TREATMENTS OF PERIPHERAL ARTERY DISEASE: COST-EFFECTIVENESS ANALYSES

- *Original publication: Burgers LT, Luyendijk M, Poley MJ, Severens JL, Redekop WK. Systematic review of cost-effectiveness analyses of treatments of peripheral artery disease. Report from Erasmus University Rotterdam, Institute of Health Policy & Management. The Netherlands, 2015.*
- *This KCE has read for you was prepared by Joan Vlayen, Nancy Thiry and Sabine Stordeur*
- *Published on 28 September 2017*

KEY MESSAGES OF THE ORIGINAL PUBLICATION

For patients with intermittent claudication:

- Supervised exercise therapy is cost-effective compared with unsupervised exercise therapy.
- Compared with supervised exercise therapy, revascularization improves health but increases costs; whether the health gain justifies the additional costs is not clear from the studies.
- Percutaneous transluminal angioplasty with stent placement for iliac revascularizations is cost-effective compared with percutaneous transluminal angioplasty alone.
- Percutaneous transluminal angioplasty is cost-effective compared with bypass for femoropopliteal interventions.

For patients with critical limb ischemia:

- Revascularisation (bypass or percutaneous transluminal angioplasty) is a cost-effective treatment compared with primary amputation.
- It is however unclear whether bypass or endovascular treatment is cost-effective.

SUMMARY OF THE ORIGINAL PUBLICATION

Context

The most common initial symptom of lower limb peripheral arterial disease (PAD) is pain in the calf, buttocks or thigh on walking, known as intermittent claudication (IC). Approximately 20% of patients with IC will progress to critical limb ischemia (CLI) [1] which is characterized by persisting pain in rest and/or trophic skin changes and an ankle systolic blood pressure below 50 mmHg. Patients with CLI are at significant risk of developing irreversible ischemic damage to the leg or foot if they do not receive appropriate treatment. Moreover, within a year, 25% of them will die and about 1/3 will require a major lower limb amputation.

Treatment of IC patients has three aims: 1) decrease cardiovascular disease risk, 2) improve walking distance, and 3) improve quality of life. Patients often receive medication (vasoactive drugs), exercise therapy, revascularization (e.g. (bypass) surgery, percutaneous transluminal angioplasty (PTA) or PTA in combination with stenting) or an amputation.



What is *KCE has read for you*?
KCE has read for you synthesises a recently published high-quality systematic review or health technology assessment with relevance for the Belgian health system. The original publication was appraised and contextualised by KCE researchers. KCE has read for you is not based on original research conducted by KCE.

More details on methodology can be found on the KCE website

CLICK TO READ MORE

This document includes:

- **Key findings** of the publication under evaluation
- **A contextualisation** within the Belgian healthcare system

Not included:

- Recommendations
- Detailed descriptions

Trustworthy original publication

The methodological quality of the systematic review was assessed with the Drummond checklist.

Method

The systematic review (until 13/1/2015) aimed to summarize the cost-effectiveness of the following treatment strategies for patients with IC or CLI: (supervised) exercise, (stented) PTA, bypass surgery, medication (symptom relief) and amputation. The reporting quality of the included cost-effectiveness studies was evaluated using the Drummond checklist.

Results

The authors included 29 original studies on the cost-effectiveness of therapeutic interventions either for patients with IC (13 studies), for patients with CLI (11 studies) or for both CLI and IC patients (5 studies).

Patients with intermittent claudication

Intervention	Comparator	ICER	N studies	Conclusion based on cost-effectiveness
Supervised exercise versus unsupervised exercise				
Supervised exercise (SE)	Unsupervised exercise (UE)	The Netherlands: €28,693/QALY gained UK: £1,780/QALY gained UK: £2,359/QALY gained UK: £711-1,608/QALY gained USA: $24,070/QALY gained	5	SE therapy is cost-effective compared with UE therapy.
Revascularization versus supervised exercise therapy				
Percutaneous transluminal angioplasty (PTA)	Supervised exercise (SE)	USA: $38,000/QALY gained The Netherlands: €231,800/QALY gained USA: SE dominant	6	Revascularization leads to more effects in terms of QALYs but also to higher costs when compared with exercise therapy. Contradictory results between studies about cost-effectiveness of revascularization compared with exercise therapy.
PTA + SE	SE	UK: €152,259/QALY gained		
Stenting	SE	USA: $122,600/QALY gained		
PTA with stent + SE	SE	UK: £7,988-8,348/QALY gained		
Revascularization versus revascularization				
Iliac artery				
PTA with stent placement	PTA alone	The Netherlands: $4,073-4,519/QALY gained USA: $7,624–8,519/QALY gained	2	PTA with stent placement is cost-effective compared with PTA alone.
Femoropopliteal artery				
PTA	Bypass surgery (BP)	USA: PTA dominant USA: PTA dominant	2	PTA is cost-effective compared with BP.
Endovascular treatments compared with each other: drug coated balloon (paclitaxel), PTA +/- stenting, bare metal stent, paclitaxel eluting stent, stent-graft, cryoplasty, sirolimus eluting stent, endovascular brachytherapy		UK: drug coated balloon (paclitaxel) dominant	1	Among the specific endovascular treatments compared, drug coated balloon (paclitaxel) is the dominant strategy.
Orbital atherectomy and balloon angioplasty	Balloon angioplasty	USA: $3,441/QALY gained	1	Orbital atherectomy + angioplasty is cost-effective compared with angioplasty alone.
Laser-assisted (Nd/YAG) PTA	PTA alone	UK: £3,040/QALY gained	1	(Nd/YAG) laser-assisted PTA is cost-effective compared with PTA alone.
Medication				
Medications compared with each other: Pentoxifylline, Cilostazol, Naftidrofuryl		UK: no ICER provided UK: Naftidrofuryl dominant	2	Cilostazol and naftidrofuryl are more effective than pentoxifylline. However, it is not clear which is the most cost-effective treatment. *Cilostazol is unavailable in Belgium

SE: supervised exercise therapy, UE: unsupervised exercise therapy, PTA: percutaneous transluminal angioplasty, BP: bypass surgery, ICER: incremental cost-effectiveness ratio, QALY: quality-adjusted life year, Nd/YAG: neodymium-doped yttrium aluminium garnet. Dominant: a strategy is dominant when it provides greater effectiveness at a lower cost compared to an alternative treatment.

Patients with critical limb ischemia

Intervention	Comparator	ICER	N studies	Conclusion based on cost-effectiveness
Primary amputation versus revascularization				
Infra-inguinal area and tibial-peroneal artery occlusive disease				
Revascularization (bypass surgery or PTA)	Primary amputation	USA: $5,475/ LYG USA: $7,836-15,881/QALY USA: dominant USA: dominant USA: $3,545/QALY gained	5	Revascularization (bypass surgery or PTA) is cost-effective compared with primary amputation.
Revascularization versus Revascularization				
Infra-inguinal area				
BP	PTA	UK : £134,257/QALY gained UK : $184,492/QALY gained USA: BP dominant USA: PTA dominant USA: PTA dominant	5	It is unclear whether BP or PTA is cost -effective. USA: contradictory results depending on populations.
Femoropopliteal area				
BP	PTA	USA: no ICER provided USA: no ICER provided	2	BP is cost-effective compared with PTA.
Subintimal angioplasty	BP	UK: €10,768/QALY gained	1	Subintimal angioplasty is cost-effective compared with BP.
Orbital atherectomy and balloon angioplasty	Balloon angioplasty	USA: $3,441/QALY gained	1	Orbital atherectomy with angioplasty is cost-effective compared with angioplasty alone.
Laser-assisted (Nd/ YAG) PTA	PTA alone	UK: £1,810/QALY gained	1	(Nd/YAG) laser-assisted PTA is cost-effective compared with PTA alone.
Endovascular treatments compared with each other: drug coated balloon (paclitaxel), PTA +/- stenting, bare metal stent, paclitaxel eluting stent, stent-graft, cryoplasty, sirolimus eluting stent, endovascular brachytherapy		UK: drug coated balloon (paclitaxel) dominant	1	Among specific endovascular treatments, drug coated balloon (paclitaxel) was the dominant strategy.
Drug eluting stent (DES)	Bail-out bare metal stent (BMS)	Greece: €6,518 (bail-out sirolimus DES) to €11,581 (primary everolimus DES) per event-free year	1	DES treatments are cost-effective compared with BMS.
Tibial area				
Cool excimer laser-assisted angioplasty	Balloon angioplasty	Ireland: €2,073/QALY gained	1	Cool excimer laser-assisted angioplasty is cost-effective when compared with balloon angioplasty.
Medication versus revascularization				
Repeated use of PTA or BP	Prostaglandin E1 (PGE1)	Germany: €10,450 (PTA) to €23,797 (BP) per QALY gained	1	Repeated PTA and BP are both cost-effective compared with PGE1.

PTA: percutaneous transluminal angioplasty, BP: bypass surgery, DES: drug eluting stent, BMS: bare metal stent, ICER: incremental cost-effectiveness ratio, QALY: quality-adjusted life year, LYG: life-year gained, Nd/YAG: neodymium-doped yttrium aluminium garnet.
Dominant: a strategy is dominant when it provides greater effectiveness at a lower cost compared to an alternative treatment.

Conclusion

Some interventions for the treatment of PAD were consistently reported as cost-effective: in patients with IC supervised versus non-supervised exercise therapy, PTA versus BP for femoropopliteal interventions, PTA with stent placement versus PTA alone for iliac revascularizations; in patients with CLI revascularisation (BP or PTA) versus primary amputation.

Evidence for the other interventions is mitigated with contrasting results, or is based on a single study per intervention, such that it is not possible to indicate which intervention is cost-effective.

KCE VIEWPOINT

Quality of the publication

This publication is a thorough systematic literature review, based on several search strategies (consultation of multiple electronic databases) to ensure exhaustive identification of all relevant studies. The selection process was performed by two independent reviewers, with conflicts resolved by consensus. Data extraction and quality assessment was performed by one reviewer, and checked by a second one. Most cost-effectiveness analyses covered by the review were estimated to be of reasonable quality by the authors; on average the studies fulfilled 77% of the Drummond criteria.

Belgian context

In 2012, 26,041 hospital stays with a revascularization procedure for PAD were registered in Belgium. However, no data are available on the total amount of patients with lower limb PAD.

In 2014, KCE recommended to first proceed with the standard medical treatment (i.e. secondary prevention of cardiovascular diseases and advices on physical activity) in patients presenting with intermittent claudication before considering more invasive treatment (such as angioplasty), a recommendation that was based on a very low level of evidence. [1] The findings of this review do not contradict or support this recommendation. However, when exercise treatment is considered, it should be clearly supervised by a health professional. Currently, supervised exercise treatment is not reimbursed in Belgium for this indication.

REFERENCES

Vlayen, J., K. Holdt Henningsen, et al. (2014). Revascularization for lower limb peripheral arterial disease. KCE Reports. Brussels, Belgian Health Care Knowledge Centre (KCE). Report 221

What is the Drummond checklist?

The Drummond et al. checklist contains 35 questions, divided under three headings (study design, data collection, and analysis and interpretation of results), and concerning the reporting quality of an economic evaluation. The checklist was not primarily developed to assess the internal validity of an economic evaluation (though it could serve as a basis for this purpose) and it does not result in an aggregated summary score.

Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. BMJ 1996; 313(7052): 275-283.

https://www.nlm.nih.gov/nichsr/edu/healthecon/drummond_list.html

What is a QALY?

QALY (Quality-adjusted Life-Year)= life year gained weighted by health-related quality of life, or "healthy year of life". This is the unit of measurement of a health benefit. It encompasses both the "quantity of life" and the "quality of life" modified by an intervention.