

Management of Biliary Tract Disease During Pregnancy

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The term “evidence-based medicine” was first coined by Sackett and colleagues¹ as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.” The key to practicing evidence-based medicine is applying the best current knowledge to decisions in individual patients. Medical knowledge is continually and rapidly expanding and it is impossible for an individual clinician to read all the medical literature. For clinicians to practice evidence-based medicine, they must have the skills to read and interpret the medical literature so that they can determine the validity, reliability, credibility and utility of individual articles. These skills are known as critical appraisal skills. Generally, critical appraisal requires that the clinician have some knowledge of biostatistics, clinical epidemiology, decision analysis, and economics as well as clinical knowledge.

The Canadian Association of General Surgeons and the American College of Surgeons jointly sponsor a program entitled “Evidence-Based Reviews in Surgery (EBRS),” supported by an educational grant from Ethicon Inc. and Ethicon Endo Surgery Inc. The primary objective of this initiative is to help practicing surgeons improve their critical appraisal skills. During the academic year, eight clinical articles are chosen for review and discussion. They are selected not only for their clinical relevance to general surgeons, but also because they cover a spectrum of issues important to surgeons; for example, causation or risk factors for disease, natural history or prognosis of disease, how

to quantify disease (measurement issues), diagnostic tests and the diagnosis of disease, and the effectiveness of treatment. Both methodologic and clinical reviews of the article are performed by experts in the relevant areas and posted on the EBRS website. A listserv discussion is held where participants can discuss the monthly article. Fellows and candidates of the College can access Evidence-Based Reviews in Surgery through the American College of Surgeons website (www.facs.org). All journal articles and reviews are available electronically through the website. Currently we have a library of 50 articles and reviews which can be accessed at any time. Each October, a new set of articles will be available each month until May. Surgeons who participate in the current (modules) packages can receive CME credits by completing a series of multiple choice questions. Additional information about EBRS is on the ACS website or by email to the administrator, Marg McKenzie at mmckenzie@mtsinai.on.ca.

In addition to making the reviews available through the ACS and CAGS websites, four of the reviews are published in condensed versions in the *Canadian Journal of Surgery* and the other four will be published in the *Journal of the American College of Surgeons* each year.

REFERENCE

1. Evidence Based Medicine Working Group. Evidence-based medicine. *JAMA* 1992;268:2420–2425.

SELECTED ARTICLE

Management of biliary tract disease during pregnancy: a decision analysis

Jelin EB, Smink DS, Vernon AH, Brooks DC. *Surg Endosc* 2008;22:54–60

ABSTRACT

Question: What is the preferred management (nonoperative management vs. laparoscopic cholecystectomy) for patients presenting with biliary tract disease (defined as

biliary colic, acute cholecystitis, or gallstone pancreatitis) in the first or second trimester of pregnancy?

Base Case: Pregnant woman in the first or second trimester presenting with biliary tract disease.

Treatment Alternatives: Nonoperative management (NM) or laparoscopic cholecystectomy (LC).

Outcomes considered: Fetal death, healthy birth, recovery without symptoms, recurrence of biliary tract symptom and status post cholecystectomy. Outcomes are expressed in quality pregnancy weeks (QPWs); one

QPW is the utility of a normal healthy week of pregnancy.

Sources for Estimating Probabilities and Utilities: The probabilities and utilities for fetal outcomes were derived from the literature, while utilities for disease and operative states were estimated in consultation with obstetricians.

Results: Fetal death rate following LC for biliary tract disease was 2.2% and following NM was 7%. Relapse rates were found to be trimester dependent and estimated to be 55%, 55% and 44% in first, second and third trimester respectively.

Sensitivity Analysis: One way sensitivity analyses were performed on the variables. Fetal death rate for LC and NM; the relapse rate; and the emergent surgery rate for NM. The findings were sensitive only to fetal death rates following both LC and NM. The fetal death rate associated with LC was permitted to vary from 0% to 20%. The fetal death rate associated with LC would have to rise to four times (8.5%) our literature-derived rate of 2.5% and for NM the fetal death rate would have to fall to 2.1% to change the outcome.

Conclusion: Laparoscopic cholecystectomy is superior to nonoperative management for pregnant women presenting in the first and second trimester with biliary tract disease.

Commentary: In the study by Jelin et al, the clinical question being addressed is "What is the preferred management (nonoperative management versus laparoscopic cholecystectomy) for patients presenting with biliary tract disease (defined as biliary colic, acute cholecystitis or gallstone pancreatitis) in the first or second trimester of pregnancy?" The objective of the study however is not explicitly stated.

All the potential clinical strategies were included and compared in this decision analysis. However, although most cholecystectomies at the present time are performed laparoscopically, some might argue that open cholecystectomy should have been considered an option. In addition, stratifying the analysis based on presenting diagnosis may have significantly altered the conclusions. Specifically, patients with gallstone pancreatitis or acute cholecystitis may require different treatment algorithms than those patients with uncomplicated biliary colic.

When performing a decision analysis, it is important to consider what the clinically relevant outcomes from the procedure could be. For this analysis, the authors neglected to discuss (except for a brief mention in their limitations section) the issues of fetal birth defects that could be associated with an abdominal operation in the first trimester.

They chose to use binary outcomes (fetal death or healthy live birth), rather than choosing a more complex analysis that would have included other outcomes such as premature birth requiring neonatal intensive care, if so, the results of the decision analysis may have changed significantly had let to significantly different recommendations.

It is unclear whether the authors used an explicit and sensible process to identify, select and combine the evidence into probabilities for this decision tree analysis. For at least one probability, an average of the two reported rates was chosen. While the methodology used was standard and the MeSH terms used to identify the 277 cases were listed, how many articles were found and what inclusion and exclusion criteria were used were not reported. It appears they used only the reports for these 277 patients to determine all of the probabilities. Where there were no data available, they used expert opinion. The lack of description of the specific methodology would make it difficult to reproduce this analysis. The utilities were explicit as the authors chose to use a dichotomous outcome.

There were wide ranges in what turned out to be their most important variable, fetal death rates with non-operative management and laparoscopic cholecystectomy. The assumption was made also that patients presenting with different severities of biliary tract disease would all behave similarly, whereas this is likely not the case (patients with acute cholecystitis or gallstone pancreatitis likely have different outcomes than those with biliary colic). The authors acknowledge these shortcomings but state small numbers of patients reported precluded any further subgroup analyses. Both of these factors raise the level of uncertainty in this analysis.

This decision analysis showed an average gain of 4 weeks of healthy pregnancy (without any biliary tract symptoms) for those patients presenting in the first trimester and 2 weeks for those presenting in the second trimester who undergo laparoscopic cholecystectomy at their initial presentation. This led the authors to conclude "Laparoscopic cholecystectomy is superior to non-operative management for pregnant women presenting in the first or second trimester with biliary tract disease."

The evidence used in this analysis is poor. There are no randomized trials in this area (nor will there likely ever be). The 277 cases included in the analysis come from a variety of sources, all of which are retrospective, uncontrolled series or case reports. They clearly represent only a fraction of pregnant women who have undergone laparoscopic cholecystectomy. As well, many of the references are 20–30 years old; more recent series include patients accrued over a long period of time so these data may not be relevant now because of changes in obstetrical and perioperative surgical

care. The authors acknowledge this, but also state that these data are the only evidence available.

The uncertainty in the evidence could change the results as already noted. The authors performed a sensitivity analysis and found that only variation in the fetal mortality rates would change their recommendations. Realistically, the fetal mortality rates *could* vary to the extent expressed by the authors that would change the recommendation. The literature cited for this analysis in fact report fetal mortality rates for non-operative management ranging from 0 to 60%.

While the probability estimates in general fit many patients' clinical features, some of the assumptions made for this modeling (lumping all diagnoses together, allowing patients to enter the model at either 6 weeks or 19 weeks) could make the estimates "fit" less well. In addition, while patients would find the outcomes of this analysis to be important, they would also be interested in (and frequently ask about) other consequences such as birth defects.

The authors conclude "Laparoscopic cholecystectomy is superior to non-operative management for pregnant women presenting in the first or second trimester with biliary tract disease." The evidence presented, although slim does support this conclusion. However, the authors have neglected a potentially important aspect of the care of such patients; that is the potentially adverse effect of exposure to a general anesthetic in the first trimester on fetal outcome (including death). Also, because the authors chose to use dichotomous outcomes (birth or death), they have avoided a potentially important in between outcome, fetal morbidity including preterm labor and/or birth and the costs and complications associated with this. Finally the conclusions are limited by the quality of the available data. Unfortunately, a randomized controlled trial will never be done and unless there is a registry of such patients, even retrospective analyses will be limited to case reports and

single institution retrospective case series. Surgeons can use the results of this analysis to more objectively counsel their patients in a similar situation, and then together, with the information available and several options outlined choose the one that appears best for that individual patient.

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