NICE National Institute for Health and Care Excellence

Surveillance report 2017 – Peripheral arterial disease: diagnosis and management (2012) NICE guideline CG147

Surveillance report

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Contents

Surveillance decision

We will plan an update of the following sections of the guideline:

- Diagnosis – assessment

Reason for the decision

Assessing the evidence

We found 54 new studies through surveillance of this guideline. Evidence that could affect recommendations was identified. Topic experts, including those who helped to develop the guideline, advised us about whether the following sections of the guideline should be updated.

Diagnosis of peripheral arterial disease

- In people with suspected peripheral arterial disease (PAD), is ankle brachial pressure index (ABPI) as an adjunct to clinical assessment better than clinical assessment alone or ABPI alone, in determining the diagnosis and severity of PAD?

New evidence on diagnosis of PAD among people with diabetes suggests that other forms of assessment may be superior to ABPI for diagnosing PAD in patients with diabetes. Currently, the recommendation suggests the ABPI measurement as an assessment tool in people with suspected PAD. Topic experts agreed that the new evidence should be reviewed looking specifically at people with diabetes as the value of ABPI might differ in those with diabetes.

Decision: This review question should be updated, specifically for people with diabetes.

Other clinical areas

We found new evidence that supports current recommendations on:

- endovascular or surgical techniques compared to or in combination with exercise or best medical treatment for the treatment of people with intermittent claudication
- angioplasty compared to bypass surgery or amputation for the treatment of critical limb ischaemia in adults with PAD.

We also found new evidence that was not thought to have an effect on current recommendations on:

- imaging for revascularisation in peripheral arterial disease
- clinical and cost effectiveness of bare metal stents compared to drug-eluting stents for the treatment of PAD in adults with intermittent claudication
- clinical and cost effectiveness of bare metal stents compared to drug-eluting stents for the treatment of PAD in adults with critical limb ischaemia.

We did not find any new evidence related to:

- information requirements for people with peripheral arterial disease
- management of ischaemic pain in critical limb ischaemia
- major amputation for critical limb ischaemia.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all the new evidence and views of topic experts, we decided that a partial update is necessary for this guideline.

See how we made the decision for further information.

Commentary on selected new evidence

With advice from topic experts we selected 2 studies for further commentary.

Management of intermittent claudication

We selected the network meta-analysis by Katsanos et al. (2014) for a full commentary because it highlights potential benefits of drug-eluting stents and balloons in the femoropopliteal artery.

What the guideline recommends

Recommendation 1.5.6 of CG147 states:

"Use bare metal stents when stenting is used for treating people with intermittent claudication."

Drug eluting angioplasty was not considered in CG147.

Methods

A network meta-analysis of randomised controlled trials (RCTs) performed comparing bare nitinol stents (BNS), covered nitinol stents (CNS), paclitaxel- or sirolimus-eluting stents (PES or SES), and paclitaxel-coated balloons (PCB) with plain balloon angioplasty (BA) or with each other in the femoropopliteal artery. Sixteen RCTs comprising 2,532 patients with 4,227 person years (py) of follow up included.

Trials with low risk of bias from 1950 to present with no restrictions on publication language were included. Study population in all 16 trials had similar baseline demographics among the treatment and control arms. However, there was significant variation between trials in both the rate of initial chronic total occlusions and the lesion length and length of antiplatelet therapy (1 to 6 months). To account for this variation meta-regression analyses were incorporated in the Bayesian modelling.

The majority of included patients were treated for intermittent claudication, and only a small percentage of patients had critical limb ischaemia.

Outcomes measures included technical success, vascular restenosis, target lesion revascularisation (TLR), and major amputations. Technical success was defined as successful recanalisation of the target vessel with no significant residual stenosis on completion angiogram (30% to 50% threshold). Vascular restenosis was evaluated on the 50% threshold by quantitative vascular angiography or colour doppler ultrasonography. TLR included any repeat procedures. Major amputations defined as any limb loss that extended above the ankle.

Results

The mean duration of follow up was 22 months (range 9 to 48 months). Data on immediate procedural technical success were reported in 14 RCTs. Compared with BA (success rate 73.9%) both covered (success rate 98%) and uncovered stents (success rate 95%) achieved higher median technical success rate. Covered stents had the highest probability (82.1%) of being best and uncovered stents with an 18% probability of being best, ranked second. There were significantly higher odds of success in both uncovered (odds ratio [OR] 7.0; 95% credible interval [CrI] 2.6 to 129) and covered stents (OR 13.6; 95% CrI 3.3 to 31.1) when compared with BA. There was no significant difference in technical success when comparing uncovered with covered stents.

Vascular restenosis was reported by all 16 RCTs. There were 45 median restenosis events per 100 py in the BA group. PES and PCB both showed 19 events per 100 py and CNS showed 27events per 100 py. Compared with BA, PCB (risk ratio [RR] 0.43; 95% CrI 0.26 to 0.67) and CNS (RR 0.60; 95% CrI 0.36 to 0.94) had significantly fewer events. However there were marginally non-significant difference in the rate of events in BNS (RR 0.78; 95% CrI 0.57 to 1.06) and PES (RR 0.43; 95% CrI 0.16 to 1.18) when compared to BA. PES had the highest probability (45%) of being the best treatment (lowest rate of events), followed by PCB, with a 42% probability.

TLR events were reported by 15 RCTs. The median TLR rates of for BA were 22 events per 100 py. PCB was associated with the highest probability (56%) of being the best treatment (lowest rate of events), followed by PES, with a 33% probability. Compared with BA, there were marginally non-significant difference in the risk of TLR in BNS (RR 0.77; 95% CrI 0.57 to 1.07), CNS (RR 0.74; 95% CrI 0.45 to 1.18), and PES (RR 0.42; 95% CrI 0.16 to 1.06). Compared to BA, PCB was the only treatment that showed consistent lower risk of TLR (RR 0.36; 95% CrI 0.23 to 0.55), BNS (RR 0.47; 95% CrI 0.27 to 0.80), and CNS (RR 0.49; 95% CrI 0.25 to 0.94). No significant difference was observed between PCB and different drug-eluting stents in the risk of TLR. Major amputations were rare in all treatment and

control groups.

The study concluded that immediate technical success is better with the use of covered stents, whereas PES and PCB offer the best long-term results in the femoropopliteal artery.

Strengths and limitations

Strengths

The network meta-analysis included a number of strengths:

- The study is the first comprehensive network meta-analysis of different endovascular options for occlusive disease in the femoropopliteal artery.
- Robust network meta-analysis, which allows combined direct and indirect comparisons of competing treatments while maintaining the benefits of randomisation.
- Studies with low risk of biases were included.

Limitations

The following limitations were identified:

- Small network meta-analysis with only 16 studies included. This can produce discrepancy in the treatment effect estimated from direct and indirect evidence.
- There was significant variation between included trials in the rate of initial chronic total occlusions, lesion length and length of antiplatelet therapy.
- Most participants in the included studies treated for intermittent claudication and a small percentage had critical limb ischaemia.
- The study did not report quality of life and mortality, which during the development of the original guideline were agreed by the committee to be important outcomes.

Impact on guideline

The study provides evidence of benefits for drug-eluting technology included drug-eluting

balloons in patients with PAD which was not reviewed in CG147.

Topic experts highlighted the ongoing National Institute for Health Research (NIHR) Health Technology Assessment (HTA)-funded BASIL-3 study, which is an RCT of clinical and cost effectiveness of drug-coated balloons, drug-eluting stents and balloon angioplasty with bail-out bare metal stent revascularisation strategies. Based on the feedback from topic experts, this review should be considered for a future update after completion of the BASIL-3 trial. The study is in the recruiting stage and updating the question now could potentially impact on the recruitment process. The surveillance team will track the findings of the BASIL-3 trial.

Management of intermittent claudication

We selected Dake et al. (2016) for a full commentary because it is a large multicentre RCT on use of bare metal stents in patients with PAD.

What the guideline recommends

Recommendation 1.5.6 of CG147 states:

"Use bare metal stents when stenting is used for treating people with intermittent claudication."

Recommendation 1.6.5 of CG147 states:

"Use bare metal stents when stenting is used for treating people with critical limb ischaemia."

Methods

A multicentre RCT including 55 cities in the US, Germany and Japan evaluated clinical durability of Zilver PTX, a paclitaxel-coated drug-eluting stent (DES) for femoropopliteal artery lesions. This study is 5-year follow up of the RCT. The original RCT with the 12-month result is included in CG147. The original study included patients with Rutherford category ≥2, ≥50% diameter stenosis, reference vessel diameter 4 to 9 mm, lesion length up to 14 cm, and at least 1 patent runoff vessel with <50% stenosis. Exclusion criteria were patients with untreated >50% stenosis of the inflow tract and previous target vessel

stenting. The detailed description of the study design and methods, endpoint at 1-year and 2-year follow up were previously reported and published separately.

Patients were randomised to DES (n=236) or percutaneous transluminal angioplasty (PTA; n=238). The patients with acute PTA failure (n=120) were then randomised to provisional DES (n=61) or provisional bare metal stent (BMS) placement (n=59). At 5-year follow up the primary DES group was compared to the PTA group and the provisional DES group to the provisional BMS group. In addition, the overall DES group (comprised of both primary and provisional DES) was compared to the standard care group (including patients with provisional BMS placement plus patients with optimal PTA). This overall comparison was non-randomised.

For patients randomised to DES, stents placed at least 1 cm below the SFA origin and above the medial femoral epicondyle to fully cover the target lesion(s). For patients in the PTA group, PTA was performed according to the institutional standard practice. Patients experiencing acute PTA failure underwent secondary randomisation to provisional BMS or provisional DES placement. Acute PTA failure was defined as ≥30% residual stenosis or a ≥5 mm Hg mean trans-stenotic pressure gradient.

Patients underwent in-clinic assessment at 6 months, 1 year, and annually thereafter through 5 years. The assessment included Rutherford classification, ankle brachial index (ABI), and Walking Impairment Questionnaire (WIQ).

Duplex ultrasound evaluation of patency was performed for all patients at 6 months, and at 1-year and 2-year follow up. To assess stent integrity, high-resolution stent radiographs were obtained at 1, 3, and 5 years.

Results

The 1-year primary endpoints of event-free survival (EFS) and primary patency showed superiority of primary DES compared to PTA; these results were constant through 5 years.

The EFS rate was greater through 5 years in the primary DES group compared to the PTA group (Kaplan–Meier estimates 81.4% versus 70.1% $p<0.01$ respectively).

The primary patency rate was also significantly greater in the DES group through 5 years compared to the PTA group (Kaplan–Meier estimates 64.9% versus 19.0% $p<0.01$ respectively).

All-cause mortality rate at 5 years was 13.6% (10.2% in the primary DES group and 16.6% in the PTA group, p=0.03). There were no differences observed between the 2 groups in the rate of freedom from thrombosis/occlusion through 5 years (p=0.68).

Five-year freedom from TLR and primary patency rate were significantly higher at the overall DES group compared to the standard care group (p<0.01).

Significantly higher number of patients in the overall DES group maintained clinical benefit compared with patients in the standard care group (Kaplan–Meier estimates 79.8 % versus 59.3% p<0.01). Clinical benefit was defined as freedom from persistent or worsening claudication, rest pain, ulcer or tissue loss after the initial study treatment.

Significantly more patients in the provisional DES group (81.8%) maintained clinical benefit compared to the provisional BMS group (63.8%; p=0.02). Clinical benefit was defined as freedom from persistent or worsening claudication, rest pain, ulcer or tissue loss after the initial study treatment.

These results for restenosis and TLR represent >40% RR reduction through 5 years for the overall DES group compared to the standard care group and provisional the DES group compared to the provisional BMS group.

Strengths and limitations

Strengths

The study is one of the largest randomised controlled trials of an endovascular device to treat patients with femoropopliteal artery disease, and the first to provide 5-year follow up. Loss to follow up and missing data are adequately reported. All of the pre-specified outcomes were reported.

Limitations

The following limitations were identified:

- The comparison of the overall DES group to the standard care group was non-randomised therefore subject to selection bias.
- There was no primary BMS group for direct comparison to the primary DES group.

- The rate of loss to follow up was high in the primary DES group (20%) and over 50% of patients in the PTA group had acute PTA failure which undermines the reliably of findings.
- The ratio of <2.0 for evaluating patency by duplex ultrasonography was used in this study; a higher ratio might have had an effect on the result and patients with moderate lesion length were only included.
- The study was sponsored by a medical device company (Cook Medical) and all 11 study investigators had conflicts of interest to declare.

Impact on guideline

The 5-year follow up results from this large study provided evidence for safety and clinical durability for drug-eluting stents compared to standard endovascular treatments. The original study with 12-month results is included in the CG147.

Topic experts highlighted the ongoing NIHR HTA-funded BASIL-3 study, which is an RCT of clinical and cost effectiveness of drug-coated balloons, drug-eluting stents and balloon angioplasty with bail-out bare metal stent revascularisation strategies. Based on the feedback from topic experts, this review should be considered for a future update after completion of BASIL-3 trial. The study is in the recruiting stage and updating the question now could potentially impact on the recruitment process. The surveillance team will track the findings of the BASIL-3 trial.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 4 years after the publication of peripheral arterial disease: diagnosis and management (2012) NICE guideline CG147.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual'.

Previous surveillance update decisions for the guideline are on our website.

New evidence

We found 47 new studies in a search for randomised controlled trials and systematic reviews published between 24 June 2014 and 31 March 2016. We also considered 1 additional study identified by members of the guideline committee who originally worked on this guideline.

Evidence identified in previous surveillance 2 years after publication of the guideline was also considered. This included 6 studies identified by search on the 2-year surveillance decision.

From all sources, 54 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: summary of new evidence from surveillance and references for all new evidence considered.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because this was a 4-year surveillance review, and the decision was to update, we did not consult on the decision.

See ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual' for more details on our consultation processes.

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