A Cost-Effectiveness Analysis of Early vs Late Reconstruction of Iatrogenic Bile Duct Injuries

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BACKGROUND: Controversy exists regarding the optimal timing of repair after iatrogenic bile duct injuries (BDI). Several studies advocate late repair (≥6 weeks after injury) with mandatory drainage and resolution of inflammation. Others indicate that early repair (<6 weeks after injury) produces comparable or superior clinical outcomes. Additionally, although most studies have reported inferior outcomes with primary surgeon repair, this practice continues. With disparate published recommendations and rising health care costs, decision analysis was used to examine the cost-effectiveness of BDI repair.

STUDY DESIGN: A Markov model was developed to evaluate primary surgeon repair (PSR), late repair by a hepatobiliary surgeon (LHBS), and early repair by a hepatobiliary surgeon (EHBS). Baseline values and ranges were collected from the literature. Sensitivity analyses were conducted to test the strength of the model and variability of parameters.

RESULTS: The model demonstrated that EHBS was associated with lower costs, earlier return to normal activity, and better quality of life. Specifically, 1 year after repair, PSR yielded 0.53 quality adjusted life years (QALYs) ($120,000/QALY) and LHBS yielded 0.74 QALYs ($74,000/QALY); EHBS yielded 0.82 QALYs ($48,000/QALY). Sensitivity analyses supported these findings at clinically meaningful probabilities.

CONCLUSIONS: This cost-effectiveness model demonstrates that early repair by a hepatobiliary surgeon is the superior strategy for the treatment of BDI in properly selected patients. Although there is little clinical difference between early and late repair, there is a great difference in cost and quality of life. Ideally, costs and quality of life should be considered in decisions regarding strategies of repair of injured bile ducts. (J Am Coll Surg 2012;214:919–927. © 2012 by the American College of Surgeons)

Calculous biliary disease is one of the most common gastrointestinal health problems in the United States today. The treatment of choice for this condition is laparoscopic cholecystectomy, and nearly 800,000 procedures are performed annually. While laparoscopic cholecystectomy is associated with less overall morbidity and decreased length of stay compared with open cholecystectomy, the rate of iatrogenic bile duct injury (BDI) is nearly double that with the open procedure. BDI in the era of laparoscopic cholecystectomy is reported to be between 0.4% and 0.6% compared with between 0.1% and 0.2% for open cholecystectomy.

Bile duct injury is associated with morbidity and costs to the patient, the medical community, and society if not addressed in an effective and timely manner. Some studies have shown a long-term decrement in health-related quality of life (HRQOL) in patients who suffer BDI, even after repair. Additionally, these injuries are often associated with high rates of litigation and jury awards ranging from $250,000 to $500,000.
Abbreviations and Acronyms
BDI = bile duct injury
EHBS = early repair (< 6 weeks after injury) by hepatobiliary surgeon
HBS = hepatobiliary surgeon
LHBS = late repair (≥ 6 weeks after injury) by hepatobiliary surgeon
PSR = primary surgeon repair
QALY = quality adjusted life year

There is considerable debate in the literature regarding the optimum setting for and timing of the repair of these injuries. Although it is clear that these injuries are better cared for by trained hepatobiliary surgeons, there is no consensus on the optimal timing of BDI repair. Some programs advocate early repair by hepatobiliary surgeons (less than 6 weeks after injury); others advocate late repair by hepatobiliary surgeons (≥6 weeks after the injury). Additionally, several studies have demonstrated poor outcomes with primary surgeon repair of BDI, but the practice continues.

The objective of this study was to evaluate the cost-effectiveness of repair by a primary nonhepatobiliary surgeon, late repair by a hepatobiliary surgeon, and early repair by a hepatobiliary surgeon. By modeling the outcomes of these 3 treatment strategies, we can better understand the determinants of costs and health-related quality of life associated with iatrogenic bile duct injury and subsequent repair.

METHODS

Markov decision model

The Markov decision analytic technique is used to model outcomes for groups of hypothetical patients and analyze time, value, and costs of patients in each state of health. These hypothetical patients are assigned to various health states, and outcomes for each patient group are simulated over prespecified time intervals or cycles. Hypothetical patients can change health states when the model is cycled. An “absorbing state” is a state the patient cannot leave once it is entered. The most common absorbing state is death. The model is run either until all hypothetical patients have reached an “absorbing state” or over a dictated time horizon (such as 1 year in our model). When the time horizon is limited, the model does not run until all patients reach an absorbing state, but instead stops when the predetermined time is complete. A comprehensive literature review is used to determine the likelihood that in a cycle of the model, a patient will either remain in his or her current state or transition to a new health state. A value, most commonly in units of quality-adjusted life years (QALYs), is assigned to a patient within a health state. These values accumulate over each cycle. At the completion of all the cycles, the cost for each patient is calculated. The costs per value (QALY) of each health state can be computed and compared with the value of the other treatment strategies.

We constructed a Markov-based decision analytic model to simulate outcomes for patients undergoing different strategies of repair after BDI: primary repair by nonhepatobiliary surgeon (PSR), late repair by hepatobiliary surgeon (LHBS), or early repair by hepatobiliary surgeon (EHBS). To construct and run the model we used TreeAge Pro 2009 (TreeAge Software, Inc), a software specifically designed to create and evaluate decision trees and models. This model was created with methods similar to those used previously by our group. The cost-effectiveness analysis was performed and reported according to the Panel on Cost-Effectiveness in Health and Medicine guidelines.

Health states

The Markov decision model is shown in Figure 1. As described earlier, patients initially underwent primary surgeon repair, late repair by a hepatobiliary surgeon, or early repair by a hepatobiliary surgeon. In each arm of the model, after operative repair the hypothetical patient was subjected to one of the following scenarios based on predetermined probabilities from the literature: death, liver transplantation, uneventful recovery, perioperative complications requiring reoperation, or perioperative complications requiring radiologic or endoscopic intervention. The modeled time horizon was 1 year.

Model assumptions

Several assumptions were made in designing the model in order to create a clinically meaningful yet cost-conscious model. The base case patient was defined to be a 42-year-old woman employed outside of the home, which describes the typical patient undergoing laparoscopic cholecystectomy. The time period considered for return to work started after the first operative repair in PSR and EHBS and after referral and onset of treatment in LHBS. In these models, injury severity was assumed to be at least a Strasberg E1 type injury. Strasberg’s classification of bile duct injuries can be separated into types amenable to endoscopic vs surgical repair. Types A to D include injuries to tangential ducts that may be amenable to interventional radiology or endoscopic repair and strictures that often do not present until months after injury. Type E bile duct injuries involve complete transaction or stricture of the common bile duct, and therefore require operative repair. We assumed that patients did not have septic physiology and therefore were candidates for any of the 3 approaches of surgical repair. All operative
repairs were Roux-en-Y hepaticojejunostomies. The interventional or endoscopic procedures were percutaneous transhepatic cholangiocatheter placement, percutaneous drain placement, and endoscopic retrograde cholangiography with stent placement. All modeled outcomes occurred during the first year after the operative repair.

**Probability and cost data**

Both probabilities and rates for the baseline analysis and the ranges of these values for all sensitivity analyses are reported in Table 1. To determine these values we performed a systematic review of the MEDLINE/PubMed database for all reports on BDI from 1995 to 2011, especially reviews and meta-analyses. Table 1 also presents all cost estimates and ranges. Published data on specific institutional costs, the Medicare database, or similar databases were used for the cost analysis. Cost data were also obtained from published studies identified by our systematic review of the literature. All monetary values were adjusted for inflation to 2010 US dollars using the Consumer Price Index for medical care (US Bureau of Labor Statistics). To account for the cost of spending money now vs in the future, health benefits and future costs were discounted at a constant rate of 3%.12

All costs were approached from a societal perspective.19 Modeling from the societal or patient perspective allows for comparisons with other similar studies often focused on patient outcomes and costs to society. Both positive and negative cost changes resulting from an intervention into the system were considered. Furthermore, instead of interpreting the findings for a particular patient population, our finding can be interpreted for the public interest.
The effectiveness of different repair strategies was measured in terms of QALYs. This measure of health value incorporates both quality of life and time into a composite statistic that allows for comparison between health interventions. Quality of life is determined by health utilities reported in the literature, which usually range from 0 (utility of death) to 1 (utility of perfect health). Utilities represent the reported health preferences of groups of patients who are either presently ill or may be ill in the future.20 (Table 1).

Sensitivity analysis
One- and 2-way sensitivity analyses were performed to test the model conclusions based on variations in the range of values and costs reported in the literature. The ranges used for these analyses are described in Table 1. Multi-way prob-

### Table 2. Costs and Cost-Effectiveness of Strategies of Bile Duct Injury Repair

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost, $</th>
<th>Incremental cost, $</th>
<th>Effectiveness, QALY</th>
<th>Incremental effectiveness, QALY</th>
<th>Cost/effectiveness, $/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early HBS</td>
<td>39,000</td>
<td>---</td>
<td>0.82</td>
<td>---</td>
<td>47,600</td>
</tr>
<tr>
<td>Late HBS</td>
<td>55,000</td>
<td>16,000</td>
<td>0.74</td>
<td>-0.08</td>
<td>74,300</td>
</tr>
<tr>
<td>Primary surgeon</td>
<td>64,000</td>
<td>9,000</td>
<td>0.53</td>
<td>-0.21</td>
<td>119,600</td>
</tr>
</tbody>
</table>

Early HBS, early repair (<6 weeks after injury) by hepatobiliary surgeon; Late HBS, late repair (≥6 weeks after injury) by hepatobiliary surgeon; OLT, orthotopic liver transplantation; PSR, primary surgeon repair; QALY, quality adjusted life year.
abiistic sensitivity analyses using Monte Carlo methods, which change all probabilities and costs within the model simultaneously, provided additional tests of model sensitivity to changes in model parameters.

RESULTS

Base case analysis
The previously described model assumptions and the base case probabilities and costs from Table 1 were used in the base-case analysis. This analysis evaluated the approach to BDI repair in a typical patient undergoing laparoscopic cholecystectomy complicated by an iatrogenic BDI. When the model is run, the program simulates the transition of hypothetical patients through the model. The results of the reference case analysis in the Markov model are essentially the averages associated with the different outcomes of these hypothetical patients, and are listed in Table 2 and depicted graphically in Figure 2. When thousands of hypothetical patients are run through the model using a 1-year time horizon and the base case probabilities and costs described in Table 1, patients treated with EHBS accrued an average of 0.82 QALYs over the year. LHBS patients accrued 0.74 QALYs and PSR patients accrued 0.53 QALYs. PSR resulted in costs of $64,000 to achieve 0.53 QALYs, or approximately $119,600/QALY. Late hepatobiliary surgeon repair resulted in costs of $55,000 to achieve 0.74 QALYs, or approximately $74,300/QALY. EHBS repair resulted in costs of $39,000 to achieve 0.82 QALYs, or approximately $47,600/QALY. Therefore, the EHBS treatment strategy arm was superior to, and dominated, both PSR and LHBS.

Sensitivity analysis
Realizing that the baseline probabilities and costs used in this model vary between centers performing these procedures, we performed 1-way sensitivity analyses to test the validity of the conclusions over a range of probabilities and costs. First we varied the probability of the need for reoperation after EHBS. Late hepatobiliary surgeon repair never became dominant (the better choice) over a clinically meaningful range of reoperative rates for EHBS (Fig. 3). Additionally, LHBS never became the dominant strategy over a clinically meaningful range of probabilities of interventional radiology or endoscopic reinterventions after EHBS (Fig. 4). Next, the probability of reoperation after PSR was varied. Repair by the primary surgeon would become the least costly treatment approach only if the rate of reoperation after PSR was below a threshold value of 14%. In the 2-way sensitivity analysis (Fig. 5), the number of days until returning to work after LHBS and the probability of reoperation after EHBS was varied simultaneously. In doing so, EHBS remains the dominant strategy for a wide range of values and LHBS only becomes dominant at low numbers of days till return to work for LHBS or very high rates of reoperation for EHBS.
DISCUSSION

Iatrogenic BDI during laparoscopic cholecystectomy is a catastrophic event associated with a great deal of cost to the patient, the hospital, and society. Even after successful repair, BDI patients continue to have diminished health-related quality of life and increased morbidity and mortality. Although there are no randomized controlled trials studying early vs late repair (and are unlikely in the future), there is an abundance of literature detailing the outcomes of BDI and the different strategies of repair, yet the optimal timing of repair after BDI has not been conclusively determined.

In a series of 175 patients treated with surgical biliary drainage after BDI between 1990 and 2003, Sicklick and colleagues noted that the timing of an operation for bile duct repair (early repair less than 1 month after injury) was not associated with postoperative complications or postoperative length of stay. In another series of 307 initial repairs of BDIs after laparoscopic cholecystectomy, Stewart and Way noted that timing of the repair was not associated with the success of the first repair. Resolution of intra-abdominal infection, use of correct surgical technique, complete cholangiography, and repair by an experienced hepatobiliary surgeon were associated with success. Conversely, Sahajpal and colleagues recommend either immediate repair (0 to 72 hours) or late repair (greater than 6 weeks after injury) due to significantly higher morbidity rates in patients repaired after 72 hours but before 6 weeks.

Although the timing of BDI repair varies on a case-by-case basis, general acceptance of late repair for all patients should be reconsidered. Additionally, costs and patient quality of life should be considered when determining timing of BDI repair.

We used a cost-effectiveness analysis to determine the most prudent financial strategy for BDI repair. We demonstrated that EHBS repair is the most cost-effective strategy, costing $47,600 per QALY gained. In our model, EHBS repair costs substantially less than the other repair strategies ($26,700/QALY less than LHBS and $72,000/QALY less than PSR). When the values were ranged over those reported in the published literature for the sensitivity analyses, the model remained robust. From these analyses, we concluded that EHBS is the most cost-effective strategy for BDI repair from the societal and patient’s perspective.

In our model, lost wages from missed days of work were the primary determinants of differences in cost. Our results are consistent with the cost analysis of Andersson and associates, in which the loss of production and subsequent lost wages was the primary cause of increased costs. In an analysis of hospital charges for 49 BDI patients, Savader and colleagues reported that the overall costs associated with the repair of iatrogenic BDIs were 4.5 to 26 times higher than costs of uncomplicated cholecystectomies. Fac-
Costs associated with increased costs were inpatient hospitalization days and outpatient care days, with significantly lower costs for BDI recognized intraoperatively. It is not surprising that intraoperative BDI recognition decreases costs, especially given our findings of decreased costs for EHBP repair, but recognition of BDI during laparoscopic cholecystectomy only occurs approximately 30% of the time. Furthermore, encouraging identification of BDI in the operating room without increasing PSR rates may be difficult because primary surgeons who identify the injury at the time of operation may be inclined to attempt repair.

Repair by the surgeon responsible for the iatrogenic biliary injury is often associated with poor outcomes. Success by the primary surgeon has been found in numerous series to be less than 20%. Flum and colleagues found an 11% increase in the risk of mortality after a biliary injury if the repair was done by the primary surgeon. Fischer and colleagues noted a delayed referral and an increased number of pre-referral procedures significantly increased the number of postoperative complications after definitive repair. Similar results were also noted by de Reuver and associates. In 1995, Stewart and Way noted a statistically increased length of hospital stay after primary surgeon repair compared with experienced hepatobiliary surgeon repair. Despite documentation of inferior outcomes, primary surgeon repair continues.

As noted in our model, there is significantly increased cost associated with primary surgeon repair, driven by the low success and high complication rates. Only until the complication rate after this strategy decreases below 20% (markedly lower than the nearly 80% reported in modern reports) will this strategy be considered cost-effective. The issues of familiarity with repair procedures and availability of skilled endoscopists and interventional radiologists may further limit this procedure to tertiary care centers. Silva and coworkers, from Queen Elizabeth Hospital in the United Kingdom, have implemented a travel consultation service to be available to surgeons regionally in an effort to bypass the issues of primary surgeon repair. Although this group demonstrated positive outcomes, costs of such a service remain in question. Cost-effectiveness models, such as the one presented here, would provide an excellent framework through which the generalizability of such programs may be evaluated.

Ultimately, patients with these complex injuries require individualized approaches and multidisciplinary management. This model identifies the significant determinants of costs within several management strategies. The driving force behind the decreased costs of the EHBS was the increased length of time required for the patient to return to work after the other strategies of repair. Furthermore, the costs of LHBS were determined by endoscopic and interventional radiologic procedures. Costs for PSR were also driven by reoperation rates. The most important factor contributing to the cost-effectiveness of EHBS was the ability to return the patient to a relatively normal life with as few interventions as possible. Given the rarity of this complication and relatively small cost when compared with national health care spending, surgeons should not look primarily to cost to determine an appropriate operative plan for BDI patients. Instead, this model can be used as a tool to guide individual case decision-making, where accounting for both costs and quality of life would benefit the patient.

A limitation of this study is that BDI repair is distilled into a very basic model. In this model we used published data and meta-analyses to approximate the most likely clinical scenarios in these procedures. Any publication bias that exists in the peer-reviewed literature on this topic would therefore be reflected in our results. Also, while some of the studies from which we derived our probabilities evaluated differences in injury characteristics, such as Strasberg level or concomitant arterial injury, we chose to make a more general model that included only Strasberg E1 or greater injuries that would require surgical repair. Other types of bile duct injuries have been shown to alter procedural outcomes and require an alternative approach than the injuries discussed in our model. Also, a major assumption of this model was that all patients had good source control and were not in a proinflammatory state, which would allow a choice of early vs late repair. Obviously, patients with septic physiology would require a delay in repair.

CONCLUSIONS

The strength of the decision analytic technique is that the cost-effectiveness models can be adapted to a wide range of clinical scenarios and patient characteristics. The models can be constructed to account for as many variables and outcomes of interest as there are data to support. Our cost-effectiveness model helps to elucidate the factors that contribute to the determination of the optimal economic strategy of BDI repair. In doing so, we have provided data that can allow centers to further tailor their practice to perform the most cost-conscious procedure for these injuries. Additionally, in an era of increasing health care costs, this model allows policy makers to further understand the costs associated with bile duct injuries and helps to identify policies and procedures that are most likely to both optimize patient care and minimize costs.
Author Contributions

Study conception and design: Dageforde, Landman, Feurer, Poulose, Pinson, Moore
Acquisition of data: Dageforde, Landman, Moore
Analysis and interpretation of data: Dageforde, Landman, Feurer, Poulose, Pinson, Moore
Drafting of manuscript: Dageforde, Landman, Moore

Critical revision: Dageforde, Landman, Feurer, Poulose, Pinson, Moore

REFERENCES

17. Landman MP, Feurer ID, Pinson CW, Moore DE. Which is more cost-effective under the MELD system: primary liver transplantation, or salvage transplantation after hepatic resection or after loco-regional therapy for hepatocellular carcinoma within Milan criteria? HPB 2011;13:785–791.