Computed Tomography Coronary Angiography in Patients with Suspected Angina due to Coronary Heart Disease

David Newby

On behalf of the The Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial Investigators
Declarations

Funder

• Chief Scientist Office, Scotland, UK (CZH/4/588)
  • Supplementary awards from Edinburgh and Lothian Health Foundation and the Heart Diseases Research Fund

Sponsors

• University of Edinburgh and NHS Lothian

Conflicts of Interest

• DEN, EvB, GMcK and GR have undertaken consultancy for one or more of the following companies: Toshiba, Bracco, Bayer-Schering, GE Healthcare and Guerbet
Clinic Assessment of Patients with Suspected Angina due to CHD

Fatal and Non-fatal Myocardial Infarction

HR* 6.76 (5.69,8.03), p<0.001
Adjusted HR 3.98 (3.09,5.14), p<0.001

Sekhri et al. Heart 2007;93:458–463
Scottish COnputed Tomography of the HEART (SCOT-HEART) Trial

First trial to assess the clinical impact of the addition of CTCA in patients presenting with suspected angina due to coronary heart disease in the Cardiology clinic

- Diagnosis (Primary Endpoint)
- Investigations
- Treatments
- Outcomes
Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

Diagnosis: Primary Endpoint

Diagnosis of Coronary Heart Disease

Diagnosis of Angina due to Coronary Heart Disease

- Yes
- Probable
- Unlikely
- No

Certainty:
Yes/No versus Probable/Unlikely

Frequency:
Yes/Probable versus Unlikely/No
Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

Entry Criteria

Inclusion Criteria
• Age 18-75 years
• Suspected angina due to coronary heart disease

Exclusion Criteria
• Inability to undergo CT scanning
• Renal failure (estimated GFR <30 mL/min)
• Allergy to contrast media
• Pregnancy
• Acute coronary syndrome within 3 months
• Previous recruitment to the trial

No restriction according to:
• Obesity (65 kg/m²)
• Calcium score (9015 AU)
• Arrhythmia (AF)
The SCOT-HEART Trial
Study Protocol

Primary Care Physician Referral

Clinic Consultation
History, Examination, 12-lead ECG

Exercise ECG if appropriate

Diagnosis, Investigations and Treatment Plan Documented

Approached for Study Inclusion
Angina Questionnaire

Randomised 1:1 to CTCA + Standard Care or Standard Care alone

Computed Tomography
Coronary Angiogram

Cardiovascular Risk Assessment: ASSIGN Score

Result to Attending Clinician

6-Week Attending Clinician Review
Diagnosis, Investigations and Treatment Plan

Clinical Outcome
NHS Health Records

6-Week Patient Review
Angina Questionnaire
Scottish COnputed Tomography of the HEART (SCOT-HEART) Trial

Trial Centers

Complete Health Record Data Capture

One National Healthcare Provider

12 Centers Across Scotland

Perth Royal Infirmary, Perth
Ninewells, Dundee
Victoria Hospital, Kirkcaldy
Forth Valley Hospital, Larbert
Western General Hospital, Edinburgh
Royal Infirmary, Edinburgh
St John’s Hospital, Livingston
Borders General Hospital, Melrose

Royal Alexandra Hospital, Paisley
Western Infirmary, Glasgow
Glasgow Royal Infirmary, Glasgow
University Hospital, Ayr
Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

**Trial Population**

Patients Referred for Evaluation of Suspected Angina due to Coronary Heart Disease  
\[ n = 9,849 \]

Eligible Patients for SCOT-HEART trial  
\[ n = 8,767 \]

Eligible Recruited Patients for SCOT-HEART trial  
\[ n = 4,146 \]

Randomization 1:1  
\[ n = 4,146 \]

Only 11% of All Patients Excluded From the Trial

Ineligible Patients  
\[ n = 1,082 \]

Eligible Non-recruited Patients  
\[ n = 4,621 \]

- Missing: 137
- Patient preference: 2613
- Clinician choice: 547
- Not Approached: 992
- Other: 332

47% of Eligible Patients Recruited Into the Trial
Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

**Trial Population**

Randomization 1:1
- n=4,146

- Standard of Care
  - n=2,073

- Standard of Care + CT Coronary Angiogram
  - n=2,073

- Computed Tomography Coronary Angiogram
  - n=3

- 100% Data for the Primary End-point
- Intention-to-Treat Analysis
  - CT Coronary Angiogram
  - n=1,778

- Data for Primary Endpoint
  - n=2,073

- Data for Primary Endpoint
  - n=2,073

- Non-completion: 295
- Ill-health/death: 6
- Patient default: 245
- Technical: 10
- Other: 34
<table>
<thead>
<tr>
<th><strong>Variable</strong></th>
<th><strong>All Participants</strong></th>
<th><strong>Standard Care + CTCA</strong></th>
<th><strong>Standard Care</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>4146 (100%)</td>
<td>2073 (50%)</td>
<td>2073 (50%)</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>2325 (56%)</td>
<td>1162 (56%)</td>
<td>1163 (56%)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>57±10</td>
<td>57±10</td>
<td>57±10</td>
</tr>
<tr>
<td><strong>Body-mass Index (kg/m²)</strong></td>
<td>30±6</td>
<td>30±6</td>
<td>30±6</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation</strong></td>
<td>84 (2%)</td>
<td>42 (2%)</td>
<td>42 (2%)</td>
</tr>
<tr>
<td><strong>Prior Coronary Heart Disease</strong></td>
<td>372 (9%)</td>
<td>186 (9%)</td>
<td>186 (9%)</td>
</tr>
<tr>
<td><strong>Prior Cerebrovascular Disease</strong></td>
<td>139 (3%)</td>
<td>91 (4%)</td>
<td>48 (2%)</td>
</tr>
<tr>
<td><strong>Prior Peripheral Vascular Disease</strong></td>
<td>53 (1%)</td>
<td>36 (2%)</td>
<td>17 (1%)</td>
</tr>
<tr>
<td><strong>Current or Ex-smoker</strong></td>
<td>2185 (53%)</td>
<td>1095 (53%)</td>
<td>1090 (53%)</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>1395 (34%)</td>
<td>712 (34%)</td>
<td>683 (33%)</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
<td>444 (11%)</td>
<td>223 (11%)</td>
<td>221 (11%)</td>
</tr>
<tr>
<td><strong>Hypercholesterolemia</strong></td>
<td>2176 (53%)</td>
<td>1099 (53%)</td>
<td>1077 (52%)</td>
</tr>
<tr>
<td><strong>Family History</strong></td>
<td>1716 (41%)</td>
<td>887 (43%)</td>
<td>829 (40%)</td>
</tr>
<tr>
<td><strong>Serum Total Cholesterol (mg/dL)</strong></td>
<td>206±46</td>
<td>206±47</td>
<td>206±44</td>
</tr>
<tr>
<td><strong>Serum High-density Lipoprotein Cholesterol (mg/dL)</strong></td>
<td>51±16</td>
<td>51±16</td>
<td>51±16</td>
</tr>
<tr>
<td>Category</td>
<td>All Participants</td>
<td>Standard Care + CTCA</td>
<td>Standard Care</td>
</tr>
<tr>
<td>---------------------------------------</td>
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</tr>
<tr>
<td><strong>Anginal Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typical</td>
<td>1462 (35%)</td>
<td>737 (36%)</td>
<td>725 (35%)</td>
</tr>
<tr>
<td>Atypical</td>
<td>988 (24%)</td>
<td>502 (24%)</td>
<td>486 (23%)</td>
</tr>
<tr>
<td>Non-anginal</td>
<td>1692 (41%)</td>
<td>833 (40%)</td>
<td>859 (41%)</td>
</tr>
<tr>
<td><strong>Electrocardiogram</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3492 (84%)</td>
<td>1757 (85%)</td>
<td>1735 (84%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>608 (15%)</td>
<td>292 (14%)</td>
<td>316 (15%)</td>
</tr>
<tr>
<td><strong>Stress Electrocardiogram</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Performed</td>
<td>3517 (85%)</td>
<td>1764 (85%)</td>
<td>1753 (85%)</td>
</tr>
<tr>
<td>Normal</td>
<td>2188 (62%)</td>
<td>1103 (63%)</td>
<td>1085 (62%)</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>566 (16%)</td>
<td>284 (16%)</td>
<td>282 (16%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>529 (15%)</td>
<td>264 (15%)</td>
<td>265 (15%)</td>
</tr>
<tr>
<td><strong>Further Investigation</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>1315 (32%)</td>
<td>633 (31%)</td>
<td>682 (33%)</td>
</tr>
<tr>
<td><strong>Stress Imaging</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radionuclide</td>
<td>389 (9%)</td>
<td>176 (9%)</td>
<td>213 (10%)</td>
</tr>
<tr>
<td>Other</td>
<td>30 (1%)</td>
<td>16 (1%)</td>
<td>14 (1%)</td>
</tr>
<tr>
<td><strong>Invasive Coronary Angiography</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>515 (12%)</td>
<td>255 (12%)</td>
<td>260 (13%)</td>
</tr>
<tr>
<td><strong>Baseline Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary Heart Disease</td>
<td>1938 (47%)</td>
<td>982 (47%)</td>
<td>956 (46%)</td>
</tr>
<tr>
<td>Angina due to CHD</td>
<td>1485 (36%)</td>
<td>742 (36%)</td>
<td>743 (36%)</td>
</tr>
<tr>
<td><strong>Predicted 10-year Coronary Heart Disease Risk</strong></td>
<td>17±12%</td>
<td>18±11%</td>
<td>17±12%</td>
</tr>
</tbody>
</table>
CT Coronary Angiography

Prevalence of Coronary Heart Disease

Clinicians Reporting CTCA

Diagnosis of Angina due to CHD
- Certainty
  RR 3.76 [95% CI, 3.61-3.89]
- Frequency
  RR 0.78 [95% CI, 0.70-0.86]
CT Coronary Angiography
Safety

**Adverse Reactions & Radiation Dose**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contrast Reactions</td>
<td>13 (0.7%)</td>
</tr>
<tr>
<td>Contrast Extravasation</td>
<td>7 (0.4%)</td>
</tr>
<tr>
<td>Vasovagal Reaction</td>
<td>4 (0.2%)</td>
</tr>
<tr>
<td>Headache</td>
<td>4 (0.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (0.2%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>31 (1.7%)</td>
</tr>
</tbody>
</table>

Median Radiation Dose: 4.1 mSv (Interquartile Range 3.0-5.6)

Dose-length Product: 291 mGy.cm (Interquartile Range 216-397)

37% Radiation Dose Attributable to Coronary Artery Calcium Score
Overall Changes in Diagnosis: 25% versus 1%, P<0.001

Attending Clinician: Diagnosis of Coronary Heart Disease

Certainty | Frequency | Relative Risk [95% Confidence Intervals]
--- | --- | ---
| | | 2.56 [2.33-2.79]
| 1.09 [1.02-1.17]

Attending Clinician: Diagnosis of Angina due to CHD (Primary End-point)

Certainty | Frequency | Relative Risk [95% Confidence Intervals]
--- | --- | ---
| | | 1.79 [1.62-1.96]
| 0.93 [0.85-1.02]
CTCA and Investigations

Baseline Compared to 6 Weeks

Overall Changes in Investigations: 15% versus 1%, P<0.001

Cancellations

CTCA Report in those with cancelled Invasive Coronary Angiogram:

- Normal: 15 (52%)
- Non-obstructive: 9 (31%)
- Obstructive: 5 (17%)
CTCA and Investigations
Baseline Compared to 6 Weeks

Overall Changes in Investigations: 15% versus 1%, P<0.001

New Investigations

CTCA Report in those with new Invasive Coronary Angiogram:

- Normal: 0 (0%)
- Non-obstructive: 11 (12%)
- Obstructive: 79 (88%)

![Graph showing frequency of new investigations with CTCA + Standard Care and Standard Care](chart.png)
CTCA and Medical Therapy
*Baseline Compared to 6 Weeks*

Overall Changes in Treatments: 23% *versus* 5%, *P*<0.001

### Cancellations

- **Preventative Therapy**
- **Anti-Anginal Therapy**
- **All Therapies**

### New Treatments

- **Preventative Therapy**
- **Anti-Anginal Therapy**
- **All Therapies**
CTCA and Symptoms

Baseline Compared to 6 Weeks

No Overall Change in Symptoms at 6 Weeks
Overall Treatment Satisfaction High (92/100) in Both Groups

Seattle Angina Questionnaire

Angina Stability

Baseline  | 6 Weeks

Angina Frequency

Baseline  | 6 Weeks

CTCA + Standard Care  | Standard Care
CTCA and Clinical Outcome
1.7 Years of Follow-up

Fatal and Non-Fatal MI

HR 0.62 [0.38-1.01]
P=0.053

CHD Death, Non-Fatal MI and Non-fatal Stroke

HR 0.64 [0.41-1.01]
P=0.056
CTCA and Clinical Outcome
Coronary Angiography & Revascularisation

Coronary Angiography
HR 1.06 [0.92-1.21], P=0.451

Coronary Revascularisation
HR 1.20 [0.99-1.45], P=0.061
Fatal and Non-fatal MI

Post-hoc 6-Week Landmark Analysis

Diagnostic Delay

Implementation of CTCA Findings

Proportion of patients with an event (%)

Follow Up (years)

HR 0.50 [0.28-0.88]
P=0.015
Conclusions

In patients presenting with suspected angina due to coronary heart disease, the addition of computed tomography coronary angiography

• Clarifies the diagnosis: 1 in 4
• Increases the diagnosis of CHD but appears to reduce the diagnosis of angina due to CHD
• Alters subsequent investigations: 1 in 6
• Changes treatments: 1 in 4
• Does not affect immediate anginal symptoms
• Appears to increase coronary revascularisation and reduce fatal and non-fatal myocardial infarction
Chief Investigator: Prof David Newby. **Trial Research Fellows:** Dr Michelle Williams, Dr Amanda Hunter, Dr Tania Pawade, Dr Anoop Shah.

**Grant Applicants:** Prof David Newby (Principal Applicant), Dr Andrew Flapan, Prof John Forbes, Dr Allister Hargreaves, Prof Stephen Leslie, Dr Steff Lewis, Dr Graham McKillop, Dr Scott McLean, Dr John Reid, Dr James Spratt, Dr Neal Uren.

**Trial Steering Committee:** Prof Adam Timmis (Chair), Prof Colin Berry, Dr Nicholas Boon, Mrs Liz Clark, Dr Peter Craig, Dr Tom Barlow, Dr Marcus Flather, Prof John Forbes, Dr Steff Lewis, Dr Chiara McCormack, Dr Scott McLean, Prof David Newby, Dr Giles Roditi, Prof Edwin van Beek, Dr Michelle Williams, Dr Amanda Hunter, Mrs Susan Shepherd, Ms Marise Bucukoglu.

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**St John’s Hospital, Livingston:** Dr Ashok Jacob, Mrs Fiona Bett, Mrs Frances Divers, Ms Katie Fairley, Ms Edith Keegan, Ms Tricia White, Ms Julia Fowler

**University Hospital, Ayr:** Dr John Gemmill, Dr James McGowan, Mrs Margo Henry

**Victoria Hospital, Kirkcaldy:** Dr Mark Francis, Mr Dennis Sandeman Ms Lorraine Dinnel

**Western General Hospital, Edinburgh:** Prof David Newby Dr Peter Bloomfield, Dr Martin Denvir, Dr Peter Henriksen, Dr Donald MacLeod, Mrs Avril Morrison

**Western Infirmary, Glasgow & Institute of Cardiovascular & Medical Sciences, University of Glasgow:** Prof Colin Berry, Dr Kenneth Mangion, Dr Ify Mordi, Dr Giles Roditi, Dr Nikolaos Tzemos, Dr Eugene Connolly, Mrs Heather Boylan, Mrs Ammani Brown, Ms Lesley Farrell, Mrs Alison Froom, Ms Caroline Glover, Mrs Janet Johnstone, Mrs Tracey Steedman, Mrs Kirsten Lanaghan, Mrs Deborah McGlynn, Ms Lorraine McGregor, Ms Evonne McLennan, Ms Laura Murdoch, Miss Victoria Paterson, Ms Fiona Teyhan, Ms Marion Teenan, Ms Rosie Woodward

**Borders General Hospital, Melrose:** Dr Paul Neary Mrs Gillian Donaldson, Mr Terry Fairbairn, Mrs Marlene Fotheringham, Mrs Fiona Hall.

**Forth Valley Royal Hospital, Larbert:** Dr Allister Hargreaves, Dr James Spratt, Dr Stephen Glen, Ms Sarah Perkins, Ms Fiona Taylor Mrs Louisa Cram, Ms Catherine Beveridge, Ms Avril Cairns, Ms Frances Dougherty

**Glasgow Royal Infirmary:** Dr Hany Eteiba, Dr Alan Rae, Ms Kate Robb, Ms Wenda Crawford, Ms Patricia Clarkin, Ms Elizabeth Lennon

**Ninewells Hospital, Dundee:** Prof. Graeme Houston, Prof Stuart Pringle, Dr Prasad Guntur Ramkumar, Dr Thiru Sudarshan, Dr Yvonne Fogarty, Ms Dawn Barrie, Ms Kim Bissett, Dr Adelle Dawson, Mr Scott Dunas, Mrs Deborah Letham, Ms Linda O’Neill, Mrs Valerie Ritchie.

**Perth Royal Infirmary, Perth:** Dr Hamish Dougall

**Royal Alexandra Hospital, Paisley:** Dr Faheem Ahmed, Dr Alistair Cormack, Dr Iain Findlay, Dr Stuart Hood, Dr Clare Murphy, Dr Eileen Peat, Ms Lynne McCabe, Ms Margaret McCubbin.
CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open label, parallel group multicentre trial

The SCOT-HEART Investigators

Summary

Background The benefit of CT coronary angiography (CTCA) in patients presenting with stable chest pain has not been systematically studied. We aimed to assess the effect of CTCA on the diagnosis, management, and outcome of patients referred to the cardiology clinic with suspected angina due to coronary heart disease.

Methods In this prospective open-label, parallel group multicentre trial, we recruited patients aged 18–75 years referred for the assessment of suspected angina due to coronary heart disease from 12 cardiology chest pain clinics across Scotland. We randomly assigned (1:1) participants to standard care plus CTCA or standard care alone. Randomisation was done with a web-based service to ensure allocation concealment. The primary endpoint was certainty of the diagnosis of angina secondary to coronary heart disease at 6 weeks. All analyses were intention-to-treat, and patients were analysed in the group they were allocated to, irrespective of compliance with scanning. This study is registered with ClinicalTrials.gov, number NCT01149590.

Findings Between Nov 18, 2010, and Sept 24, 2014, we randomly assigned 4146 (42%) of 9849 patients who had been referred for assessment of suspected angina due to coronary heart disease. 47% of participants had a baseline clinic diagnosis of coronary heart disease and 36% had angina due to coronary heart disease. At 6 weeks, CTCA reclassified the diagnosis of coronary heart disease in 558 (27%) patients and the diagnosis of angina due to coronary heart disease in 481 (23%) patients (standard care 22 [1%] and 23 [1%]; p<0.0001). Although both the certainty (relative risk [RR] 2.56, 95% CI 2.33–2.79; p<0.0001) and frequency of coronary heart disease increased (1.09, 1.02–1.17; p=0.0172), the certainty increased (1.79, 1.62–1.96; p<0.0001) and frequency seemed to decrease (0.93, 0.85–1.02; p=0.1289) for the diagnosis of angina due to coronary heart disease. This changed planned investigations (15% vs 1%; p<0.0001) and treatments (23% vs 5%; p<0.0001) but did not affect 6-week symptom severity or subsequent admissions to hospital for chest pain. After 1.7 years, CTCA was associated with a 38% reduction in fatal and non-fatal myocardial infarction (26 vs 42, HR 0.62, 95% CI 0.38–1.01; p=0.0527), but this was not significant.

Interpretation In patients with suspected angina due to coronary heart disease, CTCA clarifies the diagnosis, enables targeting of interventions, and might reduce the future risk of myocardial infarction.

Funding The Chief Scientist Office of the Scottish Government Health and Social Care Directorates (CZH/4/588) funded the trial with supplementary awards from Edinburgh and Lothian’s Health Foundation Trust and the Heart Diseases Research Fund.