North of England evidence based guidelines development project: summary version of evidence based guideline for the primary care management of stable angina

North of England Stable Angina Guideline Development Group

This is the last of three articles on developing evidence based guidelines for the primary care management of asthma and angina in adults

The aim of this guideline is to provide recommendations to aid primary health care professionals in their management of patients with chronic stable angina due to coronary artery disease (not aortic stenosis or hypertrophic obstructive cardiomyopathy). It does not deal with unstable angina or myocardial infarction. It is a summary version of the full guideline,[1] to which reference should be made for clarification or further information. The development group assumes that health care professionals will use general medical knowledge and clinical judgment in applying the general principles and specific recommendations in this document to the management of individual patients. Recommendations may not be appropriate for use in all circumstances. Decisions to adopt any particular recommendation must be made by the practitioner in the light of available resources and circumstances presented by individual patients. Throughout this guideline categories of evidence (cited as I, II, and III) and the strength of recommendations (A, B, or C) are as described in the paper in the previous issue (23 March, p 760).

Scope of guideline

Aspects covered by this guideline are investigation, risk factor identification and management, drug treatment, and referral. All recommendations are for primary health care professionals and apply to adult patients attending general practice with angina.

Initial assessment

Comment—Assessment will be based on a clinical history and relevant examination. This guideline requires that the following should be known: precipitants of anginal attacks; smoking history; occupation; amount of exercise taken; drug history; weight; blood pressure.

Age limits

Comment—The group thought that a chronological age limit for investigation or referral was not appropriate. Functional status was thought to be more appropriate.

Precipitating factors

RECOMMENDATION

- Factors that precipitate angina should be inquired about and have their management discussed (C).

Investigation of angina

RECOMMENDATION

Patients being investigated for angina should have the following investigations:

- Haemoglobin measurement to identify anaemia (C)
- Thyroid function measurements to identify thyroid disease (C)
- Blood glucose measurement to identify diabetes mellitus (C)
- Serum cholesterol measurement (see risk factor management) (A).

Comment—There was disagreement among both the group members and the reviewers about whether thyroid function tests should be performed only in patients in whom there is clinical suspicion of thyroid disease.

Resting 12 lead electrocardiogram

RECOMMENDATION

- All patients with angina should have a resting 12 lead electrocardiogram (B).
- Though a normal resting 12 lead electrocardiogram does not exclude coronary artery disease (II),[2,3] an electrocardiogram that is abnormal in any way supports the clinical diagnosis of coronary artery disease (II).[4-8] In addition, an abnormal electrocardiogram delineates a population with a poorer prognosis (II).[8-11]

Exercise testing

RECOMMENDATIONS

- Exercise testing is effective in prognostically grouping patients and can provide information in addition to that obtained from invasive testing; all patients with clinically certain angina should have an exercise test (B)
- Exercise testing will mean referral to an open access service when this is available and referral to a cardiologist when it is not (C)
- If a patient who requires an exercise test is physically incapable of performing the test he or she should be referred to a cardiologist for consideration of other forms of investigation (C)
- Patients having an exercise test for prognostic investigation and treatment should have the test performed while taking their normal medication (B)
- Whether or not a patient has diabetes and the oestrogen status of women should be recorded on a request form, as these influence the performance of the test and interpretation of the result (B).

Patients who should not have an exercise test are:

- Those whose symptoms are uncontrolled by maximal medical treatment (they should be referred to a cardiologist for angiography, not exercise testing) (C)
- Those who need further clarification of the diagnosis and in whom the diagnosis is currently uncertain (these patients should be referred to a cardiologist, not directly for an exercise test) (C)
- Those who are physically incapable of performing the test for reasons other than angina (see above) (C)
- Those with comorbid illness that is currently more important (C)
- Those who decline the test (C).

An exercise test is low risk (II).[12] Exercise testing is of value in patients with coronary artery disease to establish a prognosis and provide information in addition to that from invasive testing (II).[13-16] When interpreting an exercise test result it is important to take into account not just ST segment changes but other changes, such as duration of exercise, presence of

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BMJ 1996;312:827-32

pain, change in blood pressure, and change in heart rate (II).[17-22] However, the diagnostic usefulness of an exercise test is low in patients with a low pretest probability of coronary artery disease (II).[23 24]

An open access exercise testing service can be used appropriately by general practitioners (II).[25] When an exercise test is performed to identify whether a patient is in a group that would benefit from prognostic investigation and treatment it should be performed with the patient taking his or her usual treatment (II).[26] In addition, when requesting an exercise test on a woman the practitioner should record her oestrogen status in terms of whether or not she is menopausal or taking oestrogen replacement therapy; similarly, if an exercise test is performed on a patient with diabetes this should be stated clearly on the request form. Both instances will influence performance of the test or interpretation of the result, or both (II).[27 28]

Management of risk factors

Comment—Full systematic reviews in each aspect of risk factor management was beyond the scope of this guideline development project.

Cholesterol

RECOMMENDATIONS

- All patients with angina should have their serum cholesterol concentration measured (A)
- A raised serum cholesterol concentration should be managed in line with published guidelines (C).

Patients at high risk of cardiovascular disease benefit from having raised serum cholesterol concentrations lowered (I).[29] The subsequent management of patients with raised serum cholesterol concentrations should be addressed through published consensus guidelines on the management of hypercholesterolaemia. There was disagreement within the group on whether the diagnosis of hypercholesterolaemia should be based on a single or multiple measurements of serum cholesterol concentration.

Blood pressure

RECOMMENDATIONS

- All patients should have their blood pressure measured (C)
- If the blood pressure is raised it should be managed in line with published consensus guidelines (C).

Smoking cessation

RECOMMENDATIONS

- Patients with angina who smoke should be advised to stop (A)
- No one strategy is effective for all patients; advice and strategies should be tailored to individual circumstances (C)
- Nicotine patches can safely be used to help patients with coronary artery disease stop smoking (A)
- However, because the effectiveness of nicotine patches is limited they should be used as only one element of a broader strategy (C).

Smokers are more likely than non-smokers to have angina. Stopping smoking probably does not alter anginal symptoms (II),[30-36] but it lowers mortality in patients with ischaemic heart disease (I).[37-43] Nicotine replacement can be effective in helping patients to stop smoking (I),[44 45] and transdermal nicotine is safe in patients with ischaemic heart disease (I).[46]

Comment—The *British National Formulary* recommends caution when using nicotine products in patients with cardiovascular disease.[47]

Exercise

RECOMMENDATION

- Moderate exercise within a patient's capabilities should be recommended to improve general fitness and wellbeing (C).

Three trials suggested some benefit from exercise—namely, improvement in myocardial perfusion,[48 49] coronary blood flow, peak exercise, and arteriographic changes.[50] Five trials elicited no benefit.[51-55] All these trials were of different design and used different exercise regimens and durations. None was designed solely to study patients with stable angina (I).

The evidence from cohort and case-control studies is also conflicting. These studies showed that people defined as "highly active" lived on average 2·1 years longer than those not so defined[56] and that both sedentary work and sedentary occupation were associated with more ischaemic heart disease after correcting for risk factors.[57] However, a cohort study of over 9000 middle aged men found that after correcting for coronary heart disease risk factors there was no association between physical activity and myocardial infarction (II).[58]

Weight reduction

RECOMMENDATION

- Patients with a raised body mass index should be encouraged to reduce their weight until their body mass index is normal (C).

Occupation

Comment—A patient's occupation may be affected by angina. In some cases angina may necessitate a switch to lighter work; in others it may necessitate the patient stopping work. Whether this change is permanent will be determined by the patient's response to treatment. Vocational drivers' continued fitness to work is governed by clear regulations.[59] Special rules also apply to certain other occupations—for example, merchant seamen and airline pilots. For details the relevant authorities should be consulted.

Driving

Comment—The law requires notification by an applicant or licence holder to the Driver and Vehicle Licensing Agency immediately on diagnosis of any disability that is likely to affect safe driving either at the time of driving or in the future, except in the case of disabilities that will be completely cured within three months (for example, fractures). The medical practitioner's role is to advise the patient on the basis of the severity of the condition. If the driver's fitness is so severely affected as to present a distinct hazard to other people and the driver fails to notify the agency there may be grounds for the doctor to consider whether he or she should notify the agency direct.

Drug treatment

All recommendations for drug treatment apply only in the absence of recognised contraindications, side effects, or interactions as documented in the *British National Formulary*.[47]

RECOMMENDATIONS

- It is important to ensure that patients are complying with treatment and that any side effects are known (C)
- Within any drug class patients should be treated with the cheapest preparation that they can tolerate, will comply with, and which controls their symptoms (C).

Secondary prophylactic treatment

RECOMMENDATION

- All patients should be treated with aspirin 75-300 mg daily (A).

Aspirin in high risk groups lowers the risk of subsequent vascular events (I).[60]

Initial symptomatic treatment

Comment—The aim of symptomatic treatment is to use the least treatment necessary to minimise symptoms sufficient to allow patients to live as they wish.

RECOMMENDATIONS

- Patients with angina should take sublingual glyceryl trinitrate as required in response to pain and before engaging in activities that bring on pain (C)
- If patients do not respond to sublingual preparations buccal preparations should be considered (C)
- For all but minimal symptoms patients should be given regular symptomatic treatment (see section) (C).

Sublingual glyceryl trinitrate is effective prophylaxis against episodes of angina (I).[61] Buccal glyceryl trinitrate is more effective than sublingual (I).[62]

Regular symptomatic treatment

Monotherapy

RECOMMENDATIONS

- All patients who require regular symptomatic treatment should be treated with a β blocker (B)
- Patients should be treated with the cheapest preparation that they can tolerate, can comply with, and which controls their symptoms (C)
- Patients should be warned not to stop β blockers suddenly or allow them to run out (B)
- If β blockers need to be stopped they should be tailed off over four weeks (C).

Patients who have a myocardial infarction and are given β blockers have a subsequently lower mortality (I).[63,64] Patients taking β blockers for hypertension are less likely to have a vascular event, and those taking β blockers who subsequently have a myocardial infarction have a subsequently lower mortality (II).[65,66]

β Blockers are as effective as other drug groups when used as monotherapy (I). The following studies show the drugs to be effective as first line agents. However, differences in patient selection, study design, and drug dosages all prevent critical comparisons. Specific comparisons were β blockers and dihydropyridines,[67-71] β blockers and diltiazem or verapamil,[72-74] and studies with three drugs.[75,76] Within the time frame of our search there was no compelling evidence to choose one β blocker over another (I).[77-79] Acute β blocker withdrawal causes an increase in coronary events (II).[80]

Substitution monotherapy in patients intolerant of β blockers

RECOMMENDATION

- Patients intolerant of β blockers should be treated with verapamil (C).

Verapamil when used after infarction reduces the rate of major adverse events (I).[81] Verapamil is as effective as other drug groups when used as monotherapy (I).[82-85]

RECOMMENDATIONS

- If a patient cannot tolerate a β blocker or verapamil, then there is no clear basis from the evidence for choosing substitution monotherapy. Patients should therefore be given the cheapest drug with which they can comply and which controls their symptoms (C)
- All nitrates, both oral and patches, should be used in a way that avoids nitrate tolerance (A)
- Nitrate patches should be used in dosages of at least 10 mg (A).

Comment—All the following studies show the drugs to be effective as first line agents. However, differences in patient selection, study design, and drug dosages prevent critical comparisons.

Calcium channel blockers

Calcium channel blockers when used alone are more effective than placebo (I)[70,86-92] and are all equally effective (I).[93-95]

Nitrates

Oral nitrates are effective when used as a sustained release preparation, as an eccentrically dosed twice daily preparation, or as a thrice daily preparation (I).[84,96-99] Nitrate patches are effective in angina, though dose and dosing interval are important (I).[100-105] Though intermittent treatment with high dose patches is more effective than continuous treatment with high dose patches (I),[106] when patches are used with a patch free interval they are effective—high dose patches being more effective than lower dose patches (I).[107-109]

Comment—The *British National Formulary* discusses nitrate tolerance for both oral and transdermal preparations.[47]

Other drugs

Ulvenstam *et al* compared nicorandil against nifedipine.[110] These drugs had equal effects on exercise tolerance, workload, and angina rate (I).

Choosing a second drug

RECOMMENDATIONS

- In patients taking β blockers add a dihydropyridine (A)
- In patients taking β blockers who cannot tolerate dihydropyridines add isosorbide mononitrate (A)
- In patients taking verapamil add isosorbide mononitrate (C)
- In patients taking dihydropyridines add isosorbide mononitrate (C)
- In patients taking nitrates add any calcium channel blocker (C).

Adding dihydropyridines to β blockers produces a dose dependent improvement in exercise tolerance (I)[71,111-117] and adding diltiazem to β blockers produces a dose dependent improvement in symptom control and exercise tolerance (I).[74,117,118] If this second combination is used the cautions in the *British National Formulary* should be observed.[47] Though adding isosorbide dinitrate to β blockers or calcium channel blockers produces no additional benefit, and nitrate patches added to β blockers produce no additional benefit, adding isosorbide mononitrate to β blockers is effective (I).[76,84,92,119,120]

Choosing a third drug

RECOMMENDATIONS

- If patients are not adequately controlled by maximal therapeutic doses of two drugs, then the remaining evidence based therapeutic options are very limited. These patients should be referred rather than given a third drug (C)
- If a third drug is introduced—for instance, while the patient is awaiting an outpatient appointment—its effect should be monitored and if it has no effect it should be stopped (C).

The effectiveness of adding a third antianginal drug is not clear (I).[121-123]

Referral to a cardiologist

RECOMMENDATIONS

- All patients with clinically certain angina should be referred to identify whether they fall into a group that would benefit from prognostic investigation and treatment (B)
- All patients in whom the diagnosis is uncertain should be considered for referral for clarification of the diagnosis (C)
- All patients in whom management is currently suboptimal, as judged by symptoms, should be considered for referral for further treatment or investigation (C)
- Patients whose symptoms are uncontrolled by maximal medical treatment should be referred to a cardiologist for angiography, not exercise testing (C)
- For patients who are not adequately controlled by full doses of two drugs the remaining evidence based therapeutic options are very limited. These patients should be referred rather than given a third drug (C)
- Reasons for not referring are: patient declines referral; patient currently has a more significant condition (C).

Comment—Referral from a general practitioner to a cardiologist will be for one of three reasons: to identify whether the patient falls into a group that would benefit from prognostic investigation and treatment; to establish a diagnosis; or for management advice. The point of referral will be influenced by whether open access exercise testing facilities are available.

What influences the decision to refer?

In all patients considered for referral the decision will be influenced by:

- Clinical factors—pain on minimal exertion, nocturnal pain, rapidly progressive symptoms, possible aortic stenosis, failure to respond to medical treatment, previous myocardial infarction
- Age and duration of disease
- Comorbidity
- Risk factors
- Patient preference
- Clinician factors (such as uncertainty in the doctor)
- Threat to employment or unacceptable interference with lifestyle or recreation.

These factors represent a range for most patients and their effect on the decision to refer will be additive. The referral decision cannot be taken in isolation and needs to be set in the current context of the patient.

We thank the following people for reviewing the full version of the draft guideline: Dr R Baker (general practitioner), Dr T A Carney (general practitioner), Professor S Cobbe (cardiologist), Dr A Farmer (general practitioner), Dr G Feder (general practitioner), Professor K A A Fox (cardiologist), Dr J K Inman (general practitioner), Professor D G Julian (cardiologist), Dr D Reid (cardiologist).

We are grateful to Liz Wood for skilled secretarial work and to Carol Riccalton for proof reading the guideline. The views expressed in this report are ours and not necessarily those of the funding bodies.

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Funding: The development of this guideline was principally funded by the research and development directorate of the former Northern Regional Health Authority, now the Northern and Yorkshire Regional Health Authority. Contributions to the funding were also made by the medical audit advisory groups of Durham, Northumberland, and South Tyneside Family Health Services Authorities. The health services research unit is funded by the chief scientist's office of the Scottish Office Home and Health Department.

Conflict of interest: Dr P Adams (guideline development group) frequently receives fees from pharmaceutical companies for lecturing on coronary artery disease.

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(Accepted 9 December 1995)

Are tobacco subsidies a misuse of public funds?

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The European Union spends about 1000m ecu (£800m, $1240m) a year subsidising tobacco production but only about 1·55m ecu (£1·2m, $1·85m) on smoking prevention. The subsidies, part of the common agriculutral policy, were originally intended to encourage farmers to grow commercially valued varieties of tobacco and thus reduce imports. But they also aimed to guarantee farmers' income, a goal in direct conflict with the first. The policy has failed to adapt production to demand or reduce imports, since most tobacco grown in the union has little commercial value. Reforms introduced in 1992 have had a limited impact on expenditure, and data produced as a result of the reforms show that it would be much cheaper to give farmers direct income support than to subsidise them growing tobacco. Tobacco subsidies should be abolished and more should be spent on smoking prevention.

Exchange rates and conversions

£1=1·24 ecu 1 ecu=£0·80
$1=0·8 ecu 1 ecu=$1·24
£1=$1·54 $1=£0·65
1 tonne=1000 kg

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BMJ 1996;312:832-5

The common agricultural policy of the European Union subsidises tobacco production by about 1000m ecu a year ($1240m, £800m).[1] This is in stark contrast with the tiny sums spent on initiatives to prevent smoking related diseases. One of the key goals of the common agricultural policy in relation to tobacco was to reduce dependence on imports by subsidising farmers to grow commercially valued varieties. In spite of huge expenditure this goal has not been achieved. Almost 70% of the union's manufacturing needs for tobacco products are still met by imports, and almost two thirds of union production is still of tobacco of low commercial value.

In 1991 we concluded that the system was incapable of real reform because of its complexity, vulnerability to exploitation, and internal contradictions and because of its fundamental contradiction of European Union health policy. We recommended that tobacco subsidies should be phased out entirely by the year 2000 and that the money should be spent on direct income support for farmers, early retirement schemes, and research on reconversion.[1] We predicted that limited reforms would be announced but that the system itself would be left intact.

This happened: in 1992 the policy was simplified and a ceiling set on production, but the principle of tobacco subsidies was not challenged.[2] In 1994 the European Court of Auditors (responsible for monitoring the financial activities of union institutions) published the most serious attack yet on tobacco subsidies,[3] highlighting poor management of the policy and questioning the principle of tobacco subsidies.

We look here at the effects of the 1992 reforms and present new data, available as a result of the reforms, which show the true commercial value of the tobacco crop. These data seriously undermine the European Commission's defence of tobacco subsidies as an effective means of providing income for farmers in poor regions. We believe they leave tobacco subsidies with no credible defence and support our previous recommendation, and that of the Court of Auditors, that tobacco subsidies should be phased out and replaced with direct income support for farmers.