Angioplasty versus stenting for iliac artery lesions

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ABSTRACT

Backgound

Atherosclerosis of the iliac artery may result in a stenosis or occlusion, which is defined as iliac artery occlusive disease. A range of surgical and endovascular treatment options are available. Open surgical procedures have excellent patency rates but at the cost of substantial morbidity and mortality. Endovascular treatment has good safety and short-term efficacy with decreased morbidity, complications and costs compared with open surgical procedures. Both percutaneous transluminal angioplasty (PTA) and stenting are commonly used endovascular treatment options for iliac artery occlusive disease. A stenotic or occlusive lesion of the iliac artery can be treated successfully by PTA alone. If PTA alone is technically unsuccessful, additional stent placement is indicated. Alternatively, a stent could be placed primarily to treat an iliac artery stenosis or occlusion (primary stenting, PS). However, there is limited evidence to prove which endovascular treatment strategy is superior for stenotic and occlusive lesions of the iliac arteries.

Objectives

To assess the effects of percutaneous transluminal angioplasty versus primary stenting for stenotic and occlusive lesions of the iliac artery.

Search methods

The Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator searched the Specialised Register (last searched April 2015) and Cochrane Register of Studies (CRS) (2015, Issue 3). The TSC searched trial databases for details of ongoing and unpublished studies.

Selection criteria

We included all randomised controlled trials (RCTs) comparing percutaneous transluminal angioplasty and primary stenting for iliac artery occlusive disease. We excluded quasi-randomised trials, case reports, case-control or cohort studies. We excluded no studies based on the language of publication.

Data collection and analysis

Two authors (JB, NA) independently selected suitable trials. JB and HJ independently performed data extraction and trial quality assessment. When there was disagreement, consensus would be reached first by discussion among both authors and, if still no consensus could be reached, through consultation with BF.

Main results

We identified two RCTs with a combined total of 397 participants as meeting the selection criteria. One study included mostly stenotic lesions (95%), whereas the second study included only iliac artery occlusions. Both studies were of moderate methodological quality with some risk of bias relating to selective reporting and non-blinding of participants and personnel. The overall quality of evidence was low due to the small number of included studies, the differences in study populations and definitions of the outcome variables. Due to the heterogeneity among these two studies it was not possible to pool the data. Percutaneous transluminal angioplasty (PTA) with selective stenting and primary stenting (PS) resulted in similar improvement in the stage of peripheral arterial occlusive disease according to Rutherford's criteria, resolution of symptoms and signs, improvement of quality of life, technical success of the procedure and patency of the treated vessel. Improvement in walking distance as reported by the patient, measured claudication distance, ulcer healing, major amputation-free survival and delayed complications (> 72 hours) were not reported in either of the studies. In one trial, PTA of iliac artery occlusions resulted in a significantly higher rate of major complications, especially distal embolisation. The other trial showed a significantly higher mean ankle brachial index (ABI) at two years in the PTA group (1.0) compared to the mean ABI in the PS group (0.91); mean difference (MD) 0.09 (95% confidence interval (CI) 0.04 to 0.14; P value = 0.001, analysis performed by review authors). However, at other time points there was no difference. We consider it unlikely that this difference is attributable to the study procedure, and also believe this difference may not be clinically relevant.

Authors' conclusions

There is insufficient evidence to assess the effects of PTA versus PS for stenotic and occlusive lesions of the iliac artery. From one study it appears that PS in iliac artery occlusions may result in lower distal embolisation rates. More studies are required to come to a firm conclusion.

PLAIN LANGUAGE SUMMARY

Background

Atherosclerosis in the iliac artery (main pelvic artery towards the leg) may result in narrowing or obstruction (occlusion), leading to reduced blood flow to the leg. This is called iliac artery occlusive disease. Iliac artery occlusive disease may lead to symptoms of pain in the legs at walking (intermittent claudication), pain at rest, or even ulcers of the foot or leg. A range of surgical and endovascular (from inside the artery, e.g. angioplasty) treatment options are available. Open surgical procedures have excellent patency rates (percentage of

the vessels that remain open) but at the cost of substantial illness and death. Endovascular treatment has good safety and short-term effectiveness with decreased illness, complications and costs compared with open surgical procedures. Percutaneous transluminal angioplasty (PTA; dilation of the artery with a balloon) and stenting (insertion of a small mesh tube) are widely used endovascular treatment options for iliac artery occlusive disease. A narrowing or obstruction of the iliac artery can be treated successfully by PTA alone. If PTA alone is not successful, an additional stent can be placed. Alternatively, a stent could be placed on its own to treat an iliac narrowing or obstruction (this is called primary stenting). However, there is limited evidence to prove which endovascular treatment strategy is better for stenotic and occlusive lesions of the iliac arteries. This review investigates whether it is better to place a stent primarily, or only on specific indications.

Key results

We identified only two studies with a combined total of 397 participants relevant to this topic. Combining of data was not possible due to the differences between the two included studies. We could not demonstrate that either of the two strategies was superior to the other. Five of the pre-planned outcomes were not reported in either study (improvement in walking distance as reported by the patient, measured claudication distance, ulcer healing, major amputation-free survival (survival without above-ankle amputation), delayed complications (more than 72 hours)). In most other pre-planned outcomes no differences were shown between the treatments (improvement in the stage of the classification of the severity of the arterial occlusive disease, resolution of symptoms and signs, improvement of quality of life, technical success of the procedure, patency of the treated vessel). However, in one study, which only included iliac artery occlusions, fewer complications were observed in the group of participants that were treated with primary stenting. The other study showed a slightly higher ankle brachial index (blood pressure in the leg compared to blood pressure in the arm, higher is better) at two years after the procedure, but not at other time points. This difference might not be clinically relevant. More research is necessary on this subject.

Quality of the evidence

Both studies had some risk of bias relating to selective reporting and non-blinding of participants and personnel. We consider the overall quality of the evidence to be low due to the small number of included studies, the differences in the types of patients that were included and the way outcomes were reported.

BACKGROUND

Peripheral arterial occlusive disease (PAOD) involving the lower limbs is a manifestation of systemic atherosclerosis and can occur in up to 3% to 10% of the general population. The prevalence is higher with older age, affecting up to 15% to 20% of people aged over 70 years (Selvin 2004). In up to 30% of patients with PAOD, the iliac artery is involved. PAOD may lead to intermittent claudication (IC) or in cases of more advanced disease critical limb ischaemia (CLI). In the past, open bypass surgery was the therapy of choice. In recent years endovascular treatment has gained popularity and has been shown to be safe and effective even in advanced lesions (Gandini 2007; Jongkind 2010).

Description of the condition

Atherosclerosis commonly affects the distal aorta and the iliac arteries. Although most patients are asymptomatic, an arterial stenosis or occlusion may result in symptoms, depending on the extent of involvement and the availability of collaterals (Weitz 1996). Restriction of blood flow initially leads to IC. Further reduction in blood may result in ischaemic rest pain, ulceration, tissue loss and gangrene (Rutherford 1997). Treatment of this impaired vascularisation is important since peripheral arterial disease significantly impairs quality of life and can result in amputation of the affected limb (Norgren 2007).

Description of the intervention

A range of surgical and endovascular options are available for the treatment of stenotic and occlusive lesions in the iliac arteries. Open surgical procedures have excellent patency rates (IC: 85% to 92%, CLI: 78% to 83%), at the cost of substantial morbidity and mortality (de Vries 1997). Endovascular treatment has good safety and short-term efficacy with decreased mortality, morbidity and hospital stay compared with open surgical procedures (Jongkind 2010). Endovascular interventions can be repeated if the lesion recurs during follow-up (Mousa 2007).

How the intervention might work

Both percutaneous transluminal angioplasty (PTA) and stenting are widely used endovascular treatment options for iliac artery occlusive disease. A stenotic or occlusive lesion of the iliac artery can be treated successfully by PTA alone. If PTA alone is not successful, additional stent placement is indicated. Lack of success may be defined as either a suboptimal angiographic result without improvement of blood pressure gradient, or no clinical improvement. Alternatively, a stent could be placed primarily to treat an iliac artery stenosis or occlusion. The rationale for stent placement would be to prevent elastic recoil of the stenosis after angioplasty and thus reduce restenosis rates. On the other hand, the stent may cause the local vasculature to react with an inflammatory response that precipitates neointimal proliferation and tissue ingrowth and thus leads to in-stent restenosis (Hoffmann 1996).

Why it is important to do this review

Endovascular treatment of iliac artery occlusive disease is considered safe and effective (Jongkind 2010), and is currently the most commonly used treatment for this indication. Both selective stent placement as a bail-out treatment for unsatisfactory results of PTA and primary stenting (PS) of iliac artery occlusive disease are advocated (Bosch 1997). However, there is limited evidence to prove which endovascular treatment strategy is superior for stenotic and occlusive lesions of the iliac arteries.

One meta-analysis, based on non-randomised trials, showed higher technical success and patency rates after PS (Bosch 1997). However, a large randomised controlled trial, the Dutch Iliac Stent Trial, initiated by the same study group has shown better symptomatic success with PTA and selective stent placement compared with PS placement, although both groups showed similar rates of iliac artery patency, ankle brachial index (ABI) and quality of life (Klein 2006). A large observational series has reported that more than 70% of iliac artery lesions could be treated successfully with PTA alone (Kudo 2005), thus without costly stenting. Although guidelines on treatment of iliac artery occlusive disease are available they do not recommend a specific treatment (Tsetis 2008). As a result, the approach to treatment of iliac artery lesions varies widely between centres.

OBJECTIVES

To assess the effects of percutaneous transluminal angioplasty versus primary stenting for stenotic and occlusive lesions of the iliac artery.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs) comparing percutaneous transluminal angioplasty (PTA) and primary stenting (PS) for iliac artery stenoses and occlusions. We considered trials in which balloons or drug-eluting balloons were compared with stents or drug-eluting stents or covered stents for iliac artery stenoses and occlusions for inclusion. We also considered multi-armed RCTs if they compared between these two interventions. We did not include quasi-randomised trials, case reports, case-control or cohort studies. We excluded no studies based on the language of publication. Trials assessing angioplasty verses primary stenting for superficial femoral artery lesions and infrapopliteal arterial lesions are reviewed in separate Cochrane reviews (Chowdhury 2014; Hsu 2011).

Types of participants

We included patients with symptomatic iliac artery occlusive disease. There were no restrictions based on either gender or age.

Types of interventions

Percutaneous transluminal angioplasty, with or without selective stent placementPrimary stenting

Types of outcome measures

Primary outcomes

Clinical assessment of improvement:symptomatic improvementimprovement in the stage of PAOD: according to Rutherford's criteria (Rutherford 1997)improvement in walking distance as reported by the patientresolution of symptoms and signsimprovement of quality of lifeobjective assessment of improvementmeasured claudication distanceankle brachial index (ABI)ulcer healingmajor amputation-free survival (survival without above-ankle amputation)Technical success of the procedure (ability to restore more than 50% of the lumen)Patency of the treated vessel as assessed by duplex sonography, computed tomography angiography (CTA), magnetic resonance angiography (MRA) or digital subtraction angiography (DSA)

Secondary outcomes

Incidence of complications:Immediate (< 72 hours): e.g. dissection, thrombosis, infection, distal embolization. Delayed (> 72 hours): e.g. worsening of disease, pseudoaneurysm formationReintervention of the treated lesion

Search methods for identification of studies

Electronic searches

The Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator (TSC) searched the Specialised Register (last searched April 2015) and the Cochrane Register of Studies (CRS) (http://www.metaxis.com/CRSWeb/Index.asp) (2015, Issue 3). See Appendix 1 for details of the search strategy used to search the CRS. The Specialised Register is maintained by the TSC and is constructed from weekly electronic searches of MEDLINE, EMBASE, CINAHL and AMED, and through handsearching relevant journals. The full list of the databases, journals and conference proceedings that have been searched, as well as the search strategies used, are described in the Specialised Register section of the Cochrane Peripheral Vascular Diseases Group module in The Cochrane Library (www.cochranelibrary.com).

The following trial databases were searched by the TSC using the terms iliac and angioplasty (April 2015) for details of ongoing and unpublished studies.

World Health Organization International Clinical Trials Registry (http://apps.who.int/trialsearch/)ClinicalTrials.gov (http://clinicaltrials.gov/)ISRCTN register (http://www.controlled-trials.com/isrctn/)Nederlands Trials Register (http://www.trialregister.nl/trialreg/admin/rctsearch.asp)

Searching other resources

We searched references and bibliographies of relevant papers for additional references.

Data collection and analysis

Selection of studies

Two review authors (JB and NA) independently carried out selection of studies for inclusion. Disagreements were resolved by BF.

Data extraction and management

Two review authors (JB and HJ) extracted, assessed and coded data independently using the data collection form provided by the Cochrane PVD Group, adapted specifically for the review. Disagreements were resolved by BF.

JB entered data into RevMan 5.3 (RevMan 2014). Review author HJ cross-checked the data.

Statistical analysis followed the standard methods of the Cochrane PVD Group. We performed all analyses using RevMan 5.3.

Assessment of risk of bias in included studies

Two review authors (JB and HJ) independently used The Cochrane Collaboration's 'Risk of bias' tool for assessing risk of bias for the included studies (Higgins 2011). This tool provides a protocol for judgements on the bias domains sequence generation, allocation methods, blinding, incomplete outcome data, selective outcome reporting and any other relevant biases. We judged the domains to be at high, low or unclear risk of bias. We resolved any disagreements by discussion with BF. If necessary, we contacted the authors of the trials via email or fax for clarification.

Measures of treatment effect

For dichotomous outcomes we intended to calculate the relative risk (risk ratio (RR) or risk difference (RD)), to measure any treatment effect. However, as data were sparse we used odds ratio (OR) only. For continuous outcomes we intended to use the mean difference (MD) or standardised mean difference (SMD) if data were available.

Unit of analysis issues

We considered each individual participant a unit of analysis. In the DIST trial, reintervention rate at five years is reported per segment instead of per individual participant, and therefore data are reported as such.

Dealing with missing data

We contacted the authors of the respective trials directly by email or fax, to ask for missing data. If studies had a drop-out rate of more than 20%, we considered them of low quality and excluded them from the meta-analysis. In addition, we performed a sensitivity analysis.

Assessment of heterogeneity

We constructed a forest plot to display the results and to examine possible heterogeneity between the studies. In addition to the Chi2 test, we used the I2 statistic to measure the level of heterogeneity.

Assessment of reporting biases

We planned to construct a funnel plot to assess publication bias if sufficient studies (> 10) were available for meta-analysis (Higgins 2011).

Data synthesis

We planned to summarise the data using either the fixed-effect or the random-effects model. If heterogeneity was present (I2 > 50%), we used the random-effects model method. If not, we used a fixed-effect model.

Subgroup analysis and investigation of heterogeneity

We planned to conduct the following subgroup analyses, if sufficient data were available:

Moderate versus severe disease (Rutherford 1997).Length of the stenotic segment: short (≤ 3 cm) versus long (3 cm to 10 cm) (Norgren 2007).According to the TASC classification of aorto-iliac lesions (Norgren 2007).Stenosis versus occlusion.Location of stenosis:involving the common iliac artery alone versus external iliac artery alone versus both arteries;distance from the aortic bifurcation (< 1 cm versus > 1 cm);distance from the hip joint (< 1 cm versus > 1 cm).Usage of the intraluminal versus subintimal space for endovascular treatment.Self expandable stent versus balloon-mounted stent.Whether balloon angioplasty was done either before stenting or post stenting.

Sensitivity analysis

We planned to perform sensitivity analyses by excluding:

randomised controlled trials of low methodological quality; industry-funded studies.

RESULTS

Description of studies

Results of the search

See Figure 1.

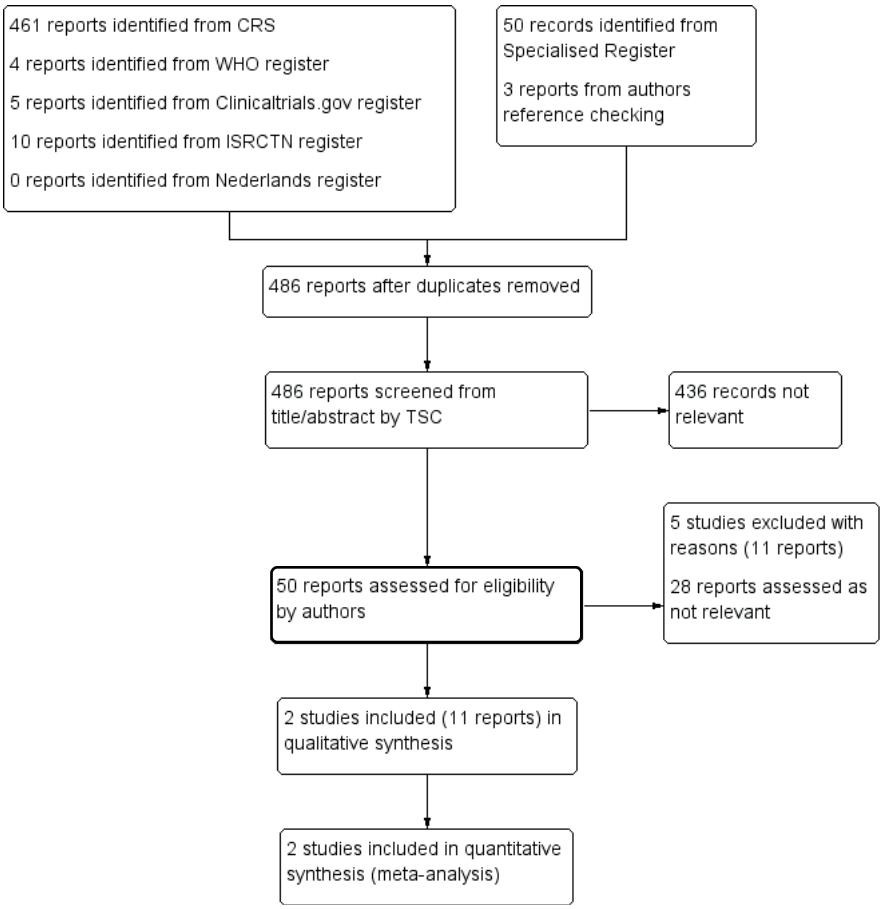


Figure 1. Study flow diagram

Included studies

See Characteristics of included studies for details of the included studies. We found two RCTs (11 publications) in the literature comparing the results of angioplasty and stenting in iliac artery occlusive disease.

We evaluated the full text of the 11 articles identified for inclusion and categorised them into two groups:

The first group was the Dutch Iliac Stent Trial (DIST), which consisted of eight publications. Three articles provided information on short-term and long-term results of percutaneous transluminal angioplasty (PTA) versus primary stenting (PS) (Klein 2004; Klein 2006; Tetteroo 1998). The other articles were about cost-effectiveness, comparisons of intra-arterial pressure gradients and haemodynamic criteria after stent placement.The second group consisted of two congress abstracts and one full publication concerning the STAG trial. We only used data from the full publication in this review.

The Dutch Iliac Stent Trial was performed from 1993 until 1997, and has published its early, mid-term and late results in 1998, 2004 and 2006. The second study is the STAG trial, which was performed from 1995 until 2002, and published its two-year follow-up in 2013.

Excluded studies

We excluded five studies. See Characteristics of excluded studies for details of the excluded studies. Two studies concerned the superficial femoro-popliteal arteries rather than the iliac arteries (Dake 2007; Katzen 2006). Two studies were RCTs comparing bare-metal and covered stents in the iliac artery (Bekken 2012; Mwipatayi 2011), not PTA with PS.

We found one quasi-randomised controlled trial (Kauffmann 1991). The publications of this study consisted of multiple conference abstracts, most of them published while the study was in progress. The most recent conference abstract consisted of 247 participants (Richter 1993). However, the only full publication was at an earlier stage when the study had recruited 131 patients (Kauffmann 1991a). The full text of this article was in the German language. JB translated this article before we made the final decision to exclude the study.

Risk of bias in included studies

See also Characteristics of included studies, Figure 2 and Figure 3.

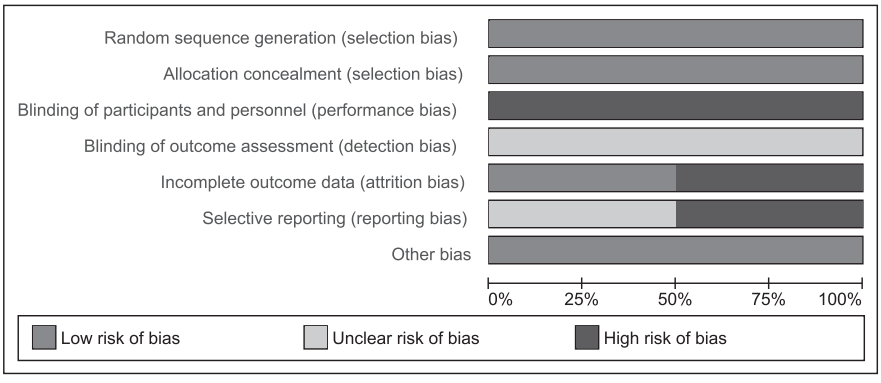


Figure 2. 'Risk of bias' graph: review authors' judgement about each risk of bias item presented as percentage across all included studies

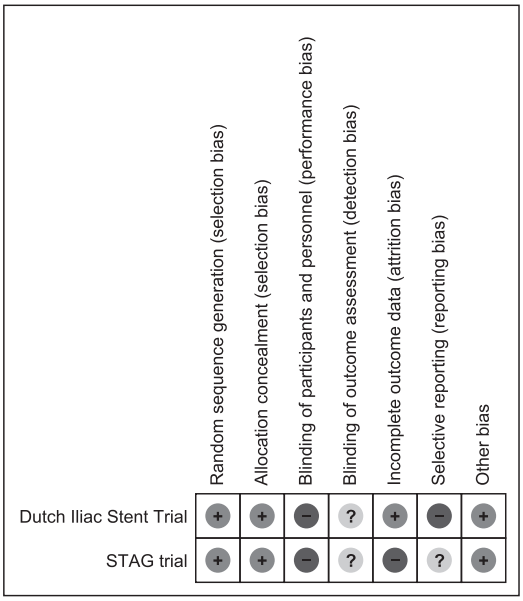


Figure 3. 'Risk of bias' summary: review authors' judgement about each risk of bias item for each included study

Allocation (selection bias)

We judged both included studies, Dutch Iliac Stent Trial and STAG trial, to be of low risk for selection bias, as both studies used random sequence generation and allocation concealment.

Blinding (performance bias and detection bias)

We judged both included studies to be of high risk for blinding of participants and personnel (Dutch Iliac Stent Trial; STAG trial). We scored the risk for blinding of outcome assessment as unclear for both studies.

Incomplete outcome data (attrition bias)

We scored the Dutch Iliac Stent Trial as low risk for incomplete outcome data, as six to eight-year results were reported on a substantial amount of patients. We scored the STAG trial as high risk, as only a limited number of patients completed full follow-up.

Selective reporting (reporting bias)

The study protocol was not published for either the Dutch Iliac Stent Trial or the STAG trial. Therefore we scored the risk as unclear for the STAG trial. However, in the final publication from Dutch Iliac Stent Trial, different outcome measures were used than in their previous

publications, and the outcomes that were reported were different from how they were defined in the methods section of the article (see paragraphs on 'improvement in the stage of PAOD' and 'resolution of symptoms and signs'). Therefore we scored this as a high risk of bias.

Other potential sources of bias

Both studies were funded by government-provided grants. The long-term follow-up from the Dutch Iliac Stent Trial was funded by Cordis, the company that manufactures Palmaz stents. However, it is stated that the investigators were in full control of the data. Therefore we scored both trials as low risk of bias on this domain.

Effects of interventions

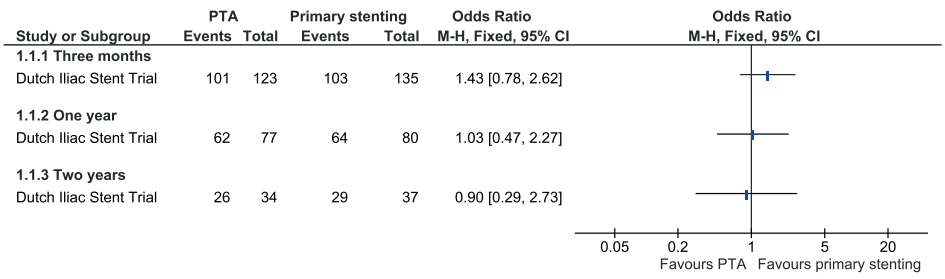
Pooling of data, planned subgroup analysis, sensitivity analysis and creation of funnel plots were not possible, due to the fact that only two studies were included and the studies were heterogeneic. The Dutch Iliac Stent Trial included mostly stenotic lesions (95%), while the STAG trial included occlusive lesions only. In addition, the definitions of the various outcomes that were reported in both studies were not comparable.

Clinical assessment of improvement

Symptomatic improvement

Improvement in the stage of PAOD according to Rutherford's criteria (Rutherford 1997)

The full publication from the STAG trial does not report on improvement in the stage of peripheral arterial occlusive disease (PAOD). In the two abstracts from congress presentations it is stated that "clinical outcome was assessed using the Rutherford scale at 1 month, 6 months, 1 year and 2 years" and that "there were no differences in clinical outcomes at 2 years" (Goode 2010; Goode 2011). However, no data have been reported to support these statements.



Analysis 1.1. Symptomatic improvement

The Dutch Iliac Stent Trial reports on improvement in the stage of PAOD, termed clinical success, at three months, one year, two years and six to eight years of follow-up. For the first three time points clinical success was defined as improvement of at least one clinical (Rutherford) category compared with the pre-treatment assessment. At three months, one year and two years no significant difference between both treatment strategies had been observed. At three months, clinical success was obtained in 82% (101/123) of patients in the percutaneous transluminal angioplasty (PTA) group compared to 76% (103/135) of patients in the primary stent group: odds ratio (OR) 1.43 (95% confidence interval (CI) 0.78 to 2.62; P value = 0.25; Analysis 1.1). At one year, clinical success was obtained in 81% (62/77) of patients in the PTA group compared to 80% (64/80) of patients in the primary stent group: OR 1.03 (95% CI 0.47 to 2.27; P value = 0.93; Analysis 1.1). At two years, clinical success was obtained in 77% (26/34) of patients in the PTA group compared to 78% (29/37) of patients in the primary stent group: OR 0.90 (95% CI 0.29 to 2.73; P value = 0.85; Analysis 1.1).

For the six to eight-year time point the methods section of the article states that symptomatic success was defined as an increase of at least one Fontaine stage. However, only the current Fontaine stage is reported, and not the proportion of patients that had an increase in Fontaine stage. This is not clinical improvement as defined in the methods section of the trial or of this review, and should actually be classified as 'resolution of signs and symptoms'; these results are therefore reported below in the appropriate section of this review. The actual improvement in the stage of PAOD rate at this time point is not reported. We contacted the study authors but no response was received.

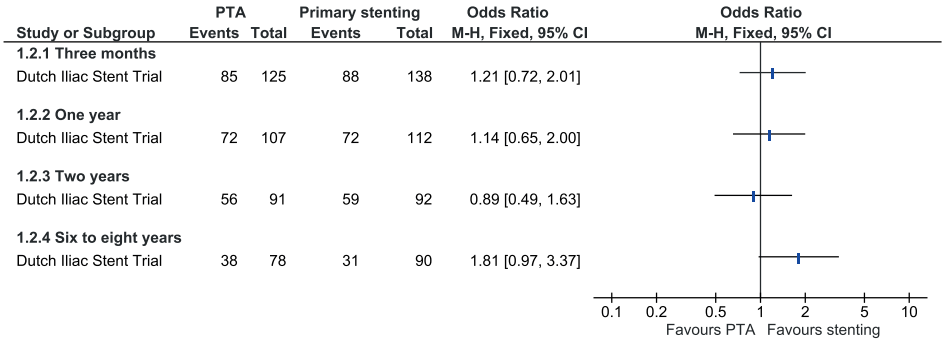
Improvement in walking distance as reported by the patient

This is not reported in the included studies.

Resolution of symptoms and signs

This is not reported in the STAG trial.

In the Dutch Iliac Stent Trial resolution of symptoms and signs, defined as Fontaine stage 1, is reported at three, 12, 24 months and six to eight years. At six to eight years it is reported as symptomatic improvement but, as stated above, we suggest that this should actually be termed as resolution of symptoms and signs. There was no significant difference between both groups at any of the time points. The study authors report that at the six to eight-year time point, there is a significant difference in the percentage of patients with resolution of symptoms and signs (Fontaine stage 1) in favour of the PTA group (31/90 versus 38/78, hazard ratio (HR) 0.8 (95% CI 0.6 to 1.0). However, no P value is given. We calculated an OR of 1.81 (95% CI 0.97 to 3.37) based on the data provided, and found a non-significant P value of 0.06 (Analysis 1.2).



Analysis 1.2. Resolution of symptoms and signs

Improvement of quality of life

Only the Dutch Iliac Stent Trial reports on quality of life. Quality of life was measured with the RAND 36-Item Health Survey at one, three, 12 and 24 months and at five years. The RAND-36 scores nine health dimensions: physical functioning, physical role functioning, emotional role functioning, social functioning, bodily pain, general health perception, mental health, vitality and health change. It is reported that all scores, except for general health perception, were still markedly higher than they were before treatment in both groups. The study authors state that survival analysis showed no differences in scores between the two treatment groups over the whole follow-up period.

Objective assessment of improvement

Measured claudication distance

This is not reported in the included studies.

Ankle brachial index

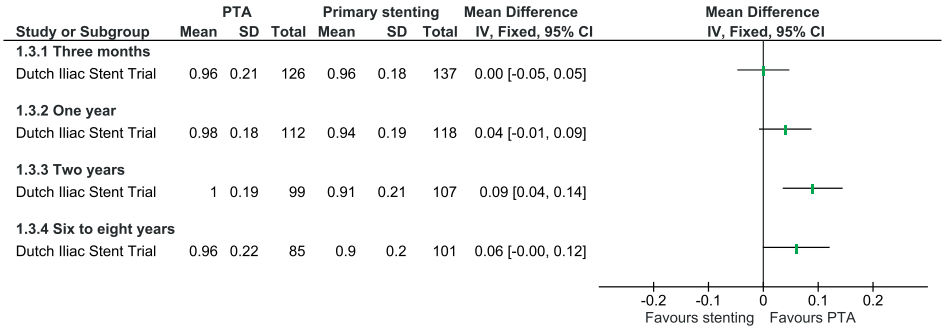
Only the Dutch Iliac Stent Trial reports on ankle brachial index (ABI) values, at three months, 12 months, 24 months and six to eight years. At 24 months there is a significant difference between the two groups with a lower mean difference (MD) in ABI value in the PS group (MD 0.09, 95% CI 0.04 to 0.14; P value = 0.001; Analysis 1.3).

Ulcer healing

This is not reported in the included studies.

Major amputation-free survival

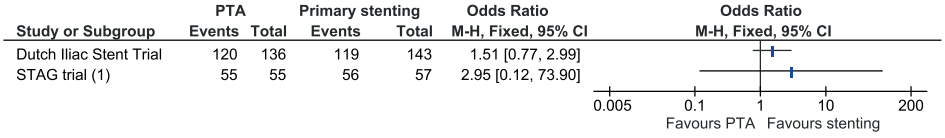
This is not reported in the included studies.



Analysis 1.3. Ankle brachial index

Technical success of the procedure

In the Dutch Iliac Stent Trial the treatment was considered a technical success when the pressure gradient across the treated segment was equal to or less than 10 mmHg after the procedure and during pharmacologically induced vasodilatation. Technical success was obtained in 120 of 136 (88%) of patients in the PTA group compared to 119 of 143 (84%) of patients in the PS group. This difference was not statistically significant: OR 1.51 (95% CI 0.77 to 2.99; P value = 0.23; Analysis 1.4).



Footnotes
(1) Secondary stenting judged to be a technical success rather than a technical failure

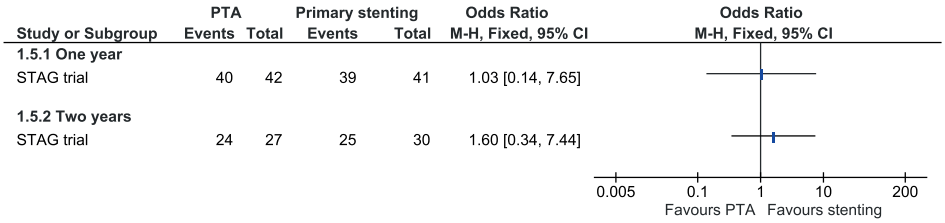
Analysis 1.4. Technical success

The STAG trial defined technical success as the presence of antegrade flow through the treated segment. Therefore patients in the PTA group who required a stent were categorised as having a technical failure. In the PTA group, 46 of 55 (84%) patients had a technical success, versus 56 of 57 (98%) in the PS group. However, in the PTA group all nine patients without flow were treated successfully by secondary stenting. We believe it would be more feasible to consider these patients a technical success, since secondary stenting was part of the treatment strategy. In that case technical success in the PTA group would be 100%, with an associated OR of 2.95 (95% CI 0.12 to 73.90; P value = 0.51; Analysis 1.4).

Patency of the treated vessel

Both the Dutch Iliac Stent Trial and the STAG trial reported on patency rates.

In the STAG trial, patency was defined as any flow through the treated segment measured by angiography after one and two years. Primary patency was defined as patency without any reintervention, secondary patency as patency after any successful reintervention. Primary patency at one year was 95% in both groups (PTA 40/42, primary stenting 39/41; OR 1.03; 95% CI 0.14 to 7.65; P value = 0.98; Analysis 1.5). At two years, primary patency was 89% (24/27) in the PTA group versus 83% (25/30) in the primary stenting group. This difference was not statistically significant: OR 1.60 (95% CI 0.34 to 7.44; P value = 0.55; Analysis 1.5). Secondary patency rates are not reported, but it is stated that there was no significant difference.



Analysis 1.5. Primary patency

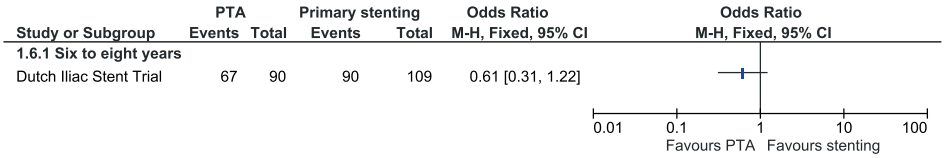
In the Dutch Iliac Stent Trial, patency was assessed by duplex ultrasonography. The iliac artery was deemed patent when the peak systolic velocity ratio was less than 2.5. Patency was reported as a life table analysis in two different publications of this study, primary patency at two years follow-up in one, and secondary patency for up to six to eight years follow-up in the other. At two years, reported primary patency rates were 71.3% in the PS group versus 69.9% in the PTA group, with a reported P value of 0.2. It is not clear how many patients had reached the two-year follow-up at the time of publication. The secondary patency rates, which are reported at six to eight years, are 83% (90/109) in the PS group versus 74% (67/90) in the PTA group, with a reported hazard ratio (HR) of 1.3 (95% CI 0.8 to 2.1).

Incidence of complications

Immediate complications (< 72 hours)

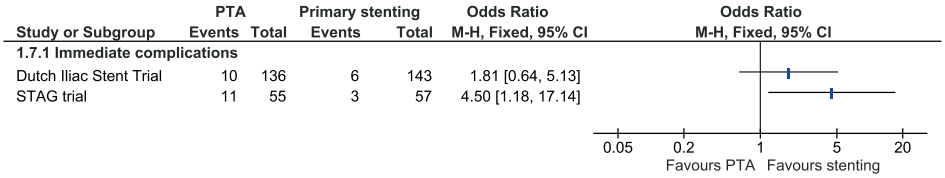
Both the Dutch Iliac Stent Trial and the STAG trial reported on early or immediate complications.

In the Dutch Iliac Stent Trial, it is not stated in the methods sections of the publications how complications were defined and no distinction was made between major or minor complications. It is stated that complications included haematoma at the puncture site, arterial-wall perforation, acute occlusion of the treated arterial segment, embolism and



Analysis 1.6. Secondary patency

vasovagal collapse. How these complications were distributed over both treatment groups is not reported. Complications occurred in 7% (10/136) of patients in the PTA group and in 4% (6/143) of patients in the PS group: OR 1.81 (95% CI 0.64 to 5.13; P value = 0.26; Analysis 1.7). Surgical intervention was necessary in two patients in the PTA group, however it is not reported for what indication. Stent occlusion as indicated by arterial thrombosis did not occur.



Analysis 1.7. Incidence of complications

In the STAG trial, major complications were defined as those resulting in death, permanent disability, unplanned amputation due to the intervention, an unexpected or unplanned secondary procedure (excluding secondary stent placement), delayed hospital discharge or blood transfusion. These occurred in 20% (11/55) of patients in the PTA group, and in 5% (3/57) of patients in the PS group: OR 4.50 (95% CI 1.18 to 17.14; P value = 0.03; Analysis 1.7). In the PTA group, nine of 11 major complications were episodes of distal embolisation. In the PS group, two episodes of distal embolisation occurred. For this reason the study was stopped prematurely. The other complications were two acute thromboses in the PTA group, and one arterial wall rupture in the PS group.

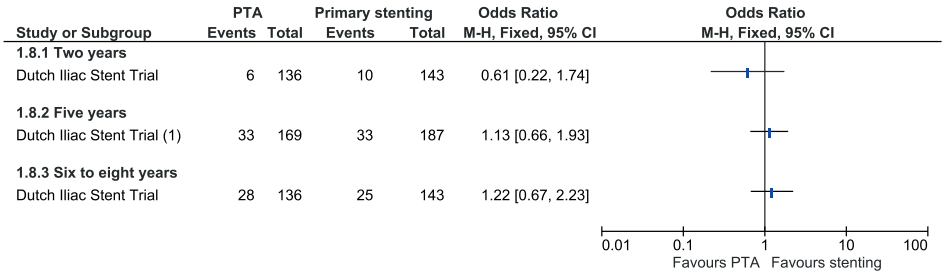
Delayed complications (> 72 hours)

Neither of the included trials reported delayed complications (Dutch Iliac Stent Trial; STAG trial).

Reintervention of the treated lesion

Reintervention rates are only reported in the Dutch Iliac Stent Trial. At two years, reintervention rates were 4% (6/136 patients) in the PTA group versus 7% (10/143 patients) in the PS group: OR 0.61 (95% CI 0.22 to 1.74; P value = 0.36; Analysis 1.8). At five years,

reinterventions were reported as treated segments - not per patient. Reintervention rates were 20% (33/169 treated segments, PTA group) versus 18% (33/187 treated segments, PS group): OR 1.13 (95% CI 0.66 to 1.93; P value = 0.65; Analysis 1.8). Finally, at six to eight years, 17% of patients (25/143) in the PS group and 21% (28/136) in the PTA group had required reintervention (HR 1.1, 95% CI 0.6 to 1.9). It is stated that there was no difference in the number of endovascular and surgical reintervention procedures between the two treatment groups.



Footnotes
(1) reported for segments rather than patients

Analysis 1.8. Reinterventions

DISCUSSION

Summary of main results

In both included studies, there were no significant differences in the primary outcomes. The Dutch Iliac Stent Trial reports significantly higher symptomatic success at six to eight years. However, the data presented by the trial authors actually reflect 'resolution of signs and symptoms', and based on the data we find no statistically significant difference. Patency rates were comparable for both strategies, and were also comparable to patency rates reported in other studies. Since additional stenting was considered a technical failure in the STAG trial, a decreased technical success rate in the percutaneous transluminal angioplasty (PTA) group was reported. We believe this should not be considered a technical failure, as it is part of the treatment strategy. In this case the technical success rates would be similar. The Dutch Iliac Stent Trial showed a significantly higher mean ankle brachial index (ABI) at two years in the PTA group (1.0 versus 0.91; mean difference (MD) 0.09; 95% confidence interval (CI) 0.04 to 0.14, analysis performed by review authors). At other time points there was no difference. It is unlikely that the difference at two years is attributable to the study procedure and it may not be clinically relevant.

The STAG trial showed a significantly increased major complication rate, especially distal embolism, in the PTA group compared to the primary stenting (PS) group (5% versus 20%). For this reason this trial was stopped prematurely. The Dutch Iliac Stent Trial did not find

any significant differences in complication rates. Reintervention rates were not significantly different between both groups as reported by the Dutch Iliac Stent Trial. Unfortunately, distribution of specific complications, such as embolism, between groups was not reported.

Overall completeness and applicability of evidence

The available evidence comes from only two studies, which were both performed in the 1990s. It is unclear whether ongoing improvements in stent design, and other innovations such as covered stents and drug-eluting balloons and stents, which were not available at the time, would affect these results.

The STAG trial compared primary stent placement with PTA and selective stenting in case of no flow through the arterial segment, and included only occlusions. In 16% of patients in the PTA group additional stent placement was performed. The Dutch Iliac Stent Trial also compared primary stent placement with PTA and selective stenting, however stenting was performed in case of a residual mean pressure gradient > 10 mmHg. This resulted in additional stent placement in 43% of patients in the PTA group. The Dutch Iliac Stent Trial included mainly stenotic lesions (95%). This makes the two studies very heterogenic and we deemed pooling of data inappropriate.

Of the 12 pre-planned outcomes, five were not assessed in either study: improvement in walking distance as reported by the patient, measured claudication distance, ulcer healing, revised level of amputation and delayed complications. Only two pre-planned outcomes were reported in both studies: technical success and patency of the treated vessel. The other outcomes were assessed in only one of the studies.

Quality of the evidence

The two studies that we included in this review did have some risk of bias, such as selective reporting and non-blinding of participants and personnel, however some of this bias is inevitable given the nature of the treatment. For example, blinding of personnel to whether or not a stent is placed is not possible. Due to the heterogeneity between the studies as discussed above, pooling was unfortunately not possible. We deemed the overall quality of the evidence to be low due to the small number of included studies, the differences in study populations and definitions of the outcome variables.

Potential biases in the review process

No biases are present. A comprehensive search was performed by the Trial Search Coordinator and we also performed a vigorous reference search, but any unpublished studies or data may have been missed.

Agreements and disagreements with other studies or reviews

A meta-analysis on the same topic, published almost 20 years ago, analysed cohort studies because no randomised controlled trials (RCTs) were available at the time (Bosch 1997). Bosch 1997 included a total of 2116 patients. They concluded that initial technical success was significantly higher in patients treated with PS than PTA (96% versus 91%, P value < 0.05). Bosch 1997 also found that long-term patency (four years) was significantly higher in the PS group. Based on their data, a relative risk reduction for loss of patency of 39% was calculated. Complication rate and mortality were not significantly different.

In our review, we did not show a difference in technical success, clinical improvement or patency. In the STAG trial, which included occlusions only, a significantly higher number of major complications was found in the PTA group.

AUTHORS' CONCLUSIONS

Implications for practice

The number of studies and total number of patients that could be included in this meta-analysis are small and results should be interpreted with caution. Also, both studies were initiated 15 to 20 years ago, and since then many improvements have been made, both in stents and percutaneous transluminal angioplasty (PTA) balloons, and new technologies such as covered stents and drug-eluting balloons and stents have been introduced. For example, in the Dutch Iliac Stent Trial the stents were mounted on the balloons by hand, whereas nowadays all stents come premounted on balloons. It is unclear how these factors influence the results from our review.Based on our results, there is insufficient evidence to assess the effects of PTA versus primary stenting (PS) for stenotic and occlusive lesions of the iliac artery.Treating occlusions with PTA only may lead to a higher major complication rate, especially distal embolisation. However, this is based on one randomised controlled trial (RCT) only.

Implications for research

Based on our results, and on the fact that much has changed in endovascular techniques and materials since the publication of the studies included in this review, we would advise the initiation of new RCTs comparing primary stenting with PTA and selective stenting. Subgroup analyses should be performed for critical ischaemia versus claudication and for stenotic versus occlusive lesions.

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Contributions of authors

JAB: article selection, data extraction, writing of the reviewNA: article selection, proof-reading the reviewHJ: data extraction, writing of the reviewCJH: provided help on statistical and methodological areas, proof-reading of the reviewVvW: writing of the reviewBF: resolved disagreements concerning article selection and data extraction, proof-reading of the review

Declarations of interest

JAB: currently involved in a RCT comparing covered versus bare-metal balloon-expandable stents in advanced PAOD in the common iliac artery (Bekken 2012). This study does employ primary stenting.NA: none knownHJ: none knownCJH: none knownVvW: none knownBF: currently involved in a RCT comparing covered versus bare-metal balloon-expandable stents in advanced PAOD in the common iliac artery (Bekken 2012). This study does employ primary stenting.

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