NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

QAngio XA 3D/ QFR and CAAS vFFR imaging software for assessing the functional significance of coronary obstructions during invasive coronary angiography

Final scope

October 2019

1 Introduction

The QAngio XA 3D/ QFR imaging software is manufactured by Medis Medical Imaging Systems. The medical technologies topic oversight group selected and routed QAngio imaging software for guidance development by the Diagnostics Assessment Programme on the basis of a topic briefing. The final scope was informed by discussions at the scoping workshop held on 5th September and the assessment subgroup meeting held on 17th September 2019.

A glossary of terms and a list of abbreviations are provided in appendices A and B.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE from the manufacturers and on information available in the public domain. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technologies

QAngio XA 3D/ QFR and CAAS vFFR are analytical software that can be used during invasive coronary angiography (ICA) to assess the functional significance of coronary obstructions (stenoses). ICA is an invasive anatomical imaging technique used to visualise coronary arteries, usually used as a third-line investigation for stable angina or during initial stages of percutaneous coronary intervention (see section 3.2.1 for details). ICA shows whether the arteries are blocked or narrowed (stenosis), and the degree of stenosis. However, visual assessment of angiograms taken during ICA has

limited ability to differentiate between functionally significant (causing inadequate blood supply) and non-significant (not substantially affecting blood supply) coronary stenoses. Stenoses that are functionally significant may benefit from revascularisation (using percutaneous or surgical techniques), while functionally non-significant stenoses should be treated medically. Currently, if it is necessary to more accurately understand the functional significance of an intermediate obstruction, fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) measurements can be done. This requires use of a pressure wire with or without a vasodilator drug, such as adenosine, and can only be done in interventional catheter laboratories.

QAngio and CAAS vFFR use angiographic images taken during the ICA, so no additional procedure is needed. It is claimed that they are more accurate than ICA alone for indicating whether intermediate anatomical obstructions (stenoses) are functionally significant and thus could improve clinical decision making relating to revascularisation. It is claimed they can give an assessment of the 3D anatomy and physiology of the coronary artery in minutes.

Because of the non-invasive nature of QAngio and CAAS vFFR, they could be used in people with stable chest pain of recent onset undergoing ICA in diagnostic-only or in interventional catheter laboratories. By improving the diagnostic accuracy of ICA, they could potentially:

- In diagnostics-only catheter laboratories, help avoid unnecessary referrals for invasive measurement of the functional significance of coronary stenoses (FFR or iFR) and/or revascularisation (percutaneous and surgical). They could also improve outcomes for people with intermediate stenoses who otherwise would not have been identified and referred for revascularisation or further assessment.
- In interventional catheter laboratories, help avoid unnecessary invasive measurement of the functional significance of coronary stenoses (FFR or iFR). For people with tandem or diffuse coronary disease, they could give per-lesion assessment in addition to per-vessel assessment, to help prioritise which lesions need to be treated. Also, they could give better assessment for people who would otherwise have treatment decisions based on ICA alone.

By avoiding unnecessary invasive measurement of FFR, the risks associated with passing the pressure wire to the coronary arteries, and with adenosine infusion could be avoided (see section 3.2.2 for details).

2.2 Product properties: QAngio XA 3D/ QFR

The QAngio software is installed on a laptop or workstation that is connected to the ICA system, so the analysis is done on site. The software uses X-ray angiographic images taken during ICA, so no additional procedure is necessary. Two images are needed, which have to be taken with at least 25 degrees difference in viewing angle and with a frame speed of at least 12.5 frames per second. High image quality is crucial for appropriate results. The QAngio software creates a 3D anatomical model of a coronary artery from these 2 images, and then estimates the quantitative flow ratio (QFR) from the 3D vessel anatomy and flow velocity. The total analysis time is claimed to take about 4-5 minutes per coronary artery. The analysis time may decrease with routine use of the software. The software is designed to be used with all ICA systems, biplane or monoplane, and is X-ray vendor independent. Medis plans to release a new version of the software (V2.0), which they claim will improve the clinical workflow and speed, as well as robustness of the software (however, the algorithms underlying QFR calculations will remain the same).

2.2.1 QFR thresholds

The QFR represents an assessment of the pressure drop over the artery, with a value of 1 representing a normally functioning artery with no pressure drop. A 20% or more drop in blood pressure (QFR value of 0.8 and less) is usually considered a significant obstruction where revascularisation should be considered.

The QAngio instructions for use document specifies that a QFR measurement close to the diagnostic cut-off point should be confirmed using invasive FFR measurement:

- QFR below 0.78: sufficiently high sensitivity to indicate revascularisation should be considered;
- QFR above 0.84: sufficiently high specificity to indicate revascularisation should not be considered (medical treatment only);
- QFR between 0.78 and 0.84: measurement should be verified by invasive FFR measurement.

It is claimed that when using these thresholds, QAngio allows pressure wire-free assessment in 2 out of 3 patients.

2.2.2 Choice of the computational flow model and QFR indices

The QAngio software offers two different flow models to calculate QFR:

- Fixed flow QFR – automatically generated by the software using data from the angiographic images and fixed flow velocity (taken from published literature)
- Contrast QFR – estimated from flow velocity in the relevant vessel using contrast frame count data from the angiogram. The analysis takes slightly longer but is claimed to be more accurate than fixed flow QFR. The manufacturer recommends that contrast QFR is calculated when the fixed flow QFR is in the range of 0.70 to 0.85.

In addition to the QFR value described above (also referred to as vessel QFR), the software provides index QFR, lesion QFR and residual vessel QFR values.

2.3 Product properties: CAAS vFFR

The CAAS vFFR software (Pie Medical Imaging) works by building a 3D reconstruction of a coronary artery as well as assessing the pressure drop across the stenosis and calculating a vessel-FFR (vFFR) value. Therefore, it gives both anatomical and functional assessments of the stenosis. It is claimed that it can be easily integrated into catheter laboratories. It uses 2 standard X-ray angiograms, and is compatible with most X-ray systems (that is, it is vendor independent). The total analysis time is claimed to take about 2 minutes per coronary artery.

It is available in CAAS Workstation 8.0, 8.1, 8.2; the algorithm for calculating vFFR is the same for all workstations. The CAAS Workstation is a platform which provides various modules (for example, quantitative coronary arteriography and left ventricular analysis) and can be installed on a laptop or desktop computer in the catheter laboratory. The vFFR module can be added to the existing CAAS workstation. In addition to the vFFR which is a measurement over the full length of the contoured coronary artery (similar to vessel QFR), CAAS vFFR also provides measurements at the end of the lesion (similar to lesion QFR) and at a chosen position in the coronary artery (similar to index QFR). Thresholds for interpretation of vFFR are not provided in the instructions for use document.

3 Target condition

3.1 Stable angina

Angina is a type of chest pain caused by insufficient blood supply to the heart (myocardial ischemia). Stable angina is brought on by physical activity or emotional stress, and goes away with rest. It is the key symptom of coronary

artery disease which remains one of the main causes of morbidity and mortality in developed countries. Other symptoms of coronary artery disease may include heart palpitations and unusual breathlessness. Some people may not have any symptoms before they are diagnosed. If left untreated, coronary artery disease can lead to cardiovascular complications such as unstable angina, myocardial infarction, heart failure and sudden cardiac death.

It is estimated that almost 2 million people in England currently have or have had angina. Angina can have a significant impact on a person's quality of life, restricting daily work and leisure activities. It is also associated with a low but appreciable incidence of acute coronary events and increased mortality.

3.2 Diagnostic and care pathway

The aim of stable angina management (and more broadly, coronary artery disease management) is to stop or minimise symptoms, and to improve quality of life and long-term morbidity and mortality. Management options include lifestyle advice, drug treatment and revascularisation using percutaneous (stent placement during percutaneous coronary intervention) or surgical techniques (such as coronary artery bypass surgery), as described in the NICE guideline on management of stable angina and the 2019 European Society of Cardiology guidelines for the diagnosis and management of chronic coronary syndromes (Knuuti et al. 2019). The choice of appropriate management option depends on correctly detecting and characterising coronary obstructions (stenoses). Therefore, the diagnostic pathway for stable angina has two functions:

- Confirm the diagnosis of stable angina,
- Define the severity of coronary stenoses to provide prognostic information and identify people who are likely to benefit from myocardial revascularization, in addition to optimal medical therapy.

The NICE guideline on assessment and diagnosis of chest pain of recent onset recommends diagnostic testing for people in whom stable angina cannot be excluded by clinical assessment alone. It recommends offering 64-slice (or above) CT coronary angiography (CTCA) as the first-line diagnostic test when clinical assessment indicates typical or atypical angina; or non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves (Figure 1).

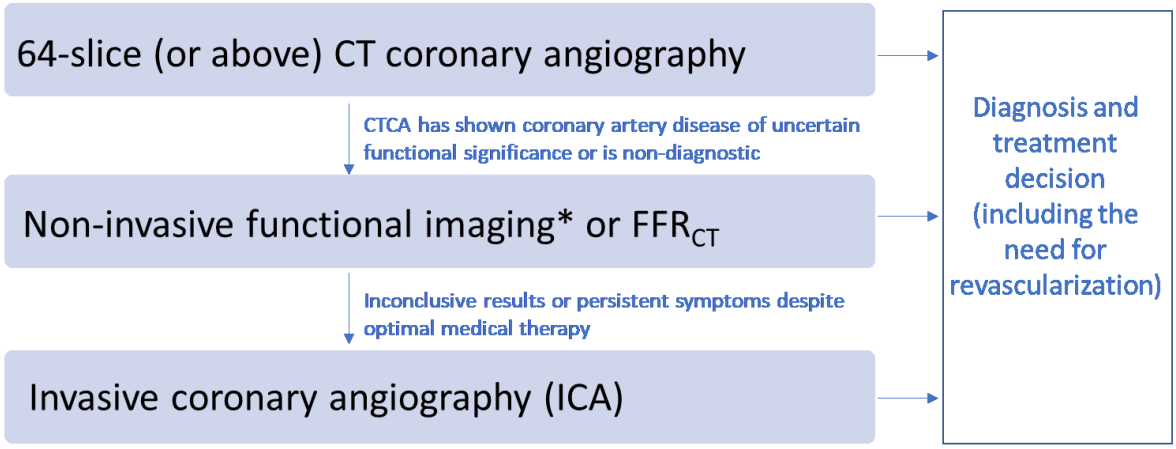
For people in whom 64-slice (or above) CTCA has shown coronary artery disease of uncertain functional significance, or is non-diagnostic, the guideline

recommends offering non-invasive functional imaging for myocardial ischaemia. This includes:

- myocardial perfusion scintigraphy with single-photon emission CT (MPS with SPECT)
- stress echocardiography
- first-pass contrast-enhanced magnetic resonance (MR) perfusion
- MR imaging for stress-induced wall motion abnormalities.

Invasive coronary angiography (ICA) should be offered as a third-line investigation when the results of 64-slice (or above) CTCA and non-invasive functional imaging are inconclusive (see section 3.2.1 for details). ICA should also be offered to guide treatment strategy for people with a confirmed diagnosis of stable angina whose symptoms are not satisfactorily controlled with optimal medical treatment.

Figure 1. Diagnostic pathway for stable angina



*Non-invasive functional imaging includes:

- myocardial perfusion scintigraphy with single photon emission computed tomography (MPS with SPECT),
- stress echocardiography,
- first-pass contrast-enhanced magnetic resonance (MR) perfusion,
- MR imaging for stress-induced wall motion abnormalities.

A diagnosis of stable angina should be made when:

- significant coronary artery disease is found during ICA or 64-slice (or above) CTCA. This is usually defined as 70% or more diameter stenosis of at least one major epicardial artery segment or 50% or more diameter stenosis in the left main coronary artery.
- reversible myocardial ischaemia is found during non-invasive functional imaging.

In addition, NICE's medical technologies guidance 32 recommends that HeartFlow FFR_{CT} should be considered as an option for patients with stable, recent onset chest pain who are offered 64-slice (or above) CTCA. It provides both functional and anatomic assessment of coronary arteries, and has better diagnostic performance than CTCA alone, or other non-invasive or invasive tests. The analysis is done using standard CTCA scans, without the need for additional imaging, radiation or medication. Using HeartFlow FFR_{CT} may avoid the need for diagnostic ICA.

Clinical experts advised that there is large regional variation in the diagnostic pathway for stable angina. This is largely driven by the availability of imaging modalities at each centre, and experience (or preferences) of the cardiologists referring for the test. However, they advised that the pathway recommended by NICE is widely recognised as current best practice, and all centres should aim to implement this pathway.

3.2.1 Invasive coronary angiography

ICA is an invasive anatomical imaging technique used to visualise coronary arteries. It shows whether the arteries are blocked or narrowed (stenosis), and the degree of stenosis. It is recommended as a third-line investigation for people with suspected stable angina in NICE's guideline on assessment and diagnosis of chest pain of recent onset (when results of CTCA and non-invasive functional imaging are inconclusive). ICA can also be used as a second-line investigation (following non-invasive functional imaging) for people who are not suitable for CTCA, or in centres where 64-slice (or above) CTCA is not available, and for people with a confirmed diagnosis of stable angina who have persistent symptoms despite optimal medical therapy.

During the procedure, a coronary diagnostic catheter is inserted into an artery, usually in the armpit or groin, and moved up the aorta and into the coronary arteries. A local anaesthetic is used to numb the skin where the catheter is inserted. A special type of dye called contrast medium is injected through the catheter and X-ray images (angiograms) are taken. Although providing valuable information on coronary artery anatomy, visual assessment of angiograms taken during ICA has limited ability to differentiate between functionally significant (causing inadequate blood supply) and non-significant (not significantly affecting blood supply) coronary stenoses.

In the UK, ICA is usually done either in diagnostic-only catheter laboratories, or in interventional catheter laboratories that can also do percutaneous coronary intervention within the same procedure, if it is indicated. In the diagnostic-only laboratories, patients who are identified as suitable for percutaneous coronary intervention would have to be then referred to the

interventional catheter laboratory for a second procedure. Clinical experts indicated that because of an increase in non-invasive functional imaging, and an increase in the number of interventional catheter laboratories across the UK, the role of diagnostic-only catheter laboratories is decreasing. However, in 2016, there were still almost 60 diagnostic-only centres in the UK that delivered about 36,000 ICA procedures (BCIS 2016). This indicates that currently, diagnostic-only catheter laboratories are still a significant part of the diagnostic pathway for stable angina.

3.2.2 Fractional flow reserve and other methods to invasively assess the functional significance of intermediate stenoses

Recognising the poor correlation between percentage diameter stenosis and their functional significance, the European and American guidelines recommend the use of FFR or instantaneous wave-free ratio (iFR) to assess the functional significance of intermediate stenoses (Neumann et al. 2018; Patel et al. 2017). The FFR or iFR measurements have not been assessed by NICE, but a Medtech innovation briefing is available for the PressureWire FFR system.

FFR assesses the reduction in blood flow resulting from a coronary artery obstruction (stenosis). It is defined as "the ratio of maximal flow achievable in the stenotic coronary artery to the maximal flow achievable in the same coronary artery if it was normal". An FFR of 1.0 is widely accepted as normal. Revascularisation can be safely deferred for stenoses with an FFR above 0.8. Stenoses with an FFR of 0.80 or less are functionally significant and revascularisation should be considered. Using this threshold, the FAME study showed that of:

- 50 to 70% diameter stenoses, 35% were functionally relevant
- 71 to 90% diameter stenoses, 80% were functionally relevant
- Above 90% diameter stenoses, most were functionally relevant

FFR is assessed invasively by advancing a pressure wire through the coronary diagnostic catheter towards the stenosis and measuring the ratio in pressure between the two sides of the stenosis during maximum blood flow (induced by adenosine infusion). This is associated with risks related to the passage of a guide wire (for example, coronary artery dissection), side effects of adenosine (including transient chest pain or shortness of breath), and additional radiation exposure. The invasive FFR measurement is also associated with increased procedural time and costs, compared with ICA alone.

iFR is an alternative method to invasively assess the functional significance of stenoses during ICA. It uses the same pressure wires (manufacturer-specific; not all pressure wires are suitable for iFR) and equipment used in FFR, but without the injection of adenosine. An iFR of 0.89 or less indicates a functionally significant stenosis. Clinical experts indicated that iFR is considered equivalent to FFR and is being increasingly used in the UK. Resting full-cycle ratio (RFR; also referred to as distal coronary to aortic pressure [P_d/P_a]) is another invasive functional assessment without adenosine administration, but it is used only in research and is not in routine clinical use.

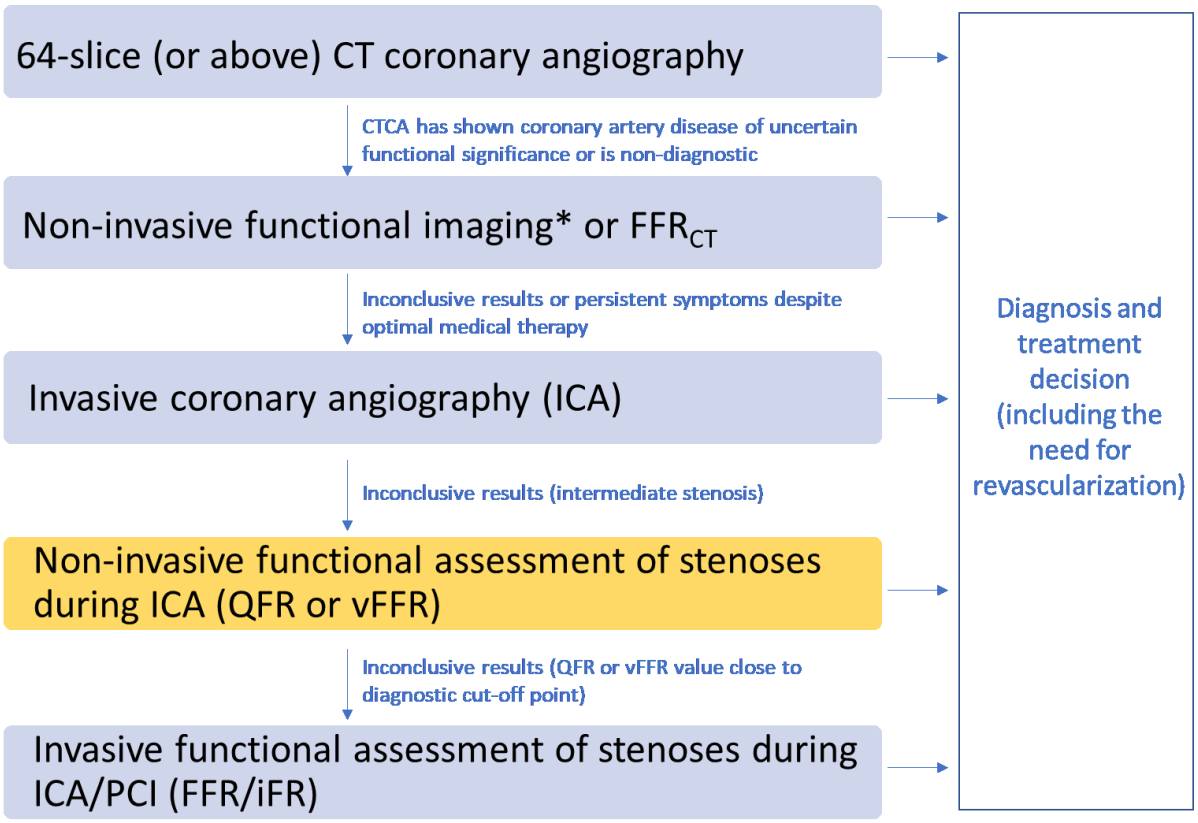
Because of their invasive nature, FFR and iFR are not used in diagnostic-only catheter laboratories, and experts indicated they may be underused in many interventional catheter laboratories. Currently, there is no consensus definition of intermediate stenoses for which FFR or iFR should be considered. Clinical experts advised that in addition to the percentage diameter stenosis, many other factors are considered when deciding whether invasive FFR or iFR measurements and/or revascularisation are needed. These factors include patient history, clinical presentation (symptoms), results of previous diagnostic investigations, position of the stenosis within the coronary tree, and whether it is single-vessel or multi-vessel disease. Also, because the percentage diameter stenosis is usually assessed visually only, there is no agreed consensus on the exact thresholds that should be used for decision making, with lower limits ranging from 30% to 50% diameter stenosis, and upper limits ranging from 70% to 90% diameter stenosis.

3.3 Position of the technology in the diagnostic pathway

The proposed position of QAngio and CAAS vFFR in the diagnostic pathway for stable angina is presented in Figure 2. They could be used during ICA for non-invasive functional assessment of intermediate stenoses, for which optimal treatment cannot be decided based on the clinical information and visual interpretation of angiographic images only.

When QFR/vFFR measurements are inconclusive, they could be verified by the invasive FFR or iFR measurement to help choose the best treatment option. This could be done within the same procedure when the ICA (or percutaneous coronary intervention) is done in the interventional catheter laboratory. A referral to an interventional lab would be needed if the ICA is done in the diagnostic-only setting.

Figure 2. Proposed position of QAngio and CAAS vFFR in the diagnostic pathway for stable angina



*Non-invasive functional imaging includes:

- myocardial perfusion scintigraphy with single photon emission computed tomography (MPS with SPECT),
- stress echocardiography,
- first-pass contrast-enhanced magnetic resonance (MR) perfusion,
- MR imaging for stress-induced wall motion abnormalities.

An intermediate stenosis is defined as any lesion stenosis identified by ICA where there is clinical uncertainty about its functional significance and the potential appropriateness of revascularization.

3.4 Patient issues and preferences

ICA is an invasive procedure which can be very distressing and unpleasant for patients, especially if invasive iFR or FFR measurements are done. iFR and FFR extend the duration of the procedure and are associated with the risk of coronary artery dissection. FFR measurement also uses vasodilator drugs to increase blood flow, such as adenosine, which are associated with a high rate of side effects (up to 30% of patients), including chest pain and shortness of breath. These are usually transient but can be very traumatic for patients. Interventions that can reduce the number and duration of ICA procedures, and avoid adenosine infusion, could be highly beneficial to patients.

The QAngio and CAAS vFFR software assess functional significance of stenoses non-invasively without the need for a pressure wire or adenosine. Therefore, they avoid the risks associated with passing pressure wire to the coronary arteries, and potential side effects and discomfort associated with adenosine infusion. They use standard X-ray angiographic images taken

during ICA, so no additional procedure is needed. They are also claimed to be faster than the invasive measurement of FFR or iFR.

QAngio may help avoid unnecessary referrals for invasive FFR measurement and/or revascularisation, compared with the use of ICA alone. This would save people additional trips to the hospital, time off work and anxiety associated with repeated invasive procedures.

4 Comparator

The comparator is clinical decision making based on the visual interpretation of the angiographic images done during invasive coronary angiography (ICA), alongside clinical judgement. The ICA allows for anatomical assessment of coronary obstructions, but does not indicate whether anatomical obstructions are functionally significant (that is, whether they cause inadequate blood supply to the heart [myocardial ischaemia]). Clinical decision making refers to decisions about the need for invasive functional assessment of stenoses (fractional flow reserve [FFR] or instantaneous wave-free ratio [iFR]) and/or revascularisation.

The reference standard for measuring diagnostic accuracy is an invasive FFR or iFR measurement (see section 3.2.2 for details). The FFR is considered a gold standard for functional assessment of coronary obstructions, and iFR has been shown to be as good as FFR for guiding revascularisation decisions.

5 Scope of the assessment

Table 1 Scope of the assessment

Decision question	Does QAngio XA 3D/QFR and CAAS vFFR imaging software for non-invasively assessing the functional significance of coronary obstructions (stenoses) during invasive coronary angiography (ICA) represent a clinically and cost-effective use of NHS resources?
Populations	People with stable angina undergoing ICA whose angiograms show intermediate coronary obstructions (stenoses). An intermediate stenosis is defined as any lesion stenosis identified by ICA where there is clinical uncertainty about its functional significance and the potential appropriateness of revascularisation. Where data permits, the following subgroups may be considered: • People with multivessel coronary artery disease • People with diffuse coronary artery disease

	• People with microvascular dysfunction (for example, caused by diabetes) • People with chronically occluded vessels If possible, the analysis should also consider the impact of sex and ethnicity on outcomes.
Interventions	Clinical decision making based on QAngio XA 3D /QFR imaging software (used during ICA), alongside clinical judgement. Clinical decision making based on CAAS vFFR workflow (used during ICA), alongside clinical judgement
Comparator	Clinical decision making based on visual interpretation of the angiographic images taken during ICA, alongside clinical judgement. Reference standard is invasive FFR or iFR measurement.
Healthcare setting	Diagnostic-only catheter laboratories Interventional catheter laboratories
Outcomes	Intermediate measures for consideration may include: • Measures of diagnostic accuracy • Proportion of patients who need invasive functional assessment of stenoses (FFR or iFR) • Proportion of patients who need revascularisation (percutaneous and surgical) • Number of vessels with stent placements • Inter-observer variability • Proportion of angiograms that were poor quality and unsuitable for QFR/vFFR (QFR/vFFR analysis not attempted) • Failure rate (due to poor angiogram quality or other reasons) • Rate of inconclusive results • Time to results • Radiation exposure
	Clinical outcomes for consideration may include: • Rates of major adverse cardiac events (definition may vary from study to study but usually include cardiovascular death, myocardial infarction, stroke, and need for urgent revascularisation) • Adverse events (related to diagnostic intervention) • Adverse events (related to revascularisation) • Mortality

	Patient-reported outcomes for consideration may include: • Health-related quality of life (related to the diagnostic interventions and treatment outcomes for stable angina)
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Costs of diagnostic interventions (including software costs [per-patient or annual license cost], time to process results, software installation, maintenance and staff training costs) • Cost of referral to interventional catheter laboratory (applicable to diagnostic-only centres) • Costs of invasive functional assessment of stenoses (FFR or iFR) • Costs of revascularisation (percutaneous and surgical) • Costs of drug treatment (optimal medical therapy) • Costs of managing major adverse cardiac events • Costs of managing side effects related to invasive functional assessment of stenoses (FFR or iFR) • Costs of managing side effects related to revascularisation (percutaneous and surgical)
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

6 Other issues for consideration

6.1 Clinical considerations

Clinical outcomes studies comparing QFR-based treatment strategies with either FFR-based treatment strategies or ICA-based treatment strategies are currently ongoing (see section 6.3). At present, there may be no published clinical outcomes studies for QFR or vFFR so a linked-evidence approach to modelling is likely to be needed.

The pre-test probability of significant stenoses needing revascularisation may be different across populations because of the:

- Prior diagnostic pathway (before referral for ICA or percutaneous coronary intervention). Note: large regional variations exist in the UK in how stable

angina is being diagnosed. For example, not all centres in the UK have access to 64-slice (or above) CT scanner, and may use different types of non-invasive functional imaging.

- Definition of intermediate stenosis for which non-invasive functional assessment would be indicated (see sections 3.2.1 and 3.2.2 for details).

The impact that pre-test probability has on the cost-effectiveness could be investigated in the economic model.

6.2 Diagnostic accuracy in the real-world setting

High X-ray angiogram image quality is crucial for appropriate results being produced by QAngio and CAAS vFFR. However, the quality of angiograms is expected to vary in real world practice, depending on training, experience and case load of the healthcare professionals doing the ICA. This may affect both the failure rate and the diagnostic accuracy of QAngio and CAAS vFFR software, which do not have any internal image quality control process. Also, QAngio and CAAS vFFR software need user inputs which may be subjective. Therefore, the accuracy of the software in the real-world setting may be subject to variation, and may be lower than in the controlled trial setting.

6.3 Ongoing clinical outcome studies

FAVOR III Europe-Japan study is an investigator-initiated, 1:1 randomised, prospective, clinical outcome, non-inferiority, multi-centre trial that will be performed at up to 40 international sites, and will include about 2,000 patients. The purpose of the FAVOR III Europe-Japan study is to investigate if a QFR-based diagnostic strategy for people with stable angina and intermediate coronary stenosis will result in non-inferior clinical outcomes after 12 months compared with a standard pressure-wire FFR guided strategy. The study is currently recruiting, with estimated completion date in 2022.

FAVOR III China is a superiority study in 4,000 patients in China in which the outcomes of treatment based on QFR will be compared with the outcomes of treatment based on standard visual interpretation of the angiographic images.

7 Potential equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. The risk of significant coronary artery disease and its presentation are related to age, sex and ethnicity. Because of this, women and people from some ethnic groups who have coronary artery

disease are potentially underdiagnosed and undertreated in current practice. An objective measurement of the functional significance of stenoses such as using QAngio or CAAS vFFR could help address this and promote equality.

NICE is not aware of any variation in the accuracy of QAngio or CAAS vFFR according to age, sex, ethnicity or other protected characteristic. The clinical effectiveness of QAngio or CAAS vFFR may be different in people with microcirculatory dysfunction, for example related to diabetes, some of whom may be covered under the disability provision of the Equality Act (2010).

Angina can sometimes have a substantial and long-term adverse effect on a person's ability to carry out normal day-to-day activities. Therefore, some people with stable angina may be covered under the disability provision of the Equality Act (2010).

8 Potential implementation issues

Evidence of clinical utility

The clinical utility of QAngio and CAAS vFFR to guide revascularisation decisions and improve clinical outcomes compared with standard care is uncertain. Clinical experts indicated that this is the biggest barrier to adoption.

Training and certification

Staff that would use QAngio software (that is, cardiac physician, lab technician [radiographer], and/or cardiologist) would need training and certification. Currently, training takes 1.5 days and is delivered in the Netherlands, but could be delivered in the UK if there are enough participants. All participants need to successfully process 8-10 analyses to gain certification. The training could be shortened if analyses were to be completed and reviewed online at a later time. and the company is also developing e-learning modules for the entire course.

Diagnostic-only catheter laboratories currently do not do invasive FFR measurements so staff in these centres may need more training and support to correctly calculate and interpret the QFR.

Depending on the QAngio volume of analyses expected (purchased upfront), there may be an additional cost related to the staff training.

Training for CAAS vFFR is provided on-line via e-learning or webex, or can be delivered on-site. It takes 2 hours to complete.

Unclear commissioning and reimbursement in the NHS

Current HRG codes split cardiac catheterisation into two categories; EY43 standard (£1,726) and EY42 Complex (£2,153). Invasive FFR is included in the latter tariff but as QAngio does not 'complicate' the catheterisation, the trusts may not be reimbursed for it under the current HRG coding. However, they may need to see offsets in the number of patients per session and reduction in the cost of consumables.

Diagnostic-only catheter laboratories wishing to adopt QAngio or CAAS vFFR software may have to bear the additional cost related to the software and the analysis time, while the potential cost savings related to avoided referrals to interventional centres may be realised in a different commissioning catchment area. This may be a barrier for adoption in diagnostic-only centres.

9 Authors

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Appendix A Glossary of terms

Adenosine
A drug used to induce maximal blood flow (vasodilator drug)

Angiography
Angiography (also referred to as arteriography) is a medical imaging technique used to visualize the lumen (central space where blood flows) of blood vessels and organs of the body, with particular interest in the arteries, veins, and the heart chambers. See also computed tomography coronary angiography and invasive coronary angiography

Chronically occluded vessel
A complete or almost complete blockage of a coronary artery for 30 or more days

Computed tomography coronary angiography
A non-invasive test that uses X-rays to give detailed pictures of the heart and the blood vessels, including information about the degree of stenosis (obstruction) in the coronary arteries

Coronary artery bypass grafting
A surgical procedure used to treat coronary heart disease. It diverts blood around narrowed or clogged parts of the major arteries to improve blood flow and oxygen supply to the heart

Coronary artery disease
A disease (also referred to as coronary heart disease or ischemic heart disease) that involves a reduction of blood flow to the heart muscle, usually because of the build-up of plaque in the arteries of the heart. It is the most common of the cardiovascular diseases

Coronary artery dissection
A split or a tear in the wall of the artery, which compresses or compromises the lumen of the artery reducing blood flow

Coronary artery stenosis (obstruction, narrowing)
A narrowing of the coronary artery leading to a reduction in blood flow, often because of the build-up of the plaque (fatty deposits) in the wall of the arteries

Diffuse coronary artery disease
Usually defined as significant obstruction (stenosis) involving the whole length of the coronary artery, significant stenosis 2 cm or longer, or presence of 3 or more significant stenoses in the same artery (tandem stenoses)

Fractional flow reserve
A technique used in coronary catheterization to measure pressure differences across a coronary artery stenosis. It is used to determine the likelihood that the stenosis results in reduced blood (and oxygen) delivery to the heart muscle (myocardial ischemia)

Functional imaging
Functional imaging (or physiological imaging), is a medical imaging technique of detecting or measuring changes in physiological activities within a certain tissue or organ, for example, changes in blood flow

Invasive coronary angiography
An invasive diagnostic test which provides anatomical information about the degree of stenosis (obstruction or narrowing) in a coronary artery. It involves manipulation of cardiac catheters from an artery in the arm or top of the leg. A contrast medium is injected into the coronary arteries, and the flow of contrast in the artery is monitored by taking a rapid series of X-rays. It is considered the ’gold standard’ for providing anatomical information about coronary artery stenosis

Microvascular dysfunction
a type of coronary artery disease that affects the small vessels (arterioles and capillaries) of the heart. It is also known as coronary small vessel disease, microvascular angina, non-obstructive coronary disease.

Multi-vessel coronary artery disease
When significant coronary artery obstructions (stenoses) are present in more than one coronary artery.

Myocardial ischaemia
Happens when blood flow to the heart is reduced, preventing it from receiving enough oxygen. The reduced blood flow is usually the result of a partial or complete blockage of coronary arteries

Myocardial revascularisation
Restores a blood flow to the heart following a myocardial ischemia. It is usually done by percutaneous coronary intervention or coronary artery bypass grafting

Percentage diameter stenosis
Percentage of the lumen reduction caused by the stenosis. For example, 30% diameter stenosis is a stenosis that compromises 30% of the normal artery lumen

Percutaneous coronary intervention (coronary angioplasty)

A non-surgical procedure used to treat stenosis (obstruction, narrowing) of the coronary arteries of the heart. It uses balloon catheter and a stent (a short wire-mesh tube) to dilate the artery and keep it open. The stent can be coated with a drug intended to reduce the risk of future blockages (drug-eluting stent) and an uncoated stent (bare-metal stent)

Pressure wire
A special guide wire which has a small sensor at its tip to measure blood pressure in the artery before and after stenosis. Comparing the two measurements can show if, and to what extent, the stenosis is limiting the blood flow

Quantitative flow ratio
A novel index of the functional severity of coronary stenosis, which can be calculated from three-dimensional quantitative coronary angiography. It is a potential non-invasive alternative to fractional flow reserve

Stable angina
A type of chest pain that results from reduced blood flow. It is usually triggered by physical activity or emotional stress, and resolves with rest

Appendix B Abbreviations

CTCA	Computed tomography coronary angiography
FFR	Fractional flow reserve
FFR_{CT}	FFR calculated from computed tomography
ICA	Invasive coronary angiography
iFR	Instantaneous wave-free ratio
QFR	Quantitative flow reserve
RFR	Resting full-cycle ratio

Appendix C References

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