Symposium: Chronic stable angina in the elderly

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The NICE guidelines on the management of stable angina: how useful for the geriatrician?

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The NICE guidance on the management of stable angina was published in July last year.[1] This is an important document yet it is a guidance that has probably been overlooked by many physicians who deal with chest pain. This is because stable angina does not have a high priority as it is considered a benign condition—yet it is not as benign as people believe.

The description of angina has been around for over 250 years and should not be difficult to recognise in clinical practice. Stable angina is pain or constricting discomfort that typically occurs in the front of the chest (but may radiate to the neck, shoulders, jaw or arms) and is brought on by physical exertion or emotional stress. Some people can have atypical symptoms, such as indigestion, breathlessness or nausea. Angina is a symptom of myocardial ischaemia and is usually caused by atherosclerotic obstructive coronary artery disease restricting blood flow and therefore oxygen delivery to the heart muscle.

However, other presentations of coronary disease and the terms used to describe them, such as acute coronary syndrome (ACS), myocardial infarction and unstable angina can confuse the picture and dominate the practice in acute hospital medicine. Stable angina has a lower emphasis even though it is a big part of people's workload especially in primary care.

Information in the guidelines relates only to people with a diagnosis of stable angina. Guidelines on correctly diagnosing angina are covered in NICE Clinical Guideline 95 entitled: "Chest pain of recent onset."[2] The two guidelines should therefore be read in conjunction.

According to the European Society of Cardiology guidelines on angina[3], typical angina meets three of the following characteristics: substernal chest discomfit of characteristic quality and duration, provoked by exertion or emotional stress and relieved by rest and/or glyceryl trinitrate (GTN). This classification has not changed with the advent of modern techniques. Atypical angina meets two of the above characteristics and non cardiac chest pain meets one or none of the above. This is useful from a history point of view as an initial diagnosis and importantly contributes to the estimation of risk of having significant coronary artery disease.

This is important as there are changes in the NICE CG95 on how we investigate coronary disease with a significant emphasis on non-invasive functional imaging (stress echo or myocardial perfusion scans). and the use of coronary CT scanning. The bedrock of assessment for many years has been exercise tolerance testing (ETT) but because of its many limitations, the guidance has eliminated this for diagnosis. Personally, I think that exercise testing still has a useful prognostic role in other settings. Nonetheless, it is currently the case that many colleagues and clinics still continue to request ETTs for the assessment of chest pain. Furthermore, a lot of older patients cannot adequately undertake ETTs. Non-invasive imaging is both safer and much more reliable in this population.

One of the important features in the NICE guidance on angina was that it has defined several treatment principles. These include not excluding people from treatment based on their age alone; not to investigate or treat symptoms

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differently based on gender or ethnic group and not to offer vitamins or fish oils, educating patients that there is no evidence that they help stable angina. Transcutaneous electrical nerve stimulation (TENS), enhanced external counterpulsation (EECP) or acupuncture should not be offered to help manage stable angina.

Another very important statement in these guidelines is that: "optimal drug treatment is one or two antianginal drugs as necessary plus drugs for secondary prevention of cardiovascular disease." A beta-blocker or calcium channel blocker are recommended as first-line treatment, based on comorbidities, contraindications and the person's preference. If both beta-blockers and calcium channel blockers are contraindicated or not tolerated, it states that physicians should consider monotherapy with a long-acting nitrate, ivabradine, nicorandil or ranolazine. Which one would be decided based on comorbidities, contraindications, person's preference and drug costs. Many of us in reality have patients on more than two anti-anginal drugs and will continue to add or increase doses over time. Thus practice differs from theory but we need to rationalise drug treatment—stop or swap drugs not just stack them up.

NICE is quite clear about not offering a third anti-anginal drug if stable angina is controlled with two anti-anginal drugs. A third anti-anginal drug should only be considered when two antianginal drugs do not satisfactorily control symptoms and the person is waiting for revascularisation or if revascularisation is not appropriate or acceptable. This is quite a departure from common clinical practice. When symptoms are not satisfactorily controlled with optimal drug treatment then it is time to consider revascularisation.

Percutaneous coronary intervention (PCI) has excellent results and there is a public perception that it is more effective. The guidance states that revascularisation (coronary artery bypass graft [CABG] or PCI) should be considered for people with stable angina whose symptoms are not satisfactorily controlled with optimal medical treatment. The NICE guidance has been influenced by the COURAGE trial,[4] which found that essentially, pills were as good as PCI. That was the perceived take home message but the results are somewhat more complicated than that.

Another ongoing study looking at this is the FAME II trial (Fractional Flow Reserve (FFR) Guided Percutaneous Coronary Intervention (PCI) Plus Optimal Medical Treatment (OMT) Verses OMT). Preliminary results from the trial reveal that in patients with one or more significant lesions as determined by FFR guidance, those treated with PCI plus optimal medical treatment experienced superior outcomes. For patients with one or more significant lesions there was a 7.6 times greater risk of hospital readmission with revascularisation for patients who received optimal medical treatment alone. Further, there was an 11.2 times greater risk of the need of unplanned hospital readmission with urgent revascularisation.[5] The decisions around offering revascularisation are thus complex.

It does seem clear that what patients get offered does depend very much on who they see. The problem is that many, especially older patients, are not sent to cardiologists and are managed by other physicians. There is still a lot of ageism, assumption and excuses used for not exploring PCI or CABG, both from patients and healthcare professionals—"I'm too old" and "they are too old." At my hospital, we have many patients in their 80s and 90s referred for PCI. In fact UK figures for outcomes in terms of safety for PCI/CABG are amongst the best in the world. Nonetheless there are often particular challenges in the elderly related to issues such as frailty that are not captured by conventional scoring systems as well as renal impairment or anaemia that can limit revascularisation options.

Finally we now have many patients, who are survivors of heart attacks and who have had often extensive revascularisation already, and who continue to have anginal symptoms despite medical therapy—so-called refractory angina. Though this is a common and difficult clinical management challenge, there are very few cardiologists who have a specialist interest or service for refractory angina.

Stable angina in the elderly: Challenges, complications and case histories

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Chest pain is a big issue in terms of resources with 1% of visits to a GP being for this condition as well as 40% of emergency admission. In addition to this, almost 2% of the population have or have had angina. The prevalence of angina is increasing particularly in the older age group due to better survival of acute events and increasing life-span, whereas that for acute coronary syndrome is decreasing.

William Heberden's classic description of angina pectoris was first presented to the Royal College of Physicians in 1768. It was published in 1772, in the Medical Transactions of the College and his description of a gripping pain in the neck and chest, coming on after exercise or with

stress and relieved by rest is as true today as ever and indeed reflects almost exactly the clinical definition of cardiac chest pain published in the most recent NICE guidance on the management of angina. The only difference is that recent descriptions describe relief by GTN as a diagnostic feature—a factor Heberden couldn't mention as GTN wasn't discovered until 100 years later!

We should now diagnose angina according to the NICE guidance CG95 "Chest pain of recent onset".[2] This was a major departure from previous practice as it no longer recommends the traditional exercise test as having any place in diagnosis, instead substituting functional imaging, such as radionuclide perfusion or stress echo. While this may be a more efficient approach, the reality is that there are major problems with appropriate resources to implement this guidance in many regions of the country and in many regions, exercise testing continues to have a role in diagnosis of chest pain.

In terms of treatment, once a diagnosis of angina has been made, NICE recommends that optimum medical therapy should be the first port of call. This should consist of secondary preventative treatments (aspirin, statins, ACE inhibitors), life-style advice to address risk factors and promote exercise and drug therapy. CG95 recommends that either a beta-blocker or a calcium antagonist should be used first, with the other class of drug being added if the first is insufficient or not tolerated. Nitrates are actually the oldest treatment for angina and short term nitrates are recommended as first line but not long term nitrates. This is not because NICE thinks that are not effective but because the treatment is so old that there has never been any randomised evidence even though we know that they appear to work.

Beta-blockers certainly improve symptoms and might improve prognosis. Beta-blockers reduce the burden of myocardial ischaemia by reducing myocardial work so reducing the myocardial oxygen demand. The most important factor in this is that they reduce heart rate, which not only reduces oxygen demand, but in fact increases supply by increasing the length of diastole, during which the coronary arteries are mainly perfused.

Heart rate was included in the targets from both the European and American guidelines on stable angina[3,6] but the recent NICE guidance on stable angina[1] did not say anything on this. This was an unfortunate omission, but for maximum effect, heart rate should be between 55-60 beats per minute (bpm) for anyone with angina and less than 50bpm with severe symptoms.

Second line therapy is decided on comorbidities, contraindications and the failure to control symptoms. Most doctors know about long acting nitrates and nicorandil, but they may not know about the two other newer drugs—ivabradine and ranolazine. They are interesting additions to the range already available and according to the NICE guidance[1] all are now equally relevant.

Ivabradine is an inhibitor of I*f*, a sodium channel in the sino-atrial node, which has the effect of slowing heart rate without having any other effect on haemodynamics and thus is particularly valuable in those who already have low blood pressure. In one add-on study of patients who were already on atenolol, but had uncontrolled heart rate, ivabradine reduced heart rate and there was a significant improvement in ischaemia and quality of life.[7] In patients who have a raised heart rate despite being on a beta-blocker than I add in ivabradine in addition to beta-blockers, although this is outwith the current licence for the drug.

A further new class of drug is ranolazine. This is a very interesting agent and currently the only one of its type. Ranolazine reduces the late sodium current and, is expected to decrease late sodium entry into ischaemic myocardial cells. As a consequence, ranolazine is proposed to reduce calcium overload indirectly via the sodium/calcium exchanger and to preserve ionic homeostasis and reverse ischaemia-induced contractile dysfunction.

The ERICA study looked at people with frequent angina and found that ranolazine significantly reduced frequency of angina and nitroglycerin consumption compared with placebo and was well tolerated. Patients with more frequent angina appeared to have a more pronounced treatment effect.[8] That is unusual in medicine as normally the people that need something the most usually have the least benefit.

The CARISA study[9] found that twice-daily doses of ranolazine increased exercise capacity and provided additional antianginal relief to symptomatic patients with severe chronic angina taking standard doses of atenolol, amlodipine, or diltiazem, without evident adverse, long-term survival consequences over one to two years of therapy. This is because it works differently to other drugs in its metabolic action. The nice thing about these new drugs are that they work and have good tolerability rates so they have a good impact on quality of life.

In the NICE guidance the final step of the care pathway is revascularisation. Before a patient gets to this point they should have had lifestyle measures and optimisation of drug therapy. This is not what happens in clinical practice as historically there is an assumption that revascularisation must be preferable to drug therapy alone in people with coronary disease. There has been an explosion over the last

30 years in PCI thus one would reasonably assume that there must be very solid evidence that this is the better course of treatment, right? Wrong! In fact there is no evidence that PCI is better than optimal medical therapy.

The recent COURAGE study was conducted in patients with stable CAD as it was unclear whether an initial management strategy of PCI with intensive pharmacologic therapy and lifestyle intervention (optimal medical therapy) is superior to optimal medical therapy alone in reducing the risk of cardiovascular events. It found that as an initial management strategy in patients with stable coronary artery disease, PCI did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when added to optimal medical therapy.[4]

A recent meta-analysis (that did not include the COURAGE trial) also found that there is not one shred of evidence that intervening on people's coronary arteries improves prognosis—it does not save lives.[10]

In terms of lifestyle therapies, many healthcare professionals might think that exercise is less relevant for older patients but many older patients can do some sort of exercise. Lots of doctors and patients have a bad attitude to exercise. An old study compared the effects of exercise training versus standard PCI with stenting on clinical symptoms, angina-free exercise capacity, myocardial perfusion and cost-effectiveness. It found that compared with PCI, a 12-month programme of regular physical exercise in selected patients with stable coronary artery disease resulted in superior event-free survival and exercise capacity at lower costs, notably owing to reduced rehospitalisations and repeat revascularisations.[11]

An increasing modern problem is that of refractory angina. It is defined as angina that is limiting and no longer amendable to conventional medical or interventional options. It is becoming more common due to advancing age, increasingly diffuse coronary disease and patients who have had multiple previous revascularisations and yet it is a problem that attracts relatively little attention—a sad truth. There is a refractory centre in Liverpool (NRAC) which uses a pain management and patient centred approach to controlling symptoms and improving quality of life. This approach has been shown to be relatively cheap and effective in this group, compared to interventional therapy and has also been shown to reduce readmissions. The quality of life of a patient with angina is what we should all be increasingly interested in. This is mainly because that is what our patients themselves care about, but also precisely because the prognosis of stable angina has been shown to be relatively benign (mortality rates in most series are between 1–2% per year), thus an obsession with prognosis is not appropriate. The mainstay of therapy in NRAC is cognitive behavioural therapy. Most physicians initially find this quite astonishing, but we have found that one of the factors that really disables people with chronic angina is not so much the symptoms themselves, but the fear of angina and the notion that they might just "drop dead". We unpick all these unhelpful (and untrue) notions and while revascularisation undoubtedly has a role to play to rapidly relieve certain symptoms, it carries an appreciable risk and is far from the panacea many patients (and doctors) appear to believe. In fact, a small study conducted in NRAC[12] showed that the quality of life benefits of this approach actually outweighed those of PCI in the COURAGE quality of life substudy, albeit in a very different patient population. The message for our patients should be that PCI is a lifestyle intervention with no intrinsic superiority to drug or any other form of therapy—it is plastic surgery for the coronaries and while there are instances when this is beneficial and the right thing to do, we all have to bear in mind it can have its disasters too. Overall then, the management of stable angina should focus on the improvement of the patients' lifestyle and quality of life, not on the method by which this is achieved. Optimal medical therapy and lifestyle adjustment, drugs and revascularisation are all equivalent and complementary strategies, but it must be acknowledged that revascularisation generally carries higher risks and costs, without improving prognosis. The choice as to which combination of these we employ should be made by properly informing our patients as to the risks and benefits and allowing them to choose what is best for them and only then can we say that we are generally practising in a patient-centred manner, as recommended by NICE.

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