



Clinical research

The initial management of stable angina in Europe, from the Euro Heart Survey

A description of pharmacological management and revascularization strategies initiated within the first month of presentation to a cardiologist in the Euro Heart Survey of Stable Angina

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KEYWORDS

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Aims In order to assess adherence to guidelines and international variability in management, the Euro Heart Survey of Newly Presenting Angina prospectively studied medical therapy, percutaneous coronary intervention (PCI), and surgery in patients with new-onset stable angina in Europe.

Methods and results Consecutive patients, 3779 in total, with a clinical diagnosis of stable angina by a cardiologist were enrolled. After initial assessment by a cardiologist, 78% were treated with aspirin, 48% with a statin, and 67% with a beta-blocker. ACE-inhibitors were prescribed by the cardiologist in 37% overall. Revascularization rates were low, with only 501 (13%) patients having PCI or coronary bypass surgery performed or planned.

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However, when restricted to patients with coronary disease documented within 4 weeks of assessment, over 50% had revascularization performed or planned. Among other factors, the national rate of angiography and availability of invasive facilities significantly predicted the likelihood of revascularization, OR 2.4 and 2.0, respectively.

Conclusion This survey shows a shortfall between guidelines and practice with regard to the use of evidence-based drug therapy and evidence that revascularization rates are strongly influenced by non-clinical, in addition to clinical, factors.

Introduction

The management of stable angina has two major objectives: to reduce or abolish the symptoms, and to improve prognosis. Some treatment options have a well proven track record in achieving both aims; for example, revascularization in anatomically defined subgroups¹⁻⁴ or beta-blockade in the post-myocardial infarction (MI) population,⁵ but many secondary prevention measures do not reduce symptoms. This absence of a direct effect on symptoms does not, however, diminish the importance of anti-platelet therapy and lipid-lowering therapy, particularly statin therapy, which should be universally prescribed in patients with clinically suspected coronary disease provided there are no contraindications,⁶⁻⁸ and possibly also angiotensin converting enzyme (ACE) inhibitor therapy.^{9,10} After such blanket secondary prevention therapy, treatment options diversify rapidly and should be guided by clinical characteristics of the patient, including cardiovascular and non-cardiovascular co-morbidity, patient tolerance, and patient preference.

With regard to pharmacological treatment of angina, there are innumerable studies of the effect of common anti-anginal drug classes (beta-blockers, calcium antagonists, and nitrates), or combinations thereof, on either symptoms or markers of ischaemia, silent or symptomatic, ambulatory or provoked.^{7,11-13} Yet despite the high prevalence of angina and frequent need for anti-anginal drug therapy, there are relatively few studies of the prognostic effect of anti-anginal drug therapy, and even fewer with long-term follow-up. Beta-blockers are recommended as first line maintenance⁶⁻⁸ therapy (after *pro re nata* nitrate) for patients with stable angina on the basis of results from post-MI studies extrapolated to the stable angina population.

The 1997 European guidelines on the management of angina suggest that revascularization should be considered in patients who will benefit prognostically,¹⁻⁴ or in whom symptoms are not controlled by medical therapy.

The purpose of this survey was to examine the initial management of newly presenting stable angina in its totality, including the adherence to guidelines and evidence-based practice in the pharmacological treatment of angina, and to attempt to examine some of the factors predictive of the decision to revascularize.

Methods

The methodology of the Euro Heart Survey (EHS) of Stable Angina is described in the companion paper.¹⁴ Briefly, to ensure that the

population studied was representative of the stable angina population, and not a pre-selected group of stable patients admitted to hospital for catheterization or revascularization, the survey was performed on community-based patients presenting to a cardiologist as an outpatient. Participating centres (197) were a mix of academic and non-academic institutions, and hospitals with and without interventional and cardiac surgical facilities.

The patient population was composed of patients at a new presentation to a cardiologist in whom a diagnosis was made of stable angina, caused by myocardial ischaemia due to coronary disease based on clinical assessment, and who did not have unstable angina. A new presentation was defined as a first ever presentation to a cardiologist, or new referral or re-referral after a period of at least 1 year of not attending (consulting) a cardiologist. Patients who required hospitalization within 24 h of the initial consultation, and were therefore considered likely to have unstable angina in a proportion of cases, were excluded from the survey, as were patients who had a prior history of revascularization, either percutaneous or surgical, or aetiology other than coronary disease, for example significant aortic stenosis, or hypertrophic cardiomyopathy. For all patients, the immediate medical treatment recommended, and follow-up arrangements were recorded. Anti-anginal drugs were defined as drugs intended to alleviate symptoms or ischaemia, such as beta-blockers, calcium antagonists, nitrates, nicorandil, or metabolic agents such as trimetazidine. In the case of guideline recommended treatments (anti-platelet therapy, statin therapy, and beta-blockade) not being prescribed, the investigator was asked to select a reason why the drug was not prescribed. The results of investigations performed, and changes to the initial management plan, including revascularization procedures performed or planned, were also recorded 4 weeks after assessment.

Data management

The data were collected electronically by the investigators and stored centrally at the European Society of Cardiology based in Nice, France. 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

Regional analyses of treatment initiated were performed according to the North, West, Central, and Mediterranean divisions as previously used in EHS methodology. Descriptive statistics were used to quantify the frequency of use of pharmacological and other treatments at presentation. The Student's *t*-test or ANOVA technique were used as appropriate to test differences in quantitative measures, and the χ^2 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. Logistic regression was employed to define determinants influencing early (within 4 weeks) decision to pursue a revascularization strategy. Forwards and backwards stepwise procedures were used to select the most significant predictors of early revascularization, using $P = 0.05$ as the significance level to enter, and $P = 0.05$ as the significance level to stay. Variables considered included clinical details such as age and sex, type of centre, comorbidity, symptom severity and duration, prior anti-anginal drug therapy, the result of exercise or other stress testing, and the rate of angiography stratified as high or low according to the median rate in the country. Separate multivariable analysis was carried out for the countries which had a high rate of referral for coronary angiography ($>$ median) and those which had a low rate of referral ($<$ median). This method avoids problems due to intra-regional heterogeneity in angiography rates, and reflects the general type practice within the national health service, and whether invasive or conservative practice is adopted (in terms of angiography at least). It is similar to methods used in previous analyses of treatment and outcome in acute coronary syndromes according to prevailing rates of PCI.¹⁵ All analyses were undertaken using STATA™ statistical software.

Results

Details of the patient population and the investigations which were performed or planned as a result of assessment by a cardiologist are briefly described. The majority of patients had been referred by a primary care physician (71%). The population was young, the mean age of the 3779 patients included in the survey was 61 years, and 58% were male. There was a high prevalence of modifiable cardiovascular risk. A large proportion, 2879 (76%), of patients had had, or were scheduled to have, an exercise ECG, and 1564 (41%) a coronary angiogram, after the initial consultation. Regarding enrolment from different types of centre, 28% of patients were from centres with non-invasive facilities only, 26% from centres with invasive facilities on site but without cardiac surgery, and 45% from centres with full facilities including cardiac surgery on site. The remaining 1% were recruited from sites which were not categorized.

Immediate medical therapy recommended

Prior to cardiology assessment, 49% of patients were taking aspirin and 22% of patients were taking a statin. *Table 1* shows the frequency of use of secondary prevention and anti-anginal drugs in individual participating countries, after initial assessment by a cardiologist. The frequency of use of other cardiovascular medication is described in *Table 2*. After assessment by a cardiologist, 81% of patients were taking or were recommended an anti-platelet agent, 78% aspirin. A statin was prescribed in 48%, beta-blockers in 67%, and 61% were on a nitrate. Only 27% were taking a calcium channel blocker and, with few international exceptions, the use of nicorandil and metabolic agents such as trimetazidine or ranolazine was limited to a small percentage of cases. The majority of patients (59%) were on two or more anti-anginal drugs after assessment by a cardiologist, and only 13% were on no anti-anginal drug (*Figure 1*). The number

of anti-anginal drugs per patient did not differ according to sex, but increased significantly with age up to 70 years ($P \leq 0.002$ for each decade increase in age up to 70 years). The intensity of anti-anginal drug therapy was also related to the severity of symptoms, with those with less severe symptoms [Canadian Cardiovascular Society (CCS) Class I] more likely to be on no anti-anginal medication, and those with more severe angina (CCS Class III) more likely to be on several drugs after assessment ($P < 0.001$ for trend). There were 307 patients with unclassified symptoms, of whom half were not prescribed anti-anginal therapy. For the majority of these patients (66%) the reason for not initiating beta-blockade was recorded as 'awaiting investigations'.

The reasons for not prescribing secondary prevention treatment and beta-blockade in the overall population are presented in *Table 3*. In the 834 patients not recommended aspirin, specific patient contraindications accounted for only 22% of the reasons given for not prescribing aspirin. Just over half (52%) of these patients were prescribed an alternative anti-platelet agent. Of the patients in whom aspirin was not considered indicated, 11% were taking an alternative anti-platelet agent.

Just one-third of the population not already taking a statin were prescribed lipid-lowering therapy. Specific patient contraindications accounted for only 19% of reasons given for not prescribing a statin. In patients with a history of hyperlipidaemia, the use of statin therapy was considerably higher (70–85%), across all regions.

ACE-inhibitors were prescribed in 40% of patients overall. However, the rate of prescription was higher (73%) in patients with clinical signs of heart failure. In diabetic patients ACE-inhibitors were also prescribed more frequently, with 56% of patients with diabetes receiving a recommendation for ACE-inhibitor therapy.

Planned follow-up

After initial assessment, a follow-up visit was scheduled with the cardiologist for the majority of patients, 2725 (72%), with a median wait for this visit of 41 days. The median wait for this review appointment varied from 70 days in Northern Europe to 35 days in Central Europe. In total, only a quarter of patients had a definitive management plan (either revascularization or conservative management with all investigations completed) in place 4 weeks after initial assessment. The remainder of patients continued to await one or more investigations 4 weeks after assessment, or were observed for clinical progress before further management was instituted (*Table 4*).

Conservative management (medical therapy only) with all investigations completed was planned in 452 patients (12%). In all, 354 (78%) of these patients had an exercise test, 35 (8%) stress echo, and 571 (3%) perfusion scan. An angiogram was performed in 281 (62%). The clinical details of patients in whom conservative management was adopted are shown in *Table 5*. In terms of guideline adherence and evidence-based practice, 400 (88%) of the conservative management group were treated with aspirin or an alternative anti-platelet agent, and 215

Table 1 Frequency of use of secondary prevention and anti-anginal drugs in patients from the EHS of Stable Angina

Country	<i>n</i>	Aspirin (%)	Statin (%)	Beta-blocker (%)	Nitrate (%)	Calcium antagonist (%)	ACE-inhibitor (%)	Nicorandil (%)	Metabolic agent (%)
Northern Europe		85	61	68	67	29	21	6	1
Denmark	70	54	24	31	43	26	10	0	3
Finland	76	82	59	83	71	24	26	0	1
Sweden	56	79	50	71	54	20	20	0	0
UK	319	94	72	72	73	33	23	10	1
Central Europe		89	55	77	77	29	61	2	17
Albania	23	96	39	96	83	52	35	0	0
Belarus	26	74	44	76	50	41	65	0	15
Bosnia and Herzegovina	20	100	50	95	100	15	75	0	0
Bulgaria	30	100	67	93	83	33	83	0	43
Croatia	52	96	69	81	67	33	56	2	0
Czech Republic	42	90	31	79	83	24	45	0	2
Georgia	45	98	51	64	84	33	56	0	38
Hungary	30	83	67	87	80	27	73	0	0
Latvia	18	83	39	83	94	22	50	0	28
Lithuania	77	97	38	88	88	30	81	3	8
Macedonia	8	100	38	75	63	63	50	0	0
Moldova	27	96	4	81	52	19	48	0	0
Poland	571	90	66	77	72	26	62	3	20
Romania	145	77	50	70	79	32	48	1	17
Russian Federation	57	89	49	90	81	39	81	0	12
Serbia and Montenegro	8	88	63	75	38	0	88	0	0
Slovakia	108	86	38	80	84	31	53	0	18
Slovenia	30	77	80	63	93	33	50	3	0
Ukraine	14	71	14	43	100	14	71	0	100
Western Europe		52	30	52	35	18	23	<1	1
Austria	22	68	36	36	59	32	32	14	0
Belgium	3	67	0	67	33	33	0	0	0
France	20	95	70	95	55	40	15	10	10
Germany	144	83	62	74	39	19	58	0	6
The Netherlands	762	44	23	46	33	17	16	0	<1
Mediterranean		85	51	66	61	33	40	1	2
Europe									
Cyprus	46	89	63	74	41	9	39	0	0
Greece	165	87	68	67	66	45	42	0	2
Israel	67	94	80	76	33	30	34	1	6
Italy	256	78	63	68	63	41	40	1	1
Lebanon	4	100	50	75	50	25	25	0	0
Portugal	77	86	47	64	64	36	52	8	6
Spain	263	83	60	54	66	25	34	2	2
Overall		78	48	67	61	27	40	2	7

(48%) were on any form of lipid-lowering therapy (predominantly statin). Although these proportions are similar to those for the population as a whole, they are significantly lower than the proportions taking anti-platelet and lipid-lowering drugs in the revascularization group (88 vs. 96%, $P < 0.001$ and 45 vs. 77%, $P < 0.001$). More than 80% of the conservatively managed patients were on two or more anti-anginal drugs.

Revascularization

Only 161 patients, 4% of the population overall, had PCI performed within 4 weeks of presentation, and 68 (2%)

had coronary artery bypass grafting (CABG) surgery. PCI was planned for an additional 155 (4%) of the population and CABG for a further 151 (4%). A small number of patients, 34 in total, had both procedures performed or planned within 4 weeks. In all, 501 patients (13%) had a revascularization procedure either performed or planned within 4 weeks of initial presentation. The proportion of men (17%) in the survey who had revascularization either performed within 4 weeks or planned was twice that of women (8%). Initially these rates of revascularization may appear low, but they refer to rates of early revascularization, PCI, or CABG that had been performed or planned within 4 weeks of

Table 2 Frequency of alternative (to aspirin and statin) secondary prevention agents and other cardiovascular drugs in patients from the EHS of Stable Angina

Country	<i>n</i>	Alternative anti-platelet (%)	Alternative lipid-lowering (%)	Oral anti-coagulant (%)	Anti-arrhythmic (%)	Angiotensin receptor antagonist (%)	Diuretic (%)
Northern Europe		3	2	1	2	5	20
Denmark	70	0	0	3	3	6	19
Finland	76	1	3	1	3	8	21
Sweden	56	4	4	0	2	7	5
UK	319	4	1	1	1	4	23
Central Europe		10	6	2	6	2	22
Albania	23	4	4	0	0	0	9
Belarus	26	32	6	0	0	3	21
Bosnia and Herzegovina	20	15	0	0	0	5	0
Bulgaria	30	0	0	0	3	0	20
Croatia	52	4	2	6	13	2	19
Czech Republic	42	10	12	0	2	2	29
Georgia	45	0	0	0	7	0	24
Hungary	30	3	7	7	10	0	27
Latvia	18	0	6	0	0	0	17
Lithuania	77	13	1	5	5	1	14
Macedonia	8	13	0	0	0	0	0
Moldova	27	15	0	4	11	0	26
Poland	571	8	8	2	4	1	22
Romania	145	20	3	1	10	1	22
Russian Federation	57	11	7	2	12	9	47
Serbia and Montenegro	8	13	0	0	0	0	25
Slovakia	108	6	6	3	7	6	21
Slovenia	30	33	0	3	3	20	27
Ukraine	14	14	14	0	50	7	43
Western Europe		7	3	5	3	8	18
Austria	22	0	5	9	9	27	18
Belgium	3	0	0	0	0	0	0
France	20	60	15	5	0	15	30
Germany	144	33	10	7	10	4	27
The Netherlands	762	1	2	4	2	8	16
Mediterranean Europe		13	4	2	3	10	18
Cyprus	46	2	4	0	0	13	15
Greece	165	19	4	1	3	9	14
Israel	67	4	7	0	0	4	15
Italy	256	14	4	5	6	12	23
Lebanon	4	0	0	0	0	0	0
Portugal	77	8	6	1	3	21	27
Spain	263	11	3	2	1	8	20
Overall		9	4	3	4	6	20

initial presentation to a cardiologist with stable symptoms. When the rate and timing of coronary angiography is considered, the converse is true. In the survey population as a whole, 1564 (or 41%) of patients had a coronary angiogram either performed or planned as a result of the initial assessment and the results of angiography were available for 799 patients overall. Of patients with results of angiography recorded within 4 weeks of presentation, revascularization was the chosen treatment strategy for 52% of patients with significant disease, i.e. >50% coronary stenosis (Table 6). The presence of

obstructive coronary disease was greater in men than women (88 vs. 66%) and increased with advancing age. The prevalence of three-vessel disease ranged from 19% among patients <50 years to 36% among the >70-year age group ($P = 0.01$ for trend).

Factors influencing early (within 4 weeks) decision to revascularize

To explore the variations in their use, determinants influencing early (within 4 weeks) decision to pursue

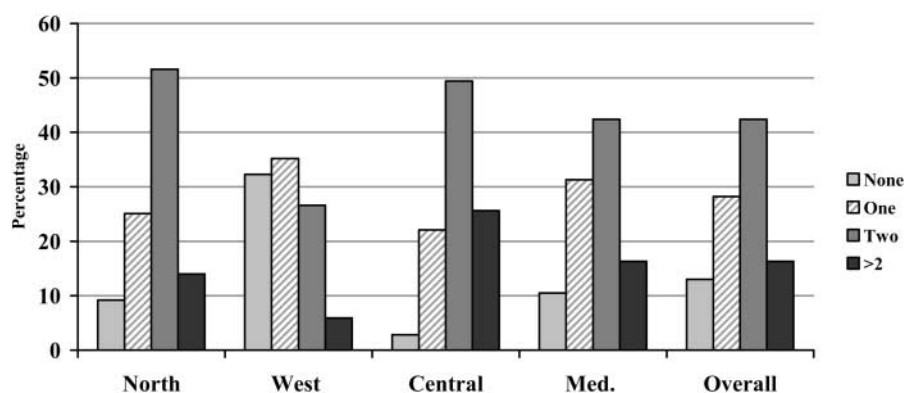


Figure 1 Regional distribution of number of anti-anginal drugs per patient after initial assessment, from the EHS of Stable Angina.

Table 3 Frequency of reasons for not prescribing aspirin, beta-blocker or statin treatments in patients from the EHS of Stable Angina

	Prior to assessment n (%)	Post-cardiology assessment n (%)		Reasons for not recommending the drug n (% of those not taking drug)			
	Taking drug	Taking drug	Not taking drug	C/I	Not indicated	Await Ix	Other/unknown
Aspirin	1803 (48)	2942 (78)	834 (22)	184 (22)	378 (45)	192 (23)	80 (10)
β-Blocker	1404 (37)	2513 (67)	1265 (33)	298 (24)	581 (46)	305 (24)	81 (6)
Statin	825 (22)	1830 (48)	1945 (52)	371 (19)	985 (51)	475 (24)	114 (6)

C/I = specific patient contraindication.

Await Ix = awaiting further investigation before prescription.

Table 4 Management status 4 weeks following initial presentation from the EHS of Stable Angina

Status	n (%) (total = 3779)
Definitive plan in place with investigations complete	953 (25)
Conservative management	452 (12)
Revascularization ^a	501 (13)
Further investigation planned during intervening period since assessment	674 (18)
Coronary angiogram	525 (14)
Stress myocardial perfusion scan	97 (3)
Stress echocardiogram	52 (1)
Awaiting clinical review and/or investigations planned at initial assessment	2152 (57)

^aRevascularization includes procedures already completed within the 4-week period.

significant independent predictor of lower rates of revascularization with an odds ratio of 0.58. A positive exercise test was associated with a greater chance of referral for revascularization (OR 2.49) as were more severe symptoms (OR 2.58 for CCS III) and use of a greater number of anti-anginal drugs (OR 1.29). The availability of invasive facilities on site and the prevailing national rate of coronary angiography were also significant and independent predictors of revascularization strategy (OR 1.72 and 2.60, respectively).

Because of the substantial variation in the rates of referral for coronary angiography between countries, separate analysis was carried out for the countries which had a high (>median) rate of referral for coronary angiography and those which had a low (<median) rate of referral (*Table 8*). A positive exercise test and sex were independently predictive of the use of revascularization in both circumstances. The availability of invasive facilities on site was also a predictive factor in countries with high national rates of angiography.

Discussion

Secondary prevention

The use of evidence-based medical therapy, particularly secondary prevention strategies, is far less than ideal in the survey. Although not so dramatic as MI, angina is

a revascularization strategy were examined using univariate and multivariable analysis (*Table 7*).

Although patients aged >70 years were less likely to receive revascularization, this was not a significant predictor of revascularization in univariate or multivariable analysis. Female sex on the other hand was a

Table 5 Clinical characteristics and treatment recommended to patients with planned conservative management or revascularization from the EHS of Stable Angina

	Conservative management (<i>n</i> = 452) % ^a	Revascularization performed/ planned (<i>n</i> = 501) % ^a	Overall population (<i>n</i> = 3779) % ^a
Male	57	74	58
Diabetic	15	26	17
Age, mean, years	61.2	61.5	61.2
Angina severity			
CCS Class I	32	29	39
CCS Class II	53	52	49
CCS Class III	15	19	12
Anti-platelet therapy	88	96	81
Lipid-lowering therapy	48	65	51
Number of anti-anginal drugs after cardiology assessment			
0	7	3	13
1	23	22	28
2	46	55	42
>2	24	20	16

^aExcept age; years.**Table 6** Proportion of patients referred for revascularization (either PCI or CABG) according to recorded severity of coronary disease from the EHS of Stable Angina

	<i>n</i>	Patients referred for revascularization (Total = 501)	% of patients revascularized according to recorded severity of CAD
Angiogram planned/performed but no result recorded	753	159	
Angiogram performed with results recorded	799	342	
0-vessel disease ^a	146	3	2
1-vessel disease ^a	217	93	43
2-vessel disease ^a	191	96	50
3-vessel disease ^a	245	150	61
Any significant CAD ^b	653	339	52

^aNumber of vessels diseased defined as number of vessels with significant coronary disease.^bSignificant coronary disease defined as >50% stenosis of a major epicardial vessel or branch thereof.

nonetheless a manifestation of coronary disease, and should trigger the implementation of secondary preventive measures. The message regarding the use of anti-platelet agents seems to have penetrated the cardiology consciousness to some extent, with 81% of patients on anti-platelet agents of one form or another after cardiology consultation, similar to the 83.9% of patients with established coronary heart disease on anti-platelet therapy in EUROASPIRE II¹⁶ and somewhat less than reported in contemporary clinical trials of patients with cardiovascular disease.⁹ However, with one in five patients not receiving anti-platelet therapy, this remains suboptimal. The use of statin therapy is even more disappointing. Only 48% of patients were prescribed statin therapy following review by a cardiologist. This figure is also similar to the 43% of patients with coronary disease on lipid-lowering drugs at hospital discharge in EUROASPIRE II, but is considerably lower than

desirable in a patient population with known or suspected coronary disease, and a high prevalence of hyperlipidaemia. Another rather disquieting feature which emerges from the data is the considerable international heterogeneity in prescription practices for secondary preventative pharmacotherapy, even in countries with large volume samples. As an example, the high average rates of aspirin prescription mask considerable variability at national level, with prescription rates varying by up to 50%. The proportion of patients prescribed aspirin ranged from 94% in the UK to 44% in The Netherlands.

Anti-anginal therapy

In terms of specific anti-anginal drugs, beta-blockers and nitrates are clearly the most frequently employed with a

Table 7 Factors influencing early decision to revascularize in patients presenting with stable angina from the EHS of Stable Angina

Variable	Comparator	Univariate			Multivariable		
		OR	95% CI	P	OR	95% CI	P
Age	≥70 years	0.84	0.67–1.07	0.164	–		
Sex	Female	0.44	0.35–0.55	<0.0001	0.56	0.44–0.70	<0.0001
Type of centre	Invasive facilities	1.42	1.13–1.78	0.002	1.70	1.34–2.17	<0.0001
Duration of symptoms	≥6 months	0.78	0.65–0.95	0.014	0.72	0.58–0.90	0.003
Symptom severity	Class II vs. I	1.54	1.23–1.92	<0.0001	1.76	1.39–2.223	<0.0001
	Class III vs. I	2.35	1.76–3.14		2.39	1.75–3.28	
Anti-anginal drugs	>1 anti-anginal	1.59	1.30–1.93	<0.0001	1.31	1.06–1.64	<0.014
Exercise ECG result	Positive	3.48	2.86–4.22	<0.0001	2.54	2.05–3.13	<0.0001
Perfusion result	Positive	10	3.04–32.85	<0.0001	–		
Stress echo result	Positive	2.15	0.58–8.03	0.251	–		
High national rate of angiography	>median	3.50	2.83–4.33	<0.0001	2.77	2.20–3.49	<0.0001

Table 8 Independent predictors of early decision to revascularize in patients presenting with stable angina in countries with high and low rates of angiography from the EHS of Stable Angina

Countries with low rates of angiography				Countries with high rates of angiography			
Variable	OR	95% CI	P	Variable	OR	95% CI	P
Positive exercise ECG	4.86	3.35–7.05	<0.0001	Positive exercise ECG	4.05	2.74–6.00	<0.001
Female	0.58	0.39–0.86	0.006	Female	0.57	0.37–0.86	0.007
				Invasive centre	1.62	1.03–2.55	0.04
				Symptom duration >6 months	0.66	0.49–0.99	0.04

smaller, but not inconsequential, proportion of patients on calcium antagonist, and combination therapy the order of the day for the majority of patients. The use of beta-blockers in this study is in line with reported usage in other studies of stable coronary disease.^{17,18} The small proportion of the population prescribed nicorandil or metabolic agents reflects the less established role of these drugs and a lack of emphasis on their use in the existing European, or even the more recent American, guidelines. It is also likely to reflect the 'newly presenting' nature of the population. Nicorandil in particular has only been shown to reduce the combined outcome of MI, death, and hospitalization for unstable angina on a background of established medical therapy¹⁹ and these classes of drugs are frequently reserved for patients who have not successfully achieved symptomatic control with conventional drugs or their combination. In a more chronic stable angina population who would have had symptoms for a longer period, and a longer period in which to try several treatment options, a somewhat greater use of these medications might be expected.

With specific patient contraindications to aspirin, statins, and beta-blockers in only 5, 8, and 10% of the overall population it seems the results of trials of secondary prevention are broadly applicable to the general angina population, although contraindication to statin therapy is higher than might be expected after the results of studies such as the Heart Protection Study²⁰

or Anglo-Scandinavian Cardiac Outcomes Trial,²¹ where a smaller proportion of patients were not randomized because of patient contraindications.

The fact that appropriate secondary preventative treatment is postponed awaiting the result of further investigation in almost a quarter of patients not commenced on such treatment is another important issue, given that most patients wait more than 6 weeks for clinical review. Although there may be good reason to withhold certain medication, in particular beta-blockers, prior to provocative stress tests, and it is not currently specifically addressed in the guidelines, it would appear reasonable, in the context of waiting periods of more than 1 month for investigations or clinical review, to commence appropriate therapy in a patient with a clinical diagnosis of angina at the time of initial diagnosis. Beta-blockade or other anti-anginal therapy could then be withdrawn for the brief time window required to perform the test if that is the practice within the individual institution.

That only 26% of patients have a definite management plan with all investigations completed within 4 weeks of the initial assessment is of concern and has important public health implications. The waiting times for non-invasive and invasive tests, and outpatient follow-up review are considerable, although the clinical impact of longer waiting times will only become available with follow-up. The scheduling of follow-up visits was subject to several variations in provision of services. It

is apparent that in some countries, patients who were due to have invasive or specialized testing such as coronary angiography, myocardial perfusion scanning, or stress echocardiography, were referred onwards for further care without follow-up arranged with the local cardiologist. For example, in the UK, more than half of patients for whom no follow-up appointment had been made were on a waiting list for a coronary angiogram in another institution.

The conservatively managed group, who have had all requested investigations completed, and have been assigned to medical therapy, receive less intensive pharmacological treatment than the revascularization group, with fewer patients receiving either anti-platelet or lipid-lowering therapy, although the use of anti-anginal drug therapy is comparable. Thus, if an excess in cardiovascular morbidity and mortality is observed in the conservatively treated group in the future, it cannot truly be described as 'failure of treatment' but rather 'failure to treat' as these patients have not been optimally medically managed.¹⁷ A possible explanation may be that patients in whom the interventional approach is adopted are more likely to be treated in university or teaching institutions, not just with greater facilities, but also with a greater emphasis on evidence-based treatment. It has also been shown in the setting of acute coronary syndromes that the availability of invasive facilities on site increases the likelihood of use of evidence-based secondary preventative therapy.²² A key factor in the success of future European Society of Cardiology guidelines will be their penetration to all strata of health care systems so that such dichotomy in treatment standards is attenuated.

Revascularization

Although the overall revascularization rates seem low, when restricted to those in whom obstructive coronary disease has been documented within 4 weeks of the initial assessment, just over half have been referred for, or have had, a revascularization procedure, mostly PCI. This is substantially greater than the 19% of patients who underwent revascularization during a much longer period of follow-up in Ghandi's study²³ of new cases of angina which included unstable angina, or other estimates of revascularization in stable angina²⁴⁻²⁶ and more in line with current studies of ACS.^{15,27-29} The overall number of revascularization procedures in the survey will inevitably rise as time progresses and more patients come to have scheduled angiography performed and analysed; however, as the highest-risk patients on clinical and non-invasive testing were prioritized for earlier angiography, it is likely that the rate of referral for revascularization may decelerate after the first month.

Clinically appropriate reasons for referral such as severe (CCS class III) symptoms or a positive exercise test are independently associated with a 2.5-fold increase in the likelihood of referral for revascularization, but women are only half as likely to be referred for revascularization, even when other potential

confounding features such as the results of exercise ECG, are adjusted for. Reports regarding a bias against revascularization in women have previously offered conflicting results.^{30,31} The results of angiography were not recorded in all patients at the 4-week follow-up and it is not possible to comment on the potential effect of angiographic results on this finding in this study. Type of centre and prevailing national rate of angiography are also independent predictors of revascularization, reflecting the influence of service capacity and availability of on-site revascularization facilities on referral patterns. In centres/countries where there is sufficient capacity to perform angiography promptly, there may be a lower threshold to proceed to revascularization for fiscal as well as clinical reasons.

Limitations

Although this was a survey of stable angina, because assessment by a cardiologist was chosen as the sampling point, the data may not be generalizable to the overall population with stable angina in the community, because of selection bias. However, the population is reflective of the patient profile presenting to cardiologists and suitable for 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 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 enrolment of consecutive patients, the increased recruitment of community hospitals, and the large population recruited over a relatively short period of time have contributed to making this survey as representative of clinical practice in Europe as possible within the constraints of feasibility, and it contributes a truly unique data source to the literature. 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 has yielded mixed results. It is apparent that guidelines regarding treatment of modifiable cardiovascular risk factors and secondary preventive measures

remain inadequately adhered to. Although the antiplatelet message appears to be widely implemented, the use of statin therapy is far below that which would be expected or desirable either at primary care level or by cardiologists. For revascularization, patient management appears to be influenced by prevailing national practice in addition to practice guidelines. It is evident that non-clinical factors, including not only national practice but also proximity to invasive centres, are influential in decisions to proceed to revascularization, in addition to clinical factors such as stress test results or symptom severity.

Appendix

Organization of the survey

Angina Expert Committee: Kim Fox (*Survey Chairman*), United Kingdom; Caroline Daly (*Research Fellow*), United Kingdom; Nicolas Danchin, France; François Delahaye, France; Anselm Gitt, Germany; Desmond Julian, United Kingdom; José-Luis Lopez Sendon, Spain; David Mulcahy, Ireland; Witold Ruzyllo, 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, United Kingdom (Chair of EHS Programme).

EHS Team (European Heart House—France): Malika Manini, Operations Manager; Claire Bramley, Data Monitor; Valérie Laforest, Data Monitor; Charles Taylor, Database Administrator; Susan Del Gaiso, Administrator.

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

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

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There was no national coordinator in the participating countries which are not mentioned in the above list.

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