Partially covered self-expandable metal stents versus polyethylene stents for malignant biliary obstruction: A cost-effectiveness analysis

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BACKGROUND/OBJECTIVE: Partially covered self-expandable metal stents (SEMS) and polyethylene stents (PES) are both commonly used in the palliation of malignant biliary obstruction. Although SEMS are significantly more expensive, they are more efficacious than PES. Accordingly, a cost-effectiveness analysis was performed.

METHODS: A cost-effectiveness analysis compared the approach of initial placement of PES versus SEMS for the study population. Patients with malignant biliary obstruction underwent an endoscopic retrograde cholangiopancreatography to insert the initial stent. If the insertion failed, a percutaneous transhepatic cholangiogram was performed. If stent occlusion occurred, a PES was inserted at repeat endoscopic retrograde cholangiopancreatography, either in an outpatient setting or after admission to hospital if cholangitis was present. A third-party payer perspective was adopted. Effectiveness was expressed as the likelihood of no occlusion over the one-year adopted time horizon. Probabilities were based on a contemporary randomized clinical trial, and costs were issued from national references. Deterministic and probabilistic sensitivity analyses were performed.

RESULTS: A PES-first strategy was both more expensive and less efficacious than an SEMS-first approach. The mean per-patient costs were US$6,701 for initial SEMS and US$20,671 for initial PES, which were associated with effectiveness probabilities of 65.6% and 13.9%, respectively. Sensitivity analyses confirmed the robustness of these results.

CONCLUSION: At the time of initial endoscopic drainage for patients with malignant biliary obstruction undergoing palliative stenting, an initial SEMS insertion approach was both more effective and less costly than a PES-first strategy.

Key Words: *Biliary obstruction; Cost-effectiveness; Gastrointestinal cancer; Stent*

Les endoprothèses de métal auto-expansibles partiellement couvertes par rapport aux endoprothèses de polyéthylène en cas d'obstruction biliaire maligne : une analyse coût-efficacité

HISTORIQUE ET OBJECTIF : Les endoprothèses de métal auto-expansibles (EMAE) partiellement couvertes et les endoprothèses de polyéthylène (EPÉ) sont toutes deux souvent utilisées pour pallier une obstruction biliaire maligne. Même si les EMAE sont beaucoup plus coûteuses, elles sont plus efficaces que les EPÉ. C'est pourquoi les chercheurs ont effectué une analyse coût-efficacité.

MÉTHODOLOGIE : Dans une analyse coût-efficacité, les chercheurs ont comparé l'EPÉ initiale à l'EMAE initiale auprès de la population à l'étude. Les patients ayant une obstruction biliaire maligne ont subi une cholangiopancréatographie rétrograde endoscopique pour insérer la première endoprothèse. Si l'insertion échouait, ils subissaient une cholangiographie transhépatique percutanée. En cas d'occlusion de l'endoprothèse, une EPÉ était insérée à la reprise de la cholangiopancréatographie rétrograde endoscopique, soit en milieu ambulatoire, soit après l'hospitalisation pour cholangite. Les chercheurs ont adopté la perspective du tiers payeur. L'efficacité était exprimée comme la probabilité d'absence d'occlusion dans l'horizon prévu d'un an. Les probabilités reposaient sur un essai clinique aléatoire contemporain tandis que les coûts étaient extrapolés des références nationales. Les chercheurs ont effectué des analyses de sensibilité déterministes et probabilistes.

RÉSULTATS : La stratégie d'installation d'une EPÉ initiale était à la fois plus coûteuse et moins efficace que celle de l'installation d'une EMAE initiale. Les coûts moyens par patient étaient de 6 701 $US pour l'EMAE initiale et de 20 671 $US pour l'EPÉ initiale, qui s'associaient à des probabilités d'efficacité de 65,6 % et de 13,9 %, respectivement. Les analyses de sensibilité ont confirmé la validité des résultats.

CONCLUSION : Au drainage endoscopique initial chez les patients ayant une obstruction biliaire maligne qui se faisaient installer une endoprothèse palliative, l'insertion initiale d'une EMAE était à la fois plus efficace et moins coûteuse que celle d'une EPÉ.

The management of patients with malignant biliary obstruction (MBO) focuses significantly on the relief of patient symptoms achieved with endoscopic drainage using different stent technologies (1,2). Polyethylene stents (PES) remain widely used, even though the newer self-expandable metal stent (SEMS) types have demonstrated improved efficacy (2,3), both covered and uncovered (4-7).

Although there are many reasons for their continued popularity, the choice of PES in the palliation of distal MBO is, no doubt, in part explained by its ease of insertion and favourable upfront cost compared with SEMS (8), with little consideration for downstream expenses attributable to differences in efficacy. Several previous analyses have suggested that SEMS were both clinically superior and more cost effective than PES, even though they do not prolong survival. Specifically, advantages of SEMS have been reported in selected health care settings and in patients with longer anticipated life expectancy (5,9-14). However, even these conclusions have been questioned by some (5,8). Since the publication of most of these reports, the advent of partially covered SEMS (15), coupled to the evolution of biliary endoscopic techniques (16,17), now justifies a more contemporary cost-effectiveness analysis that is based on a contemporary randomized clinical trial (RCT) (6).

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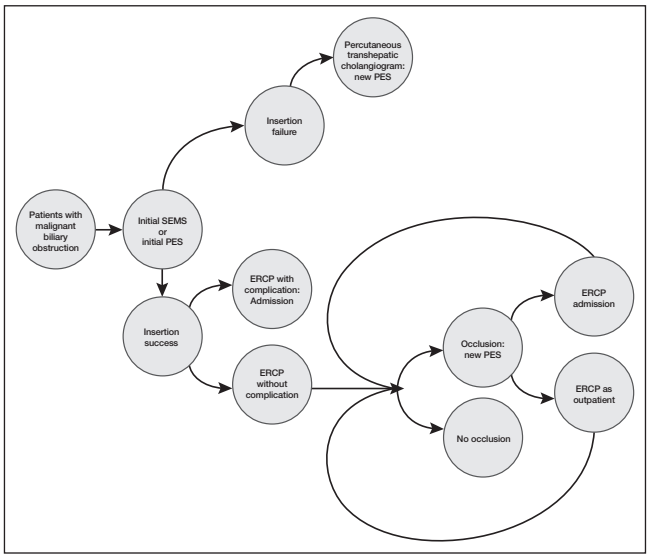

Figure 1) *Influence diagram of the adopted model structure. ERCP Endoscopic retrograde cholangiopancreatography; PES Polyethylene stent; SEMS Partially covered self-expandable metal stent*

METHODS

Overview

An incremental cost-effectiveness decision tree to compare the use of initial PES versus initial SEMS using TreeAge Pro Suite Healthcare module 2015 (18) for palliative patients deemed inoperable with MBO during a 12-month follow-up period was constructed. The outcome was the cost per stent occlusion averted. A third-party-payer perspective was adopted.

Model design

Although the RCT included one-, three-, six-, nine- and 12-month visits following randomization, these were not included in the base-case analysis because they would represent closer follow-up than in a real-life setting. At the beginning of the model, in each branch, after a first consultation an endoscopic retrograde cholangiopancreatography (ERCP) is performed to insert initially either a PES (initial PES) or an SEMS (initial SEMS). If the insertion fails, a percutaneous transhepatic cholangiogram (PTC) is performed, and it is the end of the model for this path. Figure 1 illustrates the structure of the model across a 12-month time horizon following randomization. The model allows for a possible post-ERCP adverse event state as well (pancreatitis, cholangitis, bleeding). In follow-up, the only adverse event that was modelled for was the most common one of interval stent occlusion. The treatment of stent occlusion correspondingly required a stent change to a PES, either on an outpatient basis or with an admission to hospital because of associated cholangitis. Stent occlusion could occur between each planned outpatient visit at any time over the 12-month time frame, termed time horizon. After the 12 months, the patient arrives at a terminal node and a cost per no occlusion is computed by the model for each branch. No patient death node was specifically included in the structure of the model.

Probabilities

The probabilities of failure of stent insertion (initial SEMS or initial PES) were extracted from the literature (2). All other probabilities in the model were based on a contemporary RCT of 85 patients comparing PES to SEMS (6). The inclusion criteria applied in this RCT are listed in Table 1. All of the probabilities used in the model are listed in Table 2.

Costs and lengths of stay

The national United States (US) market price of the two types of stents used for PTC or ERCP were provided by Boston Scientific, USA (19).

TABLE 1
Inclusion and exclusion criteria

Inclusion criteria
Age ≥18 years
Extrahepatic biliary obstruction by any malignant process, extending no more proximal than 1 cm below the common hepatic ductal bifurcation, as measured at the time of enrollment endoscopic retrograde cholangiopancreatography
A Karnofsky Performance Scale Index >60%
Patient physically capable and mentally willing to comply with the protocol requirements including stent insertion as well as the required three-monthly clinical follow-up visits
Signed voluntary informed consent
Exclusion criteria
Jaundice secondary to primary intrahepatic biliary obstruction (eg, patient had underlying chronic liver disease)
Active cholangitis
International normalized ratio >3.0
Multiple strictures requiring therapy
Biliary anatomy inappropriate for the available sizes of the biliary stents used in the study
Previous attempt at curative surgical resection of the malignant obstructing tumour
Patient has participated in a protocol involving an investigational drug or device 90 days before proposed entry into the present study
Allergy to any component of the individual stents, or their materials/delivery systems
Active alcohol or drug abuse
Unstable social circumstances that may preclude follow-up
Inability to understand and execute informed consent

All physicians fees were derived from the national database of the American Medical Association (20). Cost of hospitalization for cholangitis was based on specific admissions included in the Nationwide Inpatient Sample (NIS) 2008 (21). This national hospitalization database comprises eight million hospitalizations occurring in >1000 different hospitals located in 42 states of the US. Hospitalizations of patients who died during the hospital stay or who were <18 years of age were excluded from the analysis. Only hospitalizations that were recorded with Medicare, Medicaid or a private insurance as the primary payer were included. All the charges associated with the *International Classification of Diseases* 9-CM code '576.1: cholangitis' were selected. Costs were computed based on the average charges combined with a cost-to-charge ratio, which was, for the most part, specific to the hospital where the hospitalization took place; if not, a recommended (22) group average cost-to-charge ratio was applied. To obtain valid national cost estimates, discharge weights were used in the computations. The short time horizon of 12 months covering the entire study adopted obviates the need for discounting. All dollar values were expressed in 2014 US dollars utilizing the consumer price index for the medical care services published by the US Department of Labor (23). Indirect costs were not considered in the present analysis. All cost and length of stay estimates are presented in Table 3.

Cost-effectiveness analysis

The effectiveness is expressed as the probability of maintained patency occurring over the full duration of the model (one year with successful initial stent insertion). The costs are the sum of the cost items listed for all the 12 months. Results of the deterministic analysis are reported as cost, effectiveness, cost-effectiveness ratio and incremental cost-effectiveness ratio (ICER).

Sensitivity and threshold analyses

Deterministic and probabilistic sensitivity analyses were performed. All bounds used for the sensitivity analyses of the probabilities were

TABLE 2
Probability estimates of the model

Description of probability	Point estimate	Bound Low	Bound High
Initial polyethylene stent			
Failure of insertion at baseline	0.05	0.02	0.09
Cholangitis before 1 month and before first occl	0.195	0.102	0.34
Cholangitis before 1 month and after first occl	0.286	0.082	0.641
Cholangitis between 1 and 3 months	0.25	0.0456	0.699
Cholangitis between >3 and 6 months	0.286	0.082	0.641
Cholangitis between >6 and 9 months	0	0	0.5
Cholangitis between >9 and 12 months	1	0.342	1
Occl before 1 month	0.171	0.085	0.313
Occl between 1 and 3 months	0.138	0.055	0.306
Occl between >3 and 6 months	0.411	0.216	0.64
Occl between >6 and 9 months	0	0	0.435
Occl between >9 and 12 months	0.667	0.208	0.939
Initial partially covered self-expandable metal stent			
Failure of insertion at baseline	0.0597	0.03	0.1
Cholangitis before 1 month and before first occl	0.049	0.014	0.161
Cholangitis before 1 month and after first occl	0.5	0.095	0.906
Cholangitis between 1 and 3 months	0.5	0.095	0.906
Cholangitis between >3 and 6 months	0	0	0.5
Cholangitis between >6 and 9 months	0	0	0.5
Cholangitis between >9 and 12 months	0	0	0.5
Occl before 1 month	0.049	0.014	0.161
Occl between 1 and 3 months	0.074	0.021	0.234
Occl between >3 and 6 months	0.111	0.031	0.328
Occl between >6 and 9 months	0	0	0.269
Occl between >9 and 12 months	0.111	0.03	0.564

Source of the probabilities: The two probabilities of failure of the insertion were issued from the literature (2). All the other probabilities were based on a randomized clinical trial whose patients were issued from the six participating North American university centres mentioned in the method section (6). The bounds for the sensitivity analysis were based on the 95% CIs. occl Occlusion

TABLE 3
Cost and length of stay (LOS) estimates of the model

Description of cost/ LOS variable	Point estimate	Source	Bound Low	Bound High
Price of initial PES	115	BS (18)	60	230
Price of initial SEMS	2,413	BS (18)	1000	5000
Cost of outpatient follow-up	83	AMA (19)	40	170
Cost of inpatient follow-up	107	AMA (19)	50	220
Cost of outpatient first consultation	139	AMA (19)	70	280
Cost of inpatient first consultation	122	AMA (19)	60	250
Cost of emergency consultation	66	AMA (19)	30	140
Cost of physician fees PTC	467	AMA (19)	230	940
Cost of physician fees ERCP	483	AMA (19)	240	970
Cost of procedure PTC	2,471	BS (18)	1200	5000
Cost of procedure ERCP	1,170	BS (18)	500	2400
Cost of admission for cholangitis	15,100	NIS (20)	5000	30,000
LOS of cholangitis	5.5	NIS (20)	1	12

All costs are in 2014 United States dollars. The bounds for the sensitivity analysis were based on the SD for the LOS and cost of an admission for cholangitis. For all the other cost variables, the low (high) bounds were based on the point estimates divided (multiplied) by 2. AMA American Medical Association; BS Boston Scientific (USA); ERCP Endoscopic retrograde cholangiopancreatography; NIS National Inpatient Sample; PES Polyethylene stent; PTC Percutaneous transhepatic cholangiogram; SEMS Partially covered self-expandable metal stent

TABLE 4
Cost-effectiveness analysis report

Stent	Cost	IC	Eff	IE	CER	ICER
Initial SEMS	6,701	0	0.6561	0	10,213	0
Initial PES	20,671	13,971	0.1385	–0.5176	149,243	Dominated*

*All costs are expressed in 2014 United States dollars. *Incremental cost-effectiveness ratio (ICER) = − US$26,993. CER Cost-effectiveness ratio; Eff Effectiveness (probability of no occlusion during the consecutive 12 months); IC Incremental cost; IE Incremental effectiveness; PES Polyethylene stent; SEMS Partially covered self-expandable metal stent*

based on the 95% CIs. The ranges for the length of stay and cost of an admission for cholangitis were based on the standard deviations of the NIS database (21). All other cost ranges were equal to the point estimates plus 100% or less 50%.

One-way sensitivity analyses were performed on all variables used in the model to investigate the robustness of the results and to determine which factors influenced most these results.

A Tornado diagram was chosen to represent how the variation of the value of an input variable of the model across a pre-set range influences the results of the model. The widest bars of the Tornado diagram identify the variables that most changed the ICER (beyond 20%). As part of the sensitivity analysis, the influence of the time horizon chosen on the model results was specifically assessed. Threshold analyses were also performed to observe the cut-off points for which the conclusion of the model could change. Probabilistic sensitivity analysis was performed running 10,000 Monte Carlo simulations based on the uncertainty distributions of all the variables and a chosen maximal willingness to pay (WTP) value of US$50,000. A WTP represents the pre-fixed maximum dollar value that is deemed to be acceptable spending for a given treatment. Results of the probabilistic analysis are reported as an incremental cost-effectiveness scatter plot. It illustrates the probability that a stent is cost effective compared with the other one, given a WTP.

RESULTS

Base-case analysis

The report of the results (Table 4) shows that using initial SEMS over a period of 12 months for patients with MBO is a strategy significantly less expensive but also more efficacious; indeed, the initial SEMS approach dominates the initial PES strategy. On average, it would save US$13,971 per patient to opt for the initial SEMS strategy while at the same time the patient would have a 50% decrease in probability of biliary stent occlusion during the 12 consecutive month follow-up after the index ERCP. Therefore, the average cost per no occlusion is significantly more attractive with initial SEMS (US$10,213) than for initial PES (US$149,243).

Sensitivity analyses

One-way deterministic sensitivity analyses: Any variable used in the model does not change the final choice of strategy: initial PES is always dominated, even if the point estimates vary inside their respective plausible ranges. The Tornado diagram (Figure 2) shows that within the plausible ranges of all the variables of the model, the cost of hospitalization for cholangitis most influences the ICER value. It is only when the variables are made to assume values outside their predetermined ranges that there is a change in the dominance of the SEMS approach. Indeed, threshold analysis shows that the cost of initial SEMS would have to increase above US$16,240 for initial PES to be no longer dominated. The other threshold values for other variables are even less clinically plausible.

Regardless of the selected time horizon, the initial PES approach is still dominated by the initial SEMS approach (Figure 3). Adding the costs of three-monthly follow-up visits from the first to the 12th month (as in the RCT), do not alter the conclusion with a corresponding ICER of US$26,700 and an average cost strategy of US$7,060 (initial SEMS) versus US$20,880 (initial PES).

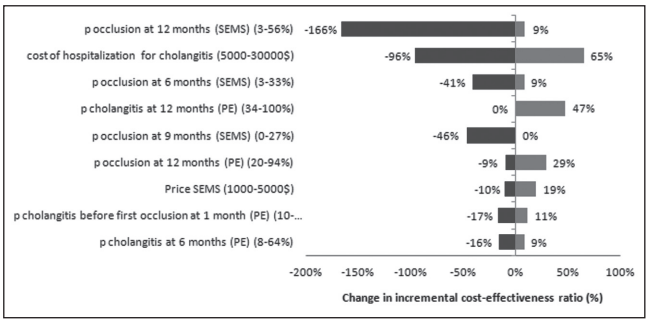

Figure 2) *Tornado diagram for variations of ≥20% and from the base-case incremental cost-effectiveness ratio (ICER) estimate. p Probability of; PES Polyethylene stent; SEMS Partially covered self expandable metal stent*

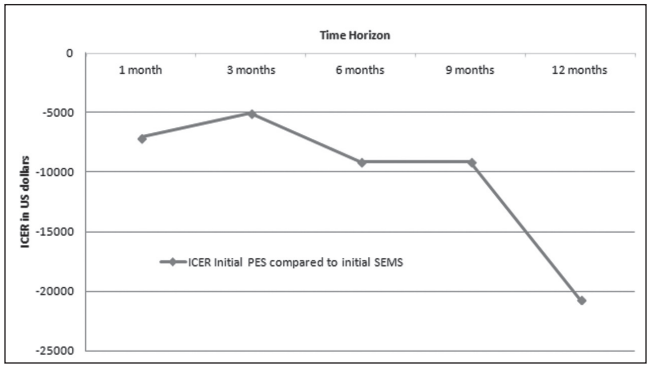

Figure 3) *Incremental cost-effectiveness ratio (ICER) as a function of the adopted time horizon for the cost-effectiveness model. PES Polyethylene stent; SEMS Partially covered self-expandable metal stent*

Probabilistic sensitivity analyses: The Monte-Carlo analysis was based on 10,000 simulations that each vary simultaneously all the variables of the model according across their adopted ranges. It represents the uncertainty about the estimates of costs and measure of effectiveness. The incremental cost-effectiveness scatter plot is presented in Figure 4: each point represents the incremental cost and effectiveness pair from the simulation results for initial SEMS relative to initial PES. The ellipse circumscribes 95% of the cloud of the results of cost and effectiveness points when simulations are performed according to the Monte Carlo analysis. All points below the WTP threshold are the simulation iterations where the initial SEMS is preferred given a WTP of US$50,000: they represent 90% of the 10,000 simulation iterations. It expresses the probabilities of preference for initial SEMS or PES, across a range of possible WTP threshold values. For every WTP threshold, the initial SEMS approach is the preferred management compared with initial PES.

DISCUSSION

The present analysis demonstrates the economic dominance of a SEMS-first approach with robust sensitivity analysis. Such a broad, overriding conclusion has not previously been adopted by other cost-effectiveness analyses and, thus, warrants a discussion of our methodology and a review of the literature.

Considering the short clinically pertinent survival time and the outcome of 'cost per no occlusion', we adopted a cost-effectiveness decision tree approach whose structure was dictated by the RCT on which it is based (6). In accordance with the concept of a theoretical decision model, we simplified some possible events: initial insertion failures are immediately followed by a PTC and a final node. The outcomes of these few patients until the 12th month was not taken into account because it would not have any impact on our comparison; this group of patients is similar between both approaches. We considered

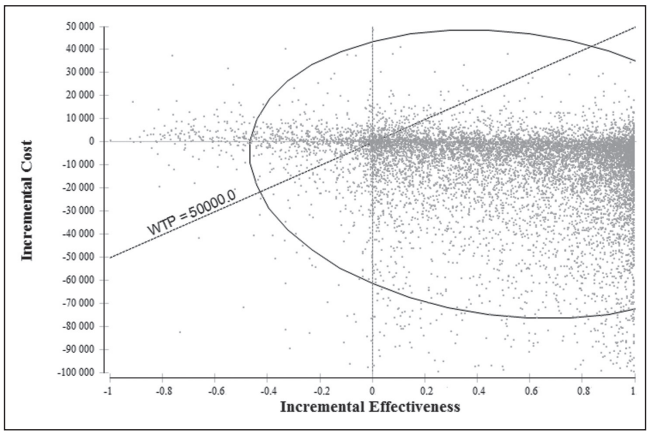

Figure 4) *Incremental cost-effectiveness scatter plot of initial partially covered self-expandable metal stent (SEMS) versus initial polyethylene stent (PES). All costs expressed in 2014 United States dollars. The willingness-to-pay (WTP) threshold (US$50,000) is the line that intersects the origin and the initial PES strategy is represented by the origin (0;0)*

the probability of all adverse events, but specifically modelled for the length of stay and costs attributable to bouts of cholangitis because it is by far the most common in this context (24); other authors have done similarly in past published economic analyses (9,14). We chose not to include death in the measure of effectiveness because this outcome introduces a lot of uncertainty (in addition to the estimation of related costs). Finally, the literature has reported no difference in mortality when comparing the use of each of the two types of stents (5,9,10,12-14,25,26).

Because the clinical trial data were available up to 12 months, it was, therefore, logical to fix the time horizon at one year, as has been performed in most cost-effectiveness analyses (9,13,27). This chosen time horizon is also consistent with the median survival duration observed in recent cohorts of patients with MBO treated with metallic stents (28).

All efficacy assumptions were based on real outcomes information observed in a contemporary RCT comparing both stent technologies (6), an important decision that is supported by the evolution of biliary endoscopic techniques and contemporary supportive care in this patient group. Although such a choice of data source decreases the external validity of the point estimates, it allows for inclusion of more uniform and clinical, currently valid assumptions; in fact, five of the seven studies included in an authoritative meta-analysis by Moss et al (2) were ≥15 years of age (2). Moreover, the RCT on which our analysis is based likely carries sufficient generalizability because patients were included from six participating North American university centres. The robustness of the cost variables of the model is based on the national representativeness of the recent data we used from the NIS 2008 (21) and that we updated for 2011, and are both, here too, more contemporary and more generalizable to a Western setting than many previous reports. In fact, as in efficacy information, many published cost analyses assessing malignant biliary stenting are significantly older, bringing into question the clinical relevance of those previous results. As examples, Prat et al (12) and Davids et al (25) based their analysis on costs markedly inferior to today's purchase costs (for example, US$20 for PES); the SEMS, at that time, also referring to an uncovered stent technology. In addition, most published cost models have not assessed relevant estimates for a North American practice with US data, focusing rather on local national costs and currencies (7,11,14,15,27,29). Other limitations are the inclusion in many analyses of sole stent costs without consideration other expenses (5,13,29,30). The summary review by Moss et al (31) in 2007 computed cost-effectiveness results in which three of the four studies were published before the turn of the century; moreover, their ICER

calculation is very approximate because it is based on the assumption that the stent price is the only difference between the two interventions. Because the patients included in the RCT (6) we used as reference were followed every three months during the study, we also added the cost of the follow-up visits from the first to the 12th month in another version of our base-case model. The comparison of the two approaches remained, however, in the same proportion.

The ICER was expressed as cost per occlusion (ie, ERCP) averted as was performed by Moss et al (31) and others (25,29,32), rather than quality-adjusted life-year (QALY) as was performed by Arguedas et al (9), who recognized the limited reliability of this measure with the available information for palliative patients with MBO. Furthermore, the ICERs expressed as cost per QALY are sometimes more difficult to interpret over short time horizons than if the ICER is based on outcomes reflecting more concrete end points. In such clinical contexts, the unit of efficacy can be chosen specific to the medical condition (28,33-37), as has been the case for MBO (11,12,14,25,27,29,31).

To confirm robustness of the results, we performed both deterministic and probabilistic sensitivity analyses consistent with existing methodological recommendations (38-41). The ranges of the probability variables were guided by the data from our RCT (6), while we used wide intervals for the cost estimates (Table 3), identifying only highly improbable, clinically irrelevant thresholds values. Because patient survival and time horizon are critical individual factors, we also assessed the impact of the duration of the time horizon, and tested the relevance of the adopted 12 months. Regardless of the time horizon chosen between one and 12 months, the initial SEMS approach remained dominant. The probabilistic sensitivity analysis leads to similar conclusions. Representative gastrointestinal disease literature have fixed values for WTP in the clinical context of gastrointestinal bleeding (33-37), gastroesophageal reflux disease (42) or adverse events in critically ill patients (43). However, we did not find reference to any set WTP that could apply to patients suffering from MBO. In fact, the choice of a threshold for a WTP often remains subjective (37,44-46). An arbitrary WTP was therefore estimated at US$50,000 based on the magnitude of the average cost of the treatment of occlusion, as suggested by Enns et al (37).

Our conclusions differ from most past economic analyses in that the increased cost effectiveness of a SEMS-first strategy (if not dominance) is found to apply regardless of patient survival or cost settings. A review of published cost analyses comparing plastic to metal stents in patients stented for distal MBO explain the reasons for such a disparity: other cost studies are derived from direct RCT results, comparing plastic with uncovered metal stents (11,12,25,27). Three RCTs (11,12,27) tabulated total costs, which were higher in the metal stent group, without calculating ICERs and without performing any sensitivity analysis. Moss et al (31) performed an extrapolated ICERs for these three studies (11,12,27), based on the assumption that, in each individual trial, the only difference in unit costs between both interventions was the stent price. They concluded that uncovered SEMS had significantly higher patency rates than PES as early as four months after insertion. A later RCT by Kaassis et al (27) concluded that placement of a PES in a patient with hepatic metastases and a metal stent in patients without hepatic metastases was cost effective solely based on extrapolations of median survival data. Three more recent RCTs (5,7,47) yielded direct cost analyses; however, once again, no modelling or sensitivity analyses were performed that recommended that the more effective uncovered SEMS be used in unresectable patients with malignant common bile duct strictures, who survived a median of 4.5 months, while less costly PES were preferable in the one-third of patients who have distant metastases.

Two true cost-effectivenesss analyses with appropriate modelling and sensitivity analyses were performed, both >10 years ago. In the first, Yeoh et al (13) concluded in 1999 that the choice of stent should be guided by the relative local costs of ERCP and metal stents, and by the prognosis of the patient, whereby metal stents were preferable for patients surviving >4 months. The authors, however, did not carry out a true cost-effectiveness analysis, as highlighted by others (9). Later in 2002, Arguedas et al (9) completed a very thorough and methodologically sound cost-effective analysis, with costs drawn from the University of Alabama (Birmingham, Alabama, USA) in 1999 and even considered the costs of home care, while using QALYs as the unit of effectiveness as discussed earlier. The authors concluded initial endoscopic placement of an uncovered metal stent was a cost-saving strategy compared to initial PES placement, particularly in patients expected to survive >6 months.

Principal differences between these previous cost-effective analyses and our own that explain the differences in findings include a higher incidence of cholangitis associated with stent obstruction in the plastic group of our recent RCT, and observed real-life probabilities at the different time points of follow-up. Moreover, as already suggested above, contemporary costs, including equipment and admissions to hospital are much greater (for example US$8,333 in the Arguedas et al [9] analysis versus our US$13,768, or the per diem of €480 in the Soderlund et al study (7) versus our US$2,500).

A more recent study by Hamada et al (15) compared a one-step versus an unusual two-step SEMS (covered and uncovered) insertion strategy in which a nasobiliary catheter is first inserted, while using local institutional charges. They concluded on the superiority of a SEMS-first approach but did not perform sensitivity analyses.

Because the majority of biliary stents inserted worldwide remain PES, an effort will need to be made to consider using the SEMS technology at the initial endoscopic procedure. In fact, decision makers need to consider the downstream cost effectiveness of an approach as opposed to the upfront cost of a piece of equipment.

Limitations of our analysis include the realization that many of the probabilities we used are based on small groups of patients whose numbers decrease gradually as patients flow through the 12-month trial duration, including complication rates (although sensitivity analyses include broad published ranges of these). The probability values in the last months of the model are therefore the most uncertain. It is also possible that very discreet subgroups of patients may benefit from an initial PES insertion; however, this appears to be unlikely based on the robustness and generalizability imparted by the uniform findings on multiple sensitivity analyses in our study. Also, the RCT data are principally based on 10 mm partially covered SEMS and 10 Fr plastic stents. Moreover, the SEMS technology adopted for the present cost analysis was that of a partially covered stent; however, the relative efficacy of covered versus uncovered SEMS remains controversial (1,48). It is important to note that partially covered SEMS are more expensive than uncovered SEMS and these latter stents are commonly used in clinical practice. Therefore, had the model included uncovered SEMS they may have been the preferred strategy and, at a minimum, partially covered SEMS would most likely not have been dominant. Similarly, because of the source data for this analysis, other relevant comparators were not assessed and this is a limitation. The costs adopted are US-based and reflect not only US currency but also a US fee structure; this realization needs to be kept in mind when the results are generalized to a Canadian setting. Moreover, our data, based on palliative patients, do not allow us to confidently conclude on the choice of stent for temporary biliary drainage while awaiting a possible curative surgery as has been increasingly practiced, with some surgeons preferring initial plastic stent insertion. Two recent cost-minimization studies examining in part this issue suggest the cost effectiveness of covered SEMS over PES and/or DoubleLayer PES (10,30), although a policy of routine preoperative drainage has not been shown to improve and may even worsen subsequent outcomes (48-50).

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CONCLUSION

Using a cost-effectiveness analysis modelled principally based on a recent RCT, a PES-first strategy was both more expensive and less efficacious than that of a SEMS-first approach in palliating patients with distal MBO. The average cost was US$6,701 for the SEMS-first and US$20,674 for PES-first, and associated with effectiveness probabilities of experiencing no occlusion over the 12 months of 65.6% and 13.9%, respectively. Extensive sensitivity analyses confirmed the robustness of these conclusions. The present analysis, based on contemporary estimates of both effectiveness and costs, expands on previous, now less-pertinent cost-effectiveness analyses, suggesting that in 2013, at the time of initial endoscopic drainage for patients with MBO undergoing palliative stenting, insertion of a partially covered SEMS is thus both more effective and less costly than that of a PES, regardless of anticipated survival or cost settings.

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