BMJ 2016;352:i205 doi: 10.1136/bmj.i205 (Published 5 February 2016)

PRACTICE

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What is the role of coronary angioplasty and stenting in stable angina?

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Introduction

Stable angina refers to chest discomfort that is classically retrosternal, triggered by exertion, and relieved by rest or nitrates within minutes. Unstable symptoms, such as those occurring at rest or persisting when activity stops, suggest an acute coronary syndrome and will not be discussed here.[1] More than one million people in the United Kingdom live with stable coronary artery disease (CAD), with an annual mortality rate of 1.5%.[2 3] It is associated with long term morbidity and has serious effects on quality of life.[4] Treatment options include medical therapy, coronary angioplasty with or without stenting (percutaneous coronary intervention; PCI), and coronary artery bypass surgery (CABG), for which guidelines from the UK's National Institute for Health and Care Excellence (NICE) and European Society of cardiology (ESC) exist.[5 6] However, patients' and doctors' expectations of potentials benefits of PCI in stable CAD are often overstated.[7] This article focuses on the limited evidence base and indications for PCI in stable angina.

Medical therapy

The two main goals are risk factor modification and symptomatic relief

Risk factor modification

- **Antiplatelet agents**—Aspirin is preferred treatment because it reduces mortality.[9] Clopidogrel may be used in those with coexistent peripheral vascular disease,[10] or in those who cannot tolerate aspirin. Dual therapy with aspirin and clopidogrel is recommended for up to one year after PCI in stable CAD.[11] No data are available yet to support newer antiplatelets, such as ticagrelor and prasugrel, in stable CAD
- **Lipid lowering agents**—Statins are used, based on NICE guidelines, because they reduce cardiovascular event rates in this group[12]
- **Angiotensin converting enzyme inhibitors**—Add these agents for patients with coexisting hypertension, left ventricular ejection fraction ≤40%, diabetes, previous MI, or chronic kidney disease as they reduce myocardial infarction (MI), stroke, heart failure, and mortality rates in these groups.[13 14]

Symptomatic treatment

This aims to relieve acute angina and reduce the frequency of attacks. Table 1⇓ summarises effects and contraindications of recommended drugs, none of which has been shown to reduce cardiovascular events, apart from β blockers, which reduce mortality after MI and in heart failure.[15]

- **First line therapy**—NICE recommends β blockers or calcium channel blockers,[5] with the choice of agent based on comorbidity and contraindications. For example, prescribe β blockers after MI or for heart failure.[15] Prescribe calcium channel antagonists in severe hypertension. Assess response to treatment soon after starting therapy.
- **Second line therapy**—If first line therapy is contraindicated or not well tolerated, consider long acting nitrates, nicorandil, ivabradine, or ranolazine instead.[5] Agents are chosen on the basis of heart rate, blood pressure, and tolerance (see figure⇓ and table 2⇓).

What is the evidence of benefit from PCI?

Multiple randomised controlled trials (RCTs) have found no reduction in mortality or MI from PCI compared with medical therapy alone in patients with stable CAD (table 2). However, some (but not all) trials, including a meta-analysis, showed improved angina relief with PCI.[8]

On the basis of current evidence the only current indication for PCI is for symptomatic relief.

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What you need to know

- First line treatment for stable CAD is optimum medical therapy to modify risk factors (for example, aspirin and statins) and relieve symptoms (for example, β blockers or calcium channel antagonists)
- There is no evidence that PCI reduces mortality or MI rates in stable angina
- PCI is indicated if symptoms persist despite treatment with two antianginals or if medical therapy is not tolerated, and perhaps earlier for patients with ischaemia in >10% of the left ventricle

Sources and selection criteria

We searched Medline and the Cochrane Library using terms from a previous systematic review of treatment of stable angina ("stable angina", "percutaneous coronary intervention", and "medical therapy"),[8] updated to March 2015. We also drew on our experience of coronary angioplasty and medical treatment of patients with stable coronary artery disease and our knowledge of NICE and ESC guidance.

The trials had serious limitations, including being underpowered to detect mortality difference, high crossover rates from medical therapy to PCI arms, outdated PCI techniques, and patients being representative of only 10% of those seen in "real life."[8 22] The trials were also unblinded and therefore susceptible to bias, particularly for subjective endpoints such as symptom severity; preconceptions on best treatment may have influenced results.[22] Thus, their findings are not easily translated to the patient in front of you, and the benefits of PCI might be underestimated by crossover or overestimated by preconceptions. A double blind RCT of PCI versus a placebo procedure with medical therapy in both groups will address some of these problems.[23]

Despite the evidence base showing no clear prognostic benefit from PCI, PCI rates in the UK continue to rise, with more than a third of procedures performed for stable CAD,

Might patient with greater myocardial ischaemia benefit more from revascularisation?

A high proportion of participants in previous trials had minimal myocardial ischaemia, perhaps explaining the similar outcomes for revascularisation and medical therapy. PCI may be more beneficial in a subset of stable CAD with evidence of high ischaemic burden (>10% ischaemic myocardium on functional imaging).[24] Older retrospective, observational studies have shown a statistically significant mortality benefit for PCI in patients with moderate myocardial ischaemia.[3 25] In a recent RCT, subgroup analysis suggested PCI in patients with moderate to severe ischaemia led to a greater reduction in MI and death compared with medical therapy at 18 months,[24] but not at five years.[26] However, a recent meta-analysis showed no improvement in MI or mortality after PCI even in patients with objective evidence of ischaemia.[20]

ESC guidelines recommend offering revascularisation to patients with evidence of ischaemia in >10% of the left ventricle and NICE recommends incorporating the results of functional testing into revascularisation decisions.[5 6] A large randomised study is in progress to evaluate PCI versus medical therapy in patients with stable CAD and ischaemia in >10% of the myocardium.[27]

Thus, a short trial of medical therapy may be the best first line treatment for this subgroup, with PCI offered early in patients who do not respond well to this approach.

What are the possible harms of PCI?

The box outlines possible complications, with the complication rate for elective PCI quoted as 1% on the day of the procedure. Although periprocedural MI can be seen in PCI, it has little impact on long term prognosis.[28] Implantation of modern drug eluting stents is associated with repeat revascularisation and stent thrombosis rates of less than 5% and 1% per annum, respectively.[29]

Who should be offered coronary angioplasty or stenting?

NICE, European, and US guidelines recommend considering PCI in stable CAD only after a trial of medical therapy, and after treatment with at least two antianginal drugs.[5 6 30] The guidelines also recommend using drug eluting stents in PCI (unless contraindicated) to obtain the best long term results.

Registry data suggest that medical therapy remains underused, with a third of patients undergoing PCI before a trial of antianginal drugs.[31] The side effect profile and interactions of many of these drugs sometimes make medical therapy difficult. However, PCI should be offered only to stable patients in whom a trial of medical therapy has not relieved symptoms or been tolerated well.

In daily practice, perhaps the only exception to this could be patients with clinically significant narrowing of the left main stem artery, subtending >50% of all heart muscle, where CABG is often offered for prognostic reasons on the basis of an old meta-analysis,[32] and PCI has been shown to be a reasonable alternative in another.[33]

Contributors: All three authors contributed to the design, writing, and revision of the paper and approved the final version.

Competing interests: We have read and understood the BMJ policy on declaration of interests and declare the following interests: JD declares consultancy fees from Volcano Corporation and holds patents pertaining to iFR technology licensed by Volcano Corporation. RAL and ISM declare no competing interests.

Provenance and peer review: Commissioned; externally peer reviewed.

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Possible complications of PCI

Acute/peri procedural

- Bleeding
- Procedural myocardial infarction
- Coronary dissection or rupture
- Acute and subacute stent thrombosis
- Transient ischaemic attack or stroke
- Death

Medium and long term

- Target vessel or target lesion revascularisation
- Spontaneous myocardial infarction
- Late and very late stent thrombosis
- Death

Discussing the evidence for stenting with patients

Stable coronary heart disease is the commonest form of heart disease. Patients with this problem may have chest pain, or breathlessness on exertion, but not at rest. There is a small rate of heart attacks and death. It is important to take drugs like aspirin and ones that lower cholesterol levels because these have been shown to reduce rates of both heart attack and death.

Balloon angioplasty and stenting are used to open up narrowed coronary arteries. Acute problems, with pain at rest, need emergency action, and this technique is well validated for treating heart attack. However, we currently have no evidence that it reduces heart attacks or death in people with stable coronary heart disease. Coronary stenting may relieve symptoms of angina; how much each person might benefit varies and can't be predicted. It also has short and long term risks, such as setting off heart attacks, stroke, bleeding, and even death. Thus it should be considered only after medical therapy has been tried and does not control symptoms or is not well tolerated, and when its benefits are thought to outweigh its risks. In these cases we select the time for stenting on the basis of symptoms and extent of coronary disease, to achieve the best possible results for each person.

How patients were involved in the creation of this article

We asked patients with stable CAD in our clinical service to review the section on discussing the evidence with patients. They provided input on whether this was understandable and gave enough information. Patients were also asked for their input on the section on discussing the evidence with patients. They gave us their views on the evidence that they wanted to know and the depth to which doctors should discuss this with them.

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Accepted: 13 October 2015

Cite this as: *BMJ* 2016;352:i205

Tables

Table 1| Drugs recommended by NICE for symptomatic treatment of stable CAD[5]: key effects, contraindications, and side effects*

Drug (action)	Clinical effect	Contraindications	Common side effects
First line therapy			
β blockers (β_1 adrenergic antagonists)	Reduce heart rate, blood pressure, and contractility; prolong diastolic filling time	Asthma, severe chronic obstructive airways disease, severe peripheral vascular disease	Hypotension, bradycardia, syncope, depression, sexual dysfunction
Ca^{2+} channel antagonist (L-type Ca^{2+} channel antagonist)	Reduce heart rate, blood pressure, and contractility; prolong diastolic filling time; systemic and coronary vasodilatation	Heart block, concurrent use of β blockers, high grade aortic stenosis, hypotension	Hypotension, flushing, peripheral oedema, dizziness, fatigue, bradycardia for rate limiting agents
Second line therapy (if first line therapy is contraindicated or not tolerated)			
Nitrate (nitric oxide donor)	Systemic and coronary vasodilatation	Concurrent use of phosphodiesterase 5 inhibitors such as slidenafil	Hypotension, headache, syncope, drug tolerance
Nicorandil (K-ATP dependent channel opener, nitric oxide donor)	Systemic and coronary vasodilatation	Concurrent use of phosphodiesterase 5 inhibitors such as sildenafil	Hypotension, headache, dizziness
Ivabradine (I_f channel antagonist)	Reduce heart rate	Moderate to severe angina (increases incidence of cardiovascular events in these patients)[16]	Bradycardia, visual disturbance
Ranolazine (late inward Ca^{2+} channel antagonist)	Improved myocardial metabolic activity; reduce diastolic wall tension	Concurrent use of class I or III antiarrhythmics, CPYP34A inhibitors (eg, ketoconazole, clarythromycin). Use with caution in severe renal disease (creatinine clearance <30 mL/min) or moderate or severe hepatic disease[17]	Dizziness, constipation, nausea

*Apart from β blockers, which reduce mortality after myocardial infarction and in heart failure, these drugs have not been shown to reduce cardiovascular events.13

Table 2| Trials comparing percutaneous coronary intervention versus medical therapy in the treatment in stable coronary artery disease

Study	Study design (N)	Intervention*	Follow-up duration	PCI *v* MT: death	PCI *v* MT: non-fatal MI	PCI *v* MT: unplanned revascularisation	PCI *v* MT: angina free at follow-up
COURAGE[18]	RCT (2287)	Revascularisation (CABG or PCI)	5 years	7.6% *v* 8.3%; P=0.38 (NS)	13.2% *v* 12.3%; p=0.33 (NS)	Favours revascularisation (21.1% *v* 32.6%, P<0.001)	59% *v* 56%; P=0.30 (NS)
MASS II[4]	RCT (611)	Revascularisation (CABG or PCI)	10 years	24.9% *v* 31%; P=0.089 (NS)	Favours PCI (13.3% *v* 20.7%; P=0.010)	41.9% *v* 39.4%; P=0.51 (NS)	Favours PCI (59% *v* 43%; P<0.001)
BARI 2D[19]	RCT (2368; all had type 2 diabetes)	Revascularisation (CABG or PCI)	5 years	11.7% *v* 12.2%; P=0.97 (NS)	Reported only as part of composite endpoint	Favours revascularisation (18% *v* 33%; P=0.001)	Favours revascularisation (66% v 58%, p=0.003)
Stergiopoulous et al[20]	Meta-analysis (5286)	PCI	Median 5 years	6.5% *v* 7.3%; P=0.42 (NS)	9.2% *v* 7.6%; P=0.06 (NS)	18.3% *v* 28.4%; P=0.14 (NS)	79.7% *v* 76.7%; P=0.67 (NS)
Windecker et al[21]	Meta-analysis (93 553)	Revascularisation (CABG or PCI)	262 090 patient years in total	No difference (except for mortality reduction in PCI with new generation DES)†	No significant difference†	Favours PCI with DES implantation†	Not assessed

*The control in all studies was medical therapy alone.

†Data given only for sub-study analyses so not directly comparable with the other studies in this table.

CABG=coronary artery bypass graft surgery; DES=drug eluting stents; NS=not significant; MT=medical therapy; PCI=percutaneous coronary intervention; RCT=randomised controlled trial.

Figure