Screening of Athlete’s Heart
Coronary Artery Disease
Role of Perfusion Tests

Danilo Neglia, Pisa, IT
EU Association of CVI - ESC
EXERCISE à Myocardial Oxygen Consumption

Myocardial Blood Flow

Coronary Disease à Myocardial Ischemia

Perfusion, Wall Motion, ECG, Symptoms
Male, 54 yrs, recent onset typical angina

Rest/Stress ECG
Male, 54 yrs, recent onset typical angina

Stress MR (WM)    Stress MR (Perfusion)

Stress/Rest PET (Qualitative)  ICA (Right Coronary Artery)
Myocardial Ischemia
Perfusion, Wall Motion, ECG, Symptoms

- CMR
- SPECT/PET
- CMR, SPECT/PET

Specificity
- ECG
- ECHO
- CMR

Sensitivity
- Normal LV function
- Angina
- Ischaemic ST depression
- Global LV dysfunction
- Regional systolic dysfunction
- Regional diastolic dysfunction
- Perfusion abnormality

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Per la Ricerca Medica e di Sanità Pubblica
The multi-modality cardiac imaging approach to the Athlete’s heart: an expert consensus of the European Association of Cardiovascular Imaging

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Document Reviewers: Rosa Sicari, (Italy), Denisa Muraru, (Romania), Massimo Lombardi, (Italy), Raluca Dulgheru, (Romania), Andre La Gerche (Australia)
Coronary Disease in Athletes

Coronary disease is reported as one of the main causes of SCD in athletes

- Congenital Coronary Anomalies in younger athletes
- ATS Coronary Artery Disease in older athletes

There is a broad range of screening recommendations for the diagnosis of myocardial ischaemia in athletes with important variations between countries, type of sport and competition level

Galderisi M, Eur Heart J CVI 2015
Sudden Cardiac Death in Athletes (by Age)

Coronary Disease

La Gerche A, JACC CVI 2013
Sudden Cardiac Death in Younger Athletes
Age < 39 yrs, Congenital Coronary Anomalies (17%)

Anomalous origin of a coronary artery from the opposite coronary sinus or the opposite coronary artery has a prevalence that ranges from 0.15% to 0.39% in invasive angiographic studies.

The majority of these individuals are symptom free

Angina and syncope may occur

Circulation 2009
Detection of Congenital Coronary Anomalies
ECHO, CT or MR Angiography (Myocardial Perfusion Test?)

39 yrs old man, effort angina
ST segment depression at exECG

Echocardiography 2012
Coceani M, Ann Thoracic Surg 2013
Younger Athletes

Tests to screen for Coronary Anomalies?

The American Heart Association has defined criteria for preparticipation screening in competitive athletes, using personal history, physical examination, and family history.

In those with a negative personal history, physical examination and family history the benefits of routine imaging for screening are not clear.

Maron BJ, Circulation 2007

In symptomatic athletes in whom coronary anomalies may be suspected, it is reasonable to consider CCT and/or CMR, as well as attenuation-corrected SPECT MPI and PET MPI.

2015 ESC-EACVI Recommendations
Athlete’s Heart
Sudden Cardiac Death in Athletes (by Age)

Coronary Disease

La Gerche A, JACC CVI 2013
Atherosclerotic CAD is the leading cause of SCD and AMI in adult athletes.

During vigorous exercise these events may be caused by **plaque disruption** or **malignant arrhythmias caused by demand ischemia** or originating in areas of **myocardial scar**

Other conditions such as coronary vasospasm, bridging, dissection, infection, etc. may cause SCD or AMI.
Asymptomatic Older Athletes (CAD 0.5%)
Tests to screen for Coronary Disease and Ischemia?

BAYES Theorem
The Positive Predictive Value of a test is very low if the Prevalence of Disease is low. It critically depends on SPECIFICITY.

Cardiac imaging cannot be recommended as a first-line screening tool.

Expected Prevalence of CAD in Asymptomatic Athletes (51 yrs) = 0.5 %
Sensitivity and Specificity Test = 95%
Positive Predictive Value = 9%
(93% of positive tests will be False Positives)

La Gerche A, JACC CVI 2013
While much recent debate has focused on the efficacy of screening with ECG, current evidence suggests that the incremental cost-effectiveness ratio of cardiac imaging modalities is too high in the context of a low prevalence of disease to justify their large use as primary screening modalities in athletes.

2015 ESC-EACVI Recommendations
La Gerche A, JACC CVI 2013
Athlete’s Heart

The 2013 ESC Guidelines on stable CAD
The ACCF/AHA guidelines for CV risk assessment in asymptomatic adults considered non invasive stress imaging, including nuclear testing, for advanced CV risk assessment of specific asymptomatic individuals such as those with diabetes or a strong family history of CAD.
Symptomatic Older Athletes (CAD 15-50%)
Detection of ATS Coronary Disease and/or Ischemia
ECG and CV Imaging
Are All the Diagnostic Tests equal?
Some are **MORE SPECIFIC** (Few False Positives)

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Diagnosis of CAD</th>
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<tbody>
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<td></td>
<td>Sensitivity (%)</td>
</tr>
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Are All the Diagnostic Tests equal?  
Some are MORE SENSITIVE (Few False Negatives)
Symptomatic Older Athletes (CAD 15-50%)
Detection of ATS Coronary Disease and/or Ischemia
Prefer More SPECIFIC Tests

SENSITIVITY
The ability to recognize the Disease
(Few False Negatives)

\[ \text{VP/FN+VP} \]

SPECIFICITY
The ability to exclude the Disease
(Few False Positives)

\[ \text{VN/FP+VN} \]
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

Task Force Members: Gilles Montalescot* (Chairperson) (France), Udo Sechtem* (Chairperson) (Germany), Stephan Achenbach (Germany), Felicita Andreotti (Italy), Chris Arden (UK), Andrzej Budaj (Poland), Raffaele Bugiardini (Italy), Filippo Crea (Italy), Thomas Cuisset (France), Carlo Di Mario (UK), J. Rafael Ferreira (Portugal), Bernard J. Gersh (USA), Anselm K. Gitt (Germany), Jean-Sebastien Hulot (France), Nikolaus Marx (Germany), Lionel H. Opie (South Africa), Matthias Pfisterer (Switzerland), Eva Prescott (Denmark), Frank Ruschitzka (Switzerland), Manel Sabaté (Spain), Roxy Senior (UK), David Paul Taggart (UK), Ernst E. van der Wall (Netherlands), Christiaan J.M. Vrints (Belgium).
Symptomatic Older Athletes (CAD 15-50%)
Detection of ATS Coronary Disease and/or Ischemia

Patients with suspected SCAD and intermediate PTP of 15% - 85%

Consider:
- Patient criteria / suitability for given test
- Availability
- Local expertise

Stress testing for ischemia → PTP 15-65% and LVEF ≥ 50%

Exercise ECG
Or Any Stress Imaging

Coronary CTA in patients at low intermediate PTP (15% - 50%)
- If suitable candidate
- If adequate technology and local expertise available

2013 ESC GL Stable CAD
Symptomatic Older Athletes

Higher Specificity = Better PPV
Higher Sensitivity = Better NPV

In athletes with suspected CAD, cardiac imaging provocative tests should be performed when the results of exercise ECG appear uncertain.

Among provocative tests, exercise ECHO may be the first choice.

The use of CCT and Stress Nuclear or CMR techniques should be restricted to athletes with unclear stress ECHO.

2015 ESC-EACVI Recommendations
Athlete’s Heart
Perfusion Predicts Outcome
(SPECT – PET)

- Regional Perfusion Defect
- Myocardial Flow Reserve Impaired (< 2)

Shaw LJ
J Nucl Cardiol 2012

Murthy VL
Circulation 2011
Sudden Cardiac Death in Athletes (by Age)

Cardiomyopathies & CMVD

La Gerche A, JACC CVI 2013
Relevance of Myocardial Perfusion

Early DCM

Patients with Endothelial/Microvascular Dysfunction

Increased relative risk of 3.5 times in 5 yrs

Dip MBF < 1.36 ml/min/g


$^{13}$NH$_3$ - PET
Relevance of Myocardial Perfusion

Myocardial Hypertrophy → Dilatation

Microvascular Remodelling

HCM

Myocardial Perfusion

Basal  Dipyridamole
Coronary Microvascular Dysfunction and Prognosis in Hypertrophic Cardiomyopathy

Franco Cecchi, M.D., Iacopo Olivotto, M.D., Roberto Gistri, M.D., Roberto Lorenzoni, M.D., Giampaolo Chiriatti, M.D., and Paolo G. Camici, M.D.

Figure 2. Myocardial Blood Flow (MBF) Values after Dipyridamole Infusion and Long-Term Prognosis.

Patients were divided into three equal groups according to MBF after dipyridamole infusion. Panel A shows overall cumulative survival, and Panel B cumulative survival free from an unfavorable outcome.
Screening Athlete’s Heart for CAD
Role of Perfusion Tests

- Asymptomatic athletes should not be screened by CV imaging unless at specific HIGH RISK (diabetics, strong Family History, etc.)

- Younger athletes with symptoms or other suspicion of coronary disease could be evaluated by stress imaging but anatomic imaging could be preferred (to detect congenital coronary anomalies)

- Older athletes with symptoms or other suspicion of coronary disease could be firstly evaluated by exercise ECG and with stress imaging after previous equivocal stress tests.

- Potential role of perfusion imaging (quantitative) in Cardiomyopathies?

...and for the FUTURE??
Better Predictive Models of CAD in Athletes

Biomarkers to Predict Probability of Disease and Individual Risk

Asymptomatics

HIGH RISK
Diabetics
Family History

Symptomatics

INT-LOW PTP
Coronary Artery Disease

Biological Markers
Myocardial damage
Genome/Epigenome
Inflammation/Metabolism
Atherosclerosis

Clinical/Biomarker MODELS

Higher Probability

Clinical Risk Markers
Age/Gender
History
Symptoms

Lower Probability

Sport Related Risk Markers
Sport Type/History
Training Load

Non Invasive Imaging

High Risk Patient
Early Disease

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Per la Ricerca Medica e di Sanità Pubblica
Better Predictive Models of CAD

Biomarkers to Predict Probability of Disease and Individual Risk

Caselli C et al.
Canadian J Cardiol 2015

Biomarkers to Predict Obstructive CAD+Ischemia

- EVINCI model, AUC=0.70
- Genders model, AUC=0.58

p <0.002

Caselli C et al.
Atherosclerosis 2015

Biomarkers to Predict CTCA Score

- Framingham Risk Score (0.63 [0.58 - 0.68])
- Euro-SCORE (0.71 [0.66 - 0.76])
- Bio-humoral model* (0.81 [0.77 - 0.85])

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Per la Ricerca Medica e di Sanità Pubblica
Better Predictive Models of CAD
Biomarkers to Predict Probability of Disease and Individual Risk

**Patient 1**
- Male, 66 yrs
- Diabetes
- Non anginal chest pain
- euroSCORE: 3.8%
- hs-cTnT: 21.76 ng/L
- NT-proBNP: 55.41 ng/L
- CTA score: 35.22
- CAC score: 841
- LVEF: 66%
- SDS: 0
- N. coronary vessels at ICA: 3

**Patient 2**
- Male, 66 yrs
- Smoke, hypercholesterolemia
- Typical chest pain
- euroSCORE: 2.4%
- hs-cTnT: 52.57 ng/L
- NT-proBNP: 220.80 ng/L
- CTA score: 26.6
- CAC score: 688
- LVEF: 38%
- SDS: 10
- N. coronary vessels at ICA: 1

Caselli C…Neglia D, ATVB 2016
Better Predictive Models of CAD
Biomarkers to Predict Probability of Disease and Individual Risk

Cardiac Troponin T and I Release After a 30-km Run

Underlying mechanisms of Tn Release in Athletes are poorly understood. Individual Susceptibility to Myocardial Damage may Stratify Risk

Klinkenberg LJJ, Am J Cardiol 2016
Possible Trial Proposal

Purpose 1:
To identify circulating biomarkers of ischemic myocardial damage and/or coronary atherosclerotic disease in competitive Athletes

Purpose 2:
To build an integrated predictive model of ischemic/atherosclerotic coronary disease in competitive Athletes

Population:
Asymptomatic non-elite Endurance and Strength Sports Athletes
High Training Load
Stratified for Age and Gender

Protocol:
Collection of Blood Samples, ECG and ECHO at rest and at different times soon after completion of training session

Coronary CT Angiography (in subjects with any abnormal test)
SAVE THE DATE  7-9 May 2017, Vienna AUSTRIA

Call for abstracts & clinical cases
15 Sept – 15 December 2016

Early registration fee deadline
27 February 2017
Are All the Diagnostic Tests equal?
Choose test according to diagnostic performance

The Ischemic Cascade

Taquety VR and Di Carli MF
Progress in CV Diseases, 2015
Are All the Diagnostic Tests equal?
Choose test according to disease probability

Pre Test Probability of CAD (60%)

Pre Test Probability of CAD (15%)

PRIVILEDGE SENSITIVITY!
The ability to recognize the Disease
(Few False Negatives)

VP/FN+VP

PRIVILEDGE SPECIFICITY!
The ability to exclude the Disease
(Few False Positives)

VN/FP+VN
Assess Pre-Test Probability of SCAD

_D&F (Genders)_

**Table 13. Clinical pre-test probabilities in patients with stable chest pain symptoms**

<table>
<thead>
<tr>
<th>Age</th>
<th>Typical angina</th>
<th>Atypical angina</th>
<th>Non-anginal pain</th>
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<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>30–39</td>
<td>59</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>40–49</td>
<td>69</td>
<td>37</td>
<td>38</td>
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<td>50–59</td>
<td>77</td>
<td>47</td>
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</tr>
<tr>
<td>60–69</td>
<td>84</td>
<td>58</td>
<td>59</td>
</tr>
<tr>
<td>70–79</td>
<td>89</td>
<td>68</td>
<td>69</td>
</tr>
<tr>
<td>&gt;80</td>
<td>93</td>
<td>76</td>
<td>78</td>
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_Per la Ricerca Medica e di Sanità Pubblica_
Detection of ATS CAD and/or Ischemia  
*In Symptomatic Patients (Prevalence of CAD 50%)*

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EVINCI Population with Symptoms
Still intermediate PTP after exECG

Neglia D, Circulation CVI 2015
Detection of ATS CAD and/or Ischemia

In Symptomatic Patients with Low Prevalence of CAD

Neglia D, Circulation CVI 2015