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Cost-effective analysis of preliminary single-operator cholangioscopy for management of difficult biliary stones

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ABSTRACT

Background and study aims Single-operator peroral cholangioscopy (SOC) is a therapeutic modality for difficult biliary stone disease. Given its high success rate and increasing availability, analysis of the economic impact of early SOC utilization is critical for clinical decision-making. Our aim is to compare the cost-effectiveness of different first and second-line endoscopic modalities for difficult-to-treat choledocholithiasis.

Patients and methods A decision-tree model with a 1-year time horizon and a hypothetical cohort of 200 patients was used to analyze the cost-effectiveness of SOC for first, second and third-line intervention in presumed difficult biliary stones. We adopted the perspective of a Canadian tertiary hospital, omitting recurrence rates associated with endoscopic retrograde cholangiopancreatography (ERCP). Effectiveness estimates were obtained from updated meta-analyses. One-way sensitivity analyses and probabilistic sensitivity analyses were also performed to assess how changes in key parameters affected model conclusions.

Results First- and second-line SOC achieved comparable clinical efficacy from 96.3 % to 97.6% stone clearance. The least expensive strategy is third-line SOC (SOC-3: $800,936). Performing SOC during the second ERCP was marginally more expensive (SOC-2: $816,584) but 9 % more effective. The strategy of first-line SOC incurred the highest hospital expenditures (SOC-1: $851,457) but decreased total procedures performed by 16.9 % when compared with SOC-2. Sensitivity analysis was robust in showing SOC-2 as the most optimal approach.

Conclusions Second-line SOC was superior to first and third-line SOC for treatment of difficult biliary stones. When based on meta-analysis of non-heterogeneous trials, SOC-2 is more cost-effective and cost-efficient. Our study warrants a larger pragmatic effectiveness trial.

Introduction

Choledocholithiasis, otherwise known as biliary stones, constitute a significant and common health problem, affecting up to 15 % of Canadian men and women by age 60 years [1]. The standard treatment of biliary stones is endoscopic retrograde cholangiopancreatography (ERCP), which achieves stone clearance via balloon sweeps or basket trawling, typically following endoscopic sphincterotomy. For large or challenging stones, mechanical lithotripsy and balloon dilation are common techniques as is stent insertion to maintain biliary drainage for post-procedure stone dissolution [2]. While largely effective, approximately 10% to 15% of stones are unyielding to traditional ERCP techniques and are thus classified as difficult biliary stones [3–6]. Reliable predictors of ERCP failure include stone impaction, diameter of biliary dilation, presence of distal strictures, and age > 65 years [7–10]. Experienced clinicians are able to gauge with relative consistency which stones will be difficult to clear prior to undergoing ERCP.

Single-operator peroral cholangioscopy (SOC) is a relatively novel technology that offers an alternative approach to difficult stone treatment; benefiting from electrohydraulic lithotripsy (EHL) and direct visualization of the bile duct lumen rather than fluoroscopic imaging. Most profoundly, the literature surrounding SOC reports an 88% to 93% clearance rate [11].

Despite high effectiveness and excellent safety profile of SOC, it is typically reserved for patients in whom traditional ERCP fails due to the added cost of cholangioscopy disposables. However, it remains unclear whether potential savings from increased effectiveness outweigh equipment costs. In the Canadian health care system, the upfront capital cost of investing in a SOC system is a significant deterrent to the acquisition of such technology, and as a result, SOC is advocated for difficult stones only after failure of conventional ERCP [12, 13]. One study out of a tertiary center in Belgium found an 27% relative reduction in total procedures and an 11% cost reduction when SOC was added as an adjunct during the index ERCP vs. when SOC was a separate procedure after ERCP failure [14]. Most recently, Alrahji et al. demonstrated how early utilization of SOC for difficult choledocholithiasis is less costly compared to postponing SOC, without significantly compromising effectiveness [15].

Given the novelty of the system and despite estimates by other authors [16, 17], the literature is divided on the estimation of financial potential SOC-EHL offers in a universal, publicly funded healthcare system. An analysis of SOC's economic impact would empower endoscopists to make an informed decision on when to incorporate SOC-EHL into their difficult stone treatment algorithm. We aim to analyze whether earlier use of SOC in presumed cases of difficult choledocholithiasis is more cost-efficient and effective than clearance achieved with a delayed approach where conventional ERCP is attempted prior to SOC introduction.

Methods

Model design

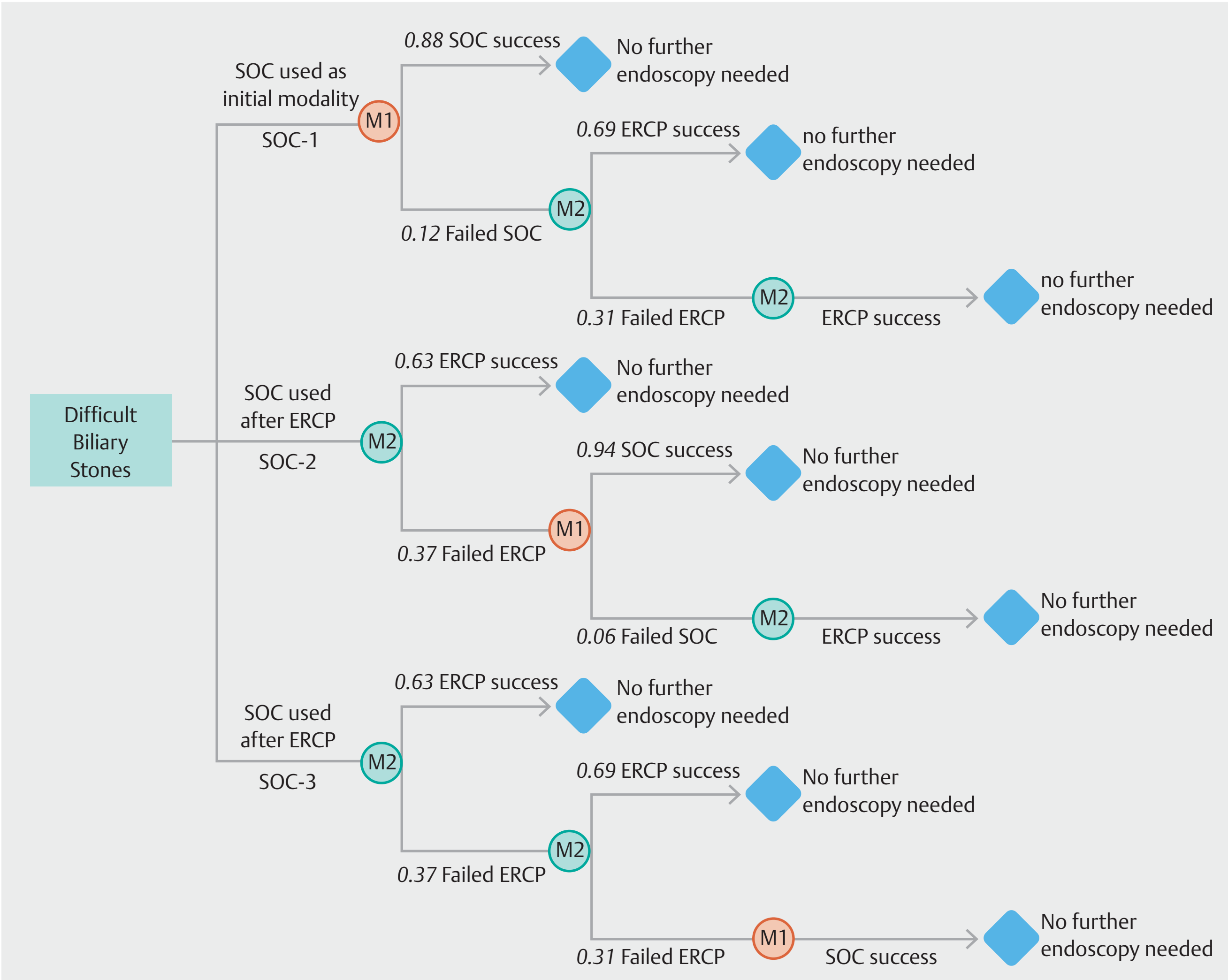
We evaluated the clinical success of first vs. second or third-line SOC in managing patients with difficult biliary stones through a decision-tree model, which estimated the annual budget from a Canadian tertiary hospital perspective. We chose this type of analysis to evaluate simultaneously the costs and efficacy of different endoscopic approaches. The impact of SOC was assessed by comparing a scenario in which SOC is given after one or two initial ERCP failure (Base Scenario 1 and 2, respectively) vs. a scenario in which SOC is given as initial treatment (Alternate Scenario). Difficult stones were defined as stones > 15 mm, impacted, of unusual shape (barrel), with distal strictures present, or with failure of complete ductal clearance using conventional ERCP methods including sphincterotomy with balloon or basket stone extraction with or without mechanical lithotripsy.

Our model outlines two management strategies with SOC: 1) one or two attempts at traditional ERCP as the first option (Base Scenario 1 and 2); or 2) SOC as the first option (Alternative Scenario) (▶ **Fig. 1**). In the base scenarios (referred to as SOC-2 and SOC-3), if ERCP is successful in stone removal (success rate: 63% of cases) then no further treatment is required and the patient exits the model. If ERCP is unsuccessful (failure rate: 1.0–0.63 = 37% of cases), then the patient undergoes SOC as a separate procedure. If SOC is successful (success rate: 88% of cases), the patient is discharged from care. For the remaining 12% of patients, if the second procedure fails, the patients are assumed to require a third traditional ERCP later in time. In the alternative scenario (referred to as SOC-1), patients are initially treated with SOC alone (success rate: 88%). Patients are then either discharge home if successfully treated, or undergo subsequent traditional ERCP at a later date. Patients undergoing ERCP as a second procedure have a 69% chance of being successfully treated and discharged. In the remaining 31% of patients, which the second intervention fails, they are assumed to undergo a third successful traditional ERCP. The current model was designed to consider a maximum of three interventions, as described above. Adverse events (AEs) were not considered in the model due to significantly low rates of complications attributable to choledocholithiasis without cholangitis [18, 19]. LucidSpark 2021 was used for construction of the model (▶ **Fig. 1**) and Microsoft Excel 2021 for the cost-effectiveness analysis.

Probability and cost assumption

Probabilities for failure were obtained from aggregating systematic reviews and meta-analyses. We used an 88% procedure success rate of POC with lithotripsy at first intervention [11], and 94% at secondary intervention to reflect the overall rate of complete stone clearance [20]. The single session clearance rate of 88% by Korrapati et al. is in keeping with other reviews of aggregated literature in a similar context. A systematic review conducted by Alrajhi et al. found a POC-EHL clearance rate of 88%, derived from screening 1870 articles and analyzing 24 full-text studies [15]. As these were both peer reviewed studies, we assumed them to be validated estimates. However, the study by Korrapati et al. was observational and investigated multiple types of cholangioscopy-guided lithotripsy. Newer studies focusing on SOC-guided lithotripsy have reported better efficacy on first intervention [21]. There continues to be a range of reported single-session clearance rates from 71% to 100% among emerging literature [20, 22–24] thus we feel 88% is a reasonable yet conservative estimate.

Our decision to set the second intervention success rate to 94% was based on the recent systematic review and meta-analysis of 24 studies by Jin et al. [20] which demonstrated a complete stone clearance was 94% (95% CI, 90.2% to 97.5%). Buxbaum et al. [25] achieved similar complete clearance rates of 93% in their randomized-controlled study. As such, we used 94% as the rate of successful clearance by POC after any index procedure.



▶ **Fig. 1** Management model for treating difficult biliary stones. SOC, peroral cholangioscopy; ERCP, endoscopic retrograde cholangioscopy. M1 indicates a decision to use ERCP. M2 indicates a decision to use SOC. SOC-1 – SOC used as initial step. SOC-2 – SOC delayed until after ERCP failure. SOC-3 – SOC delayed until two failed ERCP attempts.

Success of ERCP mechanical lithotripsy was set as 63 % at first attempt, and 68 % at second intervention to reflect overall clearance rates [15, 20, 26, 27]. These success rates are derived from literature based on biliary stones that have been defined "difficult" after at least one failed procedure. As such, they are not indicative of the true ERCP success rate for undifferentiated common bile duct (CBD) stones, rather, they reflect outcomes for patients who can be predetermined to have "difficult" CBD stones based on clinical and imaging correlates.

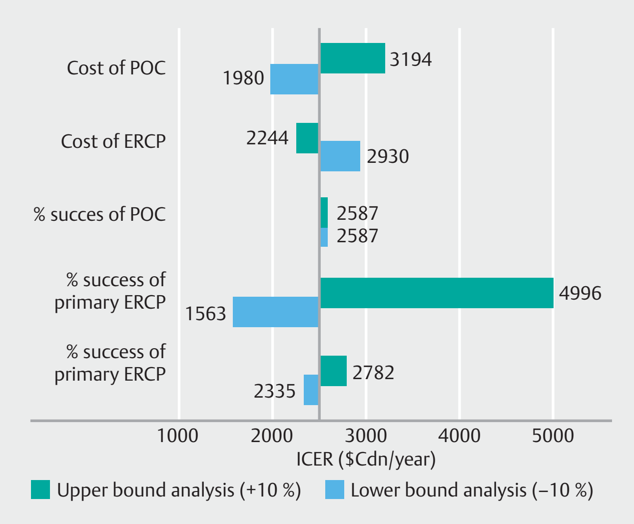
In general, cholangioscopy is seen as safe, but studies have shown a higher rate of AEs compared to ERCP based therapies – including cholangitis, pancreatitis, and hemobilia. SOC has a historically accepted AE rate of 7 % compared to 2.9 % in ERCP, and a significantly higher rate of cholangitis compared to ERCP (1 % vs. 0.2 %, respectively) [28, 29]. However, recent works by Angsuwatcharakon et al. [22] found the rate of AEs was not significantly different between the two groups (13 % in the ERCP group vs. 6 % in the SOC group, *P* = 0.76). In the same study, the median length of hospitalization was 1 day after significant AEs. In our study, we assigned SOC and ERCP procedures respectively a 1 % and 0.2 % rate of significant complications requiring one night of hospitalization. The aggregate number of SOC and ERCP procedures in each trial arm were analyzed with these rates and the resultant quantity of procedures were used to tally the added cost of complications, irrespective of the order of procedures.

For costs, we adopted the perspective of a tertiary publicly funded center (▶ **Table 1**). The cost of each procedure was calculated using a micro-costing approach i. e. multiplying the number of resources used during the procedure by unit costs. Unit costs, procedure durations, length of hospital stay, and resource consumption were derived from one Canadian hospital: Vancouver General Hospital (VGH). Equipment costs for POC were provided by the Endoscopy purchasing department of VGH for Spyglass (Boston Scientific Inc., Marlborough, Massachusetts, United States). Hospitalization costs for each endo-

▶ **Table 1** Cost data used in the model.

Resource	Unit cost ($ CAD)	Consumption of resources	
		ERCP	**SOC-EHL**
Hospital staff & stay			
RN pre-op	43.24 /h	11 min	11 min
RN intra-op	43.24 /h	47 min	47 min
RN post-op	43.24 /h	16 min	16 min
Tech intra-op	37.68 /h	47 min	47 min
Porter/ward aid	21.25 /h	20.5 min	20.5 min
SPD technician	22.70 /h	80 min	80 min
Booking clerk/admitting clerk	21.25 /h	31 min	31 min
HR chart management	18.16 /h	20 min	20 min
HR transcription	27.38 /h	12 min	12 min
HR abstracting + coding	32.41 /h	15 min	15 min
Nursing relief	20 % of totals	–	–
Staff benefits	24.9 % of totals	–	–
Leadership cost	5 % of totals	–	–
Hospital bed	3700 /night	–	–
Single-use consumables			
Basic ERCP prep supplies	170.23	1.0	1.0
Sphinctertome	218.13	1.0	1.0
Wires + guidewires	93.55	1.2	1.2
Stent delivery system[1]	150.00	1.0	1.0
Plastic Stent[1]	69.44	1.0	1.0
Rat tooth stent retriever[1]	45.01	1.0	1.0
Basket	250.52	1.0	0
CRE balloon	120.62	1.0	0
Dilation balloon	151.19	1.0	0
Balloon inflation kit	75.00	1.0	0
50cc OMNI dye	9.75	1.0	0
SpyGlass catheter	1695	0	1.0
EHL probe	395	0	1.0
Equipment repairs/case	16.42	1.0	1.0
Infrastructure + OH/case	15 % of totals	–	–
Procedure			
ERCP – Stone extraction	526.12	1.0	1.0
Visit – office, Gastroenterology	62.25	0.5	0.5
Visit – hospital, Gastroenterology	40.65	0.5	0.5
Anesthesia for ERCP/SOC	100.25	1.0	1.0
Anesthesia consultation	119.56	1.0	1.0
TOTAL		**$ 3592**	**$ 4494**

HR, human resources; OH, overhead; ERCP, endoscopic retrograde cholangioscopy; SOC, single-operator peroral cholangioscopy.
[1] The costs of stenting equipment and future stent removal were only included in calculating the cost of failed procedures.



▶ **Fig. 2** Tornado Diagram: incremental cost-effectiveness ratio (ICER) (SOC-3 vs SOC-2). Baseline model ICER is set at $ 2500/case. Secondary ERCP refers to ERCP procedures after an already failed ERCP ± SOC-EHL. Cost of ERCP and cost of SOC refer to the equipment costs.

scopic day procedure were calculated by taking the mean length of stay of the procedure (in hours) and multiplying it by the unit cost per day in a general medical ward. Physician fees and hospital bed overnight costs are publicly available and standardized across the province in a single-payer healthcare system. Costs for the cholangioscopy and lithotripsy generators were not included since they are one-time purchases and are required in all pathways. All costs were expressed in $ CAD 2018 (▶ **Table 1**).

Sensitivity analysis

One-way deterministic sensitivity analysis was performed on five variables of the model (▶ **Fig. 2**). The value of each parameter was varied by ± 10 %, while all other input variables remained unchanged. The parameters used for sensitivity analysis were: percentage of ERCP mechanical lithotripsy success at first procedure; percentage of ERCP mechanical lithotripsy success at second procedure; percentage of SOC success; cost of ERCP; cost of SOC. The models were developed in compliance with the principles of good practice for pharmacoeconomic analyses, from the International Society for Pharmacoeconomics and Outcomes Research [30].

Results

To run the model, a hypothetical cohort of 200 patients with suspected difficult biliary stones was considered. SOC-1 and SOC-2 pathways were clinically equally effective, achieving rates of stone clearance ranging from 96.3 % to 97.57 %, respectively. SOC-3 demonstrated an 88.5 % rate of stone clearance. The associated costs and procedure numbers were $ 851,457 (231 procedures) for SOC-1, $ 816,584 (278 procedures) for SOC-2, and $ 800,936 (297 procedures) for SOC-3. The strategy of SOC-1 was more expensive but represented the highest measure of effectiveness among the three options. However, upon assessment with cost-effectiveness ratios, SOC-2 was found to be economically dominant (▶ **Table 2**).

The deterministic sensitivity analysis is shown in ▶ **Table 3** and demonstrates that if the clearance rate during repeat-ERCP rises by 10 %, or if SOC clearance falls by 10 %, SOC-3 becomes optimal. A tornado diagram of the deterministic sensitivity analysis is shown in ▶ **Fig. 2**. It confirms the model trend, showing how, for nearly all tested scenarios, SOC-2 was superior to SOC-3. Furthermore, the sensitivity analysis indicates that the results are least sensitive to variation in SOC effectiveness as an index procedure and to variation in procedural cost.

Discussion

Currently, there exist no clear indications for SOC-guided lithotripsy, but rather SOC is recommended for "difficult" CBD stones. In this work, as in many others, the definition of "difficult" stones includes a heterogeneous grouping of very different clinical situations. The inclusion criteria of several studies on SOC-guided lithotripsy have suggested situations in which SOC-guided lithotripsy should be actively considered: stone size > 20 mm, multiple stones > 10 mm, stones proximal to a stricture, stones in difficult-to-access locations (cystic duct or intrahepatic duct), impacted stones in the bile or cystic duct, lumen-occupying stone casts, and at least two failed attempts of stone clearance using conventional means [21]. These indications are dependent on local availability and experience.

Most physicians and healthcare centers advocate ERCP for initial treatment of patients with difficult choledocholithiasis.

▶ **Table 2** Results of economic analysis.

Strategy	Gross Cost	Cost per case	Incremental Cost	Effectiveness	Incremental Effectiveness	Cost-Effectiveness Ratio	Incremental Cost-Effective Ratio
SOC-3	800,936	2697		0.885		3047	
SOC-2	816,584	2933	236	0.978	0.093	2998	2537
SOC-1	851,457	3679	982	0.963	0.078	3820	12590

SOC, peroral cholangioscopy. All costs are expressed in 2018 $Cdn.
SOC-3 and SOC-2 are undominated. SOC-1 is absolutely dominated.
Effectiveness is described as procedural success rate.

▶ **Table 3** Findings underscored by one-way sensitivity analysis.

Variable	Baseline value	+ 10 % value		–10 % value	
Cost of SOC-EHL equipment	2987	3286	POC-2 is optimal	2688	POC-2 is dominant
Cost of ERCP equipment	1705	1875	POC-2 is dominant	1534	POC-2 is optimal
Success rate of SOC-EHL	0.88	0.98	POC-2 is dominant	0.78	POC-3 is dominant
Success rate of conventional ERCP after first failure of ERCP ± SOC	0.69	0.79	POC-3 is optimal	0.59	POC-2 is dominant
Success rate of initial conventional ERCP	0.63	0.73	POC-2 is optimal	0.53	POC-2 is optimal

SOC, peroral cholangioscopy. All costs are expressed in 2018 $Cdn.
The use of the term dominant is reserved for scenarios in which SOC-2 or –3's Incremental Cost-Effectiveness Ratio (ICER) is less expensive than its baseline model's ICER.

This is in part due to historic physician experience, well-known high stone dissolution rates post-ERCP stent insertion, and – most significantly – presumed increased cost of cholangioscopy [26]. Despite this presumption, several analyses – including our own – support early use of cholangioscopy in scenarios where a stone is likely to be difficult to remove with traditional ERCP methods.

Most recently, Alrahji et al. demonstrated that early introduction of SOC-EHL is the least expensive strategy with a surgery-free stone clearance that clinically approximates its later introduction following repeated conventional ERCP attempts [15]. This study analyzed the impact of introducing SOC intraprocedurally during primary ERCP failure. The clinical and economic consequences of exclusive first-line SOC, however, has not been elucidated. Our study is the first analysis to specifically study the cost-effectiveness of implementing SOC-EHL prior to any traditional ERCP attempts in patients with suspected difficult biliary stones. We found that employing SOC-EHL as the second-line procedure was effective in saving annual hospital costs. Our previous hypothesis of a dominant first-line SOC-EHL strategy was ineffective in minimizing hospital costs despite excellent clinical effectiveness. The economic analysis in this study was conducted using data from a large Canadian hospital, but the underlying trade-off comparing the cost of multiple procedures versus a more effective, more expensive treatment is applicable broadly assuming an adequate procedure number to generate sufficient use of the equipment.

A previous study by Deprez et al. [14] demonstrated that laser lithotripsy reduced overall costs by 11 % when compared with mechanical lithotripsy because of the higher stone clearance rate, which resulted in a lower surgery rate. However, the analyses were based on the success rates of two different studies without direct comparison between laser and mechanical lithotripsy. Our study expands on the work by Deprez et al. by directly comparing different circumstances and variable costs that might contribute to different outcomes. These features, in conjunction with our conservative financial approach to the efficacy of SOC, make our study widely applicable to other countries.

Alternatively to SOC, the 2019 guidelines of the European Society of Gastrointestinal Endoscopy (ESGE) [31] recommend endoscopic sphincterotomy (ES) and endoscopic papillary large balloon dilatation (EPLBD) as the new standard techniques for the removal of large CBDs. EPLBD was first described by Ersoz et al. [32] in 2003 and several studies since then on difficult BDSs have demonstrated the efficacy and safety of EPLBD. Additionally, ES + EPLBD reduces the need for ERCP by 30 % to 50 % compared with ES alone [33, 34]. However, there are unique advantages and disadvantages to consider when deciding which procedure to perform. SOC-guided lithotripsy has been reported to have a better stone clearance rate than conventional EPLBD, as concluded by Buxbaum et al. [25]. Moreover, there is no significant difference in AEs with the incorporation of EPLBD. Often, SOC involves ES (if not already done during a previous ERCP) followed by papillary-dilation using a small balloon (< 12 mm). Therefore, while SOC-guided lithotripsy is the more effective and safer treatment option and should be considered when available, we recommend ERCP with EPLBD in hospital settings without SOC facilities.

With regard to biliary diseases, there is a small yet growing public health interest in the economic effects of CBD stones by a higher use of healthcare services. Our economic evaluation of the optimal timing of SOC for difficult CBD stones can help decision-makers to prioritize healthcare interventions or policies in order to achieve not only improvements in health, but also ensuring the financial sustainability of public health systems.

We acknowledge some limitations to this study. The first set of limitations relate to the assumption about which patients qualify as having difficult biliary stones. By definition, a difficult stone is one that is unyielding to traditional ERCP techniques. Thus, a patient naïve to endoscopic intervention cannot be classified as "difficult," and therefore, SOC-EHL traditionally would not be indicated until a trial of ERCP is attempted. Instead, we offer the hypothetical strategy of risk-stratifying stones based on imaging findings to predict and presumptively treat stones that are likely to be difficult. The difference in approach is subtle, given the significant overlap in equipment required for traditional ERCP compared to SOC. However, we feel it is an important question, given the not insignificant cost of multiple tools used for difficult stones (baskets, dilation balloons, multiple extraction balloons) and it also reduces the significant barrier of increased procedure time when adding SOC-EHL to a failed traditional ERCP attempt compared to a planned SOC-first strategy. Significant predictive factors for difficult-to-treat stones include strictures distal to the stone, CBD diameter >15 mm, multiple filling defects, febrile status, and age>65 years [7–10]. In real practice, not all stones presenting with these clinical characteristics are difficult-to-treat, and traditional ERCP is sufficient in this subset population. However, the risk of complications remains elevated in these types of stone presentations [4] and the financial impact from non-hospitalizing complications induced by traditional ERCP that are avoidable with SOC-EHL remains to be further elaborated. Similarly, SOC is shown to have similar AE profile than ERCP [28, 29], rendering ERCP an option that yields lower success rates for the same risk profile.

Another set of limitations is the lack of controlled data, thus placing our assumptions at risk for miscalculating clinical success. For instance, while up to 20 % of ERCP-treated patients suffer stone recurrence [8] we omitted this to give our study a more consistent and adoptable approach for different institutions. Had we included this fact, the advantages of SOC-EHL would also be greater than our analysis determined.

Finally, some of the studies from which we derived our probability statistics were strictly observational and lacked controlled data. Sensitivity analysis was performed in attempt to minimize the effects of these shortcomings. Where applicable, we used a micro-costing approach to obtain a more precise assessment of the economic costs and resources used per intervention [35].

Conclusions

In conclusion, our cost-effectiveness analysis suggests that SOC is a financially feasible modality for second-line intervention in the clearance of difficult biliary stones. This treatment strategy reduces overall procedures as well as hospital expenditures, while clinically approximating its current placement as a common third-line therapy following failures of conventional ERCP. These findings ideally require prospective randomized trials to be verified.

Competing interests

The authors declare that they have no conflict of interest.

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