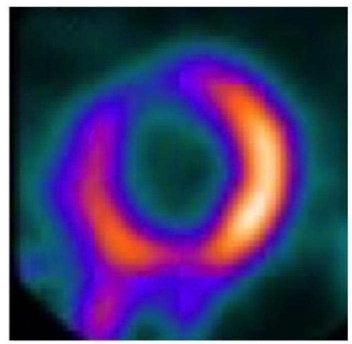
FUNCTIONAL

PERFUSION (MPI)

WALL MOTION (WMI)

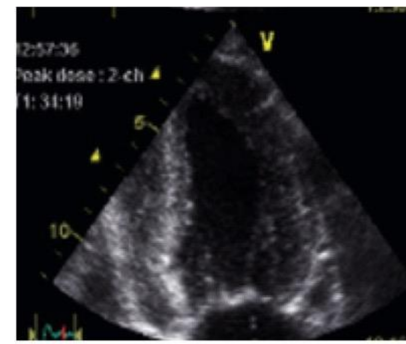
<u>CT coronary angiography</u>

- Correlates best with invasive CA
- Detects nonobstructive CAD



<u>SPECT / PET</u>
<u>Stress CMR</u>
(CT perfusion, myocardial contrast echo)

- Higher sensitivity than WMI
- Dx: Perfusion heterogeneity (not necessarily ischemia)
- Vasodilator, Dobu and exercise stress



<u>Stress Echo</u>
<u>Stress CMR (Dobu)</u>

- Higher specificity than MPI
- Dx: Ischemia
- Dobu and exercise stress

European Heart Journal (2013) 34, 2949–3003
doi:10.1093/eurheartj/eht296

ESC GUIDELINES

2013 ESC guidelines on the management of stable coronary artery disease

The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

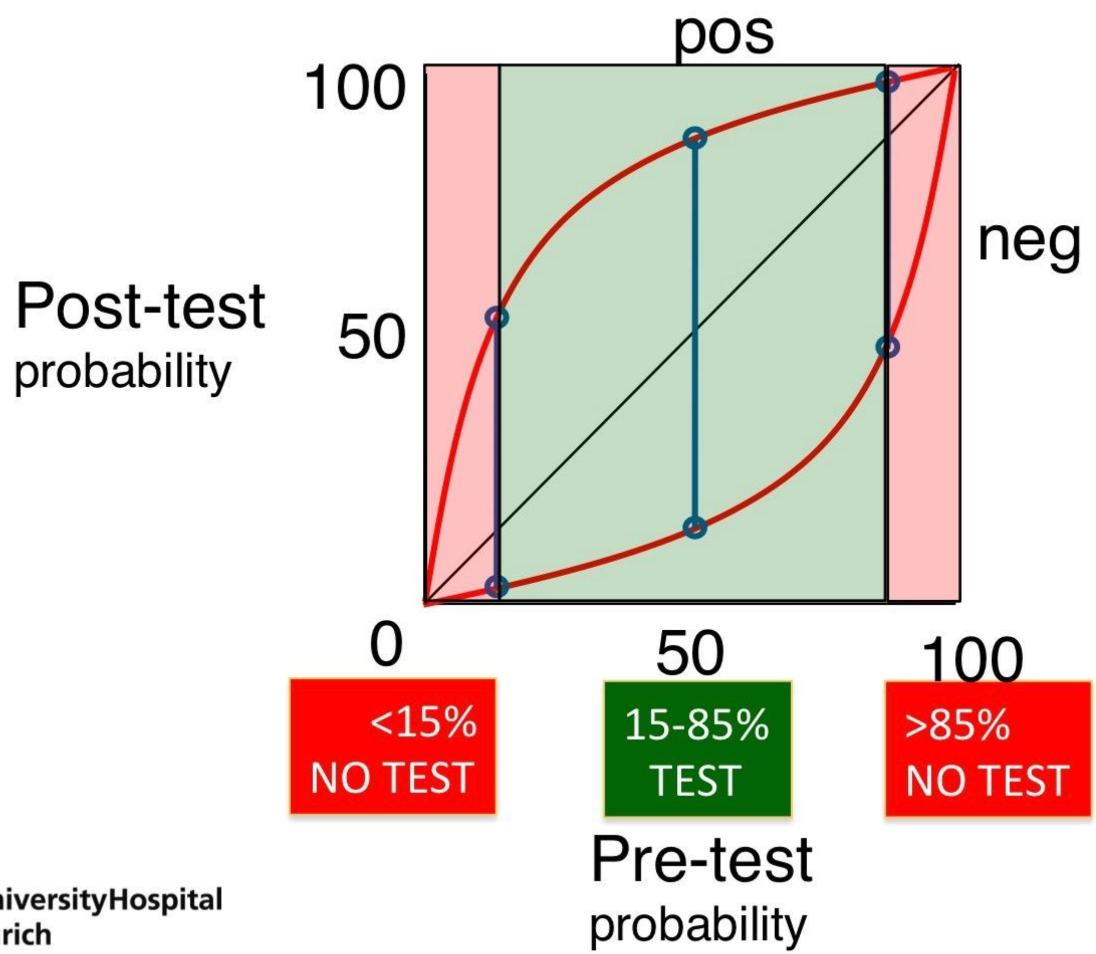
- Concept of Pre-test Probability

6.2.3 Principles of diagnostic testing

Interpretation of non-invasive cardiac tests requires a Bayesian approach to diagnosis. This approach uses clinicians' pre-test estimates [termed pre-test probability (PTP)] of disease along with the results of diagnostic tests to generate individualized post-test disease probabilities for a given patient. The PTP is influenced by the prevalence of the disease in the population studied, as well as clinical features (including the presence of CV risk factors) of an individual.[90] Major determinants of PTP are age, gender and the nature of symptoms.[90]

The Bayesien Theorem

Effect of PRE-Test-Probability on POST-Test-Probability for a given diagnosis



Recommendations 2013 ESC guidelines

European Heart Journal (2013) 34, 2949–3003
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ESC GUIDELINES

2013 ESC guidelines on the management of stable coronary artery disease

The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

Table 12 Characteristics of tests commonly used to diagnose the presence of coronary artery disease

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Exercise ECG [a, 91, 94, 95]	45–50	85–90
Exercise stress echocardiography[96]	80–85	80–88
Exercise stress SPECT[96-99]	73–92	63–87
Dobutamine stress echocardiography[96]	79–83	82–86
Dobutamine stress MRI[b,100]	79–88	81–91
Vasodilator stress echocardiography[96]	72–79	92–95
Vasodilator stress SPECT[96, 99]	90–91	75–84
Vasodilator stress MRI [b,98, 100-102]	67–94	61–85
Coronary CTA[c,103-105]	95–99	64–83
Vasodilator stress PET[97, 99, 106]	81–97	74–91

CAD = coronary artery disease; CTA = computed tomography angiography; ECG = electrocardiogram; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single photon emission computed tomography.

[a] Results without/with minimal referral bias.

[b] Results obtained in populations with medium-to-high prevalence of disease without compensation for referral bias.

[c] Results obtained in populations with low-to-medium prevalence of disease.

4.2 Computed Tomography Coronary Angiography (CTCA)

Computed tomography coronary angiography (CTCA) has emerged as the non-invasive test of choice for imaging the coronary vasculature, demonstrating clinical efficacy in multiple large-scale randomized clinical trials (Dweck et al., 2016). It provides additional information to CACS regarding stenosis severity and has an incremental prognostic value to CACS in respect of coronary artery events (Arbab-Zadeh & Fuster, 2016; Gaemperli et al., 2008; Van Werkhoven et al., 2009; Taylor et al., 2010).

…

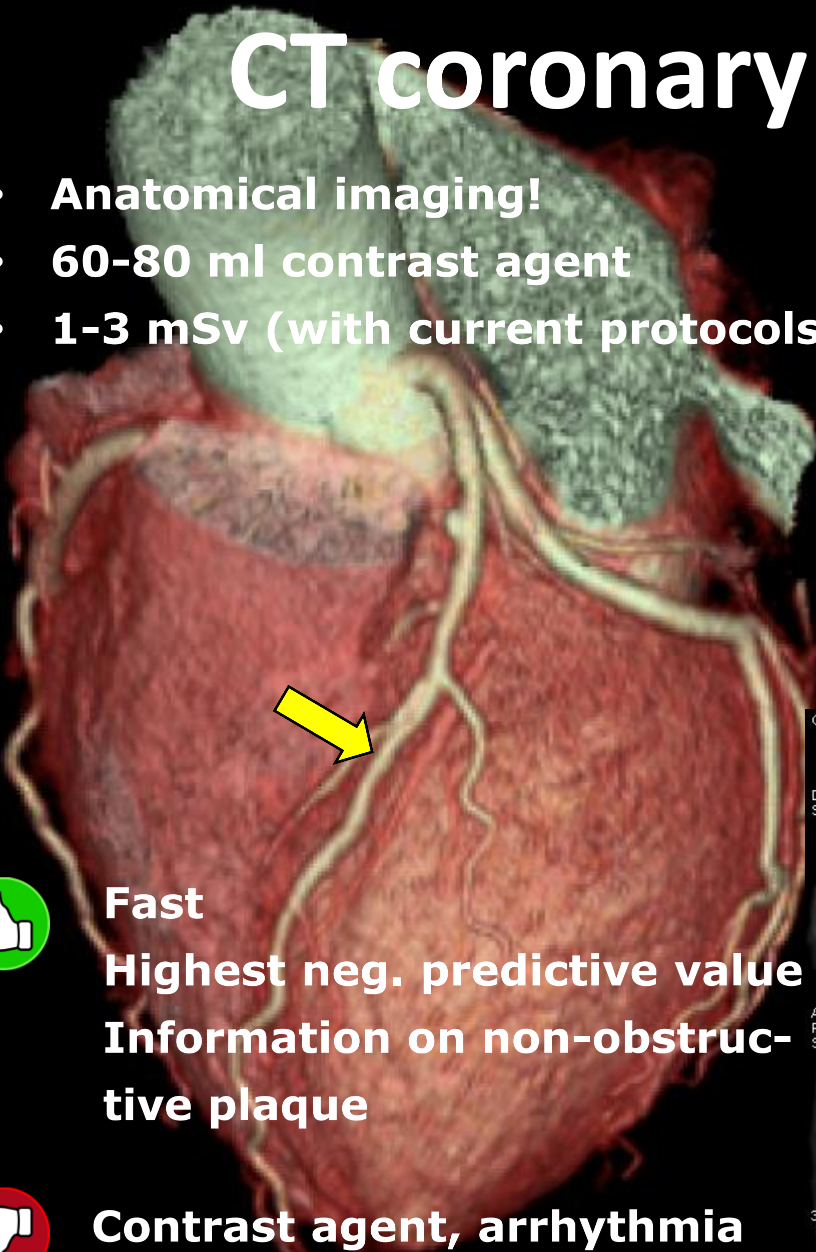
CTCA is able to both image and characterize plaques (calcified, non-calcified or mixed). This is a huge advantage of this method because it enables the detection of non-calcified soft plaques, which may cause a sudden cardiac emergency or sudden death due to a plaque rupture without any alarming symptoms before the event (Libby, 2013; Crea & Libby, 2017).

…

Comparing the cost-effectiveness of frequently used cardiological diagnostic tools, Moss et al. (2017) found that CTCA was by far the lowest-cost test per correct diagnosis due to the low cost of the test and high sensitivity and low probability of fatal or non-fatal complication.

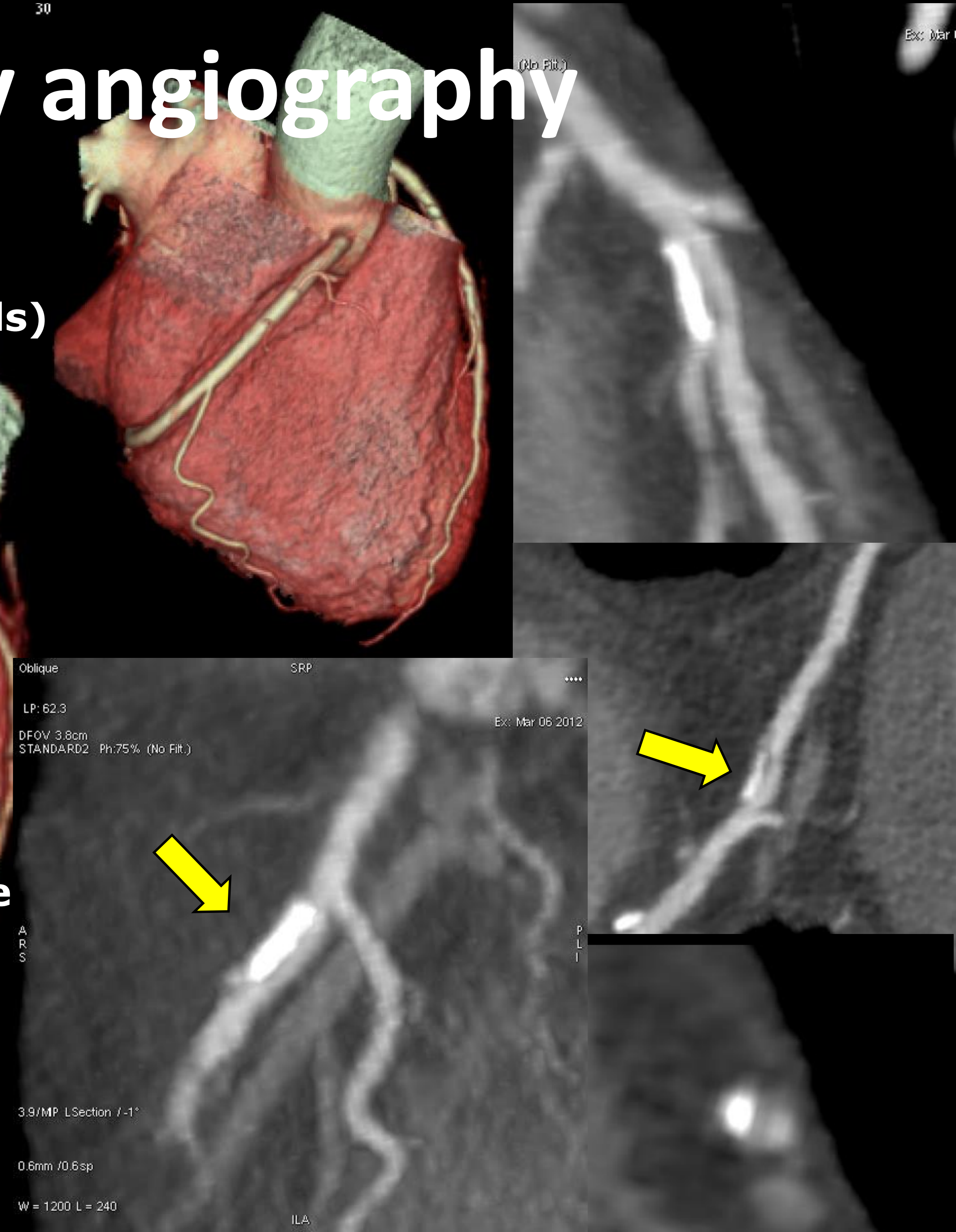
CT coronary angiography

- Anatomical imaging!
- 60-80 ml contrast agent
- 1-3 mSv (with current protocols)



Fast
Highest neg. predictive value
Information on non-obstructive plaque

Contrast agent, arrhythmia



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*

N Engl J Med 2018;379:924-33

4146 patients with stable angina were involved in the SCOT-HEART study. Half of them had a coronary CT angiography (CTCA) besides standard management. The other group had only standard management. After an observation period of 4.8 years, the rate of death from coronary heart disease or nonfatal myocardial infarction was significantly lower in the group with CTCA, without resulting in a significantly higher rate of coronary angiography or coronary revascularization.

METHODS
In an open-label, multicenter, parallel-group trial, we randomly assigned 4146 patients with stable chest pain who had been referred to a cardiology clinic for evaluation to standard care plus CTA (2073 patients) or to standard care alone (2073 patients). Investigations, treatments, and clinical outcomes were assessed over 3 to 7 years of follow-up. The primary end point was death from coronary heart disease or nonfatal myocardial infarction at 5 years.

CONCLUSIONS
In this trial, the use of CTA in addition to standard care in patients with stable chest pain resulted in a significantly lower rate of death from coronary heart disease or nonfatal myocardial infarction at 5 years than standard care alone, without resulting in a significantly higher rate of coronary angiography or coronary revascularization. (Funded by the Scottish Government Chief Scientist Office and others; SCOT-HEART ClinicalTrials.gov number, NCT01149590.)

ESC Congress Munich 2018

Day 1

ESC European Society of Cardiology

Congress News

Saturday 25 August 2018

The future of cardiovascular imaging

Prof. David Newby

Professor David Newby (University of Edinburgh, Edinburgh, UK) will tomorrow give the ESC Rene Laennec Lecture on Clinical Cardiology (Sunday, 09:30 - 10:00; Moscow - Village 5).

Over the last ten years, Prof. Newby has focussed his research interests on advanced imaging of the heart. He was Chief Investigator for the SCOT-HEART trial, which showed that the addition of CT coronary angiography (CTCA) to standard clinical care clarifies the diagnosis of angina due to coronary heart disease (CHD).[1] "Results from SCOT-HEART and the US-based PROMISE trial have shown us that with CTCA we can see whether a patient actually has CHD, and also that CTCA guided changes in management can improve clinical outcomes," he says.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*

OPEN ACCESS

The challenge of asymptomatic coronary artery disease in aircrew; detecting plaque before the accident

Gary Gray,[1] Eddie D Davenport,[2] Dennis Bron,[3] Rienk Rienks,[4] Joanna d'Arcy,[5] Norbert Guettler,[6] Olivier Manen,[7] Thomas Syburra,[8] Edward D Nicol[5]

Heart: first published as 10.1136/heartjnl-2018-313053 on 13 November 2018.

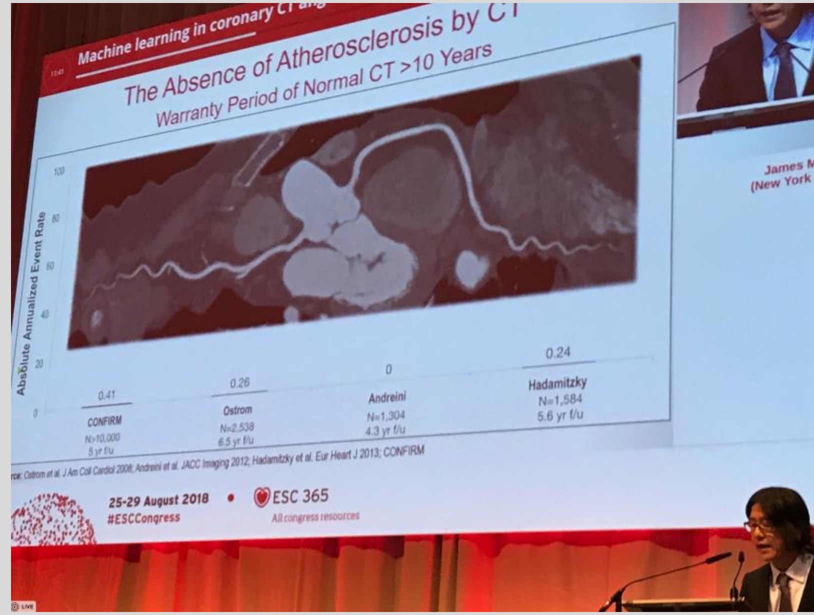
Table 6 Enhanced screening for coronary artery disease in aircrew

For aircrew identified as being at increased risk for a coronary event based on a risk prediction model, a CT imaging study is recommended to assess for the presence of atherosclerotic plaque. The choice of whether to use CT Coronary Artery Calcium Score (CACS), and/or CT coronary angiogram (CTCA) is an organisational decision.	Highly recommended

Where we go with CT angiography?

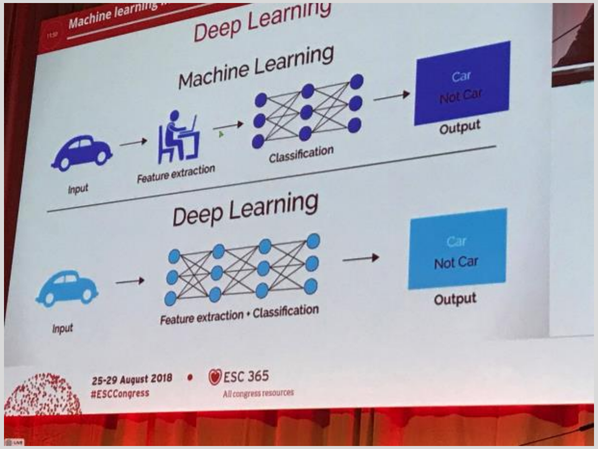
List of Presentations

Time	FP Nr	Title	Speakers
11:00	3361	Is the calcium score our optimal tool for risk stratification?	Stephen FENTON (Sydney, Australia)
11:18	3362	CT angiography in large clinical trials.	Leslee SHAW (Atlanta, United States of America)
11:36	3363	Machine learning in coronary CT angiography.	James MIN (New York, United States of America)
11:54	3364	CT plaque composition to predict coronary events	Damini DEY (Los Angeles, United States of America)
12:12	3365	FFR-CT: a critical appraisal.	Ricardo CURY (Miami, United States of America)



Machine Learning

- Machine learning is a field of computer science that gives computers the ability to learn without being explicitly programmed.



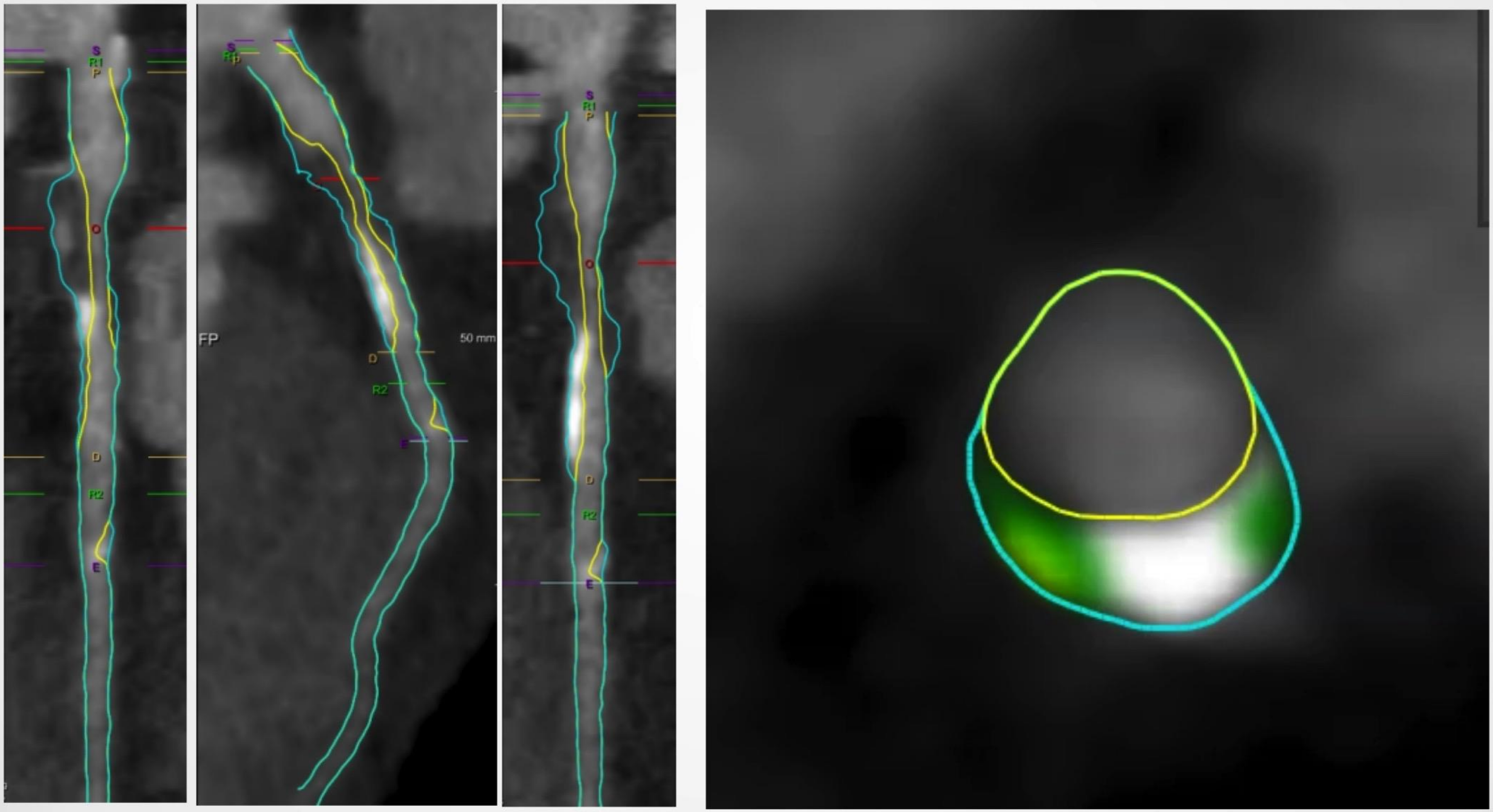
Huge amounts of data out of CT-pictures are analysed by various computer algorithm. In this process, multiple variables are created, which finally allow prognostic statements.

Tesla

Real-time Computer Vision through Machine Learning

Source: https://www.youtube.com/watch?v=VG68SKoG7vE

CT is the only method for whole-heart quantification and characterization of coronary atherosclerosis.



European Heart Journal (2016) 37, 2315–2381
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TNO innovation for life

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4.3 Vascular ultrasound imaging:

Carotid Intima-Media Thickness (IMT)

Recommendations for imaging methods

Recommendations	Class[a]	Level[b]	Ref[c]
Atherosclerotic plaque detection by carotid artery scanning may be considered as a risk modifier in CV risk assessment.	IIb	B	126–128
ABI may be considered as a risk modifier in CV risk assessment.	IIb	B	129–132
Carotid ultrasound IMT screening for CV risk assessment is not recommended.	III	A	128, 133

ABI = ankle–brachial index; CV = cardiovascular; IMT = intima–media thickness.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

4.4 Second-line investigations for Coronary Artery Disease and CVD

When enhanced screening investigations show evidence of significant CVD, further cardiological investigations have to be done to enable an advice concerning therapeutic measures (Neumann et al., 2018) and the flying status.

Investigations for the refinement of the **anatomic** coronary situation generally involve:

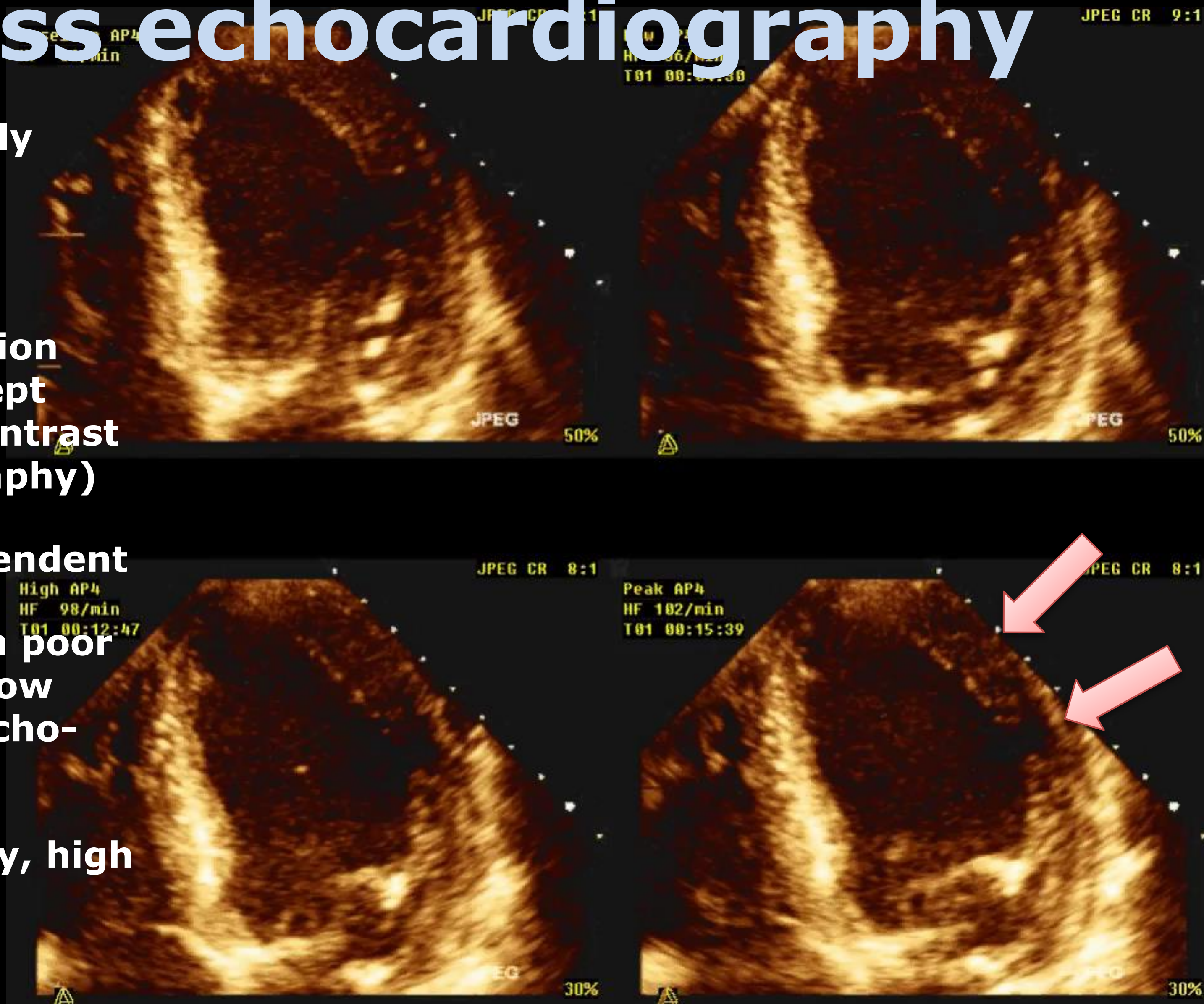
- CTCA (see § 4.2);
- Invasive coronary angiography (ICA).

Investigations for the assessment of the presence of **functional** coronary ischemia generally involve:

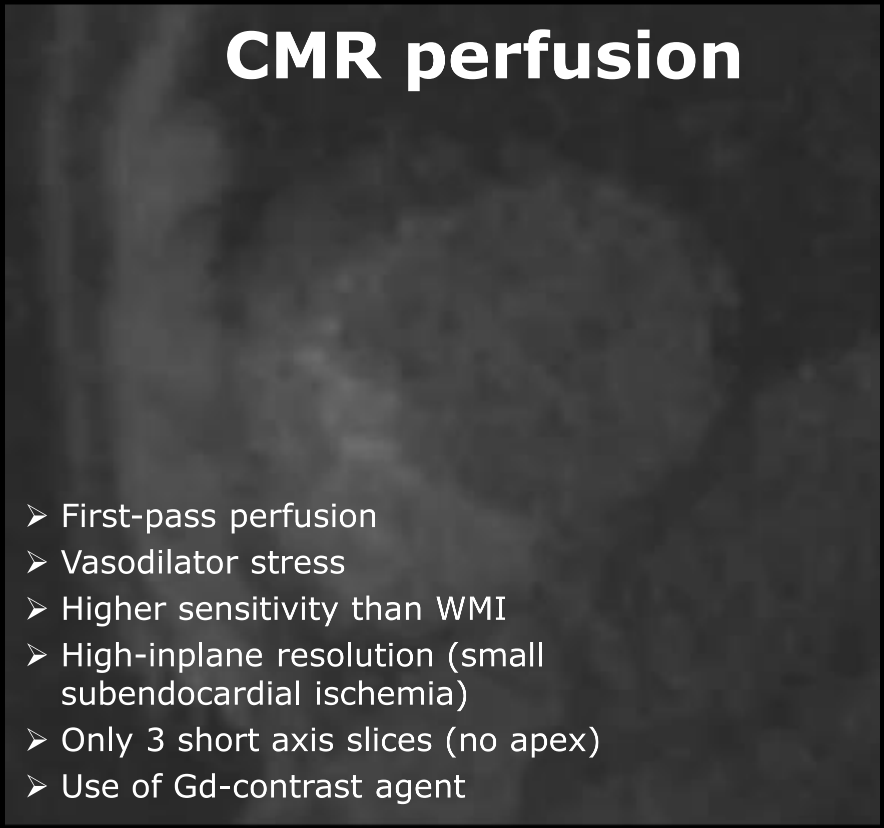
- Myocardial perfusion scintigraphy (MPS);
- Single Positron Emission Tomography (SPECT) and Positron emission tomography (PET);
- Cardiac magnetic resonance (CMR) (also known as cardiac MRI);
- Invasive coronary angiography (ICA) with application of Fractional flow reserve (FFR) or of the Instant wave-free ratio (iFR);
- Stress echocardiography;
- PET might become the first line method for the assessment of the presence of coronary ischemia in the near future (Jaarsma et al., 2012).

Stress echocardiography

- Bedside, widely available
- No radiation
- Only wall motion imaging (except myocardial contrast echocardiography)
- Operator-dependent
- Problems with poor acoustic window (potentially echo-contrast)
- Low sensitivity, high specificity

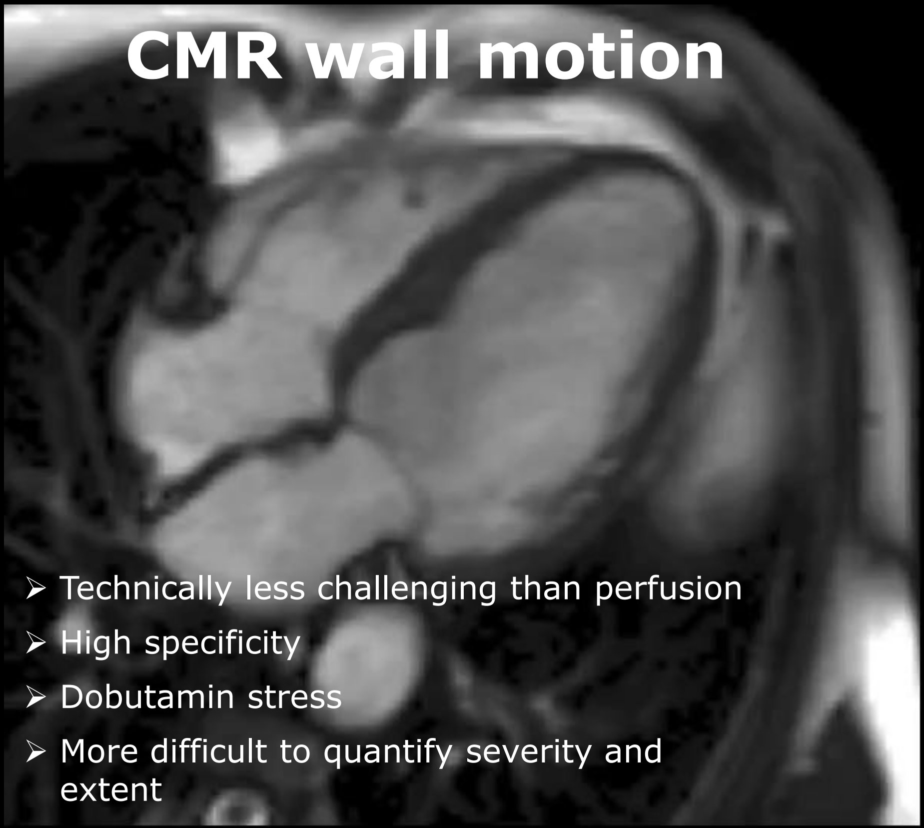


Stress CMR



CMR perfusion

- First-pass perfusion
- Vasodilator stress
- Higher sensitivity than WMI
- High-inplane resolution (small subendocardial ischemia)
- Only 3 short axis slices (no apex)
- Use of Gd-contrast agent



CMR wall motion

- Technically less challenging than perfusion
- High specificity
- Dobutamin stress
- More difficult to quantify severity and extent

No poor acoustic window, no radiation

Claustrophobia, metal implants

SPECT

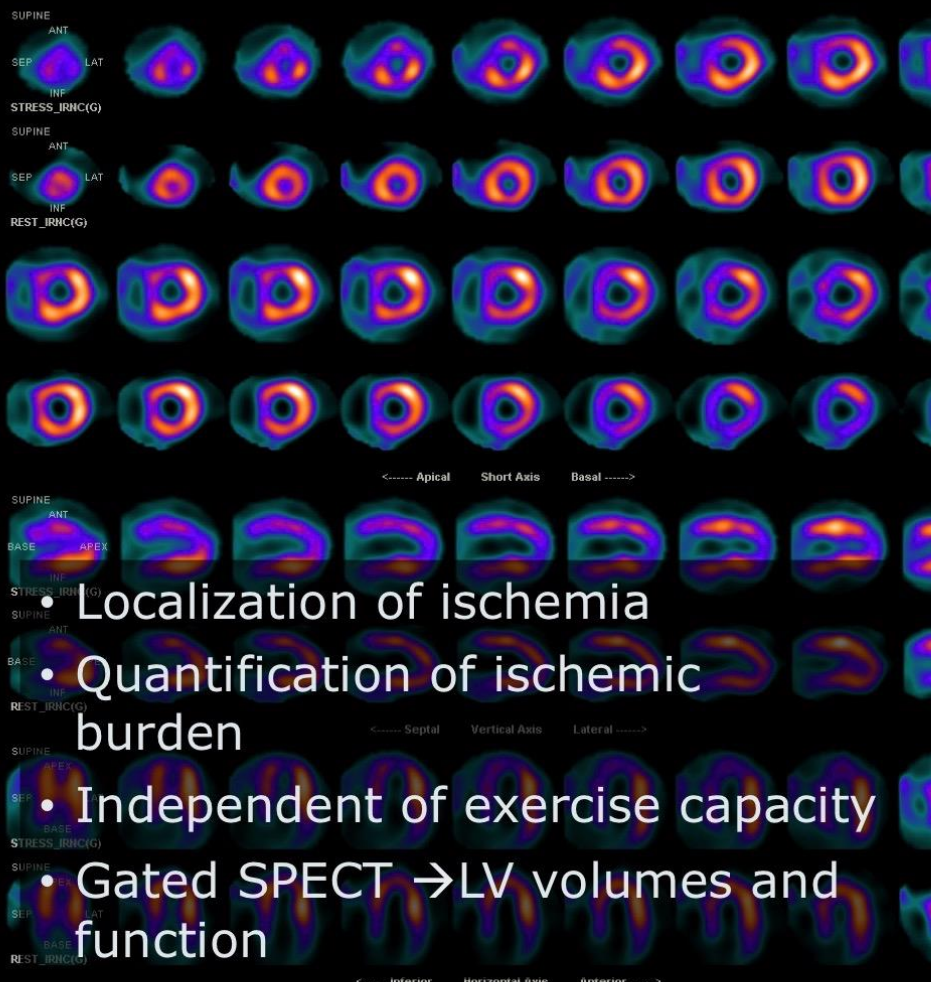
Stress modalities

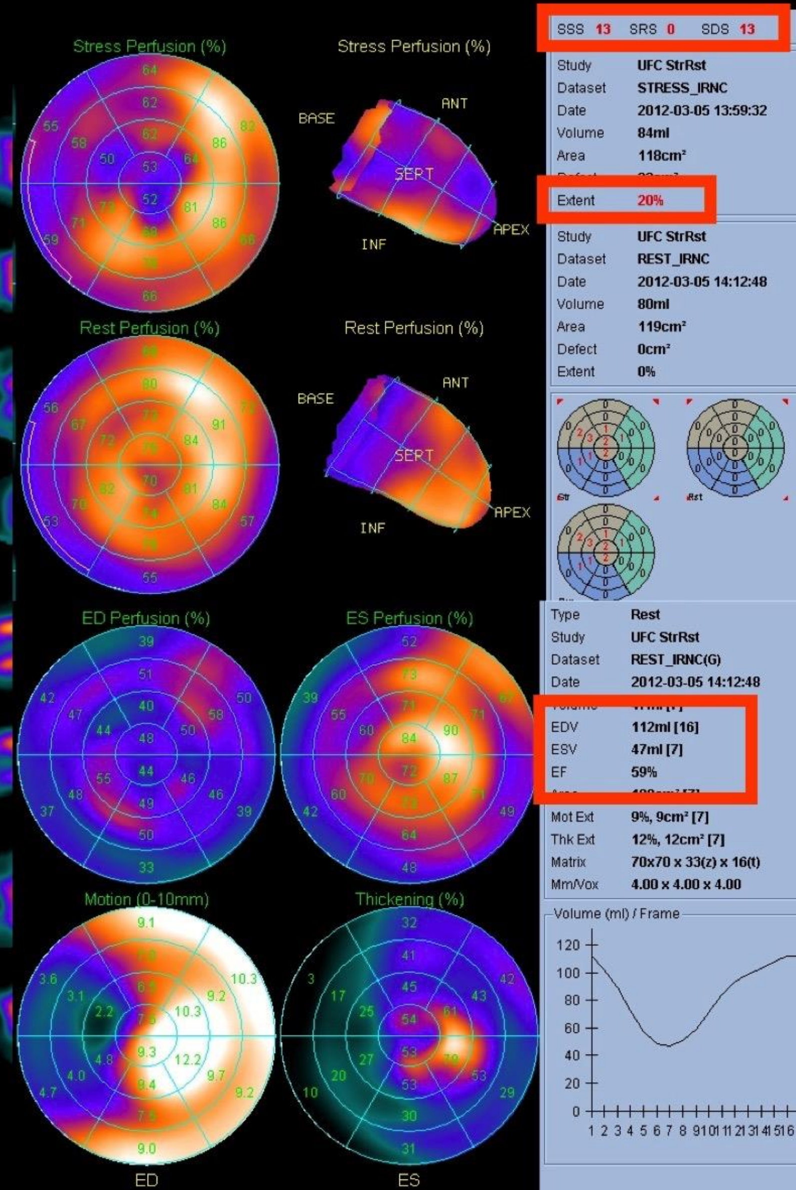
- **Physical:** e.g. bicycle ergometer, tread mill
  (more physiological, less GI uptake, 1st choice)

- **Pharmacological** (for patients who cannot exercise):
  - **Vasodilators** (hyperemic agents, un-couple O_2 supply and demand): e.g. adenosine ($t_{1/2}$=10-20 sec) , dipyridamol, regadenoson (selective A2A agonist)
  - **Dobutamine** (β1-agonist)

Contrary to stress echo and stress CMR, MP-SPECT allows de-coupling of stress injection from stress imaging by a variably long interval (generally 60-90 min)

Myocardial perfusion SPECT



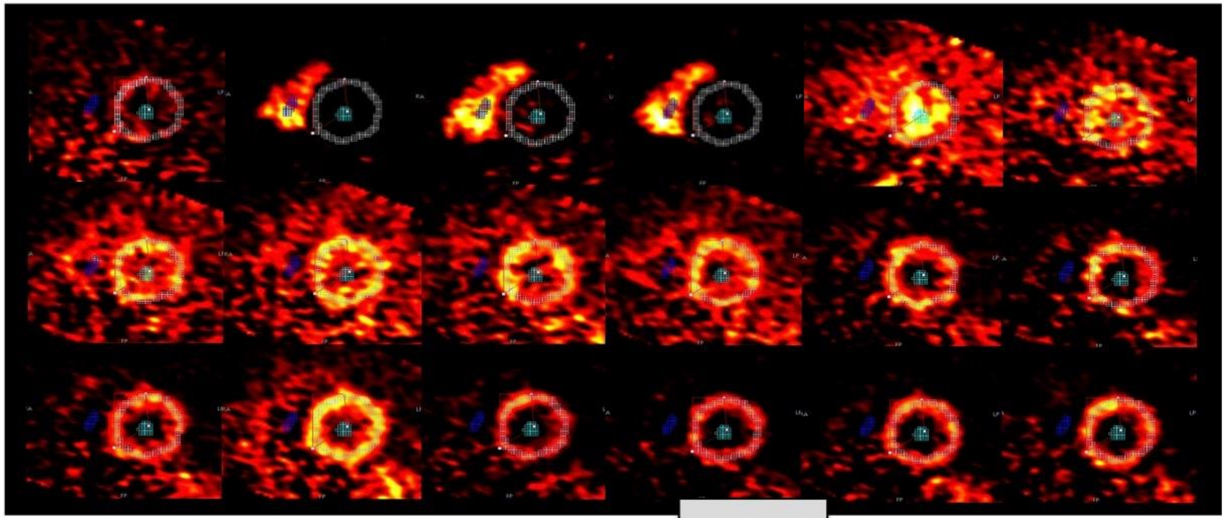


- Localization of ischemia
- Quantification of ischemic burden
- Independent of exercise capacity
- Gated SPECT →LV volumes and function

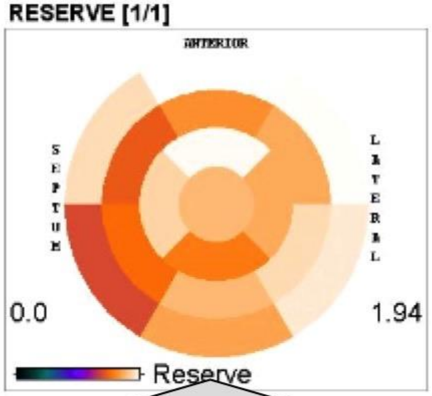
UniversityHospital Zurich

Myocardial blood flow quantification with PET

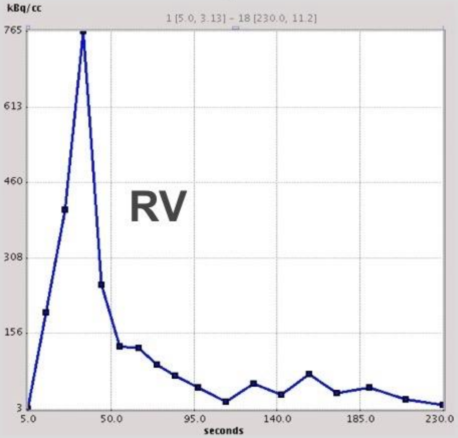
List mode dynamic acquisition – 20 frames

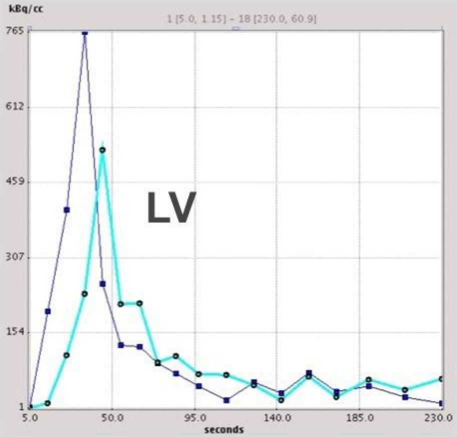


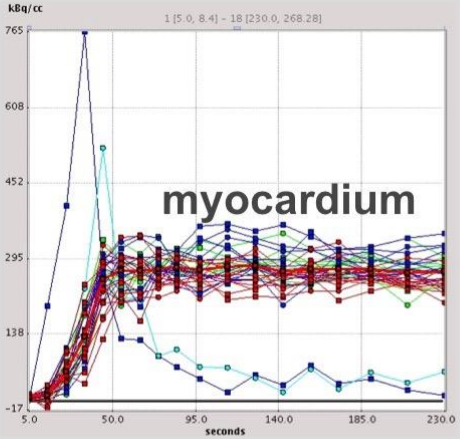
Parametric map of hyperemic MBF and coronary flow reserve



Time-activity curves







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Cardiac Imaging

Diagnostic Performance of Noninvasive Myocardial Perfusion Imaging Using Single-Photon Emission Computed Tomography, Cardiac Magnetic Resonance, and Positron Emission Tomography Imaging for the Detection of Obstructive Coronary Artery Disease

A Meta-Analysis

Caroline Jaarsma, MD,*†‡ Tim Leiner, MD, PHD,†‡ Sebastiaan C. Bekkers, MD, PHD,*‡
Harry J. Crijns, MD, PHD,*‡ Joachim E. Wildberger, MD, PHD,†‡ Eike Nagel, MD, PHD,‖
Patricia J. Nelemans, MD, PHD,‡§ Simon Schalla, MD*‡

Maastricht, the Netherlands; and London, United Kingdom

Objectives This study aimed to determine the diagnostic accuracy of the 3 most commonly used noninvasive myocardial perfusion imaging modalities, single-photon emission computed tomography (SPECT), cardiac magnetic resonance (CMR), and positron emission tomography (PET) perfusion imaging for the diagnosis of obstructive coronary artery disease (CAD). Additionally, the effect of test and study characteristics was explored.

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Patricia J. Nelemans, MD, PhD,‡§ Simon Schalla, MD*‡
Maastricht, the Netherlands; and London, United Kingdom

Conclusions

SPECT, CMR, and PET all yielded a high sensitivity, while a broad range of specificity was observed. SPECT is widely available and most extensively validated; PET achieved the highest diagnostic performance; CMR may provide an alternative without ionizing radiation and a similar diagnostic accuracy as PET. We suggest that referring physicians consider these findings in the context of local expertise and infrastructure. (J Am Coll Cardiol 2012;59:1719–28) © 2012 by the American College of Cardiology Foundation

Costs of cardiac imaging techniques (University Hospital Zurich)

CACS	300 CHF	260 Euro
CTCA	700 CHF	617 Euro
CMR	1000 CHF	881 Euro
SPECT	1300 CHF	1145 Euro
PET	2400 CHF	2115 Euro

Choice of imaging technique...

... should be rather based on local expertise, availability, and patient suitability

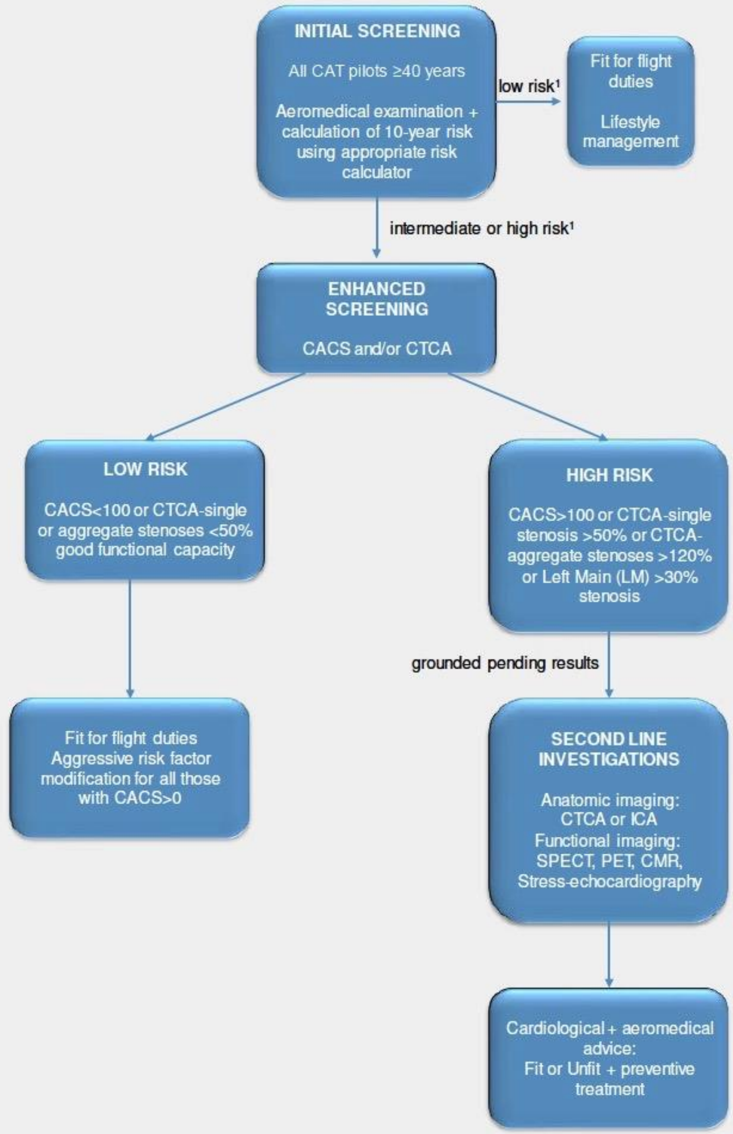
... than on assumptions of superior accuracy of one technique over the other

Technique	Advantages	Disadvantages
Stress-Echo	• Wide access, portability • No radiation • Low cost	• Patients with poor ultrasound windows • Dependent on operator skills
SPECT	• Wide access • Extensive data	• Radiation
PET	• Flow quantitation	• Radiation • Limited access • High cost
CMR	• High soft tissue contrast including scar imaging • No radiation	• Limited access • Contraindications (metal implants/GFR) • Limited 3D quantification of ischaemia
CTCA	• High NPV in pts with low PTP	• Radiation • Poor image quality with coronary calcifications, stents or arrhythmia

Adapted from 2013 ESC guidelines stable CAD

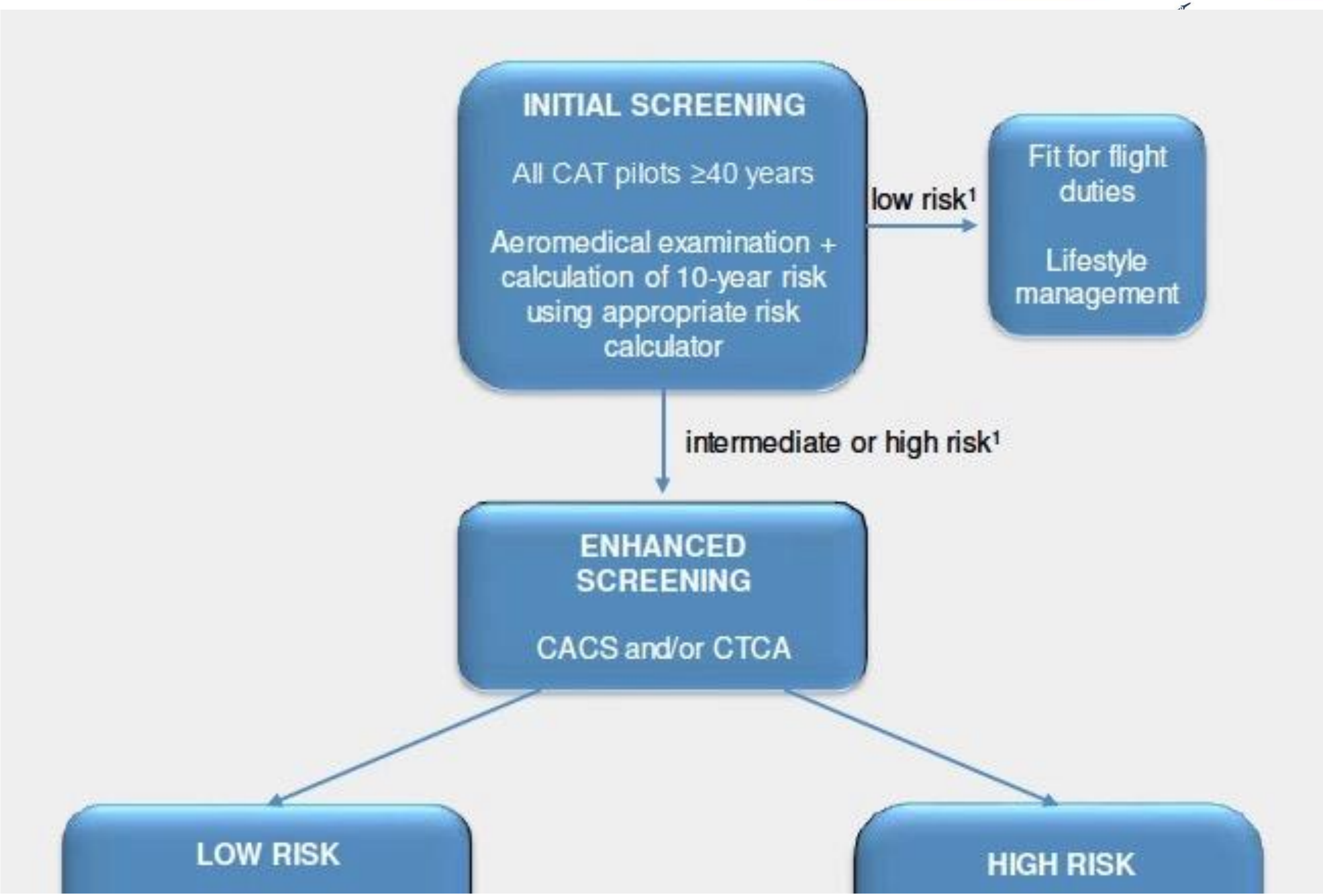
5 Conclusion/Recommendation

Figure 1 Flow chart with algorithm adapted from Gray et al. (2019). This algorithm is aimed at supporting AMEs and Medical Assessors. The second line investigations are in the realm of the consulted cardiologist



[1] The classification of a low, intermediate or high risk is given by the cardiovascular score being used. We recommend using the PROCAM score; in this case a 10-year cardiovascular risk of <10% is low, of 10-20% intermediate and of >20% high.

Figure 1 Flow chart with algorithm adapted from Gray et al. (2019). This algorithm is aimed at supporting AMEs and Medical Assessors. The second line investigations are in the realm of the consulted cardiologist



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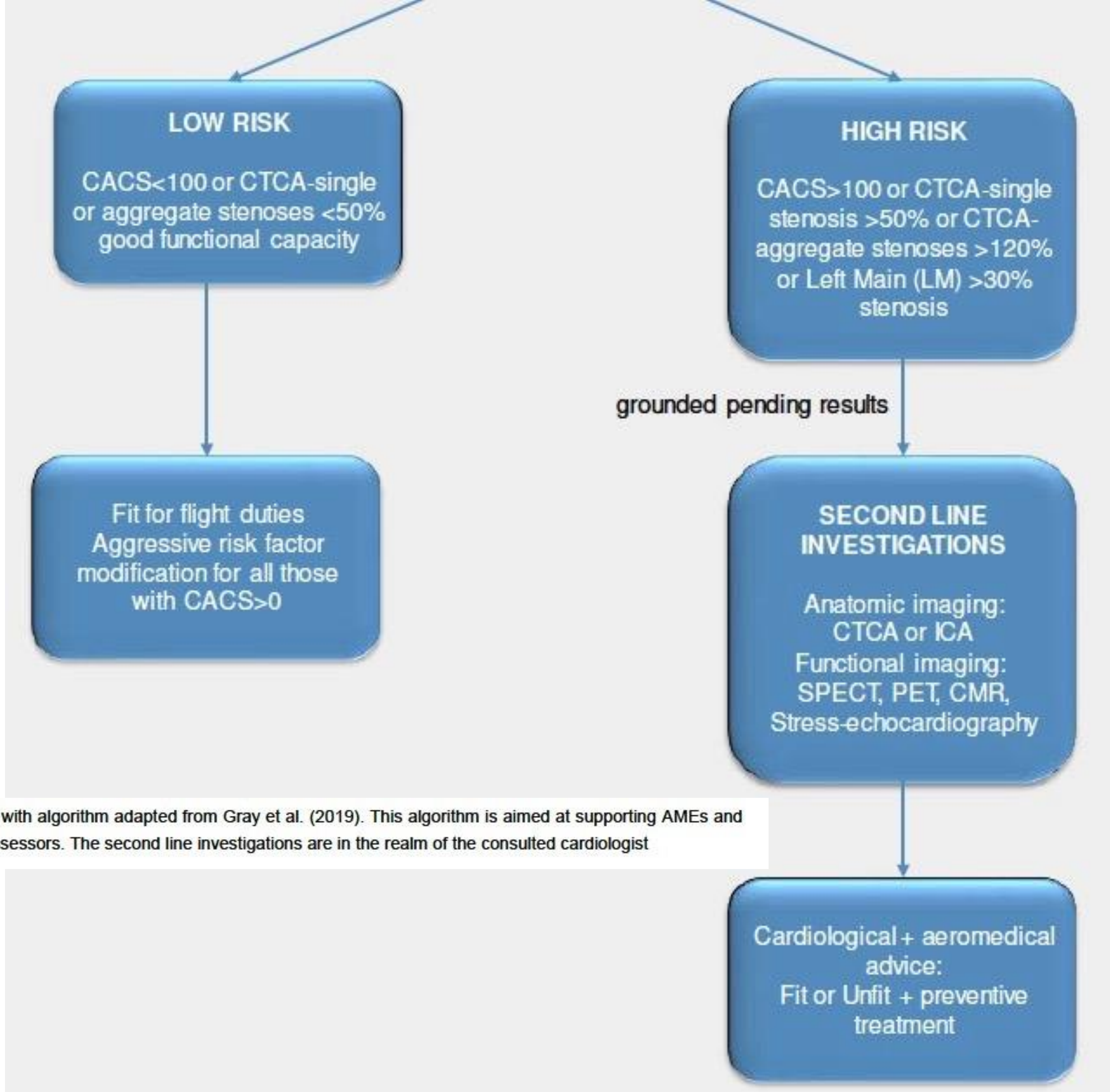

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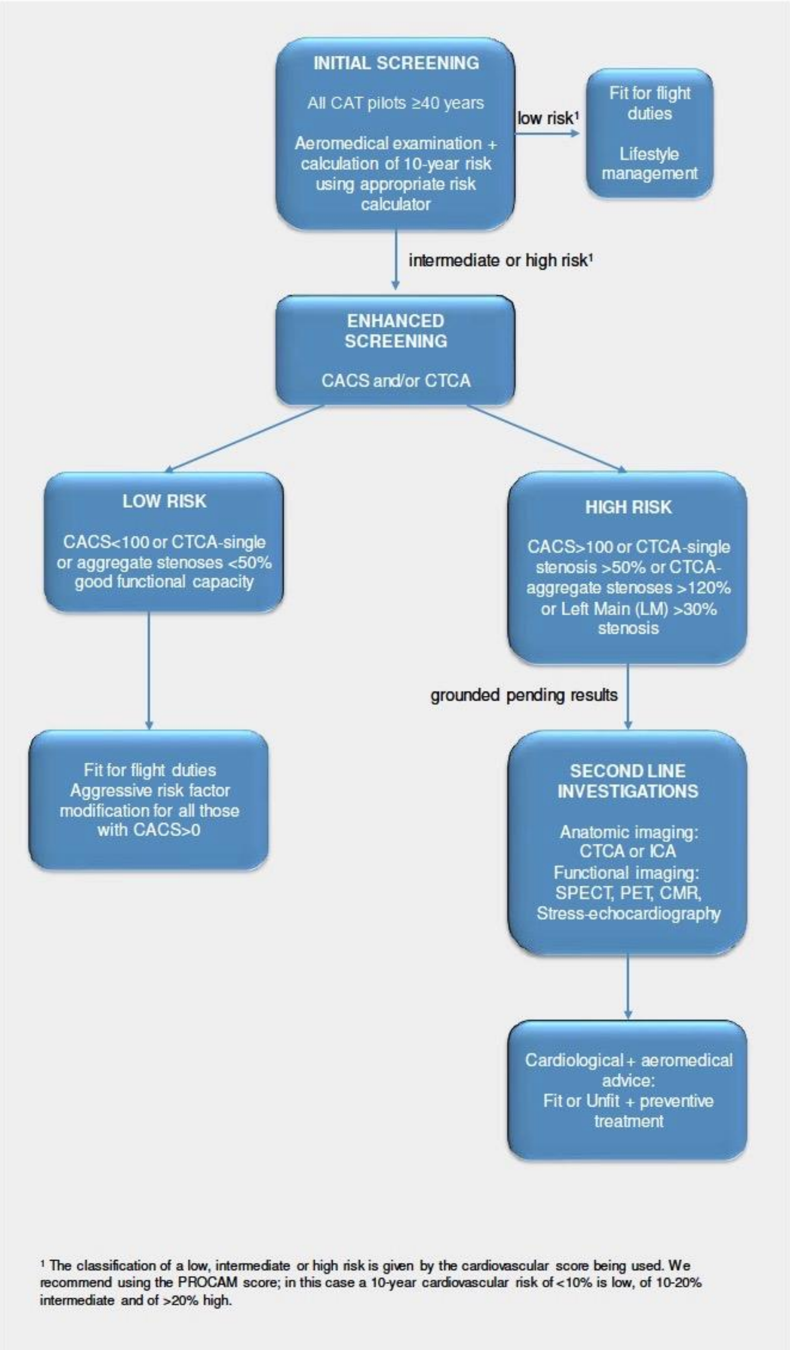

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Thank you for your attention!