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The management of stable angina – a perspective on recent guidance

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Introduction

About two million people in England are believed to have (or to have had) angina: unlike other forms of coronary artery disease, angina is not declining in incidence.[1] Further, studies from primary care indicate that patients with a diagnosis of angina may have an annual cardiovascular death rate as high as 6.5%.[2]

The Euro Heart Survey documented considerable variation in the management of patients with new-onset stable angina, due in part to uncertainties about the prognostic impact of both drug treatment and revascularisation. These uncertainties were inevitable given that much of the evidence used to guide management was incomplete and out of date.

There have been further developments since the European Society of Cardiology guidelines on angina were published in 2006: these include better understanding of the efficacy and role of newer agents such as ivabradine and ranolazine, better understanding of secondary prevention measures, and refinements in the techniques and equipment used in primary coronary intervention.

The National Institute for Health and Clinical Excellence (NICE) has recently published a new guideline, CG126,[3] to guide management of adults who have been diagnosed with stable angina due to atherosclerotic disease. Management of angina has many facets since clinicians need to manage the patient's symptoms, to minimise the ischaemia and to improve the prognosis. Evidence-based therapy is needed, and clear thinking is required since angina patients are an ageing population often with co-morbidity such as diabetes, hypertension and heart failure.

This supplement covers aspects of this recent guidance that we consider to be particularly relevant and useful for our readers, taking into account some of the key areas for implementation identified by NICE. For example, one of the NICE guidance key priorities is to: "Offer people optimal drug treatment for the initial management of stable angina. Optimal drug treatment consists of one or two anti-anginal drugs as necessary plus drugs for secondary prevention of cardiovascular disease".[3]

This supplement discusses mainly the medical management of stable angina, with a perspective given from both primary and secondary care. Other aspects of the NICE guidance including revascularisation, risk stratification, multi-disciplinary management and patient awareness of their condition, are only briefly covered. NICE has published a new care pathway algorithm to guide clinicians, who are advised to consult the guidance in full.[3]

Fundamental to the recent recommendations is the concept of patient-centred care. An article describing a community-based angina clinic is also included in this supplement to give a perspective of angina management in a 'real world' setting. High levels of patient satisfaction were reported and this model may be useful in meeting patient's needs and, with the adoption of other strategies described in recent guidance, help overcome the suboptimal management of stable angina in the UK.

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The management of stable angina

Dr Chris Arden gives a perspective from primary care on the recent NICE guidance

Introduction

Angina is a clinical syndrome with symptoms attributable to myocardial ischaemia, most commonly related to underlying occlusive coronary artery disease.

Long-term prognosis for those with stable angina is variable, with mortality rates of between 0.9%– 6.5% per annum. An individual's risk is determined by their baseline clinical, functional and anatomical characteristics, illustrating the importance of careful risk stratification to ensure optimal treatment (whether medical, interventional or a combination of both) and outcomes.

The range of treatment options in angina, and their evidence base, has evolved considerably over the last few years, with the objective of ideally not only controlling symptoms but also improving prognosis. Guideline-compliant therapy is associated with improved outcomes, including reduced rates of cardiovascular events and death.

The National Institute for Health and Clinical Excellence (NICE) recently commissioned the National Clinical Guidelines Centre (NCGC) to develop a clinical guideline on the management of stable angina.[1] In particular, the recommendations focus on the relative merits of medical therapy and revascularisation, and the role each strategy has in improving quality of life, morbidity and mortality. This article reviews the key recommendations and the implications for clinical practice, with particular emphasis on primary care.

Treatment

The aims of treatment in stable angina are two-fold, to minimise symptoms and improve quality of life, whilst also ensuring the timely institution of medical therapy or revascularisation to improve prognosis by preventing myocardial infarction or death. Both of these approaches should be supported by positive lifestyle measures, including encouraging activity within the patient's limitations, supporting smoking cessation and adopting a Mediterranean diet. There is no evidence that vitamin or fish oil supplements confer benefit in stable angina.

Optimal control and management of co-morbidities, including hypertension, diabetes and renal disease, is important in modifying the atherosclerotic disease process and improving outcomes in those with stable angina.

Pharmacological therapy to improve prognosis

The guidelines support and endorse the implementation of secondary prevention therapy in patients with stable angina, to reduce the progression of cardiovascular disease and improve prognosis. The recommendations are:

- Aspirin 75 mg daily, taking into account the risk of bleeding and co-morbidities. Treatment is associated with a statistically significant reduction in non-fatal myocardial infarction and vascular events although, due to the heterogeneity of those with stable angina, there is a relatively low-risk cohort in whom the bleeding risk may outweigh any potential gain.
- Statin treatment should be offered to all those with stable angina, in line with current lipid modification guidelines and targets.
- Angiotensin-converting enzyme (ACE) inhibitors should be considered for those with stable angina and diabetes. The evidence reviewed suggested potential benefit in this group of patients, although it is recognised there are other compelling indications for ACE inhibitors, in particular in those post-myocardial infarction, those with left ventricular (LV) systolic dysfunction, reno-vascular disease and hypertension.

Treatment of symptoms

Minimising, or ideally eradicating, symptoms in stable angina is a key objective and, for the majority of patients, results in an improvement

in their quality of life and exercise tolerance, as well as having a significant bearing on the need for further investigation or revascularisation.

The guidelines provide a useful treatment algorithm with optimal medical treatment being defined as the use of up to two anti-anginal drugs plus secondary prevention measures (**figure 1**).

Consideration to adding a third anti-anginal drug should only be given when:

- the person's symptoms are not controlled with two anti-anginal drugs and
- the person is either waiting for revascularisation or revascularisation is not considered appropriate or acceptable.

Symptoms of angina can effectively be relieved by the use of short-acting nitrates, including glyceryl trinitrate as a sublingual tablet or spray. The individual should be carefully instructed in its use and also of the potential benefit of using it before any planned exercise or activity ('situational prophylaxis'). Short-acting nitrates should be prescribed for all those with stable angina.

First-line treatment

The guidelines recommend, as first-line treatment, either beta blockers or calcium channel blockers. These are effective in reducing anginal symptoms by reducing myocardial oxygen consumption, as a result of lowering heart rate, myocardial contractility and blood pressure, coupled with increasing coronary blood flow and myocardial oxygen supply during diastole.

The decision as to which therapy to chose, either a beta blocker or a calcium channel blocker, should be based on the individual's co-morbidities, contraindications and preference. If they are unable to tolerate either of these therapies, then consideration should be given to switching to the other. The recommendation is not to routinely offer anti-anginal drugs other than a beta blocker or calcium channel blocker as first-line treatment in stable angina.

If symptoms are not satisfactorily controlled on either option alone then the recommendation is to consider using a combination of a beta blocker and a calcium channel blocker, although the latter should be a dihydropyridine calcium channel blocker (amlodipine, slow-release nifedipine or felodipine).

Second-line treatment

For those individuals in whom symptoms persist, despite optimisation of their beta blocker or calcium channel blocker dose, consideration should be given to introducing additional anti-anginal therapy. These may also be considered as initial monotherapy when the patient is intolerant of either a beta blocker or calcium channel blocker. These therapeutic options include:

- long-acting nitrates
- ivabradine
- nicorandil
- ranolazine.

The decision on which drug to use should be based on co-morbidities, contraindications and patient preference.

Long-acting nitrates reduce the severity and frequency of angina attacks, and may increase exercise tolerance, although they have not been demonstrated to confer any prognostic benefit.

Ivabradine acts by inhibition of the sinus node, reducing heart rate and myocardial oxygen demand during rest and exercise, with evidence of proven anti-anginal efficacy, and can be prescribed in combination with either a beta blocker or dihydropyridine calcium channel blocker.

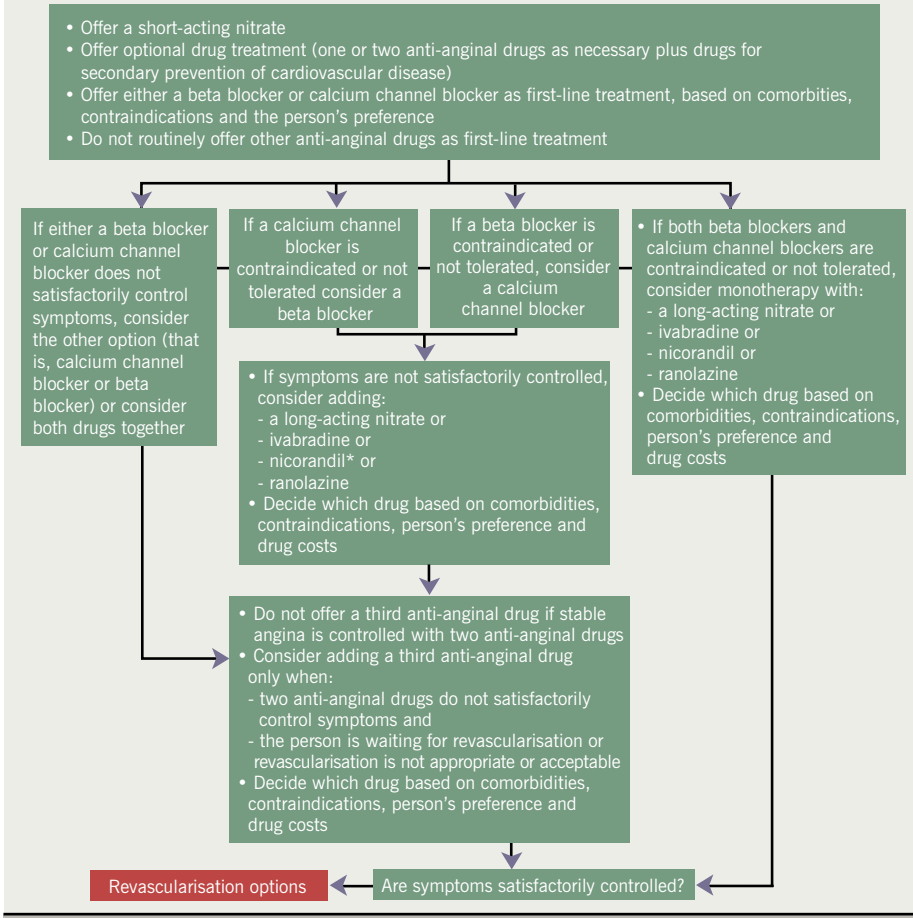
Nicorandil has a dual mechanism of action, as a potassium channel activator and also with a nitrate moiety that dilates epicardial coronary arteries, with a nitrate-like effect. Trial data have demonstrated a reduction in hospital admissions for cardiac chest pain in patients with stable angina.

Ranolazine is a metabolically acting agent, which is believed to selectively inhibit sodium channels, with minimal reductions in heart rate and blood pressure.

When counselling patients with regards to the relative merits of medical treatment, it is helpful to advise them that the aim of anti-anginal treatment is to prevent episodes of angina, and the aim of secondary prevention to prevent cardiovascular events, including myocardial infarction and stroke.

All anti-anginal therapies should be titrated, depending on the patient's symptoms, to their optimal tolerated doses (within the licensed dose range) before considering adding additional therapy.

Figure 1. Detail from the NICE care pathway for the management of stable angina showing drug treatment after confirmed diagnosis. Physicians should consult the full guidance



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*Nicorandil does not have a UK marketing authorisation for this indication. Informed consent should be obtained and documented

Medical therapy versus revascularisation

The two conventional approaches to revascularisation in patients with coronary artery disease are percutaneous coronary intervention

(PCI) and coronary artery bypass surgery (CABG). The latter procedure has been developed and refined, including more recent off-pump (avoiding the need for circulatory bypass) surgery over the last 40 years, while results with PCI started have improved significantly following the introduction of coronary artery stents 15 years ago.

Despite extensive trial data and research, there is still persisting uncertainty regarding the indications for, and optimal timing of, invasive investigation and revascularisation in stable angina, although there is clear evidence that an early investigation and intervention strategy significantly improves outcomes in patients with acute coronary syndrome and in those with high-risk coronary anatomy.

Patients who remain symptomatic despite optimal medical therapy should be considered for revascularisation and, in order to decide which procedure may be appropriate, invasive investigation (angiography) should be offered. A proportion of these patients may still require functional testing to evaluate angiographic findings and guide treatment decisions.

A proportion of patients whose symptoms appear to be controlled with medical therapy may still potentially have coronary lesions, which are prognostically significant, including left main stem or proximal three-vessel disease. These patients would benefit from a revascularisation strategy and the guidelines recommend considering a non-invasive functional (stress echo or myocardial perfusion scan) assessment to help risk-stratify these patients. In those patients in whom there is evidence of extensive ischaemia, angiography should be offered.

In patients with angina, both PCI and CABG have proven efficacy in improving symptoms although, on available evidence, PCI does not appear to provide substantial survival benefit. CABG has been shown to improve prognosis in a subset of patients including those who:

- have anatomically complex three-vessel disease, with or without involvement of the left main stem
- have diabetes mellitus
- are aged over 65.

If the patient's coronary anatomy is considered suitable for either procedure, then it is recommended that PCI should be offered in preference.

Fuctional assessment and risk stratification

Within the population with stable angina there is significant variance in respect of a particular individual's prognosis, with an up to ten-fold difference in annual mortality between those deemed to have low risk and those with high risk. This emphasises the importance of early risk stratification to identify those patients who will benefit prognostically from a more intensive treatment or interventional approach.

'It is important we employ these strategies effectively to ensure our patients achieve the greatest benefit'

The four most important pieces of information required to assess an individual's risk, and hence prognosis, accurately are:

- clinical evaluation (history, examination, ECG, lifestyle factors, smoking, diabetes, metabolic syndrome, hypertension and lipids)
- response to stress testing
- quantification of LV function (impaired LV systolic function is the strongest predictor of poor prognosis; resting left ventricular ejection fraction < 35% is associated with an annual mortality of > 3% per year)
- extent of coronary artery disease.

Non-invasive functional assessment, including stress echo, myocardial perfusion imaging or exercise ECG, is useful in identifying those individuals who may have high-risk coronary anatomy and are likely to benefit from revascularisation. The role of the exercise ECG in current practice appears increasingly to be limited to assessing functional capacity in those with established coronary disease, rather than in the diagnostic pathway, due to the test's relatively poor specificity and sensitivity as compared with other functional imaging tests.

Rehabilitation

There is good evidence that cardiac rehabilitation programmes are beneficial to individuals with cardiovascular disease, in particular post-myocardial infarction or coronary revascularisation. In stable angina the evidence is less robust and the guidelines recommend a more tailored approach to rehabilitation, depending on the individual's particular needs, including psychological support if required.

The Angina Plan[2] provides a structured programme of support for both individuals with angina and their carers, which appears to be particularly beneficial.

Summary

The increasing prevalence of angina, due to an ageing population and improved survival of those with conditions which predispose to the development of coronary atherosclerosis, including diabetes, hypertension and renal disease, provides us with challenges in ensuring patients receive timely investigation and optimal treatment, including potential intervention. Fortunately, we have a wide range of effective management options at our disposal which have the potential to significantly improve our patients' symptoms, and hence quality of life, as well as their prognosis.

It is important we employ these strategies effectively to ensure our patients achieve the greatest benefit from their given treatment or intervention, as well as taking time to accurately risk-stratify individuals to identify those at higher risk who would benefit from more intensive investigation and treatment, including revascularisation.

The guidelines are helpful in detailing the evidence base supporting the current recommendations and these will no doubt have a significant positive impact on the management, quality of life and prognosis of our stable angina patients

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The medical management of stable angina

Professor Kim Fox offers a perspective from secondary care on the recommendation for optimal medical management in the recent NICE guidance

The new guideline from the National Institute for Health and Clinical Excellence (NICE)[1] covers adults who have been diagnosed with stable angina due to atherosclerotic disease, following on from clinical guideline 95,[2] which advises on diagnosis of chest pain of recent onset.

A key priority for implementation in the latest guidance is to ensure that people with stable angina receive balanced information and have the opportunity to discuss the benefits, limitations and risks of their treatment. Initial management of stable angina should be to offer optimal drug treatment, addressing both the angina itself and secondary prevention of cardiovascular disease.

What constitutes this optimal medical treatment?

Initial drug monotherapy

Previous guidelines have suggested that beta blockers should be first-line treatment for stable angina, but the NICE guideline development group (GDG) could find no evidence to differentiate between the use of beta blockers and calcium channel blockers for this indication. The main outcomes evaluated were total and cardiovascular mortality and risk for myocardial infarction (MI) and stroke; measures of symptom severity were also included. The two drug classes were found to have similar effectiveness, similar adverse event rates and similar costs. However, randomised trials of these agents in stable angina have mainly used the older drugs in each class and relatively small numbers of patients, and data on long-term effectiveness are limited. The GDG felt unable to recommend any other agents as first-line monotherapy, suggesting that there is currently insufficient experience with the newer anti-anginal agents (nicorandil, ivabradine and ranolazine) and that the development of tolerance limits the use of long-acting nitrates.

Clinicians may choose between beta blockers or a calcium channel blocker (no specific agent was preferred by the GDG) according to contraindications, any co-morbidity and the patient's preference. Unfortunately, the guidelines take a totally pragmatic view of medical therapy and do not consider the underlying pathophysiological mechanisms that may apply to the selection of treatment. We believe this is a retrograde step to approaching pharmacological therapy: in current thinking medicine should be personalised if we are to achieve optimal and cost-effective treatment for our patients. If either beta blockers or calcium channel blockers are ineffective or not tolerated, then a switch to the other option was proposed.

> **'Recommendations from NICE differ from those of the ESC'**

These recommendations from NICE differ from those of the European Society of Cardiology (ESC), which published angina guidelines in 2006.[3] The ESC states that "there is no evidence to support the use of calcium channel blockers for prognostic reasons in uncomplicated stable angina, although rate-lowering calcium channel blockers may be used as an alternative to beta blockers post-MI in patients who do not tolerate beta blockers." Further, as regards treatment of symptoms and ischaemia, in the absence of previous MI, if factors such as individual tolerance and co-morbidity are equally weighted, then a beta blocker is recommended as first choice. Thus, NICE is more enthusiastic about the use of calcium channel blockers as first-line treatment, even though the most recent study included in this section of the guideline was the INVEST study from 2003.[4]

Combination treatment

NICE goes on to consider whether addition of a beta blocker to a calcium channel blocker, or vice versa, improved symptoms or clinical outcome in patients with stable angina. The trials analysed to formulate such recommendations are all more than 10 years old with, again, a small number of patients, the most recent being Pehrsson 2000 (which compared atenolol or amlodipine against both).[5] The GDG found no reason to recommend that patients whose symptoms were controlled on one drug should be given the other in addition, saying that the only benefit observed with combination of agents from the two drug classes was a short-term improvement in exercise tolerance. If the two classes are combined, then a dihydropyridine calcium channel blocker should be used with a beta blocker.

Is there any advantage to the patient in adding a third anti-anginal agent?

To address this question, the GDG studied the ACTION trial (published 2004),[6] which reported the effects on mortality and outcomes, such as acute MI, new heart failure and stroke, from adding nifedipine GITS to usual anti-anginal treatment (this was a beta blocker in 79% and an organic nitrate as required [56%] or daily maintenance [37%]). They also looked at evidence from trials of newer anti-anginal agents such as nicorandil, ivabradine and ranolazine. The GDG were unconvinced that routine addition of nifedipine GITS to standard treatment conferred any major clinical benefit, and recommended that a third anti-anginal drug (this advice includes the newer agents) should not be offered routinely to people whose symptoms are controlled on two anti-anginal drugs. A therapeutic trial of a third drug could be considered in certain people: these are patients in the problematic position of having symptoms not controlled on two anti-anginal drugs and who are either waiting for revascularisation or whose disease is considered inappropriate or unacceptable for revascularisation.

Newer anti-anginal agents

What is the place of ivabradine, nicorandil and ranolazine in the new NICE guideline? There are two recommendations for their use.

First, if a patient with stable angina cannot tolerate beta blockers or calcium channel blockers, or when these are contraindicated, then monotherapy with ivabradine, nicorandil or ranolazine (or a long-acting nitrate) is a possibility. The decision about which drug to use should be based on co-morbidity, contraindications, patient preferences and drug costs but not on our understanding of the pathophysiological mechanism in the individual patients. We recently presented an algorithm based on heart rate to maintain personalised medicine in the treatment of angina (**figure 1**).[7]

Second, it is suggested that these newer agents may be used for people on beta blocker or calcium channel blocker monotherapy whose symptoms are not controlled but for whom the other (beta blocker or calcium channel) option is contraindicated or not tolerated. Nicorandil does not at present have UK marketing authorisation for use as an add-on therapy in angina and therefore informed consent should be obtained and documented. When ivabradine is combined with a calcium channel blocker, then a dihydropyridine (such as slow-release nifedipine, amlodipine or felodipine) should be used.

Ivabradine

Ivabradine lowers heart rate at rest and during exercise. It acts by selectively inhibiting the I_f current, an ionic current across the sarcolemma in cells of the sinoatrial node. The GDG reviewed trial data of its clinical and cost-effectiveness.

Ivabradine was compared to placebo in two studies – by Borer *et al* (2003)[8] and Fox *et al* in BEAUTIFUL (2009).[9] The former study showed dose-dependent improvements in exercise tolerance and time to development of myocardial ischaemia during exercise in patients treated with ivabradine compared to placebo. The BEAUTIFUL trial assessed the effect of ivabradine in 10,917 patients with coronary artery disease and impaired left ventricular function. Limiting angina symptoms were identified in 13.8% of the total trial population at baseline: of these, 734 were randomised to ivabradine and 773 to placebo. There appeared to be a statistically significant difference between ivabradine and placebo for the primary end point of cardiovascular death or hospitalisation for MI or heart failure (HR 0.76, p=0.05), but no difference for all-cause mortality (hazard ratio [HR] 0.87, p=0.41), and cardiac death (HR 0.72, p=0.40); no statistical difference was found in terms of hospitalisation for heart failure (HR 0.84, p=0.45) or hospitalisation for MI or unstable angina (HR 0.9, p=0.58) but there was a statistically significant difference found in terms of hospitalisation for myocardial infarction (HR 0.58, p=0.021). The GDG took the view that since this subgroup was defined retrospectively, it only included 13.8% of the total trial population and lacked statistical power for the primary end point; the analysis did not provide definitive evidence of benefit for ivabradine.

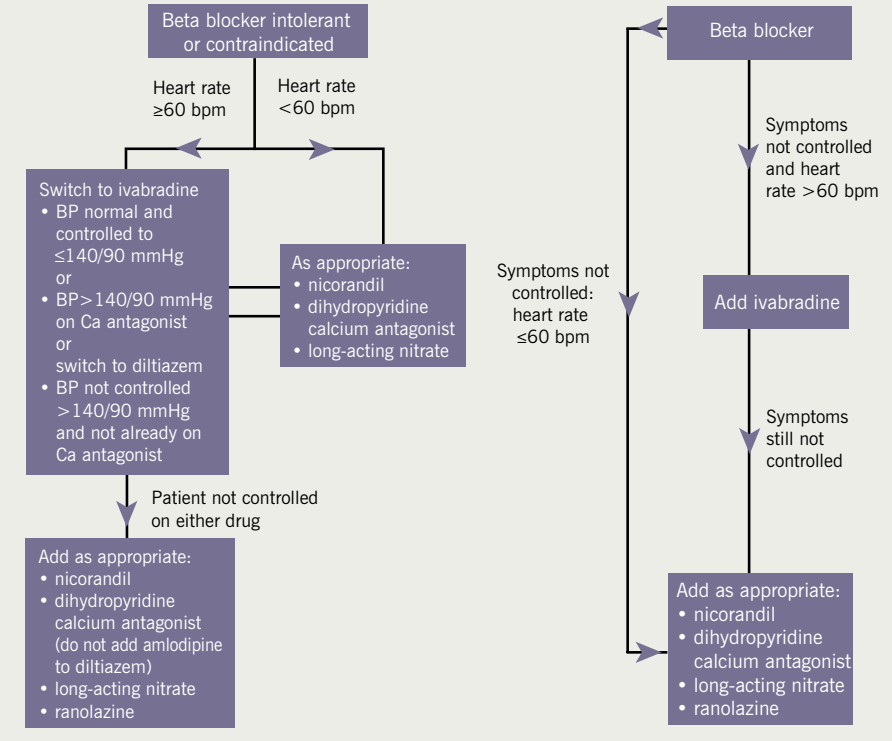
Ivabradine was compared against atenolol in a study by Tardif (2005):[10] total exercise duration, time to angina onset, number of angina attacks and short-acting nitrate consumption were similar in both treatment groups. Tardif also (2009) compared ivabradine plus atenolol (n=441) against atenolol plus placebo (n=434) in a randomised controlled trial (RCT) with follow-up to four months.[11] Results were significantly better in the group treated with beta blockers and ivabradine at four months with respect to total exercise duration at trough, time to angina onset at trough and time to 1 mm ST-segment depression, although the rate of adverse events was also higher in this group.

In one RCT considered by the GDG (Ruzyllo 2007),[12] ivabradine was compared with amlodipine. The two agents appeared comparable for the measures of efficacy that were evaluated – total exercise duration, time to onset of angina at trough, number of angina attacks and consumption of short-acting nitrates. The GDG summed up by stating that "the data suggest that ivabradine is an effective anti-anginal agent with comparable short-term efficacy to atenolol and amlodipine". However, they drew attention to the significantly higher rates of adverse events in patients treated with ivabradine, including visual symptoms. Data to confirm the efficacy and safety of ivabradine in the long term were limited, they felt.

Ranolazine

Evidence for the use of ranolazine in stable

Figure 1. Symptomatic algorithm to show how controlling heart rate can achieve symptom control



Reproduced from Fox[7] with permission
Key: BP = blood pressure; Ca = calcium

angina was reviewed. The mechanism of action of this drug is believed to be selective inhibition of late sodium influx across the sarcolemma, which attenuates the abnormalities of ventricular repolarisation and contractility associated with myocardial ischaemia. Decreases in heart rate (and systolic blood pressure) are minimal with this drug. No pro-arrhythmic effects were observed in the MERLIN-TIMI 36 study (n=3,162)[13] but ranolazine has the potential to prolong the QT interval.

The main studies identified were CARISA,[14-16] which evaluated ranolazine plus anti-anginal treatment against placebo plus anti-anginal treatment, and ERICA[17] which evaluated ranolazine plus amlodipine against amlodipine alone. In CARISA, patients treated with ranolazine had significantly better exercise duration and time to onset of angina, and fewer angina attacks. In ERICA, weekly consumption of short-acting nitrates was significantly lower in patients who received ranolazine plus amlodipine versus amlodipine alone.

The GDG stated that the improvements in exercise time and symptom severity associated with short-term ranolazine treatment were modest and of uncertain clinical significance. They were unable to recommend routine use of ranolazine but considered that it had a role in limited circumstances (see discussion above).

Heart rate and symptoms

The basis of myocardial ischaemia and development of angina is an imbalance between oxygen demand and supply. In patients with stable coronary artery disease, most episodes of exercise-induced ischaemia are preceded by a heart rate increase. The extent of myocardial ischaemia is related to baseline heart rate and the magnitude and duration of this increase.[18] Studies have found a continuous increase in cardiovascular risk with heart rate >60 bpm: it is therefore desirable to consider heart rate reduction as paramount in the treatment of angina. Our own algorithm (**figure 1)** for the management of angina in primary care is an alternative approach to the medical treatment of anginal symptoms,[7] which is equally appropriate in the initial treatment of angina in the secondary care setting.

Revascularisation

The recent NICE guidance says: "Angiography may be offered to guide the treatment strategy for patients whose symptoms are not controlled with optimal medical treatment".

The issue of revascularisation, i.e. percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG), where symptoms are not satisfactorily controlled with optimal drug treatment, is reviewed in detail in some 47 pages of the full NICE guideline. Regular multidisciplinary team meetings should discuss the risks and benefits of medical and revascularisation strategies. The GDG concluded that there is no definite evidence that one revascularisation strategy confers a prognostic advantage, although CABG provides slightly better angina relief than PCI, over the medium term, and there is a potential survival advantage with surgery for some people with multi-vessel disease e.g. in those with diabetes, those over 65 years or in those who have anatomically complex three-vessel disease with or without left main stem involvement.

The reader is referred to the guideline for full discussion of revascularisation and other recommendations, which have particular relevance for secondary care. These include: clinical risk scores, such as ACTION and the Euro Heart Angina Score, not being recommended; routine functional testing not found to be cost-effective; and lack of evidence that rehabilitation programmes are clinically or cost-effective in the management of stable angina

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Community-based angina clinics and the therapeutic management of patients with coronary artery disease

Drs Thornton-Chan and colleagues write about how well patients with coronary artery disease are being managed in the real world

The objective of this study was to look at how well patients with coronary artery disease are managed, and whether community-based angina clinics might be an alternative, or even more beneficial, to these patients compared with hospital-based clinics. Patients with coronary artery disease need regular follow-ups to review their lifestyle and medications, and to ensure angina symptoms are well controlled. Heart rates should be checked regularly as high heart rate is associated with increased risk of myocardial ischaemia. In this study, 41 patients with coronary artery disease were assessed at a community-based angina clinic. Our results showed that 27% of these patients were significantly symptomatic and a significant proportion of these symptomatic patients were not on optimal prognostic secondary prevention medication. For those on optimal medication, many were not on optimal dosage. The data suggest that patients have not been monitored closely enough. We are suggesting that community-based angina clinics, such as the one in this study, may be an alternative to – or be supplementary to – hospital-based clinics.

Introduction

Patients diagnosed with coronary artery disease should be on prognostic secondary prevention medications. We looked at four such agents: antiplatelets, statins, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), and beta blockers or other rate-limiting agents. With the latter two agents, for best prognostic outcome, close monitoring is required to ensure suitable titration to the maximum tolerated doses.

Coronary artery disease patients benefit from a low heart rate achieved by up-titration of a beta blocker to the maximum tolerated dose. Several studies suggest that heart rate is a major determinant of myocardial ischaemia.[1,2] According to a subgroup analysis of the BEAUTIFUL trial, a heart rate of over 70 beats per minute (bpm) increases the risk of experiencing a cardiovascular event in patients with coronary artery disease. There is good evidence that reduction in these patients' heart rate, by optimising the dosage of beta blockers,[3] will improve their prognosis.

The purpose of our study was to ascertain:

- whether or not patients with coronary artery disease are on optimal treatment for symptomatic control
- whether they are on optimal secondary prognostic prevention medications
- and whether a community-based angina clinic is a viable alternative to a hospital-based clinic.

Method

Patient selection

An angina clinic was held once a week in the evening at Clarendon Medical Centre in Cheshire between January and March 2011. All patients registered with this practice were included in the study provided they met all of the following criteria:

- they were previously diagnosed with coronary artery disease
- the patient had requested glyceryl trinitrate (GTN) for angina on two or more occasions in the past year
- they were capable of travelling to the clinic.

Some 86 patients fulfilled these requirements and were invited to partake in the study. A total of 41 patients from this cohort attended.

Data collection

Patients were either seen by a doctor PSI (Practitioner with Special Interest) or a nurse PSI. Data were collected on each patient's symptoms, their heart rate, their current anti-anginal medications, and their current secondary prognostic prevention medications. Each patient was also asked to complete a satisfaction questionnaire consisting of two questions:

- how satisfied were they with the clinic?
- and would they attend such clinics again in future?

To further assess the use of secondary prognostic prevention medications (specifically beta blockers/other rate-limiting agents and angiotensin-converting enzyme [ACE] inhibitors/angiotensin receptor blockers [ARBs]), information was extracted from each patient's file on the computer database at the practice. In patients who had never been on these medications, past medical notes were searched for a valid reason. In patients who had previously been prescribed these medications (but were no longer on them), the database was used to find out why these had been stopped. The beta blocker/ACE inhibitor dosages were also recorded to identify patients who were on suboptimal doses and the reasons for this. The database was also used to ascertain the reason for suboptimal dosage of these medications.

Table 1. Patient ages

Ages (years)	Number of patients
40 – 49	1
50 – 59	6
60 – 69	9
70 – 79	17
80 – 89	6
90 – 100	1

Table 2. Frequency of angina

Frequency	% of patients
5-7 times per week	7.3%
3-4 times per week	4.9%
1-2 times per week	14.6%
1-2 times per month	22.0%
< 1 times per month	34.1%
Asymptomatic	17.1%

Table 3. Patients' heart rates in beats per minute (bpm)

Heart rates (bpm)	% of patients
< 55	2.4%
55 – 60	7.3%
61 – 69	22.0%
≥ 70	51.2%

Table 4. Anti-anginal medications

Anti-anginal medication	% of patients
Glyceryl trinitrate	90
Beta blocker	61
Calcium channel blocker	54
Long-acting nitrate	29
Nicorandil	24
Ivabradine	5
Ranolazine	5

Table 5. Secondary prevention medications

Medication	% of patients
Statins	93
Antiplatelets	85
ACE inhibitors or ARBs	66
Beta blockers	59

Results

Some 41 patients attended the angina clinic out of the 86 patients initially invited to participate. High numbers declining were reported to be due to unpleasant weather and dark nights. The study cohort comprised 18 women and 23 men (age range 49–95 years) (**table 1**).

During the first visit, patients were asked whether they experienced angina. The frequency at which angina was experienced is shown in **table 2**. A significant 7.3% of our patients were experiencing angina at least five times a week, 12.2% had angina three to seven times a week, and 26.8% had angina on a weekly basis. Of the five patients with angina at least three times a week, two were being considered for referral to hospital, and one was already under hospital care.

Looking at resting heart rate, this was found to be between 55–60 bpm in 7.3% of patients, less than 70 bpm in 31.7% of patients, and 70 bpm or over in 51.2% of patients (**table 3**).

During our review of these patients' anti-anginal drugs, we found the majority (90%) were on GTN, 61% were on beta blockers, 54% were on calcium channel blockers, 29% were on long-acting nitrate, 24% were on nicorandil, whilst a small number of patients (5% each) were on ivabradine and ranolazine (**table 4**).

Table 5 illustrates the percentage of patients seen in the clinic who were taking the four prognostic secondary prevention medications. A good proportion of patients were on both statins and antiplatelet drugs (93% and 85%, respectively).

We looked in more detail at the use of ACE inhibitors/ARBs and beta blockers/other rate-limiting agents. We found that of the patients who were not on ACE inhibitors/ARBs, only 14% had a valid reason for this. The remaining 86% did not have a valid reason.

Table 6 looks at beta blocker use in more detail. Of those who were not on beta blockers, 25% had valid reasons and were on other rate-limiting agents; 44% had valid reasons but were not on other rate-limiting agents; and 31% did not have any valid reason but were on alternatives. For those on beta blockers, only 20% were on optimal dosage, 20% were on a suboptimal dose with a valid reason (such as optimal heart rate, low blood pressure and intolerance of higher dose), and 60% were on suboptimal dosage without a valid reason.

Discussion

There is good evidence that aggressive medical treatment is effective in managing symptoms and improving the prognosis of patients with coronary artery disease.[4] We identified a significant proportion of our patients whose medications had not been optimised. Although 90% of patients attending the clinic were using GTN spray for symptomatic control, the use of other anti-anginal drugs seemed low. The low use of anti-anginal medications and the high proportion (26.8%) of significantly symptomatic patients (those experiencing angina at least once a week) are no coincidence.

The use of beta blockers (59%) and ACE inhibitors/ARBs (66%) was poor. The reasons given for either suboptimal treatment or no treatment with beta blockers, included asthma, bradycardia, intolerance, no prior use of beta blockers, and discontinuation due to unspecified reasons. For ACE inhibitors/ARBs, the reasons given were intolerance, no prior use of the drug, and discontinuation due to unclear reasons.

We noticed that discontinuation of medications sometimes occurred after a hospital admission or an outpatient clinic with no reason being given. Poor or delayed communication between the hospital and GP is a recognised problem. GPs may make changes to the medications prescribed to patients by hospital clinicians, if the reason for initiating the drug is unclear.[5] The hospital discharge letters were generally clear in indicating which medications patients had been prescribed. Patients, however, may be uncertain which medications are to be continued, or may simply stop the medication when it has run out. Having community-based angina clinics could ensure continuity of care and also regularly review all the treatments patients receive. Hospitals, generally, do not have access to the patients' GP notes. As every patient's past medical notes from both hospitals and GP consultations are all readily accessible at the community clinics, it may be easier to identify why treatments have been started or stopped.

We are aware that some of our patients did not attend their hospital appointments, which may have resulted in their poor therapeutic management. Reasons for missed appointments may include the distance, patients being unfamiliar with hospital clinicians and/or not knowing the reason why they have been given

the appointment. Patients are likely to be more familiar with their own GP, which may make it less intimidating to communicate during a consultation. It may also be easier and quicker for patients to access a community-based clinic, which would reduce the waiting time between subsequent appointments, thereby allowing symptomatic patients to be assessed more rapidly in comparison to a hospital-only angina clinic.

Table 6. Analysis of beta blocker use

Total number of patients not on beta blocker	16 out of 41
– valid reason and on alternatives	25%
– valid reason and not on alternatives	44%
– no valid reason and on alternatives	31%
Total number of patients on beta blocker	25 out of 41
– on optimal dose	20%
– on suboptimal dose with valid reason	20%
– on suboptimal dose with no valid reason	60%

Figure 1. Future attendances to community-based clinics

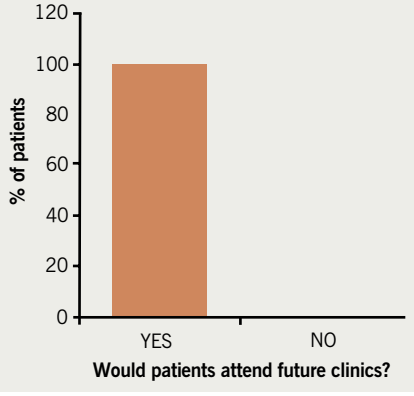
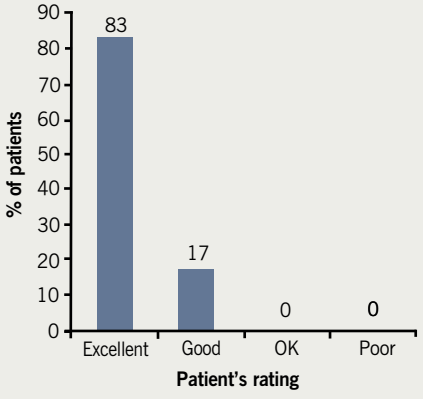


Figure 2. Patients ratings of the community-based angina clinic



Possible issues with community-based clinics are that although GPs receive hospital letters regarding patients' hospital stays, investigations or appointments, information regarding community-based consultations is not usually passed on to hospital clinicians. Another issue could be the PSI's capability and experience of managing patients with coronary artery disease. If PSIs have the prescribed qualifications, this is not generally a problem, but it could lower patients' confidence levels in community-based angina clinics.

In addition, community-based angina clinics are unlikely to have on-site echocardiogram or exercise tolerance test facilities although ECGs and 24-hour ambulatory blood pressure profiles are widely available.

Lastly, however beneficial community-based clinics are for patients, it is crucial that they are satisfied with the clinic to ensure attendance. In this respect, our angina clinic was extremely successful with 100% of the cohort of patients reporting they would attend the clinic again (**figure 1**). The majority (83%) of patients rated our clinic as excellent, whilst 100% of patients rated our clinic as excellent or good (**figure 2**).

Future considerations

To improve future attendance, we may need to provide earlier appointments during daylight hours and/or run the clinics in the summer months when it is still light in the evening. It would be interesting to look at the percentage of missed appointments at hospital clinics and the reasons for non-attendance. It would also be useful to compare our data with that of other studies similar to ours. One such study was done in Rochdale in 2011.[7] Some of their figures were comparable with ours, such as beta blocker use, which was 47% in their study (59% in ours) and ACE inhibitor use, which was 68% in their study (66% in ours).

Conclusion

Our angina clinic demonstrated that a significant number of patients were not symptomatically controlled, and a significant number of patients were not on optimal prognostic secondary prevention treatment. These results suggest poor follow-up and management. These findings are broadly in keeping with that of other studies.[6] It is possible that community-based angina clinics may be more beneficial than the current model of hospital-based clinics due to them being easier to access, and the fact that it is generally less daunting to see a GP/community-based practitioner than a hospital clinician. Our patient satisfaction was also extremely high. Thus significant unmet need we saw in patients with coronary artery disease may be improved by a community-based angina clinic

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