

RESEARCH

What's the risk? Assessment of patients with stable chest pain

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Abstract

In 2010, the National Institute for Health and Clinical Excellence published guidelines for the management of stable chest pain of recent onset. Implementation has occurred to various degrees throughout the NHS; however, its effectiveness has yet to be proved. A retrospective study was undertaken to assess the impact and relevance of this guideline, comparing the estimated risk of coronary artery disease (CAD) with angiographic outcomes. Findings were compared with the recently published equivalent European guideline. A total of 457 patients who attended a Rapid Access Chest Pain Clinic were retrospectively reviewed. CAD risk was assessed according to NICE guidelines and patients were separated into typical, atypical and non-anginal chest pain groups. Risk stratification using typicality of symptoms in conjunction with NICE risk scoring and exercise tolerance testing was used to determine the best clinical course for each patient. The results include non-anginal chest pain – 92% discharged without needing further testing; atypical angina – 15% discharged, 40% referred for stress echocardiography, 35% referred for angiogram and significant CAD revealed in 8%; typical angina – 4% discharged, 19% referred for stress echocardiography, 71% referred for angiogram and 40% demonstrated CAD. Both guidelines appear to overestimate the risk of CAD leading to an excessive number of coronary angiograms being undertaken to investigate patients with typical or atypical sounding angina, with a low pick up rate of CAD. Given the high negative predictive value of stress echocardiography and the confidence this brings, there is much scope for expanding its use and potentially reduce the numbers going for invasive angiography.

Key Words

- ▶ coronary artery disease
- ▶ risk stratification
- ▶ stress echocardiography
- ▶ coronary angiography

Introduction

The National Institute for Health and Clinical Excellence (NICE) published its guideline CG95 '*Chest Pain of Recent Onset*' (1), in which it presents an algorithm for assessing patients with intermittent chest pain or discomfort. It defines the contributing features of anginal pain as: i) constricting discomfort in the chest, neck, shoulders, jaws or arms; ii) precipitated by physical exertion; iii) pain relieved by rest or glyceryl trinitrate (GTN) spray within about 5 min. Patient's symptoms are classified as follows:

typical angina – three of the above features, atypical angina – two of the three features and non-anginal chest pain – one or none of the features (1).

The NICE 2010 guideline recommends that patients presenting with typical or atypical angina symptoms be referred for further investigation, in the form of functional imaging and/or coronary angiography (1).

Based on research by Pryor *et al.* (2), an estimated risk of coronary artery disease (CAD) is determined using the

patients' age, gender, chest pain classification and risk factors (smoking, diabetes, hyperlipidaemia) (1). Those with an estimated risk of <10% should be investigated for other causes of chest pain, 10–29% should be offered CT calcium scoring as the first-line diagnostic test, 30–60% offered functional imaging in the first instance, 61–90% offered invasive coronary angiography as first-line, if appropriate.

Those presenting with features of typical angina with an estimated risk >90% are presumed to have stable angina and should be treated accordingly (1).

The NICE 2010 guideline advises against using exercise tolerance testing (ETT) to diagnose or exclude stable angina (1); however, access to CT calcium scoring is limited across the UK. Due to this, ETT is still utilised for risk stratification in Greater Manchester & Cheshire Cardiac and Stroke Network (3), and therefore at Macclesfield District General Hospital.

In 2013, the European Society for Cardiology (ESC) produced an updated guideline on the management of stable CAD (4). The ESC 2013 guideline classifies chest pain in a similar manner to the NICE 2010 guideline, with the addition of emotional stress being listed alongside physical exertion as a possible trigger.

Using research by Genders *et al.* (5), the ESC 2013 guideline contains a similar table of estimated risk percentages to the NICE 2010 guideline.

Those with an estimated risk of <15% should be presumed not to have CAD. If >15% risk, a patient's left ventricular ejection fraction (LVEF) is a key determinant factor: 15–50% risk can be offered coronary CT angiography if suitable and/or available and 15–65% risk can be offered ETT or functional imaging if LVEF >50%. 66–85% risk should be offered functional imaging. If the estimated risk is 15–85% and LVEF <50% with typical angina symptoms, then coronary angiography is advised. >85% risk should be diagnosed as having CAD and medical therapy started.

Cardiac imaging therefore plays a pivotal role in such decision-making, through determination of left ventricular systolic function and subsequent investigation selection.

The NICE 2010 guideline has been implemented to various degrees across the NHS, and its effectiveness has previously been considered (6). The objective of this real-life, retrospective study was to assess the guideline locally, and compare its effectiveness with the ESC 2013 guideline by comparing the estimated risk of CAD with the angiographic outcomes.

Method

Study population

In this study, 457 patients (52% male, average age 59 years) who attended the RACPC at Macclesfield District General Hospital during the period January–December 2013 were retrospectively studied. All patients were referred by their general practitioner (GP) with no prior history of CAD. A variety of risk factors were recorded during the clinical assessment (Table 1).

Rapid Access Chest Pain Clinic

All patients were assessed by a specialist cardiology nurse who recorded a clinical history to determine typicality of symptoms. In line with the NICE 2010 guideline, patients were stratified to risk percentage groups depending upon their symptoms (non-anginal chest pain, atypical angina or typical angina), age, gender and risk factors. For the purpose of this study, a separate set of risk percentages was determined using the ESC 2013 guideline to permit comparison.

A resting 12-lead ECG and physical examination were performed before patients were considered suitable for ETT. ETTs were performed using the standard BRUCE protocol (7). Further investigative tests were referred on determining the typicality of symptoms, NICE estimated risk of CAD and ETT result.

Further tests included stress echocardiography and coronary angiography. Results from these investigations were recorded and the estimated risk of CAD was compared with the actual prevalence of disease within the individual classifications. Obstructive CAD was considered to be stenosis >50% diameter in at least one vessel, a threshold similar to that used in a previous large multicentre study (8).

Table 1 Population characteristics.

Characteristics	Value
Male (%)	51.5
Age (years)	59 ± 12.1
Follow-up time (months)	12.1 ± 4.0
Diabetes (%)	8.5
Smoker/ex-smoker (%)	49.9
Hyperlipidaemia (%)	35.9
Hypertension (%)	34.6
Family history (%)	61.1

A total of 457 patients attended RACPC in 2013 reporting a range of risk factors for CAD. Continuous data presented as mean ± s.d.

Results

The largest group of patients attending the clinic were considered to have non-anginal chest pain (52%), compared with atypical (26%) and typical (21%) symptoms. Five patients (1%) were admitted with suspected myocardial infarctions and therefore not classified. 11% of patients were considered unsuitable for ETT but remained in the analysis.

Non-anginal chest pain

A total of 236 patients presented with symptoms considered to be non-anginal chest pain with a NICE 2010 guideline mean estimated risk of 28% (range 1–90%) for CAD (Fig. 1): 92% of these patients were discharged after attending RACPC. 8% of patients underwent further investigations with no evidence of flow-limiting CAD. Five discharged patients later attended Accident and Emergency complaining of chest pain/discomfort, three were deemed non-cardiac related. Two patients were admitted with myocardial infarctions and received percutaneous coronary intervention (PCI) – RACPC results showed a negative ETT with hypertensive response, and another was unable to exercise but had a normal transthoracic echocardiogram.

Atypical angina

A total of 119 patients presented with symptoms atypical for angina with a NICE 2010 guideline mean estimated risk of 58% (range 5 to >90%). All patients were assessed for their suitability to undertake ETT, with 100 patients proceeding (Fig. 1). The outcomes of all ETTs are provided in Table 2 along with the number of referrals for stress echocardiograms and angiograms.

Overall, 15% patients with atypical angina symptoms were discharged without undergoing further investigations based on reassuring ETT results and/or low estimated risk. 15% were referred for transthoracic echocardiograms for murmur investigation, 40% for stress echocardiography and 35% for angiography (Fig. 1) with 5% referred following an abnormal/positive stress echocardiogram (Table 2). Referrals for further investigations were based upon estimated risk: five patients with 30–60% risk were referred straight for angiography due to their unsuitability for stress echocardiography or following a positive ETT.

Eighty-five percent of stress echocardiograms were negative for wall motion abnormalities and discharged. One patient attended Accident and Emergency complaining of chest pain/discomfort following a negative stress echocardiogram. On declining angiography they were

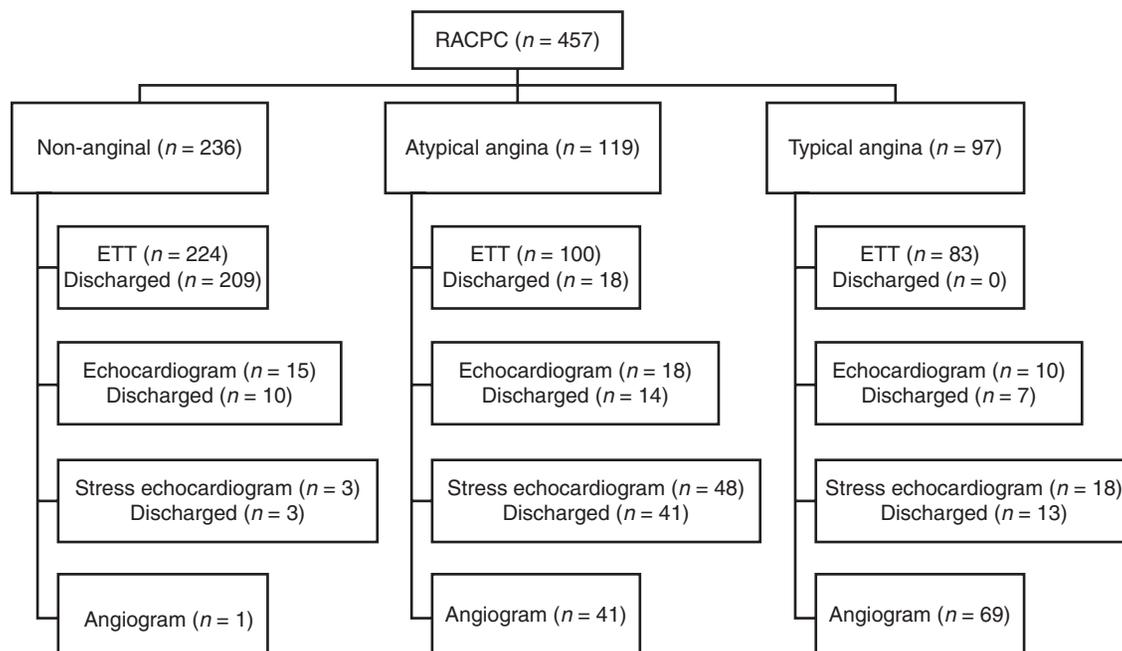


Figure 1

RACPC outcomes for each chest pain classification. A total of 457 patients attended RACPC in 2013. These were assessed and assigned to non-anginal, atypical angina or typical angina groups. If suitable, patients underwent

ETT and where necessary they were referred for further investigations (transthoracic echocardiogram, stress echocardiogram and/or coronary angiogram).

Table 2 ETT outcomes for patients with atypical angina.

	No.	Stress echocardiogram	Angiography	Unobstructed arteries	> 50% stenosis
Negative ETT	53	26 (2)	9	8	1
Inconclusive ETT	19	6	5	5	0
Abnormal ETT	19	10 (3)	10	8	2
Positive ETT	9	2 (1)	7	5	2

A total of 100 patients with atypical angina symptoms attempted ETT (inconclusive ETT – any test whereby the patient did not reach 90% of their target heart rate due to fatigue; abnormal ETT – any test whereby ST segment changes did not reach significance, or there was an arrhythmia towards peak exercise). Referrals for further investigations are broken down by ETT result (the number in brackets represents abnormal/positive stress echocardiograms). The degree of CAD determined from angiography is provided; unobstructed arteries (<50% stenosis) or flow-limiting CAD (>50% stenosis).

referred for a stress cardiac MR scan which also returned a negative result.

Thirteen percent subsequently underwent coronary angiography, one had flow-limiting CAD and was medically managed, the other five had unobstructed arteries.

Of those referred for angiography, 24% were found to have flow-limiting CAD (Fig. 2) and 10% required revascularisation.

Typical angina

A total of 97 patients presented with symptoms typical of angina with a NICE 2010 guideline mean estimated risk of 79% (range 20 to >90%) (Fig. 1): 83 patients proceeded to ETT with 15 referrals for stress echocardiograms and 64 for angiograms (Table 3).

Four percent were discharged post RACPC without referral for further investigation, one had severe anaemia, one declined angiography and two were treated outside the NHS. None of these patients presented again during the follow-up period of this study.

10% were referred for transthoracic echocardiograms for murmur investigation, 19% for stress echocardiography, and 71% for angiography (Fig. 1) with 4% referred following an abnormal/positive stress echocardiogram (Table 3). Referrals for further investigations were based upon estimated risk. Two patients with risk >61% were referred for stress echocardiography due to negative ETT.

Of those referred for stress echocardiography, 72% were negative for wall motion abnormalities and discharged. One patient with an estimated risk of 51% was referred for angiography after an inconclusive result, which provoked symptoms but was negative for wall motion abnormalities, unfortunately suffered a fatal cardiac arrest and later ascribed to CAD. Of the four who subsequently underwent coronary angiography, one had normal coronary arteries, three had flow-limiting CAD.

The majority of typical angina patients underwent angiography due to an estimated risk >61% in 78% of this group. Of these, 55% were found to have flow-limiting CAD (Fig. 2) with 34% requiring revascularisation.

Estimated risk for CAD following the NICE 2010 guideline

Considering angiographic outcomes in relation to the estimated risk of CAD, one atypical angina patient with <10% estimated risk was referred due to a run of left bundle branch block on ETT, another atypical patient with 10–29% risk was referred following a positive ETT and abnormal/positive stress echocardiogram (Fig. 3). Two patients with typical angina with a risk of 10–29% had abnormal/positive ETT and hence were referred for further investigation (Fig. 4). All of these low risk patients were found to have unobstructed arteries.

Fourteen patients estimated to be at 30–60% risk underwent coronary angiography (Figs 3 and 4), with four patients having had stress echocardiograms first. Of these four only one was considered to have flow-limiting CAD. Other referrals followed abnormal/positive ETT, wall motion abnormality on transthoracic echocardiogram or

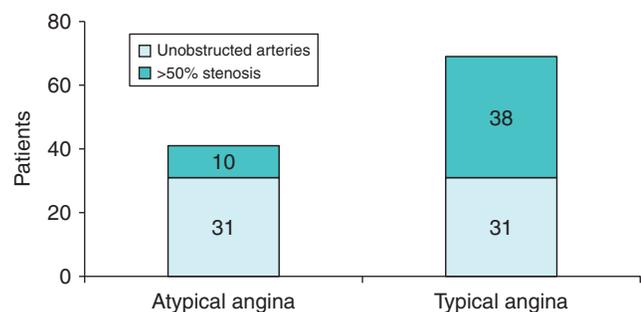


Figure 2 Coronary angiography outcomes for the 41 patients with atypical angina and 69 patients with typical angina symptoms who were referred after attending the RACPC in 2013.

Table 3 ETT outcomes for patients with typical angina.

	No.	Stress echocardiogram	Angiogram	<50% stenosis	>50% stenosis
Negative ETT	37	10 (2)	24	16	8
Inconclusive ETT	16	3	13	6	7
Abnormal ETT	8	1 (1)	7	3	4
Positive ETT	22	1 (1)	20	3	17

A total of 83 patients with typical angina symptoms attempted ETT (inconclusive ETT – any test whereby the patient did not reach 90% of their target heart rate due to fatigue; abnormal ETT – any test whereby ST segment changes did not reach significance, or there was an arrhythmia towards peak exercise). Referrals for further investigations are broken down by ETT result (the number in brackets represents abnormal/positive stress echocardiograms). The degree of CAD determined from angiography is provided; unobstructed arteries (<50% stenosis) or flow-limiting CAD (>50% stenosis).

unsuitability for stress echocardiography. 64% of this risk group had unobstructed arteries.

Eighty-four percent of patients who underwent angiography had an estimated risk >60%. However in the (61–90%) risk group, 65% were found to have unobstructed arteries. In the highest risk (>90%) group, 38% had unobstructed arteries (Figs 3 and 4).

Comparison of estimated risk according to ESC 2013 vs NICE 2010 guidance

When the ESC 2013 guideline was applied to atypical angina patients who underwent angiography, there were fewer in the higher risk groups compared with NICE 2010 guideline with no patients with estimated risk >90% and 7 with 61–90% risk. The consequence was increased numbers in the 10–29% and 30–60% risk groups. Overall, 66% would be recommended to have functional imaging in the first instance (Fig. 3).

A different outcome was revealed in typical angina patients: a large reduction in the >90% risk group, with

increased numbers in the 30–60% and 61–90% risk groups. Overall, 67% would qualify for angiography as a first-line diagnostic test (Fig. 4).

Detection of flow-limiting CAD differed when the ESC 2013 guideline was compared to the NICE 2010 guideline: the detection reduced from 36 to 35% in the 30–60% risk group and increased from 35 to 57% in the 61–90% group (Figs 3 and 4).

Age is a major risk-determining factor in both guidelines. Analysis of angiographic outcomes in relationship with age revealed patients with unobstructed arteries had a mean age of 61 years (range 36–85 years), and those with flow-limiting CAD had mean age 65 years (range 44–83 years).

Discussion

RACPC continues to prove essential in the screening process of patients suspected of stable angina. Trained and experienced staffing of these clinics is vital in determining

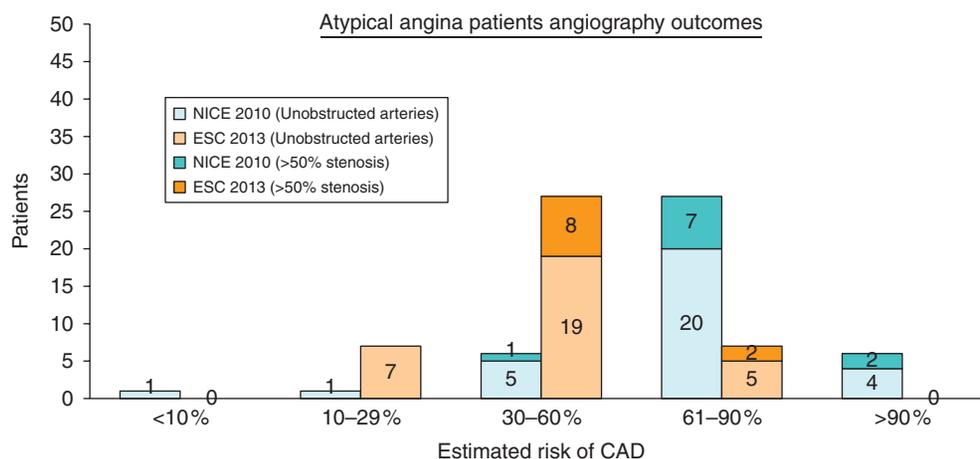


Figure 3

Comparison of the NICE 2010 guideline and ESC 2013 guideline estimated risk percentages for atypical angina patients found to have unobstructed arteries (<50% stenosis) or flow-limiting CAD (>50% stenosis) after coronary angiography.

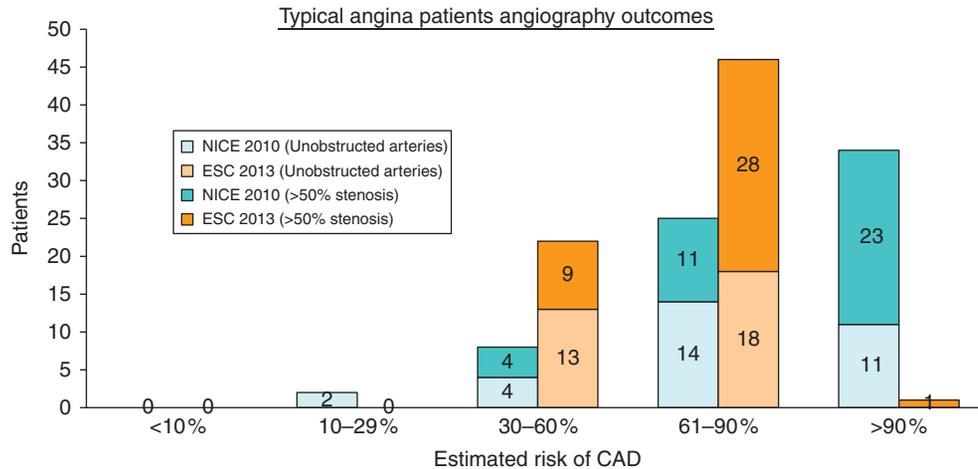


Figure 4

Comparison of the NICE 2010 guideline and ESC 2013 guideline estimated risk percentages for typical angina patients found to have unobstructed arteries (<50% stenosis) or flow-limiting CAD (>50% stenosis) after coronary angiography.

which patients require further investigation. Although NICE guidance does not recommend the use of ETT for diagnostic purposes, this easily available and inexpensive test is likely to continue to play an important role in risk stratification, currently supported by both local (3) as well as international (4) advisers.

Only 19% of patients with typical angina symptoms were referred for stress echocardiography (Fig. 1), which can be attributed to NICE guidance because 78% patients had an estimated risk >61%, and they should be offered ‘invasive coronary angiography as the first-line diagnostic investigation if appropriate’ or treated as having angina (1).

Coronary angiography had a low yield in detection of flow-limiting CAD, especially in the 61–90% risk group, to which NICE recommends coronary angiography as a first-line diagnostic test.

Of those who underwent coronary angiography, 76% presenting with atypical angina and 45% presenting with typical angina symptoms were found to have unobstructed coronary arteries, suggesting that the NICE 2010 guideline causes unnecessary invasive referrals.

A considerable number of patients were referred for angiography with typical angina symptoms along with CAD risk of >90%, which according to the NICE 2010 guideline ‘...further diagnostic investigation is unnecessary. Manage as angina’. However, more than a third of this group did not actually have flow-limiting CAD. The management would be entirely different if the NICE algorithm was strictly applied; unnecessary anxiety can be caused in addition to exposure to non-required, expensive polypharmacy.

It would appear that the NICE 2010 guideline overestimates the occurrence of flow-limiting CAD in patients considered to have typical or atypical angina symptoms. Whilst the NICE 2010 guideline states that the estimated risk percentages ‘are likely to overestimate CAD in primary care populations’, is the extent of such demonstrated in this study acceptable?

A factor which may have impacted upon this overestimation is the local demographics of the Macclesfield area where an increased ageing population predominates with a good standard of living. This can be seen by the mean age of those attending RACPC being 59 years (Table 1).

Both guidelines use age to estimate the risk of CAD, but is it acceptable of the NICE 2010 guideline to assign all patients older than 70 years with typical or atypical angina symptoms such high risk percentages whereby they will either be referred for angiography or presumed to have angina? In this study, the mean age of patients with flow-limiting CAD (65 years) would suggest it is appropriate, however this was only 4 years older than those considered to have unobstructed arteries.

Such an age threshold may need to be revised given many of us are living longer, demonstrated in a recent study considering UK health performance where life expectancy was found to have increased since 1990 (9). Another approach, adopted by ESC, raised the age limit for each group, giving those between 60 and 69 years a lower risk score with higher risk related to age being shifted to age groups 70–79 and >80 years.

Another point for consideration is the table of estimated risk percentages within the NICE 2010

guideline, which were adapted from work by Pryor *et al.* (2) more than 20 years ago. In that time great strides have been made for increasing public awareness on cardiac disease, such as the importance of a healthy diet, regular exercise and avoid smoking. Together with the availability of better medical care and treatment for people diagnosed with heart disease, the number of deaths due to CAD in the UK has reduced by 48% between 1991 and 2009 (10). Considering the great progress made in recent years, are the risk percentages used in the NICE 2010 guideline appropriate for today's patients? Recent research conducted by Genders *et al.* (5) supports this point where an updated table of risk percentages was produced based on a large cohort across multiple locations. The quality and outcome of this research has been well received and as such the updated table has been included in the ESC 2013 guideline (4).

Comparing these tables of estimated risk percentages is not straight forward as the NICE 2010 guideline includes confounding risk factor consideration (smoking, diabetes, hyperlipidaemia increases the risk). Despite this, ESC risk percentages appear to be lower overall compared with those of NICE in both typical and atypical angina patients. This would undoubtedly have an effect on the choice of investigation with the majority of patients with atypical angina being directed towards functional imaging in the first instance, a shift away from angiography. Similarly, a greater number of patients with typical angina would be recommended for functional imaging, however the majority would be eligible for angiography as a first-line diagnostic test. Very few patients with typical angina would be presumed to have stable angina.

Overall, there would be a 71% increase in the number of patients recommended for functional imaging if ESC risk percentages were applied.

For patients who underwent angiography only a small difference was seen in the detection rate of flow-limiting CAD in the 30–60% risk group, when the NICE 2010 guideline and ESC 2013 guideline risk percentages were compared. The detection rate in the 61–90% risk group was greater when ESC was applied, suggesting it is more effective than NICE; however, 43% would have unobstructed arteries. Therefore it appears that the ESC 2013 guidance-based approach also overestimates the occurrence of flow-limiting CAD in patients considered to have typical or atypical angina symptoms.

RACPC angiography referrals represent a significant amount of the Catheter Lab workload, reducing this would have a positive financial implication and free up consultant availability. Considering that 82% of those

referred for stress echocardiography were discharged following a negative result due to its high negative predictive value and the confidence this brings both the clinician and the patient, there is much scope for expanding its use to potentially reduce the numbers being sent for invasive angiography.

Of interest, the NICE 2010 guideline makes no use of the significant risk factor of existing family history, which in this study was highly prevalent. It can be argued that family history has been linked in the following years to have an important effect on the probability of having CAD with a greater understanding of genetic predisposition to CAD (11).

Limitations

This was a single-centre retrospective study with a limited sized cohort. It reflects current practice following NICE recommendations without access to CT calcium scoring. The main end-point is the outcomes from coronary angiography, but this was not performed on all patients, only those who required as per the NICE 2010 guideline algorithm. Ultimately a larger study needs to be conducted with a greater cohort size enveloping multiple centres across the UK to fully assess the effectiveness of the NICE 2010 guideline.

Follow-up was limited to further investigations performed by medical staff, and further attendances at Macclesfield District General Hospital. Long-term follow-up of discharged patients would be useful to investigate the frequency of further investigations and the prevalence of CAD.

Conclusion

RACPC is an important service which operates under NICE guidance for screening patients suspected of stable angina. Further refinement in the risk assessment may be required to establish accurate diagnosis and avoid unnecessary invasive investigations, with consideration given to a population that is living longer with healthier lifestyle choices. There is also a need to increase the spectrum and capacity of imaging and functional imaging to serve this group of patients appropriately.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contribution statement

A Cubukcu was involved in initial design and supervision. I Murray and S Anderson generated the database. I Murray completed data collection, interpretation and wrote the manuscript. A Cubukcu and S Anderson provided reviews.

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