Diagnostic Algorithms

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Montalescot G et al.
ESC Guideline on the Management of Stable Coronary Artery Disease
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2013 ESC guidelines on the management of stable coronary artery disease

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Diagnosis of Stable CAD: What is new as compared to 2006?

- Separate consideration of the processes of diagnosis and risk stratification
- Diagnostic process based on pretest probabilities of SCAD
- New data on pretest probabilities
- Broader consideration of functional CAD as cause of symptoms
- Larger role for modern imaging techniques such as CMR and CCTA but with critical appraisal of their limitations
CASE

- 59y old patient - thoracic discomfort since 3M only with intense jogging → cardiologist
Initial diagnostic management of patients with suspected SCAD (1)

- **ALL PATIENTS**
  - Assess symptoms
  - Perform clinical examination

- **Symptoms consistent with unstable angina**
  - Follow specific NSTE-ACS guidelines

- **ECG**
- **Bio-Chemistry**
- **Resting echocardiography**
- **CXR in selected patients**

- **Consider comorbidities and QoL**
  - Comorbidities or QoL make revascularization unlikely
    - **Medical therapy**

- **Cause of chest pain other than CAD?**
  - Yes → **Treat as appropriate**
  - No → **LVEF <50%?**
    - Yes → **Typical angina?**
      - Yes → **Offer ICA if revascularization suitable**
      - No → See Fig. 2 for selection of test
    - No → **Assess pre-test-probability (PTP) (see Table 13) for the presence of coronary stenoses**

**Notes:**
- May be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management.
- If diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacologic stress imaging prior to treatment may be reasonable.

This slide corresponds to Figure 1 in the full text.
CASE

- 59y old patient - thoracic discomfort since 3M with intense jogging → cardiologist
- Resting ECG: sinus rhythm, HR 98/min, normal.
- Normal values for troponin, FBC, blood sugar, creatinine.
- Resting echocardiogram: normal
- Carotid ultrasound: IMT 1,2 mm, otherwise normal
**Initial diagnostic management of patients with suspected SCAD (1)**

**ALL PATIENTS**

- Assess symptoms
- Perform clinical examination

Next steps based on symptoms:
- Symptoms consistent with unstable angina: Follow specific NSTE-ACS guidelines
- Symptoms inconsistent with unstable angina:
  - Consider comorbidities and QoL

Comorbidities or QoL make revascularization unlikely:
- Medical therapy

**Cause of chest pain other than CAD?**
- Yes: Treat as appropriate
- No:
  - LVEF <50%?
    - Yes: Typical angina?
      - Yes: Offer ICA if revascularization suitable
      - No: See Fig. 2 for selection of test
    - No: Assess pre-test-probability (PTP) (see Table 13) for the presence of coronary stenoses

---

**Notes:**

a. May be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management.

b. If diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacologic stress imaging prior to treatment may be reasonable.
### Traditional clinical classification of chest pain

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical angina (definite)</strong></td>
<td>Meets all three of the following characteristics:</td>
</tr>
<tr>
<td></td>
<td>• substernal chest discomfort of characteristic quality and duration;</td>
</tr>
<tr>
<td></td>
<td>• provoked by exertion or emotional stress;</td>
</tr>
<tr>
<td></td>
<td>• relieved by rest and/or nitrates within minutes.</td>
</tr>
<tr>
<td><strong>Atypical angina (probable)</strong></td>
<td>Meets two of these characteristics.</td>
</tr>
<tr>
<td><strong>Non-anginal chest pain</strong></td>
<td>Lacks or meets only one or none of the characteristics.</td>
</tr>
</tbody>
</table>
Clinical pre-test probabilities\textsuperscript{a} 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>
</tr>
</thead>
<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>
</tr>
<tr>
<td>50-59</td>
<td>77</td>
<td>47</td>
<td>49</td>
</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>
</tr>
</tbody>
</table>

\textsuperscript{a} Probabilities of obstructive coronary disease shown reflect the estimates for patients aged 35, 45, 55, 65, 75, and 85 years.

This slide corresponds to Table 13 in the full text.

Initial diagnostic management of patients with suspected SCAD (2)

Assess pre-test-probability (PTP) for the presence of coronary stenoses

- Low PTP (<15%)
  - Investigate other causes
    - Consider functional coronary disease

- Intermediate PTP, eg 15-85%
  - Non-invasive testing for diagnostic purposes

- High PTP (>85%)
  - Diagnosis of SCAD established
    - Proceed to risk stratification
      In patients with severe symptoms or clinical constellation suggesting high risk coronary anatomy initiate guideline-directed medical therapy and offer ICA

This slide corresponds to Figure 1 in the full text
Patients with suspected SCAD and intermediate PTP of 15% - 85%

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

Stress testing for ischaemia

PTP 15-65% and LVEF ≥50%
- Exercise ECG if feasible - stress imaging testing preferred (echo, CMR, SPECT, PET) if local expertise and availability permit

PTP 66-85% or LVEF <50% without typical angina
- Stress imaging (echo, CMR, SPECT, PET); ECG exercise stress testing possible if resources for stress imaging not available

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

Unclear
- Determine patient characteristics and preferences

Ischaemia

No ischaemia
- No stenosis
- Stenosis

Stenosis

Unclear

Diagnosis SCAD established further risk stratification (see Fig. 3)

Ischaemia testing using stress imaging if not done before

2nd (imaging) stress test (if not done before)
Coronary CTA in suitable patient (if not done before)
ICA (with FFR when necessary)

---
a. Consider age of patient versus radiation exposure.
b. In patients unable to exercise use echo or SPECT/PET with pharmacologic stress instead.
c. CMR is only performed using pharmacologic stress.
d. Patient characteristics should make a fully diagnostic coronary CTA scan highly probable (see section 6.2.5.1.2) consider result to be unclear in patients with severe diffuse or focal calcification.
e. Proceed as in lower left coronary CTA box.
f. Proceed as in stress testing for ischaemia box.
CASE 1

- 59y old patient - thoracic discomfort since 3M with intense jogging → cardiologist
- Resting ECG: sinus rhythm, HR 98/min, normal.
- Resting echocardiogram: normal
- Carotid ultrasound: IMT 1,2 mm, otherwise normal

**Exercise ECG:**
- 175 W, HR 160/min
- terminated due to dyspnoea and mild angina
- No ST-segment depression
When is an exercise ECG pathologic?


- Difficult question!
  
  - Scores of clinical and exercise test variables ⇒ superior discrimination compared with using only the ST-segment response to diagnose CAD.
  
  - However, diagnostic interpretation of the exercise test still centers around the ST response, because the clinician remains uncertain about which other variables to apply and how to include them in prediction.
Patients with suspected SCAD and intermediate PTP of 15% - 85%

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

Stress testing for ischaemia
- PTP 15-65%
  - LVEF ≥50%
  - Exercise ECG if feasible - stress imaging testing preferred (echo, CMR, SPECT, PET) if local expertise and availability permit
- PTP 66-85% or LVEF <50% without typical angina
  - Stress imaging (echo, CMR, SPECT, PET); ECG exercise stress testing possible if resources for stress imaging not available
  - Coronary CTA in patients at low intermediate PTP (15% - 50%)
    - If suitable candidate
    - If adequate technology and local expertise available

Non-invasive testing in suspected SCAD with intermediate PTP

a. Consider age of patient versus radiation exposure.
b. In patients unable to exercise use echo or SPECT/PET with pharmacologic stress instead.
c. CMR is only performed using pharmacologic stress.
d. Patient characteristics should make a fully diagnostic coronary CTA scan highly probable (see section 6.2.5.1.2) consider result to be unclear in patients with severe diffuse or focal calcification.
e. Proceed as in lower left coronary CTA box.
f. Proceed as in stress testing for ischaemia box.

This slide corresponds to Figure 2 in the full text.
CASE

● 59y old patient - thoracic discomfort since 3M with intense jogging → cardiologist

● Resting ECG: sinus rhythm, HR 98/min, normal.

● Resting echocardiogram: normal

● Carotid ultrasound: IMT 1,2 mm, otherwise normal

● MIBI-SPECT:
  - 225 W, HR 158/min
  - terminated due to maximal HR reached, RR 205/95
  - No angina, no ST-segment depression
Non-invasive testing in suspected SCAD with intermediate PTP

- Consider age of patient versus radiation exposure.
- In patients unable to exercise use echo or SPECT/PET with pharmacologic stress instead.
- CMR is only performed using pharmacologic stress.
- Patient characteristics should make a fully diagnostic coronary CTA scan highly probable (see section 6.2.5.1.2) consider result to be unclear in patients with severe diffuse or focal calcification.
- Proceed as in lower left coronary CTA box.
- Proceed as in stress testing for ischaemia box.

This slide corresponds to Figure 2 in the full text.
Obstructive Calcified Plaque by CCTA
Extensive Calcifications – No Stenosis
Resting Angina Caused by Epicardial Spasm
CCTA and Calcifications
Specificity of CCTA with Calcifications

Budoff MJ et al. – J Am Coll Cardiol 2008;52:1724–32

- Ca-Score ≤ 400
  - Sensitivity: 95.8%
  - Specificity: 86.3%

- Ca-Score > 400
  - Sensitivity: 93.6%
  - Specificity: 52.6%

p = 0.71 for Sensitivity
p = 0.0003 for Specificity
Characteristics of tests commonly used to diagnose the presence of CAD

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise ECG a, b, c, d, e, f, g, h, i,j,k,l,m,n</td>
<td>45–50</td>
<td>85–90</td>
</tr>
<tr>
<td>Exercise stress echocardiography</td>
<td>80–85</td>
<td>80–88</td>
</tr>
<tr>
<td>Exercise stress SPECT</td>
<td>73–92</td>
<td>63–87</td>
</tr>
<tr>
<td>Dobutamine stress echocardiography</td>
<td>79–83</td>
<td>82–86</td>
</tr>
<tr>
<td>Dobutamine stress MRI</td>
<td>79–88</td>
<td>81–91</td>
</tr>
<tr>
<td>Vasodilator stress echocardiography</td>
<td>72–79</td>
<td>92–95</td>
</tr>
<tr>
<td>Vasodilator stress SPECT</td>
<td>90–91</td>
<td>75–84</td>
</tr>
<tr>
<td>Vasodilator stress MRI</td>
<td>67–94</td>
<td>61–85</td>
</tr>
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<td>Coronary CTA</td>
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<td>64–83</td>
</tr>
<tr>
<td>Vasodilator stress PET</td>
<td>81–97</td>
<td>74–91</td>
</tr>
</tbody>
</table>

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.

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

Test = exercise stress echocardiography
Gold standard = ICA

Strategy:
all pts with positive stress echo ⇒ ICA
all pts with normal stress echo ⇒ no ICA

Result:
all pts with stenosis ⇒ positive stress echo
all pts without stenosis ⇒ positive stress echo

Consequence:
Sensitivity stress echo ⇒ 100%
Specificity ⇒ 0%
### Diagnostic Effectiveness of Exercise ECHO With and Without Adjustment for Referral

<table>
<thead>
<tr>
<th></th>
<th>ECHO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity, % (95% CI)</td>
</tr>
<tr>
<td>Unadjusted*</td>
<td>84 (80 to 89)</td>
</tr>
<tr>
<td>Adjusted†</td>
<td>34 (27 to 41)</td>
</tr>
</tbody>
</table>

ECHO = echocardiography.
*Diagnostic effectiveness based on random-effects meta-analysis of sensitivity and specificity reported in 15 studies of exercise ECHO and 30 studies of exercise MPI (45 studies in total).
†Adjusted for referral rates to cardiac catheterization after abnormal or normal exercise test result.
# Diagnostic Effectiveness of Exercise MPI With and Without Adjustment for Referral

<table>
<thead>
<tr>
<th></th>
<th>MPI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity, % (95% CI)</td>
</tr>
<tr>
<td><strong>Unadjusted</strong></td>
<td>85 (81 to 88)</td>
</tr>
<tr>
<td><strong>Adjusted</strong></td>
<td>38 (31 to 44)</td>
</tr>
</tbody>
</table>

MPI = myocardial perfusion imaging.

*D*Diagnostic effectiveness based on random-effects meta-analysis of sensitivity and specificity reported in 15 studies of exercise ECHO and 30 studies of exercise MPI (45 studies in total).

†Adjusted for referral rates to cardiac catheterization after abnormal or normal exercise test result.
**Guideline SIHD**

**ACC/AHA**

Fihn SD et al. – J Am Coll Cardiol 2012; 60:e44–e164
Guideline SIHD ACC/AHA
Fihn SD et al. – J Am Coll Cardiol 2012; 60:e44–e164

Suspected Ischemic Heart Disease
(or change in clinical status in a patient with known IHD)

‡See Table 2 for short-term risk of death or nonfatal MI in patients with UA/NSTEMI

Intermediate or high-risk UA?‡

Yes

See ACCF/AHA UA/NSTEMI Guideline

No

Comprehensive clinical assessment of risk, including personal characteristics, coexisting cardiac and medical conditions, and health status

Symptoms or findings suggest high-risk lesion(s)‡

OR

Prior sudden death or serious ventricular arrhythmia

OR

Prior stent in unprotected left main coronary artery

Technically adequate? Yes

Recent exercise or cardiac imaging study

No

Contraindications to stress testing?

No

Yes
Guideline SIHD ACC/AHA
Fihn SD et al. – J Am Coll Cardiol 2012; 60:e44–e164
NICE Diagnostic Pathway in Stable Chest Pain

Stable chest pain pathway

2. Diagnostic testing for people in whom stable angina cannot be diagnosed or excluded by clinical assessment alone

- Estimated likelihood of CAD 10 to 29%
  - CT calcium scoring
    - score is zero
      - Investigate other causes of chest pain
    - score is 1-400
      - Follow pathway for 61-90% CAD

- Estimated likelihood of CAD 30-60%
  - Appropriate functional imaging test (see box 5 overleaf)
    - If reversible myocardial ischaemia found, treat as stable angina
    - If not, investigate other causes of chest pain
  - Uncertain
    - Investigate other causes of chest pain

- Estimated likelihood of CAD 61-90%
  - Invasive coronary angiography if appropriate
    - Significant CAD
      - Treat as stable angina
    - Uncertain
      - Appropriate functional imaging test (see box 5 overleaf)
      - Reversible myocardial ischaemia
        - Yes
          - Treat as stable angina
        - No
          - Investigate other causes of chest pain
    - Investigate other causes of chest pain

Box 4 Definition of significant coronary artery disease

- Significant coronary artery disease (CAD) found during invasive coronary angiography is a 70% diameter stenosis of at least one major epicardial artery segment or an 50% diameter stenosis in the left main coronary artery.
  - Factors intensifying ischaemia. Such factors allow less severe lesions (e.g., 50%) to produce angina.
    - Reduced oxygen delivery: anaemia, coronary spasm
    - Increased oxygen demand: tachycardia, left ventricular hypertrophy
    - Large mass of ischaemic myocardium: proximally located lesions
    - Longer lesion length
  - Factors reducing ischaemia. Such factors may render severe lesions (e.g., 70%) asymptomatic.
    - Well developed collateral supply
    - Small mass of ischaemic myocardium: distally located lesions, old infarction in the territory of coronary artery.

- Treat as stable angina

http://www.nice.org.uk/CG95

* If coronary revascularisation is not being considered or invasive coronary angiography is not appropriate or acceptable to the person, offer non-invasive functional imaging

**Consider investigating other causes of angina, such as hypertrophic cardiomyopathy or syndrome X in people with typical angina-like chest pain if investigation excludes flow-limiting disease in the epicardial coronary arteries.
Stable chest pain pathway

2. Diagnostic testing for people in whom stable angina cannot be diagnosed or excluded by clinical assessment alone

Estimated likelihood of CAD 10 to 29%

CT calcium scoring

- Score is zero
- Score is 1 - 400
- Score is more than 400

Follow pathway for 61-90% CAD

- CT coronary angiography
- 64-slice (or above)

Appropriate functional imaging test (see box 5 overleaf). If reversible myocardial ischaemia found, treat as stable angina. If not, investigate other causes of chest pain**

Investigate other causes of chest pain**

Significant CAD

Uncertain

YES

Treat as stable angina

NO

http://www.nice.org.uk/CG95
Testing in Patients with stable AP and 30–60% PTP

- Estimated likelihood of CAD 30-60%
- Appropriate functional imaging test (see box 5 overleaf)
- Reversible myocardial ischaemia
  - NO, Investigate other causes of chest pain **
  - YES, Treat as stable angina
  - Uncertain, Invasive coronary angiography
    - Significant CAD, See box 4
      - YES, Treat as stable angina
      - NO, Investigate other causes of chest pain **

* If coronary revascularisation is not being considered or invasive coronary angiography is not appropriate or acceptable to the person, offer non-invasive functional imaging

**Consider investigating other causes of angina, such as hypertrophic cardiomyopathy or syndrome X in people with typical angina-like chest pain if investigation excludes flow-limiting disease in the epicardial coronary arteries.

http://www.nice.org.uk/CG95
Testing in Patients with stable AP and 61–90% PTP

* If coronary revascularisation is not being considered or invasive coronary angiography is not appropriate or acceptable to the person, offer non-invasive functional imaging.

**Consider investigating other causes of angina, such as hypertrophic cardiomyopathy or syndrome X in people with typical angina-like chest pain if investigation excludes flow-limiting disease in the epicardial coronary arteries.
Summary

● PTP cornerstone of diagnostic algorithms in new guidelines

● Exercise ECG
  - ESC: allowed, not promoted
  - ACC/AHA: promoted
  - NICE: forbidden

● Imaging
  - ESC: stress suggested for all, mandatory in high PTP
  - ACC/AHA: MPI, stress echo promoted, CMR/CCTA restrictive
  - NICE: CTCS mandatory in low PTP, ICA in high PTP

● Referral bias likely to be present in studies determining test characteristics of diagnostic imaging
THE END
What Is A Significant Stenosis?

Box 4 Definition of significant coronary artery disease

Significant coronary artery disease (CAD) found during invasive coronary angiography is ≥ 70% diameter stenosis of at least one major epicardial artery segment or ≥50% diameter stenosis in the left main coronary artery.

a) Factors intensifying ischaemia. Such factors allow less severe lesions (for example ≥50%) to produce angina.

- Reduced oxygen delivery: anaemia, coronary spasm
- Increased oxygen demand: tachycardia, left ventricular hypertrophy
- Large mass of ischaemic myocardium: proximally located lesions
- Longer lesion length

b) Factors reducing ischaemia. Such factors may render severe lesions (≥70%) asymptomatic.

- Well developed collateral supply
- Small mass of ischaemic myocardium: distally located lesions, old infarction in the territory of coronary supply.

http://www.nice.org.uk/CG95
Which test increases the pretest probability for this patient?

Test = Exercise ECG  
(sensitivity ≈ 50%, specificity ≈ 90%)

Pretest probability in this patient = 77%

1000 patients

- CAD: 770
  - Test +: 385
  - Test -: 385

- No CAD: 230
  - Test +: 23
  - Test -: 207

Posttest probability „CAD“ for positive test = 385/408 = 94%  
Posttest probability „No CAD“ for negative test = 207/592 = 35%
### Characteristics of tests commonly used to diagnose the presence of CAD

<table>
<thead>
<tr>
<th>Test</th>
<th>Diagnosis of CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
</tr>
<tr>
<td>Exercise ECG(^{a,91,94,95})</td>
<td>45–50</td>
</tr>
<tr>
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<td>80–85</td>
</tr>
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</tr>
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<td>Coronary CTA(^{c,103-105})</td>
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</table>

\(^{a}\) Results without/with minimal referral bias.
\(^{b}\) Results obtained in populations with medium-to-high prevalence of disease without compensation for referral bias.
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CAD = coronary artery disease; CTA = computed tomography angiography; ECG = electrocardiogram; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single photon emission computed tomography.
Which test increases the pretest probability for this patient?

Test = Exercise stress SPECT  
(sensitivity ≈ 92%, specificity ≈ 87%)

Pretest probability in this patient = 72%

1000 patients

- CAD: 720
  - Test +: 662
  - Test -: 58
- No CAD: 280
  - Test +: 36
  - Test -: 244

Posttest probability „CAD“
for positive test = 662/692 = 96%

Posttest probability „No CAD“
for negative test = 244/302 = 81%
Gold Standard Anatomy or FFR?

Christou MAC et al. – Am J Cardiol 2007; 99:450–456

Meta-analysis of FFR against noninvasive imaging

MPI (15 studies):
976 lesions, sensitivity 75%, specificity 77%.

Stress echo (6 studies):
273 lesions, sensitivity 82%, specificity 74%.