Clinical research

The clinical characteristics and investigations planned in patients with stable angina presenting to cardiologists in Europe: from the Euro Heart Survey of Stable Angina

Caroline A. Daly1*, Felicity Clemens2, Jose L. Lopez Sendon3, Luigi Tavazzi4, Eric Boersma5, Nicholas Danchin6, Francois Delahaye7, Anselm Gitt8, Desmond Julian9, David Mulcahy10, Witold Ruzyllo11, Kristian Thygesen12, Freek Verheugt13, and Kim M. Fox1 on behalf of the Euro Heart Survey Investigators

1 Royal Brompton and Harefield NHS Trust, Sydney Street, London SW3 6NP, UK
2 London School of Hygiene and Tropical Medicine, London, UK
3 Hospital Universitario Gregorio Maranon, Madrid, Spain
4 Policlinico S Matteo, Pavia, Italy
5 Department of Cardiology, Erasmus Medical Centre, Rotterdam, The Netherlands
6 Hopital Europeen Georges Pompidou, Paris, France
7 Hopital Cardiovasculaire et Pneumologique Louis Pradel, Lyons, France
8 Herzzentrum Luwigshafen, Ludwigshafen, Germany
9 University of Newcastle upon Tyne, Newcastle upon Tyne, UK
10 Adelaide and Meath incorporating National Children’s Hospital, Dublin, Ireland
11 Institute of Cardiology, Warsaw, Poland
12 Aarhus University Hospital, Aarhus, Denmark
13 University Medical Centre St Radboud, Nijmegen, The Netherlands

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Aims The Euro Heart Survey of Stable Angina set out to prospectively study the presentation and management of patients with stable angina as first seen by a cardiologist in Europe, with particular reference to adherence to existing guidelines and regional variability in patient presentation and initial assessment.

Methods and results Consecutive outpatients with a clinical diagnosis by a cardiologist of stable angina were enrolled in the study and 3779 patients were included in the analysis. The average age was 61 years and 58% were male. The majority of patients (88%) had mild to moderate angina, CCS class I or II. Despite a high prevalence of recognized risk factors, 27% did not have cholesterol and 33% did not have glucose measured within 4 weeks of assessment. The resting ECG was abnormal in 41% of patients. An exercise ECG was performed or planned as part of initial investigation in 76% of patients and 18% had a stress imaging test such as perfusion scanning or stress echo. A coronary angiogram was performed or planned in 41%, and 64% had an echo. The time from assessment to investigation varied widely, particularly for angiography. One in 10 patients had neither any form of stress test nor angiography.
with marked regional variation. Availability of invasive facilities increased the likelihood of both non-invasive and invasive investigations. Those with more severe symptoms or longer duration of symptoms or a positive non-invasive test were more likely to have angiography. In multivariable analysis, a positive stress test was the strongest predictor of the use of angiography, associated with a six-fold increase in the likelihood of invasive investigation. However, gender and availability of facilities were also predictive.

Conclusion Considerable variation in features at presentation and use of investigations has been identified in the stable angina population in Europe. The evaluation of biochemical cardiovascular risk factors was suboptimal. Overall rates of non-invasive investigation for angina and the clinical appropriateness of factors predictive of the use of invasive investigation were broadly in line with guidelines. However, the influence of access to facilities, and marked international variation in rates and timing of investigation suggest that factors unrelated to clinical need are also influential in the management of patients with stable angina.

Introduction

Stable angina is the most prevalent manifestation of coronary artery disease, occurring as an initial presentation in almost half of patients with coronary disease. Despite its prevalence, data regarding the management of angina are sparse, in contrast to the abundance of national and international surveys of the management of acute coronary syndromes. Registries exist of patients who undergo coronary angiography, or who have coronary disease detected at angiography, and there are numerous studies using either administrative or clinical data regarding the use of invasive investigation post-MI or acute coronary syndrome, but few studies document the complete sequence of investigation of stable angina. Those that have been published are either small, retrospective, and limited in scope, or restricted to a specific region. To obtain accurate and up-to-date information concerning the presentation and clinical course of stable angina, and to evaluate how the condition is managed with particular reference to the implementation of guidelines and regional or international variations in practice, the Euro Heart Survey (EHS) Programme has conducted a European Survey of Stable Angina.

Patients presenting ‘de novo’ to a cardiologist with stable angina were selected for study rather than a chronic review population, to facilitate tracing the pattern of investigations implemented, including the temporal relationships between assessment and investigation in a prospective manner. This paper reports the clinical presentation of stable angina, explores the use of investigations and factors predictive of the use of stress testing and coronary angiography in this condition, and evaluates how actual use compares to guideline recommendations.

Methods

Patient population

To ensure that the population studied was representative of the stable angina population, and not just pre-selected patients admitted to hospital for catheterization or revascularization, the survey was performed on community based, ambulatory patients on a new presentation to a cardiologist as an outpatient. Investigators were asked to enrol consecutive newly presenting patients over a 4-6 week period or until a minimum target was enrolled. A new presentation was defined as a first ever presentation, or new referral or re-referral, after a period of at least 1 year of not attending or consulting a cardiologist. Patients were suitable for inclusion if the cardiologist made a diagnosis, on the basis of clinical assessment, of stable angina, caused by myocardial ischaemia due to coronary disease. Patients were not obliged to have documented evidence of ischaemia to be included, but they did have to have stable anginal symptoms that were due to coronary disease in the opinion of the physician investigator. Exclusion criteria included unstable symptoms such as rapidly progressive symptoms, rest pain, or Canadian Cardiovascular Society (CCS) class IV symptoms. Further exclusion criteria included hospitalization within 24 h of the initial consultation (as these patients were considered potentially likely to have unstable angina in a proportion of cases); a prior history of revascularization, either percutaneous or surgical; or aetiology other than coronary disease, for example significant aortic stenosis or hypertrophic cardiomyopathy. The survey originally included only patients without any prior history of myocardial infarction, but from July 2002 to December 2002, patients with remote (>1 year) prior myocardial infarction were also included, to increase enrolment. Selection of patients with a new presentation of stable angina without prior revascularization was to facilitate the evaluation of patterns of initial assessment of stable angina, including the diagnostic approach, risk stratification procedures, the temporal relationships between assessment and investigations, and comparisons between variable patterns of investigation. Eligible patients were enrolled in the study after consent had been obtained in the manner deemed appropriate by the local regulatory authorities.

Angina severity was assessed using the CCS classification, and breathlessness classified according to the New York Heart Association (NYHA) classification. Definitions for risk factors, comorbid conditions, and ECG abnormalities are reported in Appendix B.

Participating centres

As part of the EHS Programme, the Stable Angina Survey shares many organizational and logistic features with other EHSs. National coordinators were encouraged to recruit investigators...
from a variety of clinical centres ranging from tertiary referral or university teaching hospitals to regional or district centres in a manner which reflected facilities and practice on a national level. Local investigators, who participated on a voluntary basis, then collected data. Patients were enrolled from 197 centres in 36 countries in Europe and the Mediterranean basin. The results are described from four pre-defined areas within Europe, northern Mediterranean, central and western, in line with the previous Euro Heart Surveys (EHSs) (Figure 1).7,27

Data collection

Data collection commenced in March 2002 and continued until December 2002. Participating centres completed a questionnaire regarding centre-specific information including the availability of cardiac surgery, catheterization facilities, and non-invasive diagnostic facilities. The attending physician, or a data collection officer in consultation with the attending physician, completed the case record forms (CRF), which contained information regarding demographic and clinical details of the patients, referral pathway, planned investigations, treatment recommended, and follow-up procedure observed. Attending clinicians recorded in the CRF whether a series of investigations were performed in advance of or in preparation for the initial assessment (within 4 weeks) or whether the test was planned by the cardiologist. If a test had been performed recently by the primary care physician, this could be recorded as ‘performed or planned’ by the investigator. Similarly, if the test was planned by the cardiologist but not yet performed within 4 weeks, it would still be recorded as performed or planned. For each test, the investigator recorded the timing of the test prior to assessment, <4 weeks after assessment, >4 weeks after assessment, or scheduled on a waiting list. If the result was available at assessment, or within the 4 week period afterwards, that result was recorded.

Data management

The data were collected and stored centrally at the European Society of Cardiology base in Nice. The data collection software ran initial consistency checks at data entry level, with further checking performed by submitting the database to consistency checks as per a pre-written validation plan using SAS software. Missing or inconsistent values were thus highlighted automatically and queried by the data management team using phone or e-mail contact with the investigators.

Statistical analysis

Statistical analysis was performed in collaboration with the London School of Hygiene and Tropical Medicine. Descriptive

Figure 1 Countries participating in the EHS of stable angina.
statistics were used to estimate the prevalence of risk factors, baseline clinical characteristics, and treatment at presentation. The Student’s t-test or ANOVA technique were used as appropriate to test differences in quantitative measures and the χ² test was used to test differences in proportions. Two-sided P-values are reported with 0.05 used as critical value to define statistical significance. To explore the variations in their use, logistic regression was employed to determine determinants of the use of exercise testing, stress imaging, or coronary angiography.

Univariate analysis of predictors of the use of exercise testing included nine variables, age (>70 years vs. <70 years), sex, employment, education, type of centre, comorbidity, symptom severity (CCS class), duration of symptoms (≥6 months vs. <6 months), and anti-anginal drug therapy prior to assessment (one or more anti-anginal drugs vs. one anti-anginal drug). Further variables added for analysis of stress echo and myocardial perfusion scanning as an outcome included the performance of exercise testing (yes/no) and the result of exercise testing (positive vs. negative or inconclusive). For coronary angiography, to these variables were also added the result of stress echocardiography or myocardial perfusion imaging and non-invasive estimation of LV function by echocardiography. Univariate analysis to identify the factors predictive of the use of non-invasive testing and coronary angiography was performed separately for each of the named regions. Multiple logistic regression using a stepwise procedure was used to ascertain the demographic, clinical, and investigative factors that determined the use of exercise testing, stress echo and perfusion imaging, and coronary angiography. Because of the substantial variation in the rates of referral for coronary angiography, separate analysis was also carried out for the countries which had a high rate of referral for coronary angiography (above median) and those which had a low rate of referral (below median). In order to check the robustness of the models, a uniformly distributed random variable was generated. A cutoff was imposed at a value of 0.5 for this variable, and the chosen models were re-run using the observations holding a value of ≤0.5 for this random variable. Analysis was undertaken using STATA™ version 8 statistical software.

Results

A total of 3923 patients with stable angina were enrolled in the survey. In all, 144 were excluded because the CRF had not been registered as completed, or there were multiple missing values and the results presented are for the remaining 3779 patients.

Participating centres and referral sources

Patients were enrolled in 197 centres. Of the participating centres, 35% had non-invasive diagnostic facilities only, 20% had non-invasive and invasive facilities, and 34% had, in addition to a catheterization laboratory, cardiac surgery facilities on-site. Facilities were uncategorized in 11% of centres. The majority of patients included (71%), had been referred by a primary care physician, and only 5% were referred from an emergency department for follow-up. Self referrals accounted for 10% of the population, although this figure was appreciably higher in central and Mediterranean Europe compared with northern and western Europe (15 and 17% vs. 0.2 and 2%, respectively, Figure 2). Patients were assessed in specialist chest pain clinics, non-emergency clinics specifically for the purpose of assessing patients with chest pain in 40% of cases. However, there were marked international differences in the proportions of patients assessed in such clinics, ranging from 0% in countries such as Denmark and Portugal to 93% of patients in Sweden.

Patients enrolled

Details of the numbers and basic demographics of patients enrolled from individual countries are presented

![Figure 2](https://www.oxfordjournals.org/our_journals/eurheartj/for_rent/chapter_2.png)

**Figure 2** Distribution of referral sources for patients presenting to a cardiologist with stable angina in northern, western, central, and Mediterranean Europe.
(see Supplementary material online, Table SI). The mean (SD) age of patients included in the survey was 61 (11) years, <5% were >80 years of age. Males represented 58% of the population overall (Table 1). Females included in the study were only marginally older than the males. Cardiovascular risk factors and other relevant medical history are shown in Table 1. The prevalence of diabetes and hypertension increased with increasing age with the prevalence of diabetes in >70 year age group (22%) double that in the <50 year age group (11%), and the prevalence of hypertension rising from 45% in those <50 years of age to 71% in those >70 years of age. Overall, the prevalence of comorbidity was low. Employment status was ascertained in 3511 patients, of whom 7.7% were unemployed and 48% retired.

On the whole, patients with stable angina from central Europe were slightly younger (mean age 59.5 years), more likely to be hypertensive, and to have hyperlipidaemia ($P < 0.001$ for differences in these parameters compared with other regions), whereas patients from Mediterranean Europe were slightly older (mean age 63.8 years), more often male, and more likely to have diabetes ($P < 0.001$ for differences in all of these parameters).

**Clinical details**

All patients with a clinical history of myocardial infarction within 1 year of assessment were excluded and 2398 (63%) patients were enrolled while any prior myocardial infarction was an exclusion criterion for the study. Only 4% of patients had a history of remote (>1 year) myocardial infarction. Angina class was assigned prior to presentation to a cardiologist, but just 52 patients, <2% of patients, had symptoms for >1 month. The median duration of symptoms prior to presentation to a cardiologist was 5 months and did not vary according to symptom severity. Regional variation was apparent, with symptom duration before cardiology assessment ranging from a median of 3 months in western Europe to 5 or 6 months in other regions ($P < 0.0001$). This difference was most pronounced for patients with more severe (class III) symptoms.

Severe heart failure symptoms, NYHA class III or IV, were rare, occurring in 5 and 0.6% of patients, respectively. Physical signs of heart failure, defined as a raised jugular venous pressure, crepitations in the lung fields, a third heart sound, peripheral oedema, or hepatomegaly, were reported in only 8% of cases. The population was overweight, three-quarters had a body mass index (BMI) of 25 or more, mean BMI $28.5$. Mean systolic and diastolic blood pressures were $144 \pm 21$ and $85 \pm 11$ mmHg, respectively.

**Medical therapy prior to cardiology assessment**

Almost half (49%) of patients were taking aspirin before assessment by a cardiologist. Only 22% of patients were on a statin prior to assessment by the cardiologist, and even of patients with recognized hyperlipidaemia only 41% were on a statin, and 5% on an alternative lipid lowering agent. Patients were taking at least one antianginal drug at presentation to the cardiologist in 62% of cases and two or more in 28%.

**Investigations performed**

Figure 3 is a flow diagram which depicts the overall pattern of the use of investigations.

**Biochemical tests at presentation**

Table 2 shows the numbers of patients who had lipid and glucose analyses, either performed or planned. Only 72% of patients actually had a cholesterol measurement performed within 4 weeks of assessment (Table 3). Overall mean cholesterol levels were $5.8$ mmol/L. Even in those patients who were taking a statin, mean cholesterol

### Table 1. Cardiovascular risk factors and other clinical details of patients presenting with stable angina, overall and by European region

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 3779)</th>
<th>%</th>
<th>North (n = 521)</th>
<th>%</th>
<th>West (n = 951)</th>
<th>%</th>
<th>Central (n = 1341)</th>
<th>%</th>
<th>Med (n = 966)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Male</td>
<td>2197/3779 58</td>
<td></td>
<td>315/521 60</td>
<td></td>
<td>489/951 51</td>
<td></td>
<td>784/1341 58</td>
<td></td>
<td>609/966 63</td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>61 (11)</td>
<td>62 (10)</td>
<td>61 (10)</td>
<td>60 (13)</td>
<td>64 (11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td>652/3666 18</td>
<td>74/511 14</td>
<td>142/910 16</td>
<td>209/1309 16</td>
<td>227/936 24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive</td>
<td>2267/3676 62</td>
<td>245/512 48</td>
<td>485/901 54</td>
<td>921/1321 70</td>
<td>616/942 65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>1843/3174 58</td>
<td>247/473 52</td>
<td>334/710 47</td>
<td>728/1125 65</td>
<td>534/886 62</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>819/3553 23</td>
<td>100/500 25</td>
<td>222/762 29</td>
<td>277/1326 21</td>
<td>220/965 23</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td>1337/3161 43</td>
<td>223/453 49</td>
<td>361/745 48</td>
<td>474/1119 42</td>
<td>289/844 34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>267/3779 7</td>
<td>13/521 3</td>
<td>67/951 7</td>
<td>114/1341 9</td>
<td>73/966 8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVA or TIA</td>
<td>197/3779 5</td>
<td>22/521 4</td>
<td>52/951 5</td>
<td>69/1341 5</td>
<td>54/966 6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic respiratory disease</td>
<td>313/3779 8</td>
<td>47/521 9</td>
<td>90/951 9</td>
<td>98/1341 7</td>
<td>78/966 8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic hepatic disease</td>
<td>72/3779 2</td>
<td>1/521 0.2</td>
<td>6/951 0.6</td>
<td>42/1341 3</td>
<td>23/966 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>54/3779 1</td>
<td>1/521 0.2</td>
<td>10/951 1</td>
<td>17/1341 1</td>
<td>26/966 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>61/3779 2</td>
<td>9/521 2</td>
<td>21/951 2</td>
<td>13/1341 1</td>
<td>18/966 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CVA, cerebrovascular accident; TIA, transient ischaemic attack; Med, Mediterranean.
Figure 3  Flow diagram illustrating the referral sources and use of non-invasive and invasive investigations in patients from the EHS of stable angina. Asterisk indicates investigations performed prior to assessment are included in the overall number of tests performed or planned. Non-Card. Specialist, non-cardiological specialist; FU, follow-up; CXR, chest X-ray; Ex ECG, exercise ECG; SE, stress echo; MPS, myocardial perfusion scan; Angio., angiogram.
levels were 5.7 mmol/L and just one-third of patients had achieved target (<5.0 mmol/L) cholesterol. Glucose analysis, although planned in 77% of patients, was only performed within 4 weeks in two-thirds of the population overall. Of the population without previously diagnosed diabetes, 4% were found to have a fasting glucose in the diabetic range (WHO criteria for the diagnosis of diabetes, i.e. fasting glucose of >7.0 mmol/L).

Resting ECG
A resting ECG was performed in the vast majority (99%) of patients and results recorded for 98% of patients in the study. At least one pre-defined abnormality, atrial fibrillation or other rhythm disturbance, ST depression, T-wave inversion, pathological Q-wave, or left or right bundle branch block, was recorded in 41% of ECGs.

Table 2  Number and proportion of patients who had lipid or glucose analysis performed or planned as part of cardiology assessment of stable angina

<table>
<thead>
<tr>
<th>Lipids</th>
<th>Total number planned/performed (% of population overall)</th>
<th>Number with result available to cardiologist within 4 weeks (% of population overall)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fasting</td>
<td>Fasting/non-fasting/unknown</td>
</tr>
<tr>
<td>Lipids</td>
<td>3125 (83%)</td>
<td>TC 1924 (51%) 2720 (72%)</td>
</tr>
<tr>
<td></td>
<td>LDL 1584 (42%)</td>
<td>2094 (55%)</td>
</tr>
<tr>
<td></td>
<td>HDL 1360 (36%)</td>
<td>1891 (50%)</td>
</tr>
<tr>
<td></td>
<td>TG 1786 (47%)</td>
<td>2377 (63%)</td>
</tr>
<tr>
<td>Glucose</td>
<td>2912 (77%)</td>
<td>1825 (48%) 2528 (66%)</td>
</tr>
</tbody>
</table>

Table 3  Cholesterol, lipid subfraction, and glucose levels recorded in patients with stable angina before or within 4 weeks of presentation to a cardiologist, according to fasting or statin therapy status

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Timing of specimen</th>
<th>Therapy</th>
<th>Mean (SD) (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>Fasting</td>
<td>5.8 (1.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-fasting</td>
<td>5.8 (1.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Taking statin</td>
<td>5.7 (1.4)</td>
<td></td>
</tr>
<tr>
<td>LDL-C</td>
<td>Fasting</td>
<td>3.8 (1.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-fasting</td>
<td>3.6 (1.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Taking statin</td>
<td>3.6 (1.2)</td>
<td></td>
</tr>
<tr>
<td>HDL-C</td>
<td>Fasting</td>
<td>1.3 (0.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-fasting</td>
<td>1.3 (0.5)</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Fasting</td>
<td>1.8 (1.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-fasting</td>
<td>2.2 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>Fasting</td>
<td>6.0 (1.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-fasting</td>
<td>6.1 (2.0)</td>
<td></td>
</tr>
</tbody>
</table>

ST depression and T-wave inversion were the most frequently observed abnormalities, occurring in 18 and 19% of patients, respectively, overall.

Chest X-ray
Although performed or planned in 51% of patients overall, performance of chest X-rays showed wide regional and international variability, ranging from 19 to 100% in individual countries. One-fifth of chest X-rays showed at least one abnormality, most commonly cardiomegaly, which was reported in 13% of all X-rays performed. Pulmonary congestion was reported in 5% of chest X-rays.

Echocardiography
Echocardiography was planned or performed in 2430 patients, 64% of the population overall, but only in 24% of patients in northern Europe. Of patients from western, central and Mediterranean Europe, 60, 84, and 63%, respectively, had a resting echo. At 4 week follow-up, an echo had been carried out and results were available for 80% of patients in whom the test was planned. Left ventricular hypertrophy (LVH) was detected in 32% of echos, and regional wall motion abnormality (RWMA) in 21% overall. Moderately impaired and poor ventricular function was reported in 17 and 3%, respectively.

Exercise ECG
Exercise testing was planned or performed in 76% of patients (Figure 3), with less regional variation than for other investigations (Figure 4). In northern Europe compared with other parts of Europe, a greater proportion of patients, 65% of all patients in whom an exercise test was planned, had their exercise test performed prior to being seen by a cardiologist. Results of 2328 exercise tests were available within 4 weeks of assessment. A positive result was recorded in 57%, negative in 29%, and inconclusive in 13%. Of patients with a positive test, 68% went on to have a coronary angiogram (Figure 3) compared with only 14%
of patients with a negative test ($P < 0.001$). Stress echo or perfusion scanning was performed in 8% of patients with negative result, 29% of patients with an inconclusive result, and 11% of patients with a positive exercise ECG result.

Patients who did not have an exercise test performed or planned
An exercise test was neither performed nor planned in 24% of the overall population. Among these patients, there were specific patient contra-indications to exercise ECG in 25%. Only 23 patients were reported not to have had the exercise test because it was not available. Of the patients who had no exercise test, 26% had an alternative form of non-invasive stress testing, either performed or planned, and 39% had an angiogram performed or planned. Of the patients who had no exercise test, 408 (45%) had neither another form of non-invasive stress testing nor coronary angiography (Figure 3). This group was composed of a higher proportion of elderly patients than the overall population, 45% were >70 years, and females were over-represented. Patients who had neither any form of stress testing nor angiography accounted for 11% of the overall population. Regionally, this corresponded to 18% ($n = 244$) of all patients in central Europe, 4% ($n = 19$) in northern Europe, 7% ($n = 68$) in western Europe, and 8% ($n = 77$) in Mediterranean Europe.

Stress imaging tests
The use of stress echocardiography and myocardial perfusion scanning was not widespread in this population, with one or other of these tests performed in only 18% of the population overall (Figure 5), although this rose to 34% among patients with a specific patient contra-indication to exercise ECG. Stress imaging techniques were not exclusively employed in patients who did not or could not have an exercise ECG as two-thirds of patients who were scheduled to have stress imaging also had an exercise ECG.

Exercise was the most common stressor in the case of perfusion imaging and inotropes in the case of stress echo. Myocardial perfusion scanning was more frequently used than stress echocardiography, but was less likely to be completed within 4 weeks of assessment. Results were available at 4 weeks for 71% of planned stress echos and 60% of planned perfusion scans. Inconclusive or uninterpretable stress imaging results were rare, reported in only 1-2% of tests performed. A negative result was reported in 17% of stress echos and 28% of perfusion scans, with evidence of fixed or reversible ischaemia in 81 and 71%, respectively.

Coronary angiography
Coronary angiography was either planned or performed in 1564 patients (41%) overall, with considerable regional variation as seen in Figure 6. The rate of coronary angiography was low overall in western Europe, but this masks high performance rates in certain countries with relatively smaller numbers of patients such as in Germany ($n = 144$), where 75% of patients had an angiogram performed or planned. Although coronary angiography was planned in 57% of patients with stable angina in northern Europe, there was frequently considerable delay before performance of the test. Almost 9 out of 10 patients (88%) referred for angiography in northern Europe had their angiogram scheduled >4 weeks after the time of assessment. In central Europe, 62% of patients had to wait for >4 weeks, 40% in Mediterranean, and only 18% in western Europe.

At 4 week follow-up, the results of coronary angiography were available for 799 patients. Of these patients, 72% of patients had significant coronary disease, defined as at least 50% stenosis of an epicardial vessel or branch thereof.

Factors influencing the use of non-invasive tests
In univariate analysis, females and those >70 years of age were significantly less likely to have an exercise test, as were patients with one or more comorbid condition (see Supplementary material online, Table SII). Patients with symptoms for >6 months, more severe

![Figure 5](https://example.com/figure5.png)

**Figure 5** Regional distribution of the use of stress perfusion scanning and stress echocardiography in patients presenting with stable angina. Med, Mediterranean.

![Figure 6](https://example.com/figure6.png)

**Figure 6** Regional distribution of the use, and timing relative to initial cardiology assessment, of coronary angiography in patients presenting with stable angina. >4 weeks, more than 4 weeks after cardiology assessment; <4 weeks, within 4 weeks or less of cardiology assessment; Prior, same day or before cardiology assessment; Med, Mediterranean.
angiography, gender was an independent predictor of the use of exercise testing, but not in countries with high rates of angiography. For stress imaging techniques, not having an exercise ECG performed or planned was an independent predictor of the use of either stress echo or perfusion imaging in all regions.

Independent predictors of the use of coronary angiography included a positive exercise test, symptom severity, and gender (Table 5). A positive exercise test was associated with an approximately six-fold increase in the likelihood of angiography irrespective of the overall rate of angiography within a country. Age and type of centre were independent predictors of the use of angiography only in countries with low rates of angiography. The validity of the multivariable models used was assessed using a random subset of the data as outlined previously. The models were found to be robust in the selection of which variables were predictive, and the magnitude of the effects observed were comparable to the results obtained in the analysis of the full population.

### Discussion

There is an abundance of national and international surveys of acute coronary syndromes,7–11 and indeed of heart failure27–30 in the recent literature, but remarkably few of stable angina. This survey represents the first registry of patients with stable angina in a large cohort of European countries and is unique as a prospective study with complete data on non-invasive and invasive investigations on a relatively unselected population of patients with stable angina presenting for the first time to cardiologists. It is the only report regarding investigation of angina to span multiple geographical areas and health care systems.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Multivariable determinants of the use of exercise ECG in patients with stable angina from the EHS of newly presenting angina in countries with high and low national rates of coronary angiography</th>
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<tbody>
<tr>
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<tr>
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<td>Age &gt;70</td>
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<td>Symptom duration (&gt;6 months)</td>
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<td>Countries with greater than median angiography rate</td>
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<tr>
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<tr>
<td>Symptom duration (&gt;6 months)</td>
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<tr>
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</tr>
<tr>
<td>CCS class III</td>
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<tr>
<td>Table 5</td>
<td>Multivariable determinants of the use of coronary angiography in patients with stable angina from the EHS of stable angina in countries with high and low national rates of coronary angiography</td>
</tr>
<tr>
<td>Variable</td>
<td>OR</td>
</tr>
<tr>
<td>Countries with less than median angiography rate</td>
<td></td>
</tr>
<tr>
<td>Positive Ex ECG</td>
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</tr>
<tr>
<td>≥2 Anti-anginal drug</td>
<td>2.10</td>
</tr>
<tr>
<td>CCS III</td>
<td>2.44</td>
</tr>
<tr>
<td>Female gender</td>
<td>0.56</td>
</tr>
<tr>
<td>Age &gt;70</td>
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<tr>
<td>Centres with invasive facilities</td>
<td></td>
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<td>Positive Ex ECG</td>
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<td>Age &gt;70</td>
<td>0.50</td>
</tr>
</tbody>
</table>

Ex ECG, exercise ECG; anti-anginal drugs: nitrates, beta-blockers, calcium antagonists, nicorandil, or metabolic agents.
care systems and is substantially larger than previous studies in this field.

**Patient profile**

On the whole, the patient profile was similar in the different European regions. Exceptions include a greater prevalence of diabetes in this population in Mediterranean region and a higher proportion of hypertension and hyperlipidaemia in central Europe. There is a higher proportion of women then included in most trials of secondary prevention in coronary disease, but this is not surprising if one considers that angina is the most frequent manifestation of coronary disease in women.31,32

**Risk factor assessment**

The 1997 European Society Guidelines on the management of stable angina advocate, as a minimum, an assessment of risk factors and resting electrocardiogram in addition to clinical assessment for all patients, and an initial strategy of non-invasive testing for most patients, which will assist in determining the need for coronary angiography.44

Despite the relative ease and lesser expense of lipid and glucose measurements compared with other forms of investigation, lipid analysis was not performed within 1 month in more than a quarter of patients and glucose measurement not performed in one-third of patients. Fewer than half of the 58% of patients with known hyperlipidaemia were on lipid lowering drugs, and of even among those on statin therapy only one-third had achieved target cholesterol levels, reflecting subtherapeutic dosing, and emphasizing the need for cholesterol monitoring even among those on cholesterol lowering therapy from their primary care physician. The low rate of lipid measurement is not dissimilar to that observed in the EUROASPIRE II study33 or studies of the penetration of guidelines regarding the investigation and management of hypertension.34 It is higher than reported rates of measurement during cardiac hospitalizations in the early 1990s, which report as few as 14% of patient having cholesterol measurement.35,36 However, the rate of measurement of cholesterol can be increased considerably with strategic programmes at institutional level to raise awareness of the benefits of measuring and treating cholesterol, and standardize the approach to risk factor assessment in the ischaemic heart disease population. Such targeted programmes can also increase the appropriate use of lipid lowering therapy.35

Although glucose measurement resulted in the discovery of only an additional 4% of the population with previously unknown diabetes, a lower proportion of newly discovered diabetics than in studies of myocardial infarction37 or the EHS of Diabetes and the Heart,38 this is nonetheless an important finding with consequences both for the prognosis of the individual, and for treatment. Clearly successful and effective secondary prevention cannot be achieved if lipid and glucose status are not actively investigated, and routine measurement of these biochemical parameters should be an unquestioned preliminary step in patient assessment.

**Resting echocardiography**

With the exception of northern Europe, a large proportion of patients surveyed underwent resting echocardiography as part of the work up for stable angina. It is well recognized that left ventricular function is a crucial factor in influencing prognosis in coronary disease.39-41 and it is possible to use simple reproducible echocardiographic measurements of ventricular dimensions to assign risk and to combine this information effectively with information obtained from stress testing to discriminate between high and low risk groups.42 The relatively high pick up rate of LVH (32%) and RWMA (21%) in a population for the most part without clinical heart failure or prior history of MI, are further vindication of this course of action.

**Non-invasive stress tests**

The sequence of non-invasive investigation of angina observed in the study seems at first to be in line with existing guidelines with regard to the use of functional assessment in almost all patients. Between 70 and 80% of patients had an exercise test performed or planned, and stress imaging techniques were used in 26% of the population who did not have an exercise ECG. However, imaging techniques were used more frequently as an additional test rather than an alternative to exercise ECG in the majority of patients, with the highest rate of stress imaging among patients with inconclusive exercise ECG results.

Importantly, failure to perform some form of functional assessment as a minimum was an issue for a considerable proportion of patients. This was particularly the case in central Europe where neither functional assessment nor angiography was planned in 18% of the population referred to cardiologists. These findings are reconcilable with suggestions that, although modest, the contribution of differences in medical care to the east–west health gap is not inconsequential.43,44

Nevertheless, the overall rate of non-invasive investigation stress testing compared favourably with that reported from a US study of the use of diagnostic testing within 4 weeks in a population with new onset chest pain, in which only 60% received a specific cardiac investigation, and 22% of patients who met necessity criteria for testing were not tested.45

In this survey, patients with longer symptom duration, more severe symptoms, or those already on more than one anti-anginal medication were less likely to have an exercise ECG or other stress test. This may indicate either that these patients are thought to have more severe disease and more likely to require revascularization and therefore go on to have coronary angiography
directly or that in such patients, the diagnosis is considered established and confirmatory testing not required. This latter approach does not take account of the important role exercise testing may have in risk stratifying patients. The use of the Duke treadmill score or other prognostic scores was not evaluated by this survey. As only 39% of patients who did not have an exercise test went on to have an angiogram, direct angiography does not fully account for the observed referral patterns and suggests under use of stress testing as a prognostic tool.

Invasive investigation: coronary angiography

The rate of coronary angiography recommended by cardiologists, 41%, is comparable to North American figures from 1990, which estimated that 40% of incident cases of angina undergo elective cardiac catheterization over a 5-year-period. Although there has been a progressive increase in cardiac catheterization rates in the USA, some reports suggest that referral of incident coronary disease for catheterization after stress testing has not increased dramatically after the late 1980s. The variability in length of time between assessment and angiography is a striking feature of the survey, with an almost five-fold difference in the proportion of patients having to wait more than a month for scheduled angiography between regions. This is also a cause for concern given reported rates of adverse cardiac events (including death, MI, and hospitalization for unstable angina) of 9.4% over 8.4 months in previous studies, with increased probability of events as the waiting time for angiography lengthened. Future guidelines may need to provide guidance on prioritization of patients for angiography to address this issue.

In line with previous findings, gender was a significant predictor of the use of coronary angiography in both univariate and multivariable analyses. Although less frequently documented in the literature, a bias against the use of angiography in older patients has been reported. However, in this survey, age was only independently associated with less angiography where overall rates of angiography are low, suggesting that where services are constrained, or practice more conservative, the elderly are less likely to be referred onwards for angiography or potential consideration for revascularization, but where there is more liberal use of angiography age is not a deciding factor. The availability of on-site cardiac catheterization facilities significantly increased the likelihood of referral for coronary angiography in similar fashion to that shown in studies of acute coronary syndrome. Again, however, centre type was only a predictive factor in multivariable analysis in countries where overall rates of angiography were low.

Important clinical factors related to appropriateness of use namely, a positive stress test or intensity of medical therapy (more than one anti-anginal at presentation) were universally independent predictors of the use of coronary angiography. But patient symptoms were more influential, and availability of on-site facilities not an influential factor in countries where angiography was more frequently undertaken.

Limitations

Although a survey of stable angina, this is not a population-based study and as such it is not possible to make any inferences from the data about the incidence of angina in any of the regions studied. Furthermore, as assessment by a cardiologist was chosen as the sampling point, the data regarding clinical characteristics may not be generalizable to the overall population with stable angina in the community because of selection bias, but the population is reflective of the patient profile presenting to cardiologists and suitable for the investigation of their management practices. Inclusion in the study was based on the diagnosis of angina by the attending physician and is thus also open to interpretation bias, but as patient management was based on the working diagnosis of angina, the population is suitable for the evaluation of patient management. Because of the existing infrastructure in place at the time this survey was initiated, the survey is somewhat biased towards larger teaching or university affiliated centres, with more centres with on-site catheterization facilities than would be the case in practice. The numbers of patients from some of the 36 countries which contributed data are too small to be representative of practice in that individual country, but where trends in prevalence or practices emerge between countries in a region, the larger regional sample size is likely to be representative. Finally, given the potential sources of bias in the analysis, the results must be considered as indicative rather than factual. In light of this, and as the nature of the study is exploratory rather than definitive, caution is advised in interpretation of the results, but the findings are nonetheless worthy of consideration, and generate important questions as well as providing novel information in this area.

Conclusions

The survey documents a young population with a high prevalence of modifiable cardiovascular risk factors presenting for the most part with mild to moderate anginal symptoms, uncomplicated by heart failure. This population, who have declared themselves at increased risk by virtue of their symptoms, but who for the most part have not yet suffered major adverse cardiovascular events, present a perfect opportunity to the cardiologist to improve prognosis while also reducing angina. Despite being comparable to the populations recruited in international randomized controlled trials of secondary prevention to which the existing guidelines are most applicable, there is a clear gap between the guidelines and practice with regard to the evaluation of the major biochemical measurements of cardiovascular risk, cholesterol and glucose.

The widespread use of non-invasive investigations appears broadly in line with existing guidelines, but
improvements can certainly be made, particularly among the minority of patients who have no form of non-invasive stress test or angiogram, in standardizing the use of echo-cardiography, and in improving the temporal relationships between assessment and initial investigations in some regions.

However, the influence of access to facilities, and marked international variation in rates and timing of angiography, suggest that factors unrelated to clinical need, including service capacity and patient preference, are also influential in the management of patients with stable angina. The challenge to the European cardiology community is not only to ensure that clear guidelines on the subject, backed by the available evidence, penetrate to all relevant professionals, but also to ascertain the optimal strategies to ensure that the guidelines are put into practice, through implementation of national or institutional programmes and to adapt such programmes to fit into highly variable existing services.

Supplementary material

Supplementary material is available at European Heart Journal online.

Appendix A

Organization of the survey

Angina Expert Committee: Kim Fox (Survey Chairman), UK; Caroline Daly (Research Fellow), UK; Nicolas Danchin, France; Francois Delahaye, France; Anselm Gitt, Germany; Desmond Julian, UK; Jose-Luis Lopez Sendon, Spain; David Mulcahy, Ireland; Witold Ruczyilo, Poland; Luigi Tavazzi, Italy; Kristian Thygesen, Denmark; Freek Verheugt, The Netherlands, Eric Boersma, The Netherlands (Representative of the Committee for Methodology and Data Management), David Wood, UK (Chair of Euro Heart Survey Programme).

Euro Heart Survey Team (European Heart Journal, France): Malika Manini, Operations Manager; Claire Bramley, Data Monitor; Valerie Laforest, Data Monitor; Charles Taylor, Database Administrator; Susan Del Gaiso, Administrator.

Main Investigator Centre (London, UK): Kim Fox (Chairman); Caroline Daly (Research Fellow).

Statistical Centre: London School of Hygiene and Tropical Medicine, Felicity Cleemens, Bianca de Stavola.

National Co-ordinators: Kurt Huber, Austria; Guy De Backer, Belgium; Vera Sirakova, Bulgaria; Roman Cerkar, Czech Republic; Per Thayssen, Denmark; Seppo Lehto, Finland; Francois Delahaye, France; Bondo Kobuila, Georgia; Uwe Zeymer, Germany; Dennis Cochinos, Greece; Kristof Karlocai, Hungary; Emer Shelley, Ireland; Shlomo Behar, Israel; Aldo Maggioni, Italy; Virginija Grabauskiene, Lithuania; Jaap Deckers, The Netherlands; Inger Aasmosun, Norway; Janina Stepinska, Poland; Lino Goncalves, Portugal; Vyacheslav Mareev, Russia; Igor Riecansky, Slovakia; Miran F. Kenda, Slovenia; Jose Luis Lopez-Sendon, Spain; Anna Rosengren, Sweden; Peter Buser, Switzerland; Tugrul Okuy, Turkey; Oleg Sychov, Ukraine; Kevin Fox, UK.

There was no national co-ordinator in the participating countries which are not mentioned in the previous list.

Euro Heart Survey Board Committee: Maarten Simoons (Chairman), The Netherlands; David Wood (Past Chairman), UK; Angeles Alonso, Spain; Shlomo Behar, Israel; Eric Boersma, The Netherlands; Harry Crijns, The Netherlands; Kim Fox, UK; Anselm Gitt, Germany; Malika Manini, France; Keith McGregor, France; Barbara Mulder, The Netherlands; Markku Nieminen, Finland; Sylvia Priori, Italy; Lars Ryden, Sweden; Luigi Tavazzi, Italy; Alec Vahanian, France; Panos Vardas, Greece; William Wijns, Belgium; Uwe Zeymer, Germany.

List of Industry Sponsors: Servier Laboratories Ltd.

For the purposes of recording ECG abnormalities

**ST depression:** defined as depression of the ST segment >0.5 mm or >0.05 mm below the isoelectric line.

**T wave inversion:** defined as inversion of the T wave of the QRS complex except in leads AVR, V1, and III which are >0.04 s wide and 0.2 mm deep or >20% of the accompanying R wave.

On examination, clinical signs of heart failure were defined as the following:

- Elevated venous pressure, hepatomegaly, dependent oedema, crepitations, gallop rhythm, or evidence of cardiac enlargement.

**Comorbid conditions and risk factors**

**Hepatic disease:** chronic hepatitis or cirrhosis, or other hepatic disease causing elevation of transaminases more than three times the upper limit of normal.

**Peripheral vascular disease:** claudication either at rest or exertion, amputation for arterial vascular insufficiency, vascular surgery (reconstruction or bypass) or angioplasty to the extremities, tissue diseases, polymyalgia rheumatica, etc.

**Chronic renal failure:** chronic dialysis or renal transplantation or serum creatinine >200 μmol/L.

**Chronic respiratory disease:** diagnosis within 1 year or active malignancy.

**Chronic inflammatory conditions:** chronic arthritis, systemic lupus erythematosus or other connective tissue diseases, polymyalgia rheumatica, etc.

**Peptic ulcer disease:** Active peptic ulcer disease or on treatment for peptic ulcer disease.

**Malignancy:** diagnosis within 1 year or active malignancy.

**Hypertension:** treated hypertension, on anti-hypertensive therapy.

**Hyperlipidaemia:** treated hyperlipidaemia, on lipid lowering medication, or specific dietary modification.

**Diabetes:** treated diabetes, on insulin or oral diabetic medication, or specific dietary modification.

**Family history of premature coronary artery disease (CAD):** a history of angina pectoris, myocardial infarction or sudden death among first-degree relatives under the age of 55 years for male relatives and 65 years for female relatives.
References


