Paclitaxel Drug-Eluting Stents in Peripheral Arterial Disease: OHTAC Recommendation

HEALTH QUALITY ONTARIO

ONTARIO HEALTH TECHNOLOGY ADVISORY COMMITTEE RECOMMENDATIONS

- OHTAC recommends against publicly funding paclitaxel drug-eluting stents for the treatment of above-the-knee peripheral arterial disease.

BACKGROUND

Peripheral arterial disease is a common condition in which atherosclerotic plaques in the arteries partially or completely block blood flow to the legs. There are a variety of potential treatments for peripheral arterial disease, including exercise, drugs, angioplasty, and surgery.

Angioplasty can be performed by itself or in conjunction with a bare metal or drug-eluting stent. Stents are inserted to reduce the risk of the vessel collapsing or narrowing again. The Zilver paclitaxel drug-eluting stent is the only drug-eluting stent currently licensed by Health Canada to treat symptomatic lesions in above-the-knee femoropopliteal arteries. It is an endovascular drug/device system that includes a self-expanding nitinol drug-eluting stent and a polymer-free coating of paclitaxel at a dose density of 3 µg/mm^2 on its outer surface.

KEY QUESTIONS AND FINDINGS

Health Quality Ontario reviewed the evidence (1) to answer the questions below.

- What is the clinical effectiveness and safety of Zilver paclitaxel self-expanding drug-eluting stents compared to 1) other self-expanding drug-eluting stents, 2) balloon-expanding drug-eluting stents, 3) bare metal stents, 4) percutaneous transluminal angioplasty, and 5) drug-coated balloons, in treating *de novo* or restenotic lesions in above-the-knee peripheral arterial disease?
- What is the cost-effectiveness of Zilver paclitaxel self-expanding drug-eluting stents in treating *de novo* or restenotic lesions in above-the-knee peripheral arterial disease?
- What is the budget impact of funding Zilver paclitaxel self-expanding drug-eluting stents in treating *de novo* or restenotic lesions in above-the-knee peripheral arterial disease from the perspective of the Ontario Ministry of Health and Long-Term Care?

We found a single randomized trial studying the use of the Zilver paclitaxel drug-eluting stent. In this trial, patients were randomized to receive either angioplasty alone or angioplasty with the Zilver paclitaxel drug-eluting stent. In the angioplasty group, patients whose vessels immediately collapsed were subsequently randomized to receive either a bare metal stent or a Zilver paclitaxel drug-eluting stent.

Based on this trial, we concluded the following:

- Use of the Zilver paclitaxel drug-eluting stent may improve the patency rate compared to angioplasty alone.
- Use of the Zilver paclitaxel drug-eluting stent may improve the event-free survival rate compared to angioplasty alone, where most "events" were another revascularization procedure.
- It is uncertain whether use of the Zilver paclitaxel drug-eluting stent leads to less pain, better function, or fewer amputations compared to angioplasty or bare-metal stent.

Funding of paclitaxel drug-eluting stent might result in an estimated annual savings of between $470,000 and $640,000, if the paclitaxel drug-eluting stent reduces the risk of needing a future revascularization procedure.

OHTAC DELIBERATIONS

OHTAC accepted the findings of the clinical evidence review conducted by HQO. OHTAC also accepted the findings of the budget impact analysis, but noted that the use of the paclitaxel drug-eluting stent would be cost-saving at current prices only if it did indeed substantially reduce the risk for future revascularization procedures.

OHTAC reached a consensus that the clinically meaningful comparison would be one between the paclitaxel drug-eluting stent and the bare metal stent. Given that such a trial is underway, and given that there are other options available for the treatment of peripheral arterial disease, OHTAC decided to recommend against publicly funding paclitaxel drug-eluting stents for the treatment of above-the-knee peripheral arterial disease.

Decision Determinants

Table 1: Decision Determinants for Paclitaxel Drug-Eluting Stents in Above-the-Knee Peripheral Arterial Disease

Decision Criteria	Subcriteria	Decision Determinants Considerations
Overall clinical benefit How likely is the health technology/intervention to result in high, moderate, or low overall benefit?	**Effectiveness** How effective is the health technology/intervention likely to be (taking into account any variability)?	*Patency* Higher compared to angioplasty (GRADE very low [24 months] to low [12 months]) Higher compared to bare metal stent (GRADE low) No difference compared to paclitaxel drug-coated balloon (GRADE very low) *Walking Impairment Questionnaire*[a] No difference compared to angioplasty (GRADE moderate) *Ankle-brachial index*[b] No difference compared to angioplasty (GRADE moderate) *Rutherford classification*[c] No difference compared to angioplasty (GRADE moderate) *Clinical benefit index*[d] Significant improved compared to angioplasty or bare metal stent (GRADE low)
	Safety How safe is the health technology/intervention likely to be?	*Event-free survival*[e] Higher compared to angioplasty (GRADE low) No difference compared to paclitaxel drug-coated balloon (GRADE very low)
	Burden of illness What is the likely size of the burden of illness pertaining to this health technology/intervention?	Based on administrative data, approximately 500 patients with peripheral arterial disease in Ontario would be candidates for the Zilver paclitaxel drug-eluting stent if they did not receive a bare metal stent instead
	Need How large is the need for this health technology/intervention?	Unclear, but alternative treatments are available
Consistency with expected societal and ethical values[f] How likely is adoption of the health technology/intervention to be congruent with societal and ethical values?	**Societal values** How likely is the adoption of the health technology/intervention to be congruent with expected societal values?	Untreated peripheral arterial disease causes severe pain and limits mobility, affecting work and social relationship
	Ethical values How likely is the adoption of the health technology/intervention to be congruent with expected ethical values?	None known
Value for money	**Economic evaluation**	It is uncertain whether the Zilver paclitaxel drug-eluting stent is cost-effective. Budget impact

Decision Criteria	Subcriteria	Decision Determinants Considerations
How efficient is the health technology likely to be?	How efficient is the health technology/intervention likely to be?	analyses suggest that funding of this technology would be cost-saving if it was substantially more effective than bare metal stents
Feasibility of adoption into health system How feasible is it to adopt the health technology/intervention into the Ontario health care system?	**Economic feasibility** How economically feasible is the health technology/intervention?	The only additional cost of implementing this technology would be the additional cost of purchasing this stent compared to bare metal stent. Implementing this technology is economically feasible
	Organizational feasibility How organizationally feasible is it to implement the health technology/intervention?	Adoption of the Zilver paclitaxel drug-eluting stent is feasible given that the only additional resource required is the stent

[a]Walking Impairment Questionnaire measures patient-perceived walking capacity.
[b]Ankle-brachial index measures lower-limb hemodynamic status.
[c]Rutherford classification indicates severity of peripheral arterial disease.
[d]Clinical benefit index was a composite outcome that included freedom from persistent or worsening claudication, rest pain, ulcer, or tissue loss after initial study treatment.
[e]Event-free survival was defined as freedom from major adverse events (procedure- or device-related death; amputation; clinically driven target lesion revascularization; target limb ischemia requiring surgical intervention or surgical repair of target vessel; and worsening of the Rutherford classification by two classes or to class 5 or 6).
[f]The anticipated or assumed common ethical and societal values held in regard to the target condition, target population, and/or treatment options. Unless there is evidence from scientific sources to corroborate the true nature of the ethical and societal values, the expected values are considered.

REFERENCES

(1) Health Quality Ontario. Paclitaxel drug-eluting stents in peripheral arterial disease: a health technology assessment [Internet]. Toronto (ON): Queen's Printer for Ontario; 2015 November; 62 pp. Available from: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series/drug-eluting-stent-hta.

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Citation
Health Quality Ontario. Paclitaxel drug-eluting stents in peripheral arterial disease: OHTAC recommendation [Internet]. Toronto (ON): Queen's Printer for Ontario; 2015 November; 5 pp. Available from: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series/drug-eluting-stent.