

## Diagnostic studies

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Beygui 2000<sup>22</sup></b></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1995 – Dec 1996  <b>Country:</b> France  <b>Focus:</b> Diagnostic values of ExECG and SPECT in asymptomatic patients and the discordance between follow-up functional tests and CA</p>	<p><b>Inclusion criteria:</b> Asymptomatic patients with ExECG, SPECT and CA 6 ± 2 months after PTCA. All patients were symptomatic before PTCA.  <b>Exclusion criteria:</b> Patients unable to undergo ExECG, or those with rest ECG abnormalities receiving pharmacologic stress  <b>Enrolled:</b> 179</p> <p><b>Analysed:</b> 179  <b>Age:</b> 61 ± 10  <b>Gender:</b> M 154, W 25  <b>History of:</b> MI 8; PTCA 179; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Qualitative.  <b>Equipment:</b> APEX SPX-4 HR (Elsint, Haifa, Israel) gamma camera.  <b>CA methods:</b> Judkins technique  <b>Interval between tests:</b> ECG/SPECT 1-7 days before CA  <b>Definition of positive SPECT test:</b> Qualitative analysis using a 0 to 4 scale (0 = normal, 4 = severe reduction in Tl-201 uptake). Exercise perfusion defect: segment with a score of ≥ 2. Ischaemia: minimal improvement of 1 point on a visual scale. Presence of restenosis: ischaemic redistribution in the territory of individual vessels, guided by a pre-PTCA angiogram.  <b>Definition of positive stress ECG test:</b> ≥ 0.1mV ST-segment depression with or without chest pain.  <b>Angiographic definition of significant CAD:</b> Restenosis: &gt; 50% diameter stenosis  <b>Outcome measures:</b> Sensitivity, specificity, positive predictive value, negative predictive value, accuracy for restenosis</p>
<p><b>Chae 1993<sup>23</sup></b></p> <p><b>Study design:</b> Retrospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Country:</b> USA  <b>Focus:</b> Ability of SPECT to identify high risk women with left main or 3 vessel CAD</p>	<p><b>Inclusion criteria:</b> Women who underwent SPECT within 3 months of CA  <b>Exclusion criteria:</b> History of previous CABG, recent MI, unstable angina pectoris, valvular heart disease and congenital heart disease  <b>Enrolled:</b> 243</p> <p><b>Analysed:</b> 243  <b>Age:</b> Grp 1 65 ± 11, Grp 2 61 ± 10  <b>Gender:</b> M 0, W 243  <b>History of:</b> MI 103; PTCA N/S; CABG excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual, quantitative.  <b>Equipment:</b> Large field of view gamma camera  <b>CA methods:</b> Performed in multiple projections using standard techniques  <b>Interval between tests:</b> ECG/SPECT performed within 3 months of CA  <b>Definition of positive SPECT test:</b> Perfusion pattern in each vascular territory assessed as normal or with fixed or reversible abnormalities. Multivessel abnormality: &gt;1 vascular territory involved. Quantitative analysis: perfusion abnormality – pixels with counts 2.5 SD below the mean normal value obtained from low risk women; extent – percent of total myocardium.  <b>Definition of positive stress ECG test:</b> ≥ 1mm ST segment depression of the flat or downsloping variety in ≥ 3 consecutive beats at 8ms after the J point or ≥ 1.5mm upsloping ST segment depression. Patients with baseline ST abnormalities, additional 2-mm ST depression in the leads showing changes at baseline.  <b>Angiographic definition of significant CAD:</b> ≥ 50% diameter stenosis  <b>Outcome measures:</b> Sensitivity, specificity</p>

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<p><b>Daou 2002<sup>24</sup></b></p> <p><b>Study design:</b> Prospective observational comparison</p> <p><b>Method of recruitment:</b> Consecutive</p> <p><b>Dates:</b> N/S</p> <p><b>Country:</b> France</p> <p><b>Focus:</b> Values of SPECT, indirect scintigraphic markers of extensive CAD and total MPD criteria; additive value above clinical and stress test variables, for the diagnosis of extensive CAD</p>	<p><b>Inclusion criteria:</b> Patients referred for SPECT who had CA within 3 months of SPECT</p> <p><b>Exclusion criteria:</b> Valvular heart disease, cardiomyopathy, complete LBBB, atrial fibrillation, pacemaker, severe hypertension, advanced chronic bronchopulmonary disease, prior CABG or PTCA, dialysis, or intervening acute coronary event between SPECT and CA</p> <p><b>Enrolled:</b> 338</p> <p><b>Analysed:</b> 310 (pilot group; limited CAD 38, extensive CAD 122, validation group; limited CAD 32, extensive CAD 118)</p> <p><b>Age:</b> Pilot group limited CAD 57 ± 10, pilot group extensive CAD 61 ± 9, validation group limited CAD 59 ± 12, validation group extensive CAD 60 ± 10</p> <p><b>Gender:</b> M 282, W 28</p> <p><b>History of:</b> MI 202; PTCA excluded; CABG excluded</p>	<p><b>SPECT:</b></p> <p><b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise. <b>Image interpretation:</b> Visual. <b>Equipment:</b> Elscint 1-head gamma camera (Hackensack, NJ).</p> <p><b>CA methods:</b> N/S</p> <p><b>Interval between tests:</b> within a 3 month period</p> <p><b>Definition of positive SPECT test:</b> Abnormalities in ≥ 2 vascular territories</p> <p><b>Definition of positive stress ECG test:</b> Downsloping or horizontal ST-segment depression of ≥ 1mm or upsloping ST depression of ≥ 2mm measured 80ms after the J point</p> <p><b>Angiographic definition of significant CAD:</b> ≥ 50% diameter stenosis</p> <p><b>Outcome measures:</b> Sensitivity, specificity, accuracy, incremental value (multivariable logistic regression analysis)</p>

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<p><b>De 2002</b><sup>25</sup></p> <p><b>Study design:</b> Retrospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Feb 1997 – Dec 2000  <b>Country:</b> Canada  <b>Focus:</b> Rate of CAD in women &lt;45 years referred for chest pain; prevalence of cardiac risk factors; the role of non-invasive testing and the quality of medical management</p>	<p><b>Inclusion criteria:</b> Women &lt;45 years referred for CA because of chest pain that had not yet been diagnosed  <b>Exclusion criteria:</b> Known history of CAD  <b>Enrolled:</b> 187  <b>Analysed:</b> 187  <b>Age:</b> &lt;45 years  <b>Gender:</b> M 0, W 187  <b>History of:</b> MI N/S; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> N/S. <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S  <b>CA methods:</b> N/S  <b>Interval between tests:</b> SPECT/ECG within 6 months before CA  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> <math>\geq 70\%</math> diameter stenosis in <math>\geq 1</math> coronary artery  <b>Outcome measures:</b> Sensitivity, specificity</p>
<p><b>Gentile 2001</b><sup>26</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Jan 1990 – Dec 1998  <b>Country:</b> Italy  <b>Focus:</b> Diagnostic accuracy and prognostic significance of stress ECG and SPECT in an elderly population</p>	<p><b>Inclusion criteria:</b> Patients aged &gt;65 years hospitalised because of cardiac events  <b>Exclusion criteria:</b> Previous MI, revascularisation, significant valvular disease, idiopathic dilated cardiomyopathy, LBBB, equivocal ECG or SPECT, or borderline lesion of a single vessel.  <b>Enrolled:</b> 195  <b>Analysed:</b> 132  <b>Age:</b> M 72.4 (range 62-to 76), W 68.2 (range 65 to 73)  <b>Gender:</b> M 90, W 42  <b>History of:</b> MI excluded; PTCA excluded; CABG excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle), pharmacologically (dipyridamole). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Rotating large field gamma camera (Starcam 2000, G.E., Milwaukee, WI, USA).  <b>CA methods:</b> Judkins technique  <b>Interval between tests:</b> CA performed within 2 weeks of ECG/SPECT  <b>Definition of positive SPECT test:</b> An area of decreased activity seen during the peak stress that resolved, either partially or totally, during redistribution  <b>Definition of positive stress ECG test:</b> &gt; 1mm horizontal or downsloping depression of the ST segment 0.08s after the J point  <b>Angiographic definition of significant CAD:</b> Obstruction of 60% of lumen diameter.  <b>Outcome measures:</b> Sensitivity, specificity, true positives for 1, 2 and 3 vessel disease. Sensitivity, specificity, true and false positives and negatives, and accuracy by gender and overall</p>

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<p><b>Hamasaki 1996</b><sup>27</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Oct 1988 – Sept 1994  <b>Country:</b> Japan  <b>Focus:</b> Clinical usefulness of the increase in the <math>\Delta ST/\Delta HR</math> index from several days after angioplasty to follow-up for detection of restenosis after successful PTCA</p>	<p><b>Inclusion criteria:</b> Patients with single-vessel CAD, no prior MI, positive ExECG and SPECT, receiving antianginal therapy, previous PTCA and consent to 1) undergo ExECG after PTCA; 2) follow-up CA; 3) able to perform maximal exercise; and 4) ability to achieve <math>\geq 85\%</math> of the maximum age-predicted HR in the absence of diagnostic ECG.  <b>Exclusion criteria:</b> L or R BBB or non-specific intraventricular block patterns on resting ECG, taking digitalis or <math>\beta</math>-blocking agents  <b>Enrolled:</b> 125</p> <p><b>Analysed:</b> 125  <b>Age:</b> <math>64 \pm 9</math>  <b>Gender:</b> M 95, W 30  <b>History of:</b> MI excluded; PTCA 125; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Gamma camera (ZLC-75; Shimadzu, Kyoto, Japan)  <b>CA methods:</b> N/S  <b>Interval between tests:</b> CA performed <math>7.5 \pm 3.6</math> days after SPECT and <math>5.4 \pm 1.3</math> days after ECG  <b>Definition of positive SPECT test:</b> Perfusion defect on stress study absent on redistribution images, or defect on stress study larger than on redistribution study  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression of <math>\geq 0.10</math>mV and an upsloping ST-segment depression of <math>\geq 0.20</math>mV measured 60ms after the J point compared with the resting value  <b>Angiographic definition of significant CAD:</b> Restenosis: increase in stenosis to <math>&gt; 60\%</math> diameter  <b>Outcome measures:</b> Sensitivity, specificity, positive predictive value, negative predictive value, true and false positives and negative.</p>
<p><b>Hambÿe 1996</b><sup>28</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Country:</b> Belgium  <b>Focus:</b> Incremental value of testing strategies for diagnosis of CAD in patients with an intermediate probability of CAD</p>	<p><b>Inclusion criteria:</b> Patients referred for suspected or known CAD  <b>Exclusion criteria:</b> History of MI, abnormal Q wave on the 12-lead ECG, LBBB, valvular or congenital heart disease, severe arrhythmias, or non-ischaemic cardiomyopathy  <b>Enrolled:</b> 128</p> <p><b>Analysed:</b> 128  <b>Age:</b> <math>60 \pm 9.2</math> (range 34 to 80)  <b>Gender:</b> M 90, W 38  <b>History of:</b> MI excluded; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual, quantitative. <b>Equipment:</b> Single-head rotating gamma camera, 40cm detector size (Orbiter Digitrac 7500; Siemens, Chicago, Ill.) or a triple-head camera, 40x20cm detector size.  <b>CA methods:</b> Performed in multiple views according to standard techniques  <b>Interval between tests:</b> CA performed within 2 months of ECG/SPECT  <b>Definition of positive SPECT test:</b> Reduced tracer uptake in <math>\geq 2</math> contiguous slices on two different orthogonal projections on the stress study that disappeared or improved by <math>\geq 10\%</math> on a colour scale on the rest image  <b>Definition of positive stress ECG test:</b> Presence of clinical symptoms (typical angina, atypical chest pain, nonanginal pain, or miscellaneous) and ECG findings (significant changes, dubious results, no changes)  <b>Angiographic definition of significant CAD:</b> <math>\geq 50\%</math> stenosis of <math>\geq 1</math> major epicardial coronary arteries or main side branches; <math>\geq 70\%</math> stenosis.  <b>Outcome measures:</b> Sensitivity, Specificity</p>

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<p><b>Hecht 1990<sup>29</sup></b></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Country:</b> USA  <b>Focus:</b> Detection of restenosis after PTCA and differentiation from other sources of myocardial ischaemia</p>	<p><b>Inclusion criteria:</b> Patients referred for possible restenosis receiving SPECT and CA  <b>Exclusion criteria:</b> N/S  <b>Enrolled:</b> 116</p> <p><b>Analysed:</b> 116  <b>Age:</b> 58 ± 9  <b>Gender:</b> M 93, W 23  <b>History of:</b> MI 49; PTCA 116; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual, quantitative.  <b>Equipment:</b> Siemens Orbiter large field-of-view tomographic camera  <b>CA methods:</b> Judkins or Sones approach  <b>Interval between tests:</b> ECG/SPECT 1 week before CA  <b>Definition of positive SPECT test:</b> Each segment scored on a 0 to 4 scale. Scores of ≥ 2 (mildly reduced uptake) abnormal. Myocardial ischaemia was categorized as either total or partial normalization of a segment from exercise to redistribution imaging  <b>Definition of positive stress ECG test:</b> ≥ 1mm of horizontal or downsloping ST depression for ≥ 0.08 second after the J point compared with the resting tracing  <b>Angiographic definition of significant CAD:</b> Restenosis; return of previously dilated vessel to a ≥ 50% diameter reduction  <b>Outcome measures:</b> Sensitivity, specificity and accuracy for all, complete/partial revascularisation</p>
<p><b>Huang 1992<sup>30</sup></b></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Country:</b> Taiwan  <b>Focus:</b> Accuracy of SPECT in diagnosis of CAD; the extent the level of exercise affects the sensitivity of the test</p>	<p><b>Inclusion criteria:</b> Patients with chest pain receiving CA and SPECT  <b>Exclusion criteria:</b> Cardiomyopathy, valvular or congenital heart disease  <b>Enrolled:</b> 179</p> <p><b>Analysed:</b> 179  <b>Age:</b> Grp 1 58 ± 9, Grp 2 57 ± 9; Control 56  <b>Gender:</b> M 144, W 35  <b>History of:</b> MI 70; PTCA 0; CABG 0</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Computerized dual-head imaging system (Picker International).  <b>CA methods:</b> Judkins' technique  <b>Interval between tests:</b> ECG/SPECT within 2 months of CA  <b>Definition of positive SPECT test:</b> ≥ 50% decrease of thallium uptake in ≥ 2 contiguous slices and ≥ 2 tomographic planes  <b>Definition of positive stress ECG test:</b> A horizontal or down-sloping ST-segment depression of ≥ 1mm or upsloping depression of ≥ 1.5mm, persisting ≥ 0.08 second after the J point  <b>Angiographic definition of significant CAD:</b> ≥ 50% stenosis in ≥ 1 major coronary artery  <b>Outcome measures:</b> Sensitivity, specificity, true and false positives and negatives. SPECT sensitivity for 1, 2 and 3 vessel CAD for all patients and those without MI, SPECT sensitivity for individual coronary artery stenosis</p>

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<p><b>Kajinami 1995<sup>31</sup></b></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> May 1991 – May 1993  <b>Country:</b> Japan  <b>Focus:</b> Usefulness of electron beam computed tomography, ECG and SPECT for prediction of coronary stenosis</p>	<p><b>Inclusion criteria:</b> Patients receiving elective CA and 1) chest pain suggesting angina pectoris, or 2) possible myocardial ischaemia based on rest ECG  <b>Exclusion criteria:</b> Patients in unstable condition, previous CABG or PTCA, abnormal Q waves in <math>\geq 2</math> ECG leads  <b>Enrolled:</b> 251  <b>Analysed:</b> 251  <b>Age:</b> <math>56 \pm 14</math> (range 16 to 86)  <b>Gender:</b> M 174, W 77  <b>History of:</b> MI N/S; PTCA excluded; CABG excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Rotating gamma-camera SNC-510R (Shimadzu Co., Kyoto, Japan)  <b>CA methods:</b> Performed in multiple projections using standard techniques  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> Abnormal area in the initial images demonstrating complete or partial redistribution in the delayed images .  <b>Definition of positive stress ECG test:</b> 1) <math>\geq 0.1</math>mV depression 0.08s from the J point, or 2) <math>\geq 0.1</math>mV elevation in a non Q-wave lead in those without previous MI  <b>Angiographic definition of significant CAD:</b> <math>\geq 75\%</math> occlusion in major coronary artery  <b>Outcome measures:</b> Sensitivity, specificity, positive predictive value, negative predictive value, accuracy</p>
<p><b>Karlsson 1995<sup>32</sup></b></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Country:</b> Sweden  <b>Focus:</b> Additional value of SPECT one month after an episode of unstable CAD over conventional ExECG for the identification of severe coronary lesions at CA</p>	<p><b>Inclusion criteria:</b> Men 40-70 years; ongoing chest or angular pain during the last 48 hours; occurrence of earlier unknown ST-depression <math>\geq 0.1</math>mV or T wave inversion by <math>&gt; 0.1</math>mV in <math>\geq 2</math> adjacent leads in rest ECG  <b>Exclusion criteria:</b> Increase risk of bleeding; indication for thrombolysis; acute Q wave MI; Q wave in <math>\geq 2</math> adjacent precordial leads or LBBB in ECG at rest; left ventricular failure; valvular heart disease; cardiomyopathy, pacemaker; CABG; poor short-term prognosis; or logistic difficulties with investigations or follow-up  <b>Enrolled:</b> 205  <b>Analysed:</b> 170  <b>Age:</b> 59  <b>Gender:</b> M 170, W 0  <b>History of:</b> MI 14%; PTCA N/S; CABG excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Qualitative.  <b>Equipment:</b> Siemens Rotacamera (Siemens AC, The Netherlands) or Picker SX300 gamma-camera (Picker International Inc, Ohio, USA)  <b>CA methods:</b> Judkins technique  <b>Interval between tests:</b> CA performed 1 day after ECG/SPECT  <b>Definition of positive SPECT test:</b> Left ventricular myocardium divided into 9 segments. Each segment classified as: 0 = normal uptake, 1 = reduced uptake, 2 = uptake defect. SPECT score = summation of score from all segments.  <b>Definition of positive stress ECG test:</b> ST segment depression <math>\geq 0.1</math>mV 0.06s after the J point  <b>Angiographic definition of significant CAD:</b> <math>\geq 50\%</math> occlusion. Severe lesions defined as left main stenosis, 3 vessel disease, or 2 vessel disease with proximal LAD stenosis before first diagonal branch  <b>Outcome measures:</b> Sensitivity, specificity</p>

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<p><b>Khattar 1998</b><sup>33</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Country:</b> UK  <b>Focus:</b> SPECT and/or echocardiography for detection of multivessel disease versus clinical and ExECG data alone</p>	<p><b>Inclusion criteria:</b> Patients with chest pain undergoing ExECG and subsequent CA  <b>Exclusion criteria:</b> Unstable angina, significant arrhythmias, heart failure, uncontrolled hypertension, MI within 30 days, cardiomyopathy, significant valvular disease  <b>Enrolled:</b> 100  <b>Analysed:</b> 100  <b>Age:</b> 62.2 (8.9)  <b>Gender:</b> M 70, W 30  <b>History of:</b> MI 29; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (treadmill) for ECG, pharmacologically (dobutamine, arbutamine) for SPECT. <b>Image interpretation:</b> Semiquantitative. <b>Equipment:</b> Large field of view gamma camera  <b>CA methods:</b> Judkins technique  <b>Interval between tests:</b> CA performed within 3 months of SPECT/ECG  <b>Definition of positive SPECT test:</b> Resting or stress induced perfusion defect, multivessel disease if abnormalities in <math>\geq 2</math> coronary artery territories at peak stress  <b>Definition of positive stress ECG test:</b> Multivessel disease: 1. ST depression <math>\geq 2</math>mm, ST depression <math>\geq 1</math>mm in <math>\geq 5</math> leads; 2. workload <math>&lt; 6</math> MET; or 3. fall of systolic blood pressure <math>&gt; 20</math>mm Hg compared to the previous stage  <b>Angiographic definition of significant CAD:</b> <math>\geq 50\%</math> stenosis, multivessel disease if <math>\geq 2</math> major coronary arteries involved  <b>Outcome measures:</b> Sensitivity, specificity and accuracy for detecting multivessel disease in the total study group and excluding previous MI, incremental value</p>
<p><b>Koskinen 1987</b><sup>34</sup></p> <p><b>Study design:</b> Retrospective observational comparison  <b>Method of recruitment:</b> N/S  <b>Dates:</b> 1983 to 1984  <b>Country:</b> Finland  <b>Focus:</b> SPECT versus CA</p>	<p><b>Inclusion criteria:</b> Patients receiving SPECT and CA  <b>Exclusion criteria:</b> CABG between CA and SPECT, patients whose imaging data had not been stored on magnetic tape, required stress level not achieved  <b>Enrolled:</b> 117  <b>Analysed:</b> 117  <b>Age:</b> Proximal 3 vd 50.1, peripheral 3 vd 49.1, peripheral 2 vd 49.1, peripheral 1 vd 47.6, CA healthy vessels 48.8, reference group 52.1, range 33-64  <b>Gender:</b> N/S  <b>History of:</b> MI N/S; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> N/S. <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S  <b>CA methods:</b> N/S  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> Vessels with a 50% stenosis  <b>Outcome measures:</b> Sensitivity and specificity</p>

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<p><b>Lind 1990</b><sup>35</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Country:</b> Austria  <b>Focus:</b> SPECT versus ExECG for detection of silent myocardial ischaemia in patients with vascular risk factors</p>	<p><b>Inclusion criteria:</b> Patients showing vascular risk factors, pathologic ergometric findings without angina or signs of silent MI in the resting ECG  <b>Exclusion criteria:</b>  <b>Enrolled:</b> 106</p> <p><b>Analysed:</b> 106  <b>Age:</b> Grp I 55 ± 10, Grp II 60 ± 9  <b>Gender:</b> Grp I M 38, W 8, Grp II M 43, W 17  <b>History of:</b> MI N/S; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Elscint Apex 409 AG rotating gamma camera  <b>CA methods:</b> Judkins  <b>Interval between tests:</b> Maximum of 14 days between SPECT/ECG and CA  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> &gt;75% coronary stenosis  <b>Outcome measures:</b> Sensitivity, specificity plus true and false positives and negatives for ECG.</p>
<p><b>Mairesse 1994</b><sup>36</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Country:</b> Belgium  <b>Focus:</b> Optimal ECG criteria for the diagnosis of CAD in association with dobutamine stress by use of precise computer measurements and compare their accuracy with those of stress echocardiography and MPS</p>	<p><b>Inclusion criteria:</b> Patients referred for diagnostic CA  <b>Exclusion criteria:</b> Clinical history or ECG evidence of previous Q wave MI, unstable angina, malignant arrhythmias, cardiomyopathy, severe valvular disease or severe hypertension, stress test interrupted prematurely, or uninterpretable ECG  <b>Enrolled:</b> 129</p> <p><b>Analysed:</b> 129  <b>Age:</b> 56 ± 9 (range 31-78)  <b>Gender:</b> M 95, W 34  <b>History of:</b> MI (Q wave) excluded; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Pharmacologically (dobutamine). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Large-field single-crystal camera.  <b>CA methods:</b> Judkins technique  <b>Interval between tests:</b> CA within 2 days of stress ECG/SPECT  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> Empiric ROC based on 0.2 to 1.8mm of absolute ST segment shift of peak stress to define CAD at 0, 20, 40, 60 and 80 ms after the J point.  <b>Angiographic definition of significant CAD:</b> &gt;50% stenosis of major epicardial coronary segment  <b>Outcome measures:</b> Sensitivity, specificity, accuracy, true and false positives and negatives, sensitivity for 1 vessel disease and multivessel disease.</p>



Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>McClellan 1996</b><sup>37</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Country:</b> USA  <b>Focus:</b> 1. Use of SPECT in a community hospital; 2. Accuracy and additive value of SPECT versus ExECG.</p>	<p><b>Inclusion criteria:</b> Patients referred for treadmill exercise testing with SPECT. Indications for SPECT: diagnosis of CAD; evaluation and follow-up of patients with known CAD; and evaluation after MI, PTCA and CABG  <b>Exclusion criteria:</b>  <b>Enrolled:</b> 492  <b>Analysed:</b> 492  <b>Age:</b> 58.9 (range 22 to 82)  <b>Gender:</b> M 322, W 179  <b>History of:</b> MI 170; PTCA 123; CABG 103</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual, quantitative.  <b>Equipment:</b> Rotating large field of view camera (GE 400 AC)  <b>CA methods:</b> N/S  <b>Interval between tests:</b> CA performed within 3 months of SPECT/EC  <b>Definition of positive SPECT test:</b> Presence of exercise-induced defects and partial, complete or absence of redistribution on delayed images  <b>Definition of positive stress ECG test:</b> Normal resting ECG and <math>\geq 0.1</math>mV horizontal or downsloping depression during exercise  <b>Angiographic definition of significant CAD:</b> <math>\geq 50\%</math> stenosis in <math>\geq 1</math> coronary artery  <b>Outcome measures:</b> True and false positives and negatives, specificity, positive predictive value, diagnostic accuracy</p>
<p><b>Michaelides 1999</b><sup>38</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Country:</b> Greece  <b>Focus:</b> Sensitivity of exercise testing in the detection of CAD using right precordial leads V<sub>3</sub>R, V<sub>4</sub>R and V<sub>5</sub>R and left precordial leads</p>	<p><b>Inclusion criteria:</b> Patients Referred to hospital with symptoms resembling angina  <b>Exclusion criteria:</b> R or LBBB, R or LVH, ventricular pre-excitation, history of MI or valvular or congenital heart disease, CABG or PTCA, and those receiving digitalis and those refusing CA.  <b>Enrolled:</b> 268  <b>Analysed:</b> 245  <b>Age:</b> 52 <math>\pm</math> 8 (range 32 to 74)  <b>Gender:</b> M 218, W 27  <b>History of:</b> MI excluded; PTCA excluded; CABG excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Qualitatively, quantitatively. <b>Equipment:</b> model 400 AC/T, General Electric, Milwaukee  <b>CA methods:</b> Judkins technique  <b>Interval between tests:</b> CA within 2 months after ECG/SPECT  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression of <math>\geq 1</math>mm 60msec after the J point; upsloping ST segment with a depression of <math>\geq 1.5</math>mm 80msec after the J point. In the presence of ST-segment depression at rest, an additional 2mm of ST-segment depression; or an ST-segment elevation of <math>\geq 1</math>mm at the J point as compared with the base-line ECG recorded at rest  <b>Angiographic definition of significant CAD:</b> narrowing of <math>\geq 70\%</math> of the diameter of the lumen in the LAD, LCX, or RCA or narrowing of <math>\geq 50\%</math> of the diameter of the lumen in the left main coronary artery  <b>Outcome measures:</b> Overall sensitivity and specificity plus sensitivity for 1, 2 and 3 vessel disease, any CAD and LAD, RCA and LCX for single vessel disease.</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Nallamothe 1995<sup>39</sup></b></p> <p><b>Study design:</b> Retrospective observational comparison</p> <p><b>Method of recruitment:</b> Identified from complete database according to inclusion criteria</p> <p><b>Dates:</b> N/S</p> <p><b>Country:</b> USA</p> <p><b>Focus:</b> 1. Diagnostic accuracy of SPECT and ExECG response in patients with normal baseline ECG results; 2. Differences in ability of each method to identify high risk patients with extensive CAD</p>	<p><b>Inclusion criteria:</b> Patients with 1. SPECT and CA within 3 months of each other; 2. normal baseline ECG results (no evidence of previous MI, conducting defects, ST-T wave changes, pre-excitation or pacemaker rhythm)</p> <p><b>Exclusion criteria:</b> Patients taking digitalis</p> <p><b>Enrolled:</b> 321</p> <p><b>Analysed:</b> 321</p> <p><b>Age:</b> 57 ± 10</p> <p><b>Gender:</b> M 241, W 80</p> <p><b>History of:</b> MI N/S; PTCA 0; CABG 0</p>	<p><b>SPECT:</b></p> <p><b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual, quantitative.</p> <p><b>Equipment:</b> N/S</p> <p><b>CA methods:</b> Performed in multiple projections using standard techniques</p> <p><b>Interval between tests:</b> Stress ECG was part of SPECT test, CA within 3 months</p> <p><b>Definition of positive SPECT test:</b> Presence and nature (fixed or reversible) of perfusion defects, site (vascular territory) of perfusion abnormality, size of perfusion defect (by polar maps), lung thallium uptake and left ventricular dilation. Multivessel thallium abnormalities were considered present when there were perfusion defects in &gt; 1 vascular territory</p> <p><b>Definition of positive stress ECG test:</b> ≥ 1mm downsloping or horizontal or ≥ 1.5mm upsloping ST segment depression measured at 80ms after the J point for ≥ 3 consecutive beats during or after exercise</p> <p><b>Angiographic definition of significant CAD:</b> ≥ 50% diameter narrowing in any of the major coronary arteries of their major branches</p> <p><b>Outcome measures:</b> Sensitivity, specificity, accuracy, positive predictive value, negative predictive value. Sensitivity in patients with 1, 2 and 3 vessel disease.</p>
<p><b>Psirropoulos 2002<sup>40</sup></b></p> <p><b>Study design:</b> Prospective observational comparison</p> <p><b>Method of recruitment:</b> N/S</p> <p><b>Dates:</b> Sept 1995 – Dec 2000</p> <p><b>Country:</b> Greece</p> <p><b>Focus:</b> 1. MI development in elderly versus younger patients undergoing treatment for known CAD through conventional treadmill testing and scintigraphy; 2. Relationship between the above non-invasive tests and CA confirmed important CAD</p>	<p><b>Inclusion criteria:</b> Patients who had undergone CA, ExECG testing using Bruce protocol, and scintigraphy</p> <p><b>Exclusion criteria:</b> Uncontrolled arterial hypertension, hypertrophic cardiomyopathy, severe valve disease, severe chronic obstructive lung disease, severe anaemia, peripheral atherosclerosis, orthopedic problems and Parkinson's disease</p> <p><b>Enrolled:</b> 606</p> <p><b>Analysed:</b> 606</p> <p><b>Age:</b> Grp A 70.3 ± 5.3, Grp B 54.4 ± 9.1</p> <p><b>Gender:</b> M 440, W 252</p> <p><b>History of:</b> MI 309; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b></p> <p><b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S</p> <p><b>CA methods:</b> N/S</p> <p><b>Interval between tests:</b> ECG/SPECT performed 1 week to 2 months before CA</p> <p><b>Definition of positive SPECT test:</b> N/S</p> <p><b>Definition of positive stress ECG test:</b> 1) ST segment depression ≥ 0.15 mV at 80ms after J point, 2) 0.1mV flat or down-sloping ST segment depression, and 3) ST segment upward slope &gt; 1mV/s</p> <p><b>Angiographic definition of significant CAD:</b> Important CAD was defined as a) left main stem stenosis ≥ 50% with or without disease elsewhere, b) proximal 3 vessel disease, c) 3 vessel disease including the proximal left anterior descending artery (LAD), d) proximal 2 vessel disease including LAD, and e) 2 vessel disease including the proximal LAD</p> <p><b>Outcome measures:</b> Sensitivity, specificity, positive predictive accuracy, negative predictive accuracy</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Santana-Boado 1998</b><sup>18</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1992 – Mar 1995  <b>Country:</b> Spain  <b>Focus:</b> Diagnostic accuracy of SPECT between sexes and the influence of analysing only the patients with CA instead of all the patients who are submitted to study</p>	<p><b>Inclusion criteria:</b> Patients without previous MI in whom SPECT had been performed  <b>Exclusion criteria:</b> previous MI  <b>Enrolled:</b> 702</p> <p><b>Analysed:</b> 163  <b>Age:</b> M 60 ± 10, W 58 ± 8  <b>Gender:</b> M 100, W 63  <b>History of:</b> MI excluded; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (bicycle) plus pharmacologically (dipyridamole) in 72 patients who performed an insufficient exercise test. <b>Image interpretation:</b> Visual. <b>Equipment:</b> Elscint SP4 (Haifa, Israel) scintillation camera  <b>CA methods:</b> Standard Seldinger's technique  <b>Interval between tests:</b> Stress ECG was part of SPECT test, CA within less than 3 months after SPECT  <b>Definition of positive SPECT test:</b> Mild, moderate or severe defect in ≥ 2 of 3 axes or 3 consecutive tomographic sections of the same axis, with reversibility at rest  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> Stenoses &gt; 50%  <b>Outcome measures:</b> Sensitivity, specificity, positive predictive value, negative predictive value, accuracy globally and for gender.</p>
<p><b>Vaduganathan 1996</b><sup>41</sup></p> <p><b>Study design:</b> Prospective observational comparison  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1990 – Dec 1994  <b>Country:</b> USA  <b>Focus:</b> Diagnostic accuracy of exercise, adenosine and dobutamine imaging for the detection of LAD stenosis in patients with LBBB</p>	<p><b>Inclusion criteria:</b> Patients with LBBB referred for perfusion scintigraphy  <b>Exclusion criteria:</b> N/S  <b>Enrolled:</b> 383</p> <p><b>Analysed:</b> 154 with CA  <b>Age:</b> Exercise 61 ± 12, adenosine 69 ± 10, dobutamine 69 ± 10  <b>Gender:</b> M 94, W 60  <b>History of:</b> MI 47; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201, Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (treadmill), pharmacologically (adenosine or dobutamine). <b>Image interpretation:</b> Visual, quantitatively. <b>Equipment:</b> Single-crystal rotating gamma camera  <b>CA methods:</b> Performed in multiple views using standard techniques  <b>Interval between tests:</b> CA performed within 1 month of SPECT  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> Non-diagnostic because of underlying LBBB  <b>Angiographic definition of significant CAD:</b> ≥ 50% lumen diameter stenosis  <b>Outcome measures:</b> Overall sensitivity, specificity, positive predictive value, and negative predictive value for each type of stress. Sensitivity and specificity for LAD, RCA and LCX for each type of stress</p>

## Prognostic studies

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Amanullah 1998<sup>42</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Follow-up:</b> N/S  <b>Country:</b> USA  <b>Focus:</b> Predictors of early revascularisation; to compare early revascularisation patients with those who had medical therapy</p>	<p><b>Inclusion criteria:</b> Patients undergoing CA and SPECT for the evaluation of CAD  <b>Exclusion criteria:</b> Patients with normal CA, previous CABG, or recent MI or unstable angina  <b>Enrolled:</b> 860  <b>Lost to follow-up:</b> 44  <b>Analysed:</b> 816  <b>Age:</b> 60 ± 10  <b>Gender:</b> M 630, W 186  <b>History of:</b> MI 410; PTCA N/S; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Quantitative; visual.  <b>Equipment:</b> N/S  <b>CA:</b> Judkins methods  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> .  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> &gt; 50% stenosis of major epicardial coronary artery or one of its major branches. <b>Multivessel CAD:</b> presence of significant CAD in ≥ 2 of the 3 major coronary arteries or their major branches  <b>Multivariate analysis:</b> Multivariate logistic regression analysis  <b>Outcome measures:</b> PTCA or CABG within 3 months of nuclear testing</p>
<p><b>Amanullah 1999<sup>43</sup></b></p> <p><b>Study design:</b> Cohort  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Jan 1987 – Mar 1993  <b>Follow-up:</b> 36±26 months  <b>Country:</b> USA  <b>Focus:</b> Predictors of outcome of medically treated patients with left main and/or 3-vessel CAD</p>	<p><b>Inclusion criteria:</b> Patients who had documented left main and/or 3-vessel CAD noted on CA and had undergone SPECT within 3 months  <b>Exclusion criteria:</b> History of previous MI, recent unstable angina, or coronary revascularisation  <b>Enrolled:</b> 186  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 186  <b>Age:</b> 64 ± 9  <b>Gender:</b> M 136, W 50  <b>History of:</b> MI Excluded; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill) 127; pharmacologically (adenosine) 59.  <b>Image interpretation:</b> Quantitative; visual. <b>Equipment:</b> N/S  <b>CA:</b> Judkins methods  <b>Interval between tests:</b> 3 months  <b>Definition of positive SPECT test:</b> Reversible abnormality: perfusion abnormality in the initial image that showed complete or partial redistribution on the delayed image involving 25% of the segment. Fixed abnormality: perfusion abnormality that remained unchanged in the delayed image. <b>Multivessel abnormality:</b> perfusion defects in &gt; 1 vascular territory.  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> &gt; 50% stenosis of major epicardial coronary artery or one of its major branches  <b>Multivariate analysis:</b> Cox proportional hazards regression analysis  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Ben-Gal 2001</b><sup>44</sup></p> <p><b>Study design:</b> Cohort  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jul 1996 – Sept 1997  <b>Follow-up:</b> Mean 11.7 ± 5.3 months  <b>Country:</b> Israel  <b>Focus:</b> Utility of SPECT for predicting outcome of hospitalised patients with chest pain and a normal or non-diagnostic ECG</p>	<p><b>Inclusion criteria:</b> Patients admitted due to angina-like chest pain and a normal or non-diagnostic 12 lead ECG  <b>Exclusion criteria:</b> Patients with suspected acute MI, known previous MI, PTCA or CABG  <b>Enrolled:</b> 109  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 109  <b>Age:</b> 60.7 ± 13.7  <b>Gender:</b> M 57, W 52  <b>History of:</b> MI Excluded; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill 37 patients); pharmacologically (dipyridamole 72 patients). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Digital gamma camera (Apex SP 4-HR, Elscint)  <b>CA:</b> Judkins technique  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> Fixed defects: defects in ≥ 2 consecutive images present and unchanged in stress and rest scans. Reversible defect: defect on stress images absent or less prominent on rest images. Scans abnormal if any perfusion defect present  <b>Definition of positive stress ECG test:</b> 1 mV of horizontal or downsloping ST-segment depression that persisted for 80 msec after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Y  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI, PTCA, CABG</p>
<p><b>Berman 1995</b><sup>45</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1991 – Jan 1993  <b>Follow-up:</b> ≥ 1 year, mean 20 ± 5 months.  <b>Country:</b> USA  <b>Focus:</b> Prognostic implications of normal and equivocal SPECT scans</p>	<p><b>Inclusion criteria:</b> Patients in whom SPECT was performed  <b>Exclusion criteria:</b> Previous PTCA or CABG  <b>Enrolled:</b> 1811 of whom 7 had a technically inadequate study for interpretation or incomplete data  <b>Lost to follow-up:</b> 102  <b>Analysed:</b> 1702  <b>Age:</b> Normal scan results 60 ± 13; abnormal scan results 65 ± 12  <b>Gender:</b> M 1037, W 665  <b>History of:</b> MI 182; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 rest, Tc-99m sestamibi stress. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Scintillation camera/computer system  <b>CA:</b> No  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> Tomograms divided into 20 segments for each study and scored on a 5-point scale at rest and stress (0=normal, 4=absence of detectable tracer uptake). Study results normal, probably normal, equivocal, probably abnormal or definitely abnormal on the basis of number of segments with scores ≥ 2.  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> No  <b>Outcome measures:</b> Hard events - cardiac mortality; nonfatal MI. Soft events - PTCA or CABG &gt; 60 days after testing</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Candell-Riera 1998</b><sup>46</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Nov 1993 – Nov 1995  <b>Follow-up:</b> ≥ 6 months, max 5.5 years (mean 3.6 years)  <b>Country:</b> Spain  <b>Focus:</b> Prognosis of medically treated patients with clandestine myocardial ischaemia compared to patients with silent myocardial ischaemia and angina pectoris</p>	<p><b>Inclusion criteria:</b> Medically treated patients with confirmed CAD demonstrated by SPECT and CA  <b>Exclusion criteria:</b> Previous MI; previous revascularisation; another type of heart disease; normal CA; negative SPECT, patients who received dipyridamole simultaneously  <b>Enrolled:</b> 112  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 112  <b>Age:</b> 57 ± 10  <b>Gender:</b> M 95, W 17  <b>History of:</b> MI Excluded; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual.  <b>Equipment:</b> Elscint SP4 scintillation camera  <b>CA:</b> Seldinger's technique  <b>Interval between tests:</b> within 3 months  <b>Definition of positive SPECT test:</b> SPECT image divided into 13 segments and scored from 1 to 5 (1=normal, 5=severe defect) according to the severity of the ischaemia  <b>Definition of positive stress ECG test:</b> Horizontal or descending ST-segment depression ≥ 1mm at 0.08 seconds after the J-point  <b>Angiographic definition of significant CAD:</b> = 50% stenoses  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; need for revascularisation</p>
<p><b>Chatziioannou 1999</b><sup>47</sup></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Feb 1996 – June 1996  <b>Follow-up:</b> 18 ± 2.7 months (range 15 to 24 months)  <b>Country:</b> USA  <b>Focus:</b> Predictive value of SPECT versus ExECG in patients with high exercise tolerance</p>	<p><b>Inclusion criteria:</b> Patients receiving SPECT who reached at least Bruce stage IV  <b>Exclusion criteria:</b> N/S  <b>Enrolled:</b> 388  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 388  <b>Age:</b> 54 ± 10  <b>Gender:</b> M 337, W 51  <b>History of:</b> MI 19% of 348 patients with no event; 48% of 21 patients with event; PTCA N/S; CABG 17% of 348 patients with no event; 34% of 21 patients with event</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc99-m sestamibi. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual.  <b>Equipment:</b> 1. PRISM 3000XP triple-headed detector camera, 2. Starcam 3000 (General Electric) single-headed detector camera  <b>CA:</b> No  <b>Interval between tests:</b> Same day protocol  <b>Definition of positive SPECT test:</b> Abnormal MPI scans had = 1 reversible, fixed or mixed defects  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression of ≥ 1mm or an upsloping ST-segment depression of ≥ 2mm 0.08 seconds after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Hard events – cardiac mortality; nonfatal MI. Soft events – PTCA or CABG. Revascularisations due to SPECT or to the patients' condition at the time of SPECT not included in the analysis, and the patients involved were excluded from follow-up</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Chiamvimonvat 2001</b><sup>48</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> 1994 - 1996  <b>Follow-up:</b> Min 12 months, average 15 ± 3 months  <b>Country:</b> Canada  <b>Focus:</b> Utility of SPECT in a low-risk population after MI</p>	<p><b>Inclusion criteria:</b> Patients who were stable with no complications 3–21 days after MI  <b>Exclusion criteria:</b> CABG; other significant life-threatening illnesses; found on CA to require revascularisation  <b>Enrolled:</b> 203  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 203  <b>Age:</b> 56 ± 11  <b>Gender:</b> M 178, W 25  <b>History of:</b> MI 17; PTCA 2; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 rest, Tc 99-m sestamibi stress. <b>Stress induced:</b> Pharmacologically (dipyridamole).  <b>Image interpretation:</b> Visual; quantitative. <b>Equipment:</b> N/S  <b>CA:</b> Predetermined protocol  <b>Interval between tests:</b> Same day  <b>Definition of positive SPECT test:</b> Fixed defect: no change between rest and stress images. Reversible defect: decrease in stress score by ≥ 1. Abnormality: uptake of ≥ 2.5 SDs below lower limits of normal  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Multivariate logistic regression  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; PTCA; CABG; occurrence of unstable angina requiring hospitalisation. Late revascularisation occurring &gt; 1 month after study entry, CA, and SPECT included. Patients excluded after the first occurrence of any of the above endpoints</p>
<p><b>Diaz 2001</b><sup>49</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Sept 1990 - Dec 1993  <b>Follow-up:</b> Mean 6.7 years. Min 4.5 years  <b>Country:</b> USA  <b>Focus:</b> Value of SPECT for prediction of all-cause mortality when considered along with functional capacity and heart rate recovery</p>	<p><b>Inclusion criteria:</b> Adults aged ≥ 30 years referred for SPECT in conjunction with symptom-limited exercise testing  <b>Exclusion criteria:</b> Heart failure, left ventricular dysfunction, valvular disease, pacemaker, or foreign nationals  <b>Enrolled:</b> 7163  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 7163  <b>Age:</b> 60 ± 10  <b>Gender:</b> M 5354, W 1809  <b>History of:</b> MI N/S; PTCA 1196; CABG 1736</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> N/S. <b>Image interpretation:</b> Quantitative. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Heart divided into 12 segments, each segment weighted according to its relative contribution to total left ventricular mass. Segments coded as normal, fixed or reversible. Normal: count variation within the segment ≤ 20% compared to segment with highest count rate. Reversible: count increased by 20% on redistribution. Fixed: count increased by &lt; 20% on redistribution. Segments abnormal if defect on ≥ 2 consecutive slices and verified in an orthogonal plane  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Mortality</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Gibbons 1999</b><sup>50</sup></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Jan 1985 - Jan 1995  <b>Follow-up:</b> 3 ± 2 years (min 1 year, median 2 years)  <b>Country:</b> USA  <b>Focus:</b> The hypothesis that normal or near-normal SPECT in a patient with an intermediate-risk treadmill test would be associated with a very low long-term risk of subsequent cardiovascular events</p>	<p><b>Inclusion criteria:</b> Patients who underwent SPECT for evaluation of known or suspected CAD, had a calculable Duke treadmill score, and had an intermediate-risk treadmill score and normal or near-normal SPECT  <b>Exclusion criteria:</b> Previous PTCA or CABG, valvular heart disease, cardiomyopathy, congenital heart disease, uninterpretable exercise test due to LBBB, paced rhythm or preexcitation syndrome  <b>Enrolled:</b> 4649  <b>Lost to follow-up:</b> 176  <b>Analysed:</b> 4473  <b>Age:</b> 61.2 ± 11.4  <b>Gender:</b> M 2046, W 2427  <b>History of:</b> MI 241; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 and/or Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Images were categorised as normal, near-normal or abnormal. Near-normal: nonspecific abnormalities judged subjectively not to represent evidence of CAD.  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; PTCA; CABG; number of CAs performed</p>
<p><b>Giri 2002</b><sup>51</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> 2.5 ± 1.5 years (minimum 6 months)  <b>Country:</b> USA  <b>Focus:</b> Incremental role of SPECT in diabetic patients in the prediction of cardiac events and the possibility of a sex-ischaemia interaction</p>	<p><b>Inclusion criteria:</b> Patients with symptoms suggestive of CAD  <b>Exclusion criteria:</b> Hospitalised for unstable angina or MI or received revascularisation within 3 weeks of presentation  <b>Enrolled:</b> 4755 (diabetic 929 (20%), nondiabetic 3826 (80%))  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 4755  <b>Age:</b> Diabetic 65 ± 11, nondiabetic 64 ± 11  <b>Gender:</b> M 2669, W 2086 (diabetic M 478, W 451; nondiabetic M 2191, W 1635)  <b>History of:</b> MI 1414 (diabetic 329, nondiabetic 1085); PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 and/or Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (treadmill), pharmacologically (adenosine or dipyridamole). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> Method N/S (597 patients)  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> Stress defects: defects present at rest and remained unchanged during stress. Ischaemic: new or worsening defects (40% activity reduction) after stress. Extent of perfusion defects coded as 0, 1, 2, and 3 vascular territory involvement.  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; PTCA</p>



Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Groutars 2000</b><sup>52</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Apr 1996 – Dec 1996  <b>Follow-up:</b> Mean 25 ± 3 months  <b>Country:</b> The Netherlands  <b>Focus:</b> Prognostic significance of normal SPECT studies in patients with suspected or known CAD</p>	<p><b>Inclusion criteria:</b> Patients referred for SPECT  <b>Exclusion criteria:</b> Unstable angina pectoris, recent MI (within 6 weeks)  <b>Enrolled:</b> 246  <b>Lost to follow-up:</b> 10  <b>Analysed:</b> 236  <b>Age:</b> 61 ± 11 (range 27 – 85)  <b>Gender:</b> M 106, W 140  <b>History of:</b> MI (Q wave) 14; PTCA 22; CABG 9</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 rest, Tc 99-m sestamibi stress. <b>Stress induced by:</b> Exercise (bicycle) 125; pharmacologically (adenosine) 121. <b>Image interpretation:</b> Semiquantitative visual. <b>Equipment:</b> Toshiba triple-detector gamma camera  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG part of SPECT test  <b>Definition of positive SPECT test:</b> Semiquantitative visual analysis of myocardial scintigrams with a 5-point scoring system (1 = normal, 5 = absence of tracer uptake) over 20 segments  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression of ≥ 1mm lasting &gt; 80ms after the J-point for ≥ 3 consecutive beats  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> No  <b>Outcome measures:</b> Primary end points – cardiac mortality; nonfatal MI. Secondary end points – PTCA; CABG.</p>
<p><b>Hachamovitch 1996</b><sup>33</sup></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1991 – Dec 1993  <b>Follow-up:</b> ≥ 1 year. Mean 20 ± 5 months  <b>Country:</b> USA  <b>Focus:</b> Prognostic value of SPECT over clinical and exercise data in women versus men</p>	<p><b>Inclusion criteria:</b> Patients who underwent SPECT  <b>Exclusion criteria:</b> Valvular heart disease, primary cardiomyopathy.  <b>Enrolled:</b> 4620 of whom 16 excluded because of missing data and 270 excluded because of early revascularisation  <b>Lost to follow-up:</b> 198  <b>Analysed:</b> 4136  <b>Age:</b> M 61.7 ± 12.2, W 64.5 ± 11.8  <b>Gender:</b> M 2742, W 1394  <b>History of:</b> MI M 666, W 198; PTCA M 398, W 91; CABG M 466, W 86</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 rest, Tc 99-m sestamibi stress. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Semiquantitative visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG part of SPECT test  <b>Definition of positive SPECT test:</b> Summed stress score obtained by adding the score of the 20 segments of the stress images. Summed rest score obtained by adding the score of the 20 segments of the rest images. Summed difference score: sum of the differences between each of the 20 segments on the stress and rest images and represents amount of ischaemia present  <b>Definition of positive stress ECG test:</b> &gt; 1mm horizontal or downsloping ST-segment elevation or depression except in leads without significant Q waves or in lead aVR  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI. Patients receiving revascularisation within 60 days of index SPECT censored from analysis</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Hachamovitch 1998<sup>54</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1991 – Dec 1993  <b>Follow-up:</b> ≥ 1 year, mean 642 ± 226 days  <b>Country:</b> USA  <b>Focus:</b> 1. Incremental prognostic value of SPECT for the prediction of cardiac death. 2. Ability of SPECT to risk stratify patients. 3. Impact on cost of testing if patients at low risk for cardiac death but intermediate risk for nonfatal MI are not referred to CA as initial therapy</p>	<p><b>Inclusion criteria:</b> Patients who underwent SPECT  <b>Exclusion criteria:</b> Valvular heart disease; nonischemic cardiomyopathy; early (&lt; 60 days after SPECT) revascularisation.  <b>Enrolled:</b> 5456 of whom 4 excluded because of missing data  <b>Lost to follow-up:</b> 269  <b>Analysed:</b> 5183  <b>Age:</b> Exercise 62.6 ± 12.1; Adenosine 70.4 ± 11.3  <b>Gender:</b> Exercise M 2723, W 1381; Adenosine M 541, W 538  <b>History of:</b> MI Exercise 850; Adenosine 346; PTCA Exercise 473; Adenosine 143; CABG Exercise 544; Adenosine 219</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 rest, Tc 99-m sestamibi stress. <b>Stress induced by:</b> Exercise (treadmill) 4104; pharmacologically (adenosine) 1079. <b>Image interpretation:</b> Semiquantitative visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Summed stress score obtained by adding the score of the 20 segments of the stress images. Summed stress scores &lt; 4 normal; between 4 to 8 mildly abnormal; 9 to 13 moderately abnormal; and &gt; 13 severely abnormal. Summed rest score obtained by adding the scores of the 20 segments of the rest images. Summed difference score: sum of the differences between each of the 20 segments on stress and rest images  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI.</p>
<p><b>Hachamovitch 2002<sup>55</sup></b></p> <p><b>Study design:</b> Cohort  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1991 – Dec 1993  <b>Follow-up:</b> 1.6 ± 0.5 years  <b>Country:</b> USA  <b>Focus:</b> 1. Incremental prognostic value of SPECT in patients with normal resting ECG over pre-SPECT information; 2. Ability to risk-stratify patients; 3. Cost-effectiveness of SPECT as part of a testing strategy</p>	<p><b>Inclusion criteria:</b> Patients who underwent SPECT  <b>Exclusion criteria:</b> Abnormality on rest ECG other than sinus bradycardia; early (&lt; 60 days after SPECT) revascularisation  <b>Enrolled:</b> 3224  <b>Lost to follow-up:</b> 166  <b>Analysed:</b> 3058  <b>Age:</b> No hard event 61 ± 12; hard event 64 ± 13  <b>Gender:</b> No hard event M 1956, W 1032; Hard event M 52, W 18  <b>History of:</b> MI No hard event 520; hard event 33; PTCA No hard event 347; hard event 18; CABG No hard event 299; hard event 11</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 rest, Tc99-m sestamibi stress. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Semiquantitative visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> 20 segments scored on a 5-point scale (0 = normal, 4 = absence of tracer uptake in a segment). Summed score obtained by summing scores of 20 segments. Summed stress scores &lt; 4 normal, 4 to 8 mildly abnormal, and &gt; 8 moderately to severely abnormal  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression analysis  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Ho 1999</b><sup>56</sup></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Jan 1989 – Dec 1991  <b>Follow-up:</b> Median duration of 7.3 years in patients alive at follow-up  <b>Country:</b> USA  <b>Focus:</b> Prognostic value of SPECT performed 1-3 years after PTCA</p>	<p><b>Inclusion criteria:</b> Patients who had performed an exercise tomographic TI-201 test and had undergone PTCA 1–3 years preceding the TI-201 study  <b>Exclusion criteria:</b> Technically poor images, LBBB or paced ventricular rhythm, valvular heart disease, MI sustained between PTCA and SPECT study. CABG before PTCA  <b>Enrolled:</b> 211  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 211  <b>Age:</b> 60 ± 10  <b>Gender:</b> M 158, W 53  <b>History of:</b> MI 68; PTCA 211; CABG Excluded if CABG before PTCA</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> 14 segments graded subjectively on a 5-point scale (0 = absent uptake, 4 = normal). Redistribution: improved uptake ≥ 1 grade. Segments with mild fixed defects (scored as 3) considered normal and recoded 4 for this study. Summed stress scores obtained by adding the stress scores (normal = 56). Summed reversibility score: difference between summed stress and delayed scores  <b>Definition of positive stress ECG test:</b> ≥ 1mm horizontal or downsloping ST-segment depression 0.08 seconds after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> No. Cox univariate proportional hazards regression model  <b>Outcome measures:</b> Mortality; cardiac mortality; nonfatal MI; repeat PTCA; repeat CABG; survival free of cardiac death</p>
<p><b>Iskandrian 1993</b><sup>57</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> 28 ± 15 months (range 1 to 60)  <b>Country:</b> USA  <b>Focus:</b> Ability of SPECT to provide independent and incremental prognostic information above clinical, exercise and CA data in medically treated patients with CAD</p>	<p><b>Inclusion criteria:</b> Patients receiving, within a 3 month period, SPECT and CA for evaluation of stable chest pain due to suspected or proved CAD  <b>Exclusion criteria:</b> Normal angiograms, previous CABG or PTCA, recent acute MI (within 3 months) or unstable angina.  <b>Enrolled:</b> 316  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 316  <b>Age:</b> 62 ± 10  <b>Gender:</b> - No cardiac event M 217, W 64; cardiac event M 21, W 14  <b>History of:</b> MI N/S; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Quantitative.  <b>Equipment:</b> N/S  <b>CA:</b> Method N/S  <b>Interval between tests:</b> Within 3 months  <b>Definition of positive SPECT test:</b> Reversible abnormality: perfusion abnormality in the initial image showing complete or partial redistribution on the delayed image involving ≥ 25% of the segment. Fixed abnormality: perfusion abnormality that remained unchanged in the delayed image. Multivessel abnormality: perfusion defects in ≥ 1 vascular territory. Abnormality: data points 2.5 SD below the mean normal limit  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> ≥ 50% diameter stenosis of ≥ 1 major coronary artery  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Survival free of cardiac events. Patients receiving revascularisation (CABG or PTCA) within 3 months excluded.</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Iskandrian 1994<sup>58</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> Mean follow-up 29 months  <b>Country:</b> USA  <b>Focus:</b> Value of the treadmill exercise score versus SPECT in medically treated patients with CAD</p>	<p><b>Inclusion criteria:</b> Patients receiving SPECT and CA for evaluation of chest pain caused by suspected or proved CAD  <b>Exclusion criteria:</b> Previous revascularisation, recent acute MI, unstable angina pectoris, or revascularisation within 3 months of stress test  <b>Enrolled:</b> 437  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 437  <b>Age:</b> 61 ± 10  <b>Gender:</b> M 310, W 127  <b>History of: MI (Q wave) 77; PTCA Excluded; CABG Excluded</b></p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Quantitative.  <b>Equipment:</b> N/S  <b>CA:</b> Method N/S  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> Treadmill angina index: a score of 0 for no angina, 1 for nonlimiting angina, and 2 for exercise-limiting angina.  <b>Angiographic definition of significant CAD:</b> ≥ 50% diameter stenosis of ≥ 1 vessel  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI</p>
<p><b>Kamal 1994<sup>59</sup></b></p> <p><b>Study design:</b> Cohort  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Feb 1989 - Jan 1993  <b>Follow-up:</b> Average follow-up interval 22 ± 13 months  <b>Country:</b> USA  <b>Focus:</b> Prognostic value of adenosine SPECT in medically treated patients with CAD</p>	<p><b>Inclusion criteria:</b> Patients receiving SPECT and CA within 3 months of each other for evaluation of chest pain  <b>Exclusion criteria:</b> Coronary revascularisation within 3 months of SPECT, sick sinus syndrome, second-degree or greater atrioventricular block in the absence of a functioning pacemaker, or bronchospasm  <b>Enrolled:</b> 177  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 177  <b>Age:</b> 64 ± 11  <b>Gender:</b> M 109, W 68  <b>History of: MI (Q wave) No cardiac event 45 of 163; cardiac event 4 of 14; PTCA N/S; CABG N/S</b></p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced:</b> Pharmacologically (adenosine). <b>Image interpretation:</b> Semiquantitative. <b>Equipment:</b> N/S  <b>CA:</b> Performed in multiple projections according to standard techniques  <b>Interval between tests:</b> Within 3 months  <b>Definition of positive SPECT test:</b> Perfusion pattern in each of vascular territories assessed as normal or showing fixed or reversible abnormalities. Multivessel thallium abnormality present when ≥ 1 vascular territory involved.  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression ≥ 1mm 80msec after the J-point  <b>Angiographic definition of significant CAD:</b> ≥ 50% diameter stenosis in any major coronary arteries or their branches  <b>Multivariate analysis:</b> Cox proportional hazards regression analysis  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Lauer 1996<sup>60</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Sept 1990 - Dec 1993  <b>Follow-up:</b> 1.8 years (for all-cause mortality)  <b>Country:</b> USA  <b>Focus:</b> Possible post-test gender bias for referral for CA</p>	<p><b>Inclusion criteria:</b> Patients referred for SPECT  <b>Exclusion criteria:</b> Prior invasive cardiac procedures, congestive heart failure, cardiomyopathy, valvular disease, heart transplant evaluation, or congenital heart disease  <b>Enrolled:</b> 3669  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 3669  <b>Age:</b> - M 58 ± 12, W 59 ± 12  <b>Gender:</b> M 2351, W 1318  <b>History of:</b> MI M 167, W 41; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Quantitative.  <b>Equipment:</b> 3-headed camera  <b>CA:</b> Method N/S  <b>Interval between tests:</b> Within 90 days  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> ≥ 1mm of horizontal or downsloping ST-segment depression 80 ms after the J-point  <b>Angiographic definition of significant CAD:</b> ≥ 50% stenosis in proximal or middle coronary vessel or major branch. Severe coronary disease: (1) ≥ 50% left main stenosis, (2) 3-vessel disease (≥ 70% stenosis in each major coronary artery system), or (3) 2-vessel disease with a ≥ 70% proximal LAD artery lesion  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Mortality; cardiac catheterisation performed within 90 days of stress testing</p>
<p><b>Lauer 1997<sup>61</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Sept 1990 - Dec 1993  <b>Follow-up:</b> Approximately 2 years  <b>Country:</b> USA  <b>Focus:</b> Associations between age and referral to CA among adults undergoing noninvasive evaluation of known or suspected coronary disease</p>	<p><b>Inclusion criteria:</b> Adults, ≥ 30 years old, under the care of cardiologists, with abnormal symptom-limited SPECT  <b>Exclusion criteria:</b> Prior cardiac procedures (including CA), congestive heart failure, or valvular congenital heart disease  <b>Enrolled:</b> 416  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 416  <b>Age:</b> 30-49 years grp, 43 ± 5; 50-64 years grp, 58 ± 4; 65-74 years grp, 69 ± 3; ≥ 75 years grp, 78 ± 3  <b>Gender:</b> M 354, W 62  <b>History of: prior coronary events</b> 155; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> Method N/S  <b>Interval between tests:</b> Within 90 days  <b>Definition of positive SPECT test:</b> Ischaemia: presence of &gt; 20% reversibility. Scarring: presence of counts &lt; 80% of maximum (&lt; 70% for the posterior wall). 12 segment system - each segment coded as normal ischaemic or scarred  <b>Definition of positive stress ECG test:</b> ≥ 1mm horizontal or downsloping ST-segment depression occurring 80 msec after the J-point, or if ≥ 1mm of additional ST-segment elevation occurred in leads without pathological Q waves  <b>Angiographic definition of significant CAD:</b> ≥ 50% stenosis in any proximal or middle coronary vessel or major branch. Severe coronary disease: ≥ 50% left main artery stenosis, 3-vessel disease (≥ 70% stenosis in each major coronary artery system), or 2-vessel disease with a ≥ 70% proximal LAD artery lesion  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Mortality; cardiac mortality; CA performed within 90 days of SPECT</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Machecourt 1994<sup>62</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1987 – Dec 1989  <b>Follow-up:</b> Mean 33 ± 10 months  <b>Country:</b> France  <b>Focus:</b> Prognostic value of SPECT in patients with suspected stable CAD  <b>Note:</b> A subset of these patients is reported on in Vanzetto 1999<sup>76</sup></p>	<p><b>Inclusion criteria:</b> Patients with suspected stable CAD  <b>Exclusion criteria:</b> Prior CABG or PTCA; revascularisation performed &lt; 2 months after SPECT; MI &lt; 1 month; age &gt; 76 years; SPECT at rest; planar scintigraphy; missing administrative data  <b>Enrolled:</b> 2013  <b>Lost to follow-up:</b> 87  <b>Analysed:</b> 1926  <b>Age:</b> 56.8 ± 9  <b>Gender:</b> M 1303, W 623  <b>History of:</b> MI 357; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle) 1121 (58%), pharmacologically (dipyridamole) 805 (42%). <b>Image interpretation:</b> Visual. <b>Equipment:</b> Rotating gamma camera.  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Left ventricle divided into 6 segments, each segment classified as normal or abnormal  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression &gt; 1mm  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Main criteria – mortality; cardiac mortality. Ancillary criteria – nonfatal MI; PTCA or CABG beyond the second month following the SPECT test</p>
<p><b>Marie 1995<sup>63</sup></b></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> 1982 – 1987  <b>Follow-up:</b> 70 ± 19 months  <b>Country:</b> France  <b>Focus:</b> Long term prognostic value of SPECT in patients with known or suspected CAD compared with clinical history, exercise testing, CA and radionuclide ventricular angiography</p>	<p><b>Inclusion criteria:</b> 1. Presence of known or suspected CAD and SPECT, CA and rest radionuclide angiographic results over a &lt; 1.5 month period. 2. Subsequent medical therapy  <b>Exclusion criteria:</b> Previous cardiac surgery or PTCA; congenital or valvular heart disease; hypertrophic or idiopathic dilated cardiomyopathy; decision to revascularise at hospital discharge; or revascularisation within 3 months.  <b>Enrolled:</b> 221  <b>Lost to follow-up:</b> 4  <b>Analysed:</b> 217  <b>Age:</b> 53 ± 9 (range 25 – 72)  <b>Gender:</b> M 188, W 29  <b>History of:</b> MI 143; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> Method N/S  <b>Interval between tests:</b> Within 1.5 months  <b>Definition of positive SPECT test:</b> Tl-201 uptake scored using a 4-point scale on a 20 segment division of the left ventricle (0 = normal, 3 = severely reduced). Extent of exercise defects: percent of segments with an uptake score ≥ 2 after exercise. Extent of reversible defects: percent of segments with exercise defects with a ≥ 1 point decrease in the uptake score at redistribution  <b>Definition of positive stress ECG test:</b> ≥ 1mm horizontal or downsloping depression occurring 0.08s after the J-point compared with baseline values  <b>Angiographic definition of significant CAD:</b> Number of diseased coronary segments and vessels calculated using ≥ 70% and ≥ 50% diameter reduction  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Major ischaemic event (cardiac death or MI; other major cardiac events)</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Marwick 1999<sup>64</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> 1990 – 1995  <b>Follow-up:</b> Mean 2.4 ± 1.5 years  <b>Country:</b> USA  <b>Focus:</b> Value of SPECT for prediction of cardiac mortality in men and women and whether this is independent of clinical evaluation and exercise testing  <b>Note:</b> Shaw 2000 reports on the same patient population and is considered as part of Marwick 1999</p>	<p><b>Inclusion criteria:</b> Patients with cardiac symptoms of known or suspected CAD  <b>Exclusion criteria:</b> Recent hospitalisation for unstable angina, MI and coronary revascularisation  <b>Enrolled:</b> 8411  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 8411  <b>Age:</b> M 60.3 ± 12, W 62.9 ± 12  <b>Gender:</b> M 5009, W 3402  <b>History of:</b> MI 1428 (M 952, W 476); PTCA 571 (M 401, W 170); CABG 671 (M 501, W 170)</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 (17% of patients), Tc-99m sestamibi (83% of patients). <b>Stress induced by:</b> Exercise (treadmill 7486 patients), pharmacologically (dipyridamole 925 patients). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Fixed defects: similar defects on both stress and redistribution images. Stress-induced defects: defects present in the stress image and absent in the redistribution image, or defects greater following stress than at redistribution. Fixed and stress-induced defects in each of the vascular territories of the 3 major coronary arteries coded 1, 2, or 3  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Mortality; cardiac mortality</p>
<p><b>Miller 1998<sup>65</sup></b></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Dec 1985 – Dec 1993  <b>Follow-up:</b> Median duration of follow-up 5.8 years  <b>Country:</b> USA  <b>Focus:</b> Prognostic value of SPECT performed relatively early after CABG</p>	<p><b>Inclusion criteria:</b> Patients receiving SPECT and undergone CABG within the 2 years preceding the SPECT  <b>Exclusion criteria:</b> Technically poor images, LBBB or paced ventricular rhythm on the rest ECG, valvular heart disease, or PTCA before CABG  <b>Enrolled:</b> 411  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 411  <b>Age:</b> 62 ± 9  <b>Gender:</b> M 329, W 82  <b>History of:</b> MI 189; PTCA Excluded; CABG 411</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> 14 short axis segments. Redistribution: improved uptake of ≥ 1 grade. Mild fixed defects (score of 3 on stress and delayed images) considered normal. Ischaemia proximal to bypass graft insertion defined as redistribution confined to a basal segment or segments without redistribution in the apical or mid segments of a coronary artery distribution.  <b>Definition of positive stress ECG test:</b> ≥ 1mm horizontal or downsloping ST-segment depression 0.08s after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; PTCA/repeat CABG early (≤ 3 months following the SPECT test; PTCA/repeat CABG late (&gt; 3 months following the SPECT test)</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Miller 2001</b><sup>66</sup></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> Jan 1989 - Dec 1991  <b>Follow-up:</b> Median follow-up 4.9 years  <b>Country:</b> USA  <b>Focus:</b> Identification of high-risk patients by worsening clinical, exercise or SPECT variables</p>	<p><b>Inclusion criteria:</b> Symptomatic patients receiving SPECT and a second SPECT <math>\geq 6</math> months later without revascularisation or MI during this period  <b>Exclusion criteria:</b> Congenital, cardiomyopathic or valvular heart disease; prior PTCA or CABG; LBBB, pacemaker, LVH or ventricular preexcitation; technically poor SPECT images; or refusal of research authorisation  <b>Enrolled:</b> 375 of whom 47 patients were excluded because magnitude of ST-segment depression was not retrievable  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 328  <b>Age:</b> <math>62 \pm 10</math>  <b>Gender:</b> M 262, W 113  <b>History of:</b> MI 65; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill) . <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Tl-201 uptake in 24 segments for resting and exercise SPECT graded on a 5-point scale (0 = absent uptake, 4 = normal uptake). Summed stress and resting scores calculated by adding the grades in each of the 14 short-axis segments. Summed reversibility score calculated as the difference between the summed resting and stress scores.  <b>Definition of positive stress ECG test:</b> <math>\geq 1</math>mm horizontal or downsloping ST-segment depression 0.08 seconds after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Mortality; nonfatal MI; early PTCA <math>\leq 3</math> months of SPECT test; late PTCA <math>&gt; 3</math> months of SPECT test; early CABG <math>\leq 3</math> months of SPECT test; late CABG <math>&gt; 3</math> months of SPECT test</p>
<p><b>Mishra 1999</b><sup>67</sup></p> <p><b>Study design:</b> Retrospective comparative observational  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> 3 months for CA, 2 weeks for revascularisation  <b>Country:</b> USA  <b>Focus:</b> Down-stream utilisation rate in cohorts of patients with intermediate pretest probability of CAD, receiving either CA or SPECT for initial screening.</p>	<p><b>Inclusion criteria:</b> Patients being evaluated for chest pain suspected of being due to CAD  <b>Exclusion criteria:</b> Previous revascularisation, cardiomyopathy, or valvular heart disease  <b>Enrolled:</b> Group 1 (CA) 4572; group 2 (SPECT) 2022  <b>Lost to follow-up:</b> N/S  <b>Analysed:</b> Grp 1 4572; Grp 2 2022  <b>Age:</b> Grp 1 <math>59 \pm 11</math>; Grp 2 <math>57 \pm 12</math>  <b>Gender:</b> Grp 1 M 62%, W 38%; Grp 2 M 55%, W 45%  <b>History of:</b> MI N/S; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> N/S. <b>Stress induced by:</b> N/S. <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S  <b>CA:</b> Using standard techniques  <b>Interval between tests:</b> CA within 3 months of SPECT (group 2)  <b>Definition of positive SPECT test:</b> Presence, extent, site(s) and nature of abnormality (fixed or reversible)  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> <math>\geq 50\%</math> diameter stenosis in <math>\geq 1</math> of the major vessels  <b>Multivariate analysis:</b> No  <b>Outcome measures:</b> Coronary revascularisation (group 1); CA and coronary revascularisation (group 2)</p>



Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Nallamothu 1995<sup>68</sup></b></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Follow-up:</b> Mean 37 ± 29 months  <b>Country:</b> USA  <b>Focus:</b> Impact of SPECT on patient management and outcome</p>	<p><b>Inclusion criteria:</b> Patients with suspected CAD receiving SPECT.  <b>Exclusion criteria:</b> N/S  <b>Enrolled:</b> 2700  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 2700  <b>Age:</b> 59 ± 13  <b>Gender:</b> M 1510, W 1190  <b>History of:</b> MI 0; PTCA 0; CABG 0</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S  <b>CA:</b> Method N/S  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> No  <b>Outcome measures:</b> Mortality; nonfatal MI; PTCA; CABG; need for subsequent CA (following SPECT study)</p>
<p><b>Nallamothu 1997<sup>69</sup></b></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> Mean 41 ± 28 months (mean of 5 years after CABG (58 ± 50 months) )  <b>Country:</b> USA  <b>Focus:</b> Prognostic value of SPECT after CABG</p>	<p><b>Inclusion criteria:</b> Prior CABG for angina pectoris, SPECT and CA within 3 months of each other after CABG, and no repeat CABG within 3 months of SPECT  <b>Exclusion criteria:</b> Patients not receiving repeat CA  <b>Enrolled:</b> 255  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 255  <b>Age:</b> 64 ± 9  <b>Gender:</b> M 206, W 49  <b>History of:</b> MI (Q-wave) 64; PTCA N/S; CABG 255</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill) 134 (53%), pharmacologically (adenosine 100 (39%), dipyridamole 21 (8%)). <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S  <b>CA:</b> Multiple projections using standard techniques  <b>Interval between tests:</b> Within 3 months  <b>Definition of positive SPECT test:</b> N/S  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> ≥ 50% diameter stenosis in any one of the nongrafted coronary arteries, grafted vessels distal to the graft anastomoses, or in the grafts  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MIPTCA or CABG &gt; 3 months after stress testing</p>

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<p><b>O'Keefe 1998</b><sup>70</sup></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jun 1991 - Aug 1993  <b>Follow-up:</b> Mean 19 ± 10 months  <b>Country:</b> USA  <b>Focus:</b> Outcomes of patients with mild or moderate ischaemia but without high-risk features on SPECT as a function of whether they were managed medically or invasively</p>	<p><b>Inclusion criteria:</b> Patients with non-high-risk classification from SPECT  <b>Exclusion criteria:</b> CA &lt;90 days before SPECT  <b>Enrolled:</b> 1352 (medically managed 1236, invasively managed 116)  <b>Lost to follow-up:</b> 28  <b>Analysed:</b> 1324  <b>Age:</b> Medically managed 64.4 ± 10.2, invasively managed 61.8 ± 10.5  <b>Gender:</b> M 1078, W 274 (medically managed M 974, W 262, invasively managed M 104, W 12)  <b>History of:</b> MI 615 (medically managed 577, invasively managed 38); PTCA 743 (medically managed 679, invasively managed 64); CABG 375 (medically managed 347, invasively managed 28)</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 (97% of patients), Tc-99m sestamibi (3% of patients). <b>Stress induced by:</b> Exercise (type N/S), pharmacologically (adenosine or dipyridamole or dobutamine). <b>Image interpretation:</b> Visual, quantitative. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Perfusion defects scored: severe = 3, moderate = 2, mild/equivocal = 1, normal = 0. Ischaemia: change in segmental score between stress and rest of 3 - 0, 3 - 1, 2 - 0 and 2 - 1. Nonreversible: scores of 3 - 3, 3 - 2 and 2 - 2. Scans categorised into 3 classifications: 1. high risk - 2 or 3 of multivessel ischaemia, ischaemia in the LAD coronary territory, or abnormal lung uptake of thallium on the stress anterior view; 2. non-high risk - ischaemic but not meeting criteria for high risk; 3. normal/nonischaemic  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; PTCA or CABG excluding procedures performed within first 30 days in invasively managed group</p>
<p><b>Olmos 1998</b><sup>71</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> 1986 - 1993  <b>Follow-up:</b> Up to 8 years, mean 3.7 ± 2  <b>Country:</b> USA  <b>Focus:</b> Incremental prognostic value of exercise echocardiography and SPECT with clinical variables and ExECG in patients with suspected or known CAD</p>	<p><b>Inclusion criteria:</b> Patients evaluated for suspected or know CAD  <b>Exclusion criteria:</b> Recent MI (&lt; 2 months), valvular heart disease, dilated or hypertrophic cardiomyopathy, or previous cardiac transplantation  <b>Enrolled:</b> 248  <b>Lost to follow-up:</b> 23  <b>Analysed:</b> 225  <b>Age:</b> 56.3 ± 12  <b>Gender:</b> M 189, W 59  <b>History of:</b> MI 86; PTCA/CABG 57</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual. <b>Equipment:</b> ADAC, ARC 3000-3300 large-field-of-view, single-crystal, rotating gamma camera  <b>CA:</b> Method N/S  <b>Interval between tests:</b> Within 3 months (84 patients had CA)  <b>Definition of positive SPECT test:</b> Tl-201 uptake was scored: 1 = normal, 2 = mildly reduced, 3 = moderately reduced, and 4 = severely reduced. Perfusion defects analysed for complete redistribution (ischaemia), no redistribution (fixed defect), or partial redistribution (mixed defect)  <b>Definition of positive stress ECG test:</b> ≥ 1mm horizontal or downsloping ST-segment depression 0.08 seconds after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Stepwise logistic regression model  <b>Outcome measures:</b> Mortality; cardiac mortality; nonfatal MI; PTCA; CABG; unstable angina requiring hospitalisation; congestive heart failure; cardiac transplantation.</p>

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<p><b>Parisi 1998<sup>74</sup></b></p> <p><b>Study design:</b> Cohort  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> 5 years  <b>Country:</b> USA  <b>Focus:</b> Prognostic ability of SPECT and ExECG after commonly accepted treatments in low-risk men with CAD</p>	<p><b>Inclusion criteria:</b> Men with chronic stable angina referred for CA found to have single- or double-vessel disease and no prior revascularisation. Positive baseline test with stress ECG or SPECT required for study entry  <b>Exclusion criteria:</b> N/S  <b>Enrolled:</b> 328 of whom 3, with uninterpretable ECGs, excluded  <b>Lost to follow-up:</b> 3  <b>Analysed:</b> 297  <b>Age:</b> 60  <b>Gender:</b> M 297  <b>History of:</b> MI N/S; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> N/S. <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> <math>\geq 1</math> regional perfusion deficit apparent in the exercise images  <b>Definition of positive stress ECG test:</b> <math>\geq 1</math>mm exercise-induced ST-segment depression 0.08 seconds after the J-point persisting for <math>\geq 15</math> seconds and reverting to baseline thereafter  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Yes  <b>Outcome measures:</b> Mortality; MI; PTCA; CABG; occurrence of unstable angina</p>
<p><b>Pattillo 1996<sup>75</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> <math>41 \pm 22</math> months  <b>Country:</b> USA  <b>Focus:</b> Relative independent and incremental prognostic value of clinical evaluation, exercise testing, CA, and SPECT with quantitative assessment</p>	<p><b>Inclusion criteria:</b> Patients receiving SPECT, during symptom-limited exercise testing, and CA within 3 months of each other because of chest pain  <b>Exclusion criteria:</b> Previous CABG, PTCA, acute MI within 3 months, unstable angina pectoris, or revascularisation within 3 months of exercise testing  <b>Enrolled:</b> 732  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 732  <b>Age:</b> <math>59 \pm 11</math>  <b>Gender:</b> M 519, W 213  <b>History of:</b> MI 343; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> TI-201. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Quantitative.  <b>Equipment:</b> N/S  <b>CA:</b> Performed with standard techniques  <b>Interval between tests:</b> Within 3 months  <b>Definition of positive SPECT test:</b> Interpreted as normal or showing fixed or reversible abnormality, multivessel abnormality, left ventricular dilation, and increased lung thallium uptake. Size of the perfusion abnormality determined from polar map plots, by sum of number of segments with abnormal perfusion pattern and sum of number of segments with reversible defects  <b>Definition of positive stress ECG test:</b> Treadmill exercise score calculated according to the method of Mark et al. A score of <math>&lt; -10</math> was considered high risk; <math>-10</math> to <math>4</math> moderate risk; and <math>\geq 5</math> low risk.  <b>Angiographic definition of significant CAD:</b> Number of vessels with <math>\geq 50\%</math> diameter stenosis and by the Gensini score. Gensini score based on the number, degree and sites of stenoses and collateral vessels. Score of <math>&lt; 10</math> mild disease; <math>10</math> to <math>34</math> moderate disease; and <math>\geq 35</math> severe disease.  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Schinkel 2002</b><sup>76</sup></p> <p><b>Study design:</b> Cohort  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> 1994 - 2000  <b>Follow-up:</b> 37 ± 17 months  <b>Country:</b> The Netherlands  <b>Focus:</b> Prognostic value of dobutamine-atropine SPECT in patients with known or suspected CAD</p>	<p><b>Inclusion criteria:</b> Patients with limited exercise capacity  <b>Exclusion criteria:</b> Coronary revascularisation within 3 months of SPECT  <b>Enrolled:</b> 721  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 693  <b>Age:</b> 60 ± 10  <b>Gender:</b> M 419, W 274  <b>History of:</b> MI 194; PTCA 111; CABG 100</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m tetrofosmin. <b>Stress induced:</b> Pharmacologically (dobutamine-atropine). <b>Image interpretation:</b> Semiquantitative. <b>Equipment:</b> PRISM 3000 XP (Picker International) triple-headed gamma camera system  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Reversible perfusion defect: perfusion defect on stress images that partially or completely resolved at rest in ≥ 2 contiguous segments or slices in the 47-segment model. Fixed perfusion defect: perfusion defect on stress images in ≥ 2 contiguous segments or slices, which persisted on rest images in the 47 segment model. <b>Abnormal study:</b> presence of a fixed or reversible perfusion defect (or both)  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Mortality; cardiac mortality; nonfatal MI;PTCA/CABG later than 3 months following the SPECT test</p>
<p><b>Shaw 1999</b><sup>78</sup></p> <p><b>Study design:</b> Prospective comparative observational  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Follow-up:</b> 2.5 ± 1.5 years and was a minimum of 6 months after initial testing for each patient  <b>Country:</b> USA  <b>Focus:</b> Medical costs and clinical outcomes of women referred for CA or noninvasive stress myocardial imaging to evaluate chest pain, incremental costs of diagnostic testing and subsequent medical care of 2 testing strategies, and impact on cardiac outcomes</p>	<p><b>Inclusion criteria:</b> Women referred for testing to evaluate known or suspected CAD based on stable chest pain consistent with angina pectoris  <b>Exclusion criteria:</b> Women undergoing predischarge risk stratification after recent (&lt;3 weeks) MI, prior coronary revascularisation, recent valvular disease, or cardiac catheterisation  <b>Enrolled:</b> 4638  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 4638. Strategy 1. 3375, Strategy 2. 1263  <b>Age:</b> 66 ± 11  <b>Gender:</b> W 4638  <b>History of:</b> MI N/S; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (type N/S), pharmacologic (dipyridamole) 525. <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S  <b>CA:</b> Method N/S  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> ≥ 1 reversible myocardial perfusion defect  <b>Definition of positive stress ECG test:</b> ≥ 1mm electrocardiographically detected ST-segment depression beyond baseline  <b>Angiographic definition of significant CAD:</b> ≥ stenosis of &gt; 70% luminal diameter reduction  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; revascularisation</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Shaw 1999<sup>77</sup></b></p> <p><b>Study design:</b> Prospective comparative observational  <b>Method of recruitment:</b> N/S  <b>Dates:</b> N/S  <b>Follow-up:</b> Mean 2.5 ± 1.5 years  <b>Country:</b> USA  <b>Focus:</b> Observational differences in costs of care by the coronary disease diagnostic test modality</p>	<p><b>Inclusion criteria:</b> Patients with typical cardiac symptoms enrolled into a registry of stable angina pectoris patients including patients receiving initial direct diagnostic CA and those receiving SPECT.</p> <p><b>Exclusion criteria:</b> Patients undergoing a predischage evaluation or recently hospitalised for unstable angina, MI, or revascularisation</p> <p><b>Enrolled:</b> Group 1 (CA) 5423; group 2 (MPI) 5826</p> <p><b>Lost to follow-up:</b> N/S  <b>Analysed:</b> Grp 1 5423; Grp 2 5826  <b>Age:</b> Grp 1 62 ± 12; Grp 2 64 ± 12  <b>Gender:</b> Grp 1 M 62%, W 38%; Grp 2 M 64%, W 36%  <b>History of:</b> MI N/S; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 (17%), Tc-99m sestamibi (83%). <b>Stress induced by:</b> Exercise (treadmill 4901); pharmacologically 925 (agent N/S). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> Method N/S  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> Fixed defects: defects at rest and remained unchanged during stress. Reversible defects: new or worsening defects after stress. Perfusion defect extent coded as none, 1, 2 or 3 vascular territory involvement  <b>Definition of positive stress ECG test:</b> ≥ 1mm of horizontal or downsloping ST depression  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; death or MI; revascularisation</p>
<p><b>Shaw 2000<sup>79</sup></b></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> 1991 - 1996  <b>Follow-up:</b> Mean 2.5 ± 1.5 years  <b>Country:</b> USA  <b>Focus:</b> Value of noninvasive risk stratification relative to clinical assessment in a stable chest pain population  <b>Note:</b> this study reports on the same patient population as Marwick 1999, which is considered as the primary report</p>	<p><b>Inclusion criteria:</b> Patients with typical cardiac symptoms referred for SPECTI</p> <p><b>Exclusion criteria:</b> Undergoing a predischage evaluation, or recently hospitalised for acute coronary syndromes or coronary revascularisation</p> <p><b>Enrolled:</b> 8411</p> <p><b>Lost to follow-up:</b> N/S  <b>Analysed:</b> 8411  <b>Age:</b> 69 ± 11  <b>Gender:</b> M 5009, W 3402  <b>History of:</b> MI 1414; PTCA 4458; CABG 5467</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 (17% of patients); Tc-99m sestamibi (83% of patients). <b>Stress induced by:</b> Exercise (treadmill); pharmacologically (adenosine or dipyridamole). <b>Image interpretation:</b> Visual.  <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Fixed defects: defects at rest and unchanged during stress. Ischaemic: new or worsening defects after stress. Perfusion defect extent coded as none, 1, 2 or 3 vascular territory abnormalities  <b>Definition of positive stress ECG test:</b> ≥ 1mm horizontal or downsloping ST-segment depression at 80ms after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; MI; coronary revascularisation</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Stratmann 1994</b><sup>80</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Mar 1991 - Sept 1992  <b>Follow-up:</b> 13 ± 5 months (range 1 - 24 months), ≥ 6 months for patients without cardiac events  <b>Country:</b> USA  <b>Focus:</b> Relative prognostic value of exercise stress with SPECT and clinical risk variables in patients presenting for evaluation of stable chest pain consistent with angina pectoris</p>	<p><b>Inclusion criteria:</b> Patients with stable chest pain consistent with angina pectoris referred for exercise testing and SPECT  <b>Exclusion criteria:</b> Unstable angina, acute MI ≤ 3 months before testing, or early (&lt; 6 months after SPECT) revascularisation  <b>Enrolled:</b> 531  <b>Lost to follow-up:</b> 10  <b>Analysed:</b> 521  <b>Age:</b> No cardiac event 59 ± 11; cardiac event 62 ± 8  <b>Gender:</b> No cardiac event M 487, W 10; cardiac event M 24  <b>History of: MI</b> No cardiac event 172; cardiac event 12; <b>PTCA</b> N/S; <b>CABG</b> N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual.  <b>Equipment:</b> Siemens Orbiter-75 single-headed SPECT gamma camera  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Presence of perfusion defect. Fixed defect: defect present and unchanged on both stress and rest images. Reversible defect: defect on stress images absent or less prominent on rest images  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression ≥ 1mm  <b>Angiographic definition of significant CAD:</b> ≥ 50% stenosis (as determined in ≥ 2 angiographic views)  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; PTCA/CABG performed ≥ 6 months after exercise testing; survival free of cardiac events at 1 year</p>
<p><b>Travin 1995</b><sup>81</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Follow-up:</b> 15 ± 10 months (range &lt; 1 - 37 months)  <b>Country:</b> USA  <b>Focus:</b> Clinical utility of SPECT in patients undergoing exercise stress testing after recent acute MI</p>	<p><b>Inclusion criteria:</b> Patients who had an acute MI within 14 days and were referred for SPECT  <b>Exclusion criteria:</b> N/S  <b>Enrolled:</b> 134 of whom 33 underwent coronary revascularisation  <b>Lost to follow-up:</b> 14  <b>Analysed:</b> 87  <b>Age:</b> 60.5 ± 11.9  <b>Gender:</b> M 90, W 44  <b>History of: MI</b> 17 although all patients in the study had recent MI; <b>PTCA</b> N/S; <b>CABG</b> N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (treadmill). <b>Image interpretation:</b> Visual.  <b>Equipment:</b> ADAC ARC 4000 or Cirrhys camera.  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Left ventricular myocardium divided into 5 segments. Each segment classified as normal, ischaemic (perfusion defect on stress images that improved ≥ 30% visually on rest images), or fixed  <b>Definition of positive stress ECG test:</b> ≥ 3 consecutive beats showing ≥ 0.1mV of horizontal or downsloping ST-segment depression beyond baseline that persisted for ≥ 80 ms after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; hospital admissions for unstable angina</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Underwood 1999</b><sup>82</sup></p> <p><b>Study design:</b> Retrospective observational comparison  <b>Method of recruitment:</b> Consecutive within each centre  <b>Dates:</b> Presenting after 1 July 1993  <b>Follow-up:</b> 2 years  <b>Country:</b> France, Germany, Italy, UK  <b>Focus:</b> Cost-effectiveness of 4 diagnostic strategies in patients newly presenting with possible CAD, and to compare cost-effectiveness in centres that routinely use MPI with those that do not.</p>	<p><b>Inclusion criteria:</b> Patients newly presenting with symptoms suggestive of CAD  <b>Exclusion criteria:</b> Presenting with MI or unstable angina; those in whom coronary disease had been previously confirmed or excluded  <b>Enrolled:</b> - Strategy 1. 146, strategy 2. 131, strategy 3. 48, strategy 4. 76.  <b>Lost to follow-up:</b> - Strategy 1. 2, strategy 2. 1, strategy 3. 0, strategy 4. 1  <b>Analysed:</b> - Strategy 1. 144, strategy 2. 130, strategy 3. 48, strategy 4. 75  <b>Age (mean):</b> Strategy 1. 55 years, strategy 2. 53 years, strategy 3. 61 years, strategy 4. 61 years  <b>Gender:</b> Strategy 1. M 85, W 61; strategy 2. M 85, W 46; strategy 3. M 31, W 17; strategy 4. M 48, W 28  <b>History of:</b> MI Excluded; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> N/S. <b>Stress induced by:</b> N/S. <b>Image interpretation:</b> N/S. <b>Equipment:</b> N/S  <b>CA:</b> Yes  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> Taken as recorded in the notes  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> No  <b>Outcome measures:</b> Hard events - mortality; MI; occurrence of unstable angina. Soft events - PTCA; CABG; worsening of angina; complications; other</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Vanzetto 1999</b><sup>84</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> 1987 - 1989  <b>Follow-up:</b> 72 ± 18 months (11 days to 8 years)  <b>Country:</b> France  <b>Focus:</b> Prognostic value of SPECT in patients with low-to-intermediate likelihood of future cardiac events at long-term follow-up; incremental prognostic value of SPECT over clinical and ETT data  <b>Note:</b> This study focuses on a subset of the patient population reported on by Machecourt 1994</p>	<p><b>Inclusion criteria:</b> Patients referred for SPECT  <b>Exclusion criteria:</b> Myocardial revascularisation within 3 months of SPECT, MI &lt; 3 months before SPECT, or age &gt; 75 years  <b>Enrolled:</b> 1182  <b>Lost to follow-up:</b> 45  <b>Analysed:</b> 1137  <b>Age:</b> 55.3 ± 9.2  <b>Gender:</b> M 857, W 280  <b>History of (&gt; 3 months):</b> MI 270; PTCA 91; CABG 148</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> N/S whether stress ECG was within SPECT test  <b>Definition of positive SPECT test:</b> Left ventricle divided into 6 segments. Segments scored as abnormal in the event of decreased tracer uptake in a surface large enough to be considered significant. Abnormal segments defined as reversible (partial or total normalisation on redistribution images) or fixed  <b>Definition of positive stress ECG test:</b> Positive: horizontal or downsloping ST-segment depression of 1 to 2 mm measured 0.08 seconds after the J-point, occurring for a workload &gt; 75W, with or without chest pain. Strongly positive: ST-segment depression &gt; 2mm at any workload, or &gt; 1mm for a workload ≤ 75W, or ST depression post exercise duration &gt; 6 minutes  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Mortality; cardiac mortality; nonfatal MI; PTCA/CABG &gt; 3 months after SPECT</p>



Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Vanzetto 1999</b><sup>83</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> N/S  <b>Dates:</b> 1989 - 1994  <b>Follow-up:</b> 23 ± 17 months (range 3 - 78 months)  <b>Country:</b> France  <b>Focus:</b> Prognostic value of exercise stress testing and SPECT for the prediction of cardiac events in a homogeneous cohort of high-risk NIDDM patients</p>	<p><b>Inclusion criteria:</b> NIDDM patients presenting with ≥ 2 of the following risk factors: age ≥ 65 years; active smoker; high blood pressure, hypercholesterolaemia or LDL cholesterol &gt; 3.10 mmol/l; history of CAD; PVD; abnormal rest ECG; microalbuminuria  <b>Exclusion criteria:</b> Myocardial revascularisation &lt; 3 months; episode of unstable angina &lt; 3 months; acute MI &lt; 3 months; severe angina under medical therapy  <b>Enrolled:</b> 158  <b>Lost to follow-up:</b> 0  <b>Analysed:</b> 158  <b>Age:</b> 63 ± 9  <b>Gender:</b> M 105, W 53  <b>History of:</b> MI 20; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle, n = 78); pharmacologically (dipyridamole, n = 80). <b>Image interpretation:</b> Visual. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Left ventricle divided into 9 segments. Each segment classified as normal or abnormal, and if abnormal as reversible (partial or total normalisation after reinjection) or fixed (persistent defect after reinjection)  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression &gt; 1mm measured 0.08 second after the J-point. In patients with ST segment abnormalities on rest ECG, stress ECG positive when ST depression &gt; 2mm during exercise  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; need for revascularisation; occurrence of unstable angina; acute congestive heart failure</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Wagner 1996</b><sup>85</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Feb 1992 - Dec 1994  <b>Follow-up:</b> Mean 13.5 months  <b>Country:</b> Germany  <b>Focus:</b> Relative predictive power of 3 types of stress tests without knowledge of contributory risk factors 1 year after transmural MI and subsequent to treatment with thrombolytics</p>	<p><b>Inclusion criteria:</b> Patients hospitalised with acute transmural MI, treated with thrombolytic therapy, clinically stable in the post MI course, and able to exercise  <b>Exclusion criteria:</b> Death, unstable angina, &gt;75 years, severe concomitant disease, or refusal  <b>Enrolled:</b> 106</p> <p><b>Lost to follow-up:</b> 4  <b>Analysed:</b> 102  <b>Age:</b> 57 ± 11  <b>Gender:</b> M 89, W 13  <b>History of:</b> MI N/S; PTCA N/S; CABG N/S</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual.  <b>Equipment:</b> APEX 409 AG-system  <b>CA:</b> Performed by Judkins technique  <b>Interval between tests:</b> Within 18 days  <b>Definition of positive SPECT test:</b> Persistent defects: defects at stress and at rest. Reversible defects (ischaemia): difference to rest ≥ 10%  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression ≥ 1mm in any lead measured 80 ms after the J-point. Occurrence of angina pectoris an additional parameter for stress-induced ischaemia  <b>Angiographic definition of significant CAD:</b> Stenoses of ≥ 50% of the arterial intraluminal diameter  <b>Multivariate analysis:</b> Yes  <b>Outcome measures:</b> Mortality; PTCA; CABG; occurrence of unstable angina; occurrence of reinfarction</p>
<p><b>Zanco 1995</b><sup>86</sup></p> <p><b>Study design:</b> Cohort (prospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> Jan 1988 – Dec 1990  <b>Follow-up:</b> ≥ 36 months. Mean 43 months (range 36 – 60 months).  <b>Country:</b> Italy  <b>Focus:</b> Incremental prognostic value of SPECT in CAD patients</p>	<p><b>Inclusion criteria:</b> Patients who underwent SPECT for diagnosis or evaluation of CAD  <b>Exclusion criteria:</b> Previous revascularisation  <b>Enrolled:</b> 176</p> <p><b>Lost to follow-up:</b> 29  <b>Analysed:</b> 147  <b>Age:</b> 53 ± 9 (range 27 – 68)  <b>Gender:</b> M121, W 26  <b>History of:</b> MI 61; PTCA Excluded; CABG Excluded</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual.  <b>Equipment:</b> Single-head large field of view rotating gamma camera.  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> 18 segments per study. Each segment scored on a 4-point scale, in comparison with a linear colour scale (0 = activity &gt; 80% of the maximum, 1 = 80%- 50%, 2 = 50%-20%, and 3 &lt;20%). Parameters evaluated: (1) presence of abnormal scan (fixed or reversible defect); (2) presence of reversible defect (increase ≥ 2 in total score of stress images compared with rest images); (3) extent of stress perfusion defect (number of segments with score ≥ 1); (4) score of stress perfusion defect, including extent and severity of defect (calculated by sum of score of all segments in stress images)  <b>Definition of positive stress ECG test:</b> N/S  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Stepwise logistic regression  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; occurrence of unstable angina</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Zellweger 2002</b><sup>87</sup></p> <p><b>Study design:</b> Cohort (retrospective)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Follow-up:</b> Mean 667 ± 185 days. Minimum follow-up of 1 year  <b>Country:</b> USA  <b>Focus:</b> 1. Incremental prognostic value of SPECT over clinical assessment. 2. Potential usefulness and cost-effectiveness in clinical risk stratification. 3. Impact of SPECT on the subsequent referral to early CA</p>	<p><b>Inclusion criteria:</b> Patients with remote prior MI receiving their first SPECT study &gt; 6 months after MI  <b>Exclusion criteria:</b> Early (&lt; 60 days after SPECT) revascularisation  <b>Enrolled:</b> 1663  <b>Lost to follow-up:</b> 59  <b>Analysed:</b> 1413  <b>Age:</b> - Exercise 66.8 ± 10.5, adenosine 71.9 ± 10.5  <b>Gender:</b> M 1068, W 345  <b>History of:</b> MI 1413; PTCA 383; CABG 571</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 or Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (treadmill 899 (64%), pharmacologically (adenosine 514 (36%)). <b>Image interpretation:</b> Semiquantitative. <b>Equipment:</b> N/S  <b>CA:</b> No  <b>Interval between tests:</b> Stress ECG was part of SPECT test  <b>Definition of positive SPECT test:</b> Perfusion images scored on a 20-segment, 5-point model (0 = normal, 5 = no uptake) for the left ventricle. Summed stress score (SSS) and summed rest score (SRS) calculated by adding scores of segments in stress and rest image respectively. Summed difference score (SDS) derived as the difference between stress and rest scores. SSS &lt; 4 = normal, 4 - 8 mildly abnormal, 9 - 13 moderately abnormal, &gt; 13 severely abnormal. Degree of reversibility: SDS &lt; 2 = nonischaemic, 2 - 6 mildly ischaemic, &gt; 6 = moderately or severely ischaemic  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression of ≥ 1mm or upsloping of ≥ 1.5mm at 80ms after the J-point  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality; nonfatal MI; PTCA; CABG</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Zerahn 2000</b><sup>88</sup></p> <p><b>Study design:</b> Cohort (prospective)</p> <p><b>Method of recruitment:</b> Consecutive</p> <p><b>Dates:</b> Jan 1991 – Aug 1997</p> <p><b>Follow-up:</b> Mean 59.1 months ± 22.1. Follow-up until death or end Dec 1998</p> <p><b>Country:</b> Denmark</p> <p><b>Focus:</b> Prognostic power of SPECT in combination with ExECG</p>	<p><b>Inclusion criteria:</b> Patients referred for SPECT</p> <p><b>Exclusion criteria:</b> N/S</p> <p><b>Enrolled:</b> 697</p> <p><b>Lost to follow-up:</b> N/S</p> <p><b>Analysed:</b> N/S</p> <p><b>Age:</b> 56.9 ± 9.6</p> <p><b>Gender:</b> N/S</p> <p><b>History of:</b> MI 356; PTCA 6; CABG 30</p>	<p><b>SPECT:</b></p> <p><b>Tracer:</b> Tc-99m sestamibi. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual.</p> <p><b>Equipment:</b> N/S</p> <p><b>CA:</b> No</p> <p><b>Interval between tests:</b> Stress ECG was part of SPECT test</p> <p><b>Definition of positive SPECT test:</b> Reversible or irreversible perfusion defect present</p> <p><b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression 80ms after the J-point of ≥ 1mm compared with the rest ECG</p> <p><b>Angiographic definition of significant CAD:</b> N/S</p> <p><b>Multivariate analysis:</b> Cox proportional hazards regression model</p> <p><b>Outcome measures:</b> Cardiac mortality</p>

## ECG -gated SPECT

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Sharir 1999<sup>89</sup></b></p> <p><b>Study design:</b> Cohort (prognostic)  <b>Method of recruitment:</b> Consecutive  <b>Dates:</b> N/S  <b>Follow-up:</b> Minimum of 1 year. Mean follow-up interval was 569 ± 106 days (range 365 to 968 days)  <b>Country:</b> USA  <b>Focus:</b> Incremental prognostic value of post-stress ejection fraction and left ventricular volume, measured by gated SPECT, over clinical, exercise and perfusion data in predicting cardiac death in patients referred for SPECT</p>	<p><b>Inclusion criteria:</b> Patients receiving separate acquisition gated SPECT  <b>Exclusion criteria:</b> Nonischaemic cardiomyopathy, or revascularised &lt; 60 days after SPECT  <b>Enrolled:</b> 1924  <b>Lost to follow-up:</b>  <b>Analysed:</b> 1680  <b>Age:</b> 244  <b>Gender:</b> M 1034, W 646  <b>History of:</b> MI 418; PTCA 305; CABG 336</p>	<p><b>SPECT:</b>  <b>Tracer:</b> Tl-201 (rest), Tc-99m sestamibi (stress). <b>Stress induced by:</b> Exercise (treadmill, 1029); pharmacological (adenosine, 651). <b>Image interpretation:</b> Quantitative, visual. <b>Equipment:</b> 2-detector (Vertex, ADAC), 3-detector (PRISM, Picker) or single detector (Orbiter, Siemens) camera  <b>CA:</b> No  <b>Interval between tests:</b> N/S  <b>Definition of positive SPECT test:</b> Perfusion images scored on 20-segment, 5-point model for LV (0 = normal uptake, 4 = no uptake). Summed stress score (SSS) and summed rest score (SRS) calculated by adding the scores of segments in stress and rest images, respectively. Summed difference score (SDS) was derived as the difference between stress and rest scores. SSS &lt; 4 normal, SSS 4 to 13 mildly/moderately abnormal, and &gt; 13, severely abnormal  <b>Definition of positive stress ECG test:</b> Horizontal or downsloping ST-segment depression ≥ 1mm or upsloping ≥ 1.5 mm at 80 ms after the J-point was considered positive. Failure to achieve 85% of maximal predicted heart rate or ischaemic ECG response during exercise was followed by conversion to an adenosine stress test  <b>Angiographic definition of significant CAD:</b> N/S  <b>Multivariate analysis:</b> Cox proportional hazards regression model  <b>Outcome measures:</b> Cardiac mortality, nonfatal MI, PTCA later than 60 days following SPECT, CABG later than 60 days following SPECT</p>

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Shirai 2002</b><sup>90</sup></p> <p><b>Study design:</b> Prospective observational comparison</p> <p><b>Method of recruitment:</b> Consecutive</p> <p><b>Dates:</b> Jan 1999 – Oct 2000</p> <p><b>Country:</b> Japan</p> <p><b>Focus:</b> Incremental diagnostic value of worsening of regional wall motion, assessed by an automated algorithm in ECG-gated SPECT, over perfusion data for detection of multivessel CAD</p>	<p><b>Inclusion criteria:</b> Patients with normal sinus rhythm and known or suspected CAD who received SPECT and CA</p> <p><b>Exclusion criteria:</b> Previous CABG</p> <p><b>Enrolled:</b> 201</p> <p><b>Analysed:</b> 201</p> <p><b>Age:</b> 63 ± 10</p> <p><b>Gender:</b> M 153, W 48</p> <p><b>History of:</b> MI 63; PTCA 97; CABG Excluded</p>	<p><b>SPECT:</b></p> <p><b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (bicycle). <b>Image interpretation:</b> Visual (perfusion defects and LV regional wall motion. Quantitative (LV ejection fraction). <b>Equipment:</b> 2-detector gamma camera (Vertex, ADAC).</p> <p><b>CA:</b> Yes. Method N/S</p> <p><b>Interval between tests:</b> Within 10 weeks</p> <p><b>Definition of positive SPECT test:</b> LV divided into 9 segments. Tl-201 uptake of each segment assessed with a 4-point scoring system (3 = normal, 0 = severely reduced or absent). Reversible perfusion defect: ≥ 1 grade improvement in any segment on the delayed images or reinjection images compared with the initial images.</p> <p><b>Regional wall motion:</b> Regional wall motion graded as: 3 = normal or hyperkinetic, 2 = mildly hypokinetic, 1 = severely hypokinetic, 0 = akinetic or dyskinetic. Worsening of wall motion: ≥ 1 grade worsening in any segment on initial images compared with rest images. Individual segments assigned to 3 coronary territories</p> <p><b>Angiographic definition of significant CAD:</b> ≥ 70% narrowing of the internal diameter of the LAD, the LCX, the RCA, or their major branches and ≥ 50% narrowing of the left main coronary artery. Multivessel disease: significant left main CAD or 3- or 2-vessel disease</p> <p><b>Outcome measures:</b> True positives, false positives, true negatives, false negatives, sensitivity, specificity, diagnostic accuracy</p>

## Attenuation corrected SPECT

Study id and Methods	Participants	Test characteristics and Outcome measures
<p><b>Gallowitsch 1998<sup>91</sup></b></p> <p><b>Study design:</b> Prospective observational comparison</p> <p><b>Method of recruitment:</b> Consecutive</p> <p><b>Dates:</b> N/S</p> <p><b>Country:</b> Austria</p> <p><b>Focus:</b> Sensitivity and specificity of attenuation-corrected SPECT, impact on the extent and severity of perfusion abnormalities, and comparison with CA</p>	<p><b>Inclusion criteria:</b> Patients in whom CA was planned because of suspected CAD</p> <p><b>Exclusion criteria:</b> LBBB</p> <p><b>Enrolled:</b> All: 107</p> <p><b>Analysed:</b> 107</p> <p><b>Age:</b> All: <math>63.8 \pm 9.5</math> (range 33 – 77).</p> <p><b>Gender:</b> All: M 69, W 38.</p> <p><b>History of:</b> MI 42; PTCA 22; CABG 8</p>	<p><b>SPECT:</b></p> <p><b>Tracer:</b> Tl-201. <b>Stress induced by:</b> Exercise (treadmill, 69); pharmacological (dipyridamole, 39).</p> <p><b>Image interpretation:</b> Visual, quantitative. <b>Equipment:</b> Biplane high-resolution gamma camera (APEX SP-X , Cardia-L, Elscint).</p> <p><b>CA:</b> Seldinger technique</p> <p><b>Interval between tests:</b> 1 to 14 days</p> <p><b>Definition of positive SPECT test:</b> Positivity and reversibility on the redistribution images. Semiquantitative analysis using polar maps for non-corrected and attenuation-corrected images. Segmental perfusion defects classified as moderate (50-75% of maximal counts), severe (25-50%), or complete (0-25%). Extent of ischaemia determined by number of segments affected out of 31 segments. Segments assigned to vascular territories</p> <p><b>Angiographic definition of significant CAD:</b> <math>\geq 70\%</math> narrowing of lumen diameter</p> <p><b>Outcome measures:</b> True positives, false positives, true negatives, false negatives, sensitivity, specificity</p>