Indications for Selected Medical and Surgical Procedures—A Literature Review and Ratings of Appropriateness

Cholecystectomy

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Rand

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PREFACE

The Rand/UCLA Health Services Utilization Study (HSUS), supported by the Commonwealth Fund, the John A. Hartford Foundation, the Health Care Financing Administration of the U.S. Department of Health and Human Services, the Pew Memorial Trust, and the Robert Wood Johnson Foundation, enlists the assistance of the medical profession in studying geographic differences in the use of medical and surgical procedures. The primary goal of the study is to discover the extent to which appropriateness of use of procedures is related to overall rates of use among different geographic areas. The study is designed to answer the following question: To what extent does greater inappropriate use of procedures in high-use areas explain geographic differences in rates of use?

To help answer this question, panels of physicians were assembled to discuss and rate the appropriateness of performing each of six procedures for a wide variety of clinically specific indications. These six procedures were: coronary angiography, coronary artery bypass graft surgery, cholecystectomy, diagnostic upper gastrointestinal endoscopy, colonoscopy, and carotid endarterectomy. To facilitate the process, a comprehensive review of the medical literature was conducted for each of the procedures and given to the panelists.

The six procedures are discussed in depth in the six volumes of the R-3204 series, which has the overall title *Indications for Selected Medical and Surgical Procedures—A Literature Review and Ratings of Appropriateness*. Each volume in the series contains a literature review, a comprehensive list of potential indications for the procedure, and appropriateness ratings.

To answer the study's primary question, a sample of medical records for patients receiving selected procedures will be reviewed in high-, average-, and low-use areas; the panels' appropriateness ratings will be used to assess the use of these procedures in each case; and, finally, appropriateness of use will be compared with overall rates of use among geographic areas.

PUBLICATIONS OF THE RAND/UCLA HEALTH SERVICES UTILIZATION STUDY

Brook, R. H., M. R. Chassin, A. Fink, J. Kosecoff, R. E. Park, and D. H. Solomon, "A Method for the Detailed Assessment of the Appropriateness of Medical Technologies," *International Journal of Technology Assessment in Health Care,* 1986; 2:53–63.

Brook, R. H., K. N. Lohr, M. R. Chassin, J. Kosecoff, A. Fink, and D. H. Solomon, "Geographic Variations in the Use of Services: Do They Have Any Clinical Significance?" *Health Affairs,* 1984; 3(4):63–73.

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Merrick, N. J., R. H. Brook, D. H. Solomon, and A. Fink, "Use of Carotid Endarterectomy in Five California Veterans Administration Medical Centers," *Journal of the American Medical Association* (forthcoming).

Merrick, N., A. Fink, R. E. Park, R. H. Brook, J. Kosecoff, M. R. Chassin, and D. H. Solomon, "Derivation of Clinical Indications for Carotid Endarterectomy by an Expert Panel," *American Journal of Public Health* (forthcoming).

Park, R. E., A. Fink, R. H. Brook, D. H. Solomon, M. R. Chassin, K. Kahn, N. Merrick, and J. Kosecoff, "Physician Ratings of Appropriate Indications for Six Medical and Surgical Procedures," *American Journal of Public Health,* 1986; 76:766-772.

SUMMARY

This volume contains a literature review of cholecystectomy, a comprehensive set of indications for performing this procedure, and ratings of the appropriateness of each indication.

THE LITERATURE REVIEW

We review the published literature on the role of cholecystectomy in the treatment of biliary tract disease. The review concentrates on the literature on cholecystectomy from 1955 (after the introduction of antibiotics) through 1981, but discusses some later investigations. It provides data on cholecystectomy's indications, utilization, efficacy, pathological findings, complications, and costs. The data came from 118 articles and four textbooks, 66 percent of which were published between 1971 and 1981. Fully 84 percent were research studies (instead of editorials or reviews), with about 12 percent of these being randomized, controlled trials.

Indications

We defined the indications for cholecystectomy in clinical rather than pathological terms. Acute cholecystitis is a clinical presentation for which an operation is always recommended; the main unresolved issue is when to perform surgery: while the acute symptoms are present or after they have subsided. A history of acute cholecystitis and a history of recurrent biliary pain are clinical categories not commonly found in the literature; instead, the pathological term "chronic" cholecystitis is used. We culled statements regarding chronic cholecystitis and biliary tract disease and applied them to a history of acute cholecystitis and recurrent biliary pain. We found that early cholecystectomy was generally recommended for biliary tract disease, partly because surgery might decrease the incidence of gallbladder cancer. Cholecystectomy and choledocholithotomy were considered the treatment of choice for patients with stones in the common bile duct. Cholecystectomy was generally recommended for asymptomatic gallstones unless strongly contraindicated, although without evidence that this was efficacious. Recently, opinion appears to be shifting away from surgical treatment of asymptomatic gallstones.

Utilization

In 1980, cholecystectomy was performed on over 20 persons per 10,000 in the United States. The procedure was performed twice as often on women as on men. Certain census regions perform cholecystectomy more often than others; the ratio of highest to lowest use-rate is 1.3.

Efficacy

To study the benefits of cholecystectomy, we specified the major options available for treating patients with each of five clinical presentations: a current diagnosis of acute cholecystitis, history of acute cholecystitis, recurrent biliary pain, common bile duct obstruction, and asymptomatic or vaguely symptomatic gallstones.

For patients currently diagnosed as in an episode of acute cholecystitis, no experimental studies could be found comparing a surgical approach with a medical one. The nonexperimental literature suggests that surgery is preferred for these patients, and most experimental studies assume that cholecystectomy is efficacious in this circumstance and focus on the timing of the operation. The conclusion of these studies is that early surgery is recommended over delayed surgery for acute cholecystitis. It is not clear, however, whether the results are generalizable and if the same conclusions would be drawn if the surgery were performed by an average surgeon in the average hospital.

The therapeutic alternatives are the same for patients with a previous diagnosis of acute cholecystitis, recurrent biliary pain, and asymptomatic gallstones, and so, their efficacy is discussed together. The only research in these areas relates to the chemical dissolution of stones for patients with a history of acute cholecystitis. It appears that chemical therapy with ursodeoxycholic or chenodeoxycholic acid is not effective enough to be recommended to these patients as an alternative to surgical treatment. Cholecystectomy with choledocholithotomy is the treatment of choice for patients with stones in the common bile duct, whether obstructing or not. Routine rather than selective operative cholangiography to search for stones in the common bile duct is generally advocated during cholecystectomy for cholelithiasis.

The question of surgery's role in the treatment of patients with mild or no symptoms is still being debated, even though the literature supports it unless strongly contraindicated. Reports of large operative series indicate that very few operations are performed for asymptomatic gallstones. These data, however, derive from major academic medical centers; we do not know if findings from community hospitals would be similar. The decision regarding the form of therapy to be used requires a comparison of the costs, risks, and benefits of doing surgery when the diagnosis of gallstones has been made versus the costs, risks, and benefits of no treatment. One must also consider that the risk of surgery increases with age.

Pathological Findings

The overwhelming majority of gallbladders removed at surgery show acute or chronic cholecystitis. Some researchers estimate that calculi are present in 85 to 95 percent of inflamed gallbladders. Acalculous cholecystitis is found to come from anatomic conditions, such as an obstruction of the cystic duct due to tumor; thrombosis of major blood vessels; fibrosis of the sphincter of Oddi in patients with a "common channel"; systemic disease such as diabetes mellitus; and specific infections.

Complications: Mortality

The mortality ascribed to cholecystectomy for patients with acute cholecystitis is 2.6 percent. Age is an important predictor of mortality. However, regardless of age, the mortality rate for patients with other clinical conditions associated with biliary tract disease is less than 0.9 percent.

Costs

We found little information on the costs of cholecystectomy. The cost of early surgery for acute cholecystitis is less than for delayed surgery.

THE INDICATIONS AND APPROPRIATENESS RATINGS

The indications and ratings for cholecystectomy reflect the findings of a nine-member panel of physicians who rated indications twice using a nine-point scale where 1 = extremely inappropriate, 5 = equivocal, and 9 = extremely appropriate. The panelists were chosen because of their clinical expertise, community influence (in professional organizations, for example), and geographic location. Further, they represented academic and community medicine and different specialties: one family physician, two internists, three gastroenterologists, two general surgeons, and one radiologist.

The initial ratings of appropriateness were done individually and without group discussion. The second round of ratings used a structured method that was based on procedures often used to bring people closer to agreement.

The results showed that physicians were able to formulate detailed lists of indications for cholecystectomy and rate their appropriateness. The dispersion in ratings decreased slightly (but not statistically significantly) between the two rounds.

The panelists agreed on final ratings for more than half the indications and disagreed on about one-fifth. On the whole, panelists disagreed least on indications with very low or very high median ratings.

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PART I

LITERATURE REVIEW

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Chapter 1

INTRODUCTION AND METHODS

Approximately 20 million Americans—5 million men and 15 million women—have gallstones (the prime manifestation of gallbladder disease), and new gallstones develop in approximately one million Americans per year. Gallstones are classified, based on their composition, as either cholesterol or pigment stones. Cholesterol stones account for about 80 percent of the stones found in Americans. Pigment stones are composed primarily of calcium bilirubinate and usually contain less than 20 percent cholesterol. Cholesterol gallstones appear to run in families. Their prevalence increases with age, obesity, and possibly multiparity, and is doubled in women who take estrogens or oral contraceptives. Forty percent of patients who have Crohn's disease (an inflammatory disease of the intestine of unknown cause) or who have had their ileum resected develop cholesterol gallstones. Finally, type IV hyperlipidemia is associated with the formation of cholesterol stones. Unlike cholesterol stones, pigment stones occur in association with hemolysis and chronic liver disease. Both types are often concurrent with evidence of biliary tract infection.

Stones that remain in the gallbladder and do not block either the cystic or common bile duct are likely to be asymptomatic; complete or partial obstruction of either duct by a gallstone usually produces symptoms (e.g., biliary colic, acute cholecystitis, obstructive jaundice). The common bile duct becomes obstructed (choledocholithiasis) in up to 20 percent of patients with stones in the gallbladder. Obstruction of the cystic duct occurs in 90 percent of patients with acute cholecystitis and is probably its cause in most instances.

The major diagnostic modalities for identifying a patient with gallstones are ultrasonography and oral cholecystography. The use of these tests, coupled when necessary with other tests of gallbladder function, such as cholescintigraphy, identifies gallstones when they are present in over 99 percent of such patients.

The removal of the gallbladder, for those patients who can tolerate it, is the procedure of choice for patients whose gallstones produce symptoms of acute cholecystitis, biliary colic, or jaundice caused by obstruction of the common bile duct. The use of cholecystectomy is controversial, however, for the millions of Americans who have gallstones and either have no symptoms or have symptoms (such as belching or fatty food intolerance) whose relationship to the stones is equivocal.

This literature review was one source of information for the Health Services Utilization Study (HSUS). The primary goal of HSUS is to investigate the national use of selected medical and surgical procedures. The purpose of the review herein was to summarize, for a panel of experts, what research published from 1970 through 1981 had to say about cholecystectomy with respect to its indications, utilization, efficacy, pathological findings, complications (mortality), and costs. Thus, only articles with information on these topics were included. The panelists used that information, together with data on the national utilization of cholecystectomy from Blue Shield claims, to prepare a comprehensive list of indications for performing the procedure and then to rate each one according to how appropriate it was in 1981. This restriction was imposed because HSUS will ultimately use the panelists' findings as the basis for a study of physicians' actual practices in 1981.

Several methods were used to search the medical literature about cholecystectomy. A first source was MEDLINE, a computerized data base maintained by the National Library of Medicine. A second source was the references listed in the articles and texts identified by the MEDLINE search. Third, subject-matter experts were asked to identify other studies and relevant textbooks. Finally, we checked indexes of *Gastroenterology; The New England Journal of Medicine; Surgery, Gynecology and Obstetrics; American Journal of Surgery;* and *Archives of Surgery.*

We used 122 references in this review, of which four [8, 91, 92, 97] are textbooks. Table 1 shows the distribution of references according to time of publication. As can be seen, the majority of references, 80 or 66 percent, were published between 1971 and 1981. Since the goal of this review was to assemble what was known about cholecystectomy in 1981, studies published later were usually included because they elaborated on conclusions already evident in 1981 from prior work. Later studies are always discussed separately from the data that were available in 1981. In no instances have they been included in the summaries of data reported in the tables.

The 122 references were classified as original research studies, editorials, reviews, and textbooks. Original research studies producing primary data were further subclassified as randomized, controlled trials (RCTs); prospective non-RCT studies; retrospective studies with clearly defined sources of information; probably retrospective studies with unspecified or unclear data sources; and surveys. The defining characteristics for assigning references according to this classification system were:

- *Randomized, controlled trials.* Patients or physicians are randomly assigned to one or more experimental and control groups and all data are collected prospectively.
- *Prospective non-RCT studies.* The research is organized at a certain point in time, all data are collected thereafter, and data are specifically targeted to obtain information that the investigator needs. Patients or physicians are not randomly assigned to study groups.
- *Retrospective studies with clearly defined sources of information.* Research studies in which the data are collected from specifically named sources after the events being studied have already taken place.
- *Probably retrospective studies with unspecified or unclear data sources.* Research in which the design or data sources are not mentioned at all or are not clearly defined.

Table 1

DISTRIBUTION OF RESEARCH ARTICLES AND TEXTS ON CHOLECYSTECTOMY BY YEAR OF PUBLICATION

Period	Articles	Texts
1955–1960	9	0
1961–1965	6	0
1966–1970	17	0
1971–1975	26	0
1976–1981	51	3
1982–1985	9	1
Total	118	4

- *Surveys.* Research studies in which physicians are polled about their opinions, knowledge, and experience.
- *Editorials.* Essays describing personal viewpoints concerning cholecystectomy.
- *Reviews.* Compendia of research about cholecystectomy. (One article [84], a decision analysis, has been classified as a review.)
- *Textbooks.* Books that are designed primarily to give instruction in basic principles of cholecystectomy or gastroenterology.

Table 2 gives the distribution of references according to this classification scheme. Fully 103 (84 percent) describe the results of research studies. Of them, the majority (84 or about 82 percent) were retrospective studies with clearly defined data sources. Among all research studies, 12 or 12 percent were randomized, controlled trials.

Table 2

CLASSIFICATION OF RESEARCH ARTICLES ON CHOLECYSTECTOMY ACCORDING TO METHOD USED TO COLLECT OR REVIEW DATA

Category	Number	Percent
Research Studies	103	84
Randomized, controlled trials	(12)	—
Prospective, non-RCT studies	(2)	—
Retrospective studies with clearly defined sources of information	(84)	—
Probably retrospective studies with unspecified or unclear data sources	(4)	—
Surveys	(1)	—
Editorials	3	2
Reviews	12	10
Textbooks	4	3
Total	122	99

Chapter 2

INDICATIONS

DEFINITIONS

We defined the indications for cholecystectomy in clinical rather than pathological terms, although many papers and textbooks have done otherwise.

We divided the indications for operation into five categories (Fig. 1):

1. Current diagnosis of acute cholecystitis
2. Previous diagnosis of acute cholecystitis
3. One or more episodes of biliary pain
4. Common bile duct obstruction
5. Asymptomatic gallstones

The first four of these clinical entities are most commonly associated with gallstones but may occur in their absence.

Acute Cholecystitis

Acute cholecystitis is usually, but not always, caused by obstruction of the cystic duct by a gallstone. It is typically characterized by right upper quadrant pain (colicky or steady) and tenderness, low-grade fever (100 to 102 degrees), anorexia, nausea, and vomiting. Pathologically, the gallbladder wall shows all the signs of acute inflammation.

Biliary Pain

Pain from the biliary tract is either steady or colicky. The steady pain is ordinarily due to inflammation of the gallbladder or ducts, while the colicky pain is due to an obstruction of the cystic or common bile duct undergoing peristaltic contraction. The pain is typically located in the right upper quadrant of the abdomen and may radiate to the right scapula, interscapular region, or shoulder. When biliary colic is due to obstruction of the cystic duct and is not associated with acute cholecystitis, it tends to be self-limited, usually lasting from one to three hours. Biliary pain, steady or colicky, may be recurrent.

Common Bile Duct Obstruction (Choledocholithiasis)

The majority of common bile duct stones originate in the gallbladder and then pass into the duct. Choledocholithiasis may be asymptomatic, but it usually causes biliary pain, cholangitis, jaundice, or pancreatitis. When clinical signs suggest duct stones, ultrasonography or cholangiographic procedures are used for confirmation.

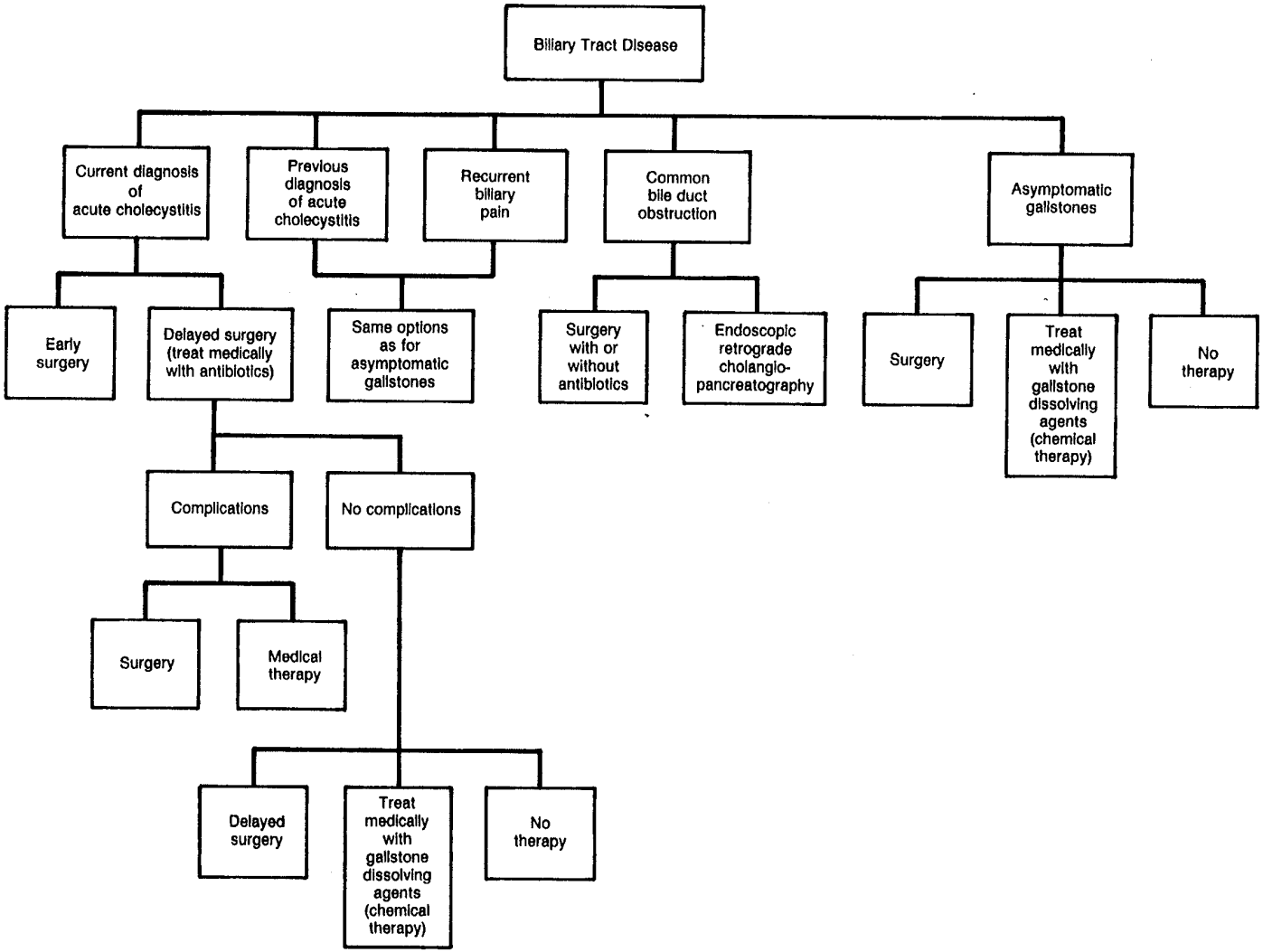

Fig. 1—A classification of indications for cholecystectomy in patients with biliary tract disease

Asymptomatic Gallstones

In practice, this condition is defined by the X-ray or ultrasound finding of stones in the gallbladder or biliary system in a patient without symptoms attributable to biliary tract disease. Since dyspepsia and fatty food intolerance occur with approximately equal frequency in patients with or without gallstones, patients with such symptoms are grouped in this review with those who are asymptomatic.

DATA SOURCES

Information about the clinical indications for the performance of cholecystectomy was summarized from 66 sources. Four were randomized, controlled trials (RCTs) [53, 55, 64, 110]; two were prospective studies [10, 21]; 46 were retrospective studies with clearly defined sources of information [1, 2, 5, 7, 9, 12, 16, 22, 24, 27, 30, 31, 33–36, 42, 44–47, 49, 50, 54, 56, 58, 60, 63, 65, 68–70, 80, 83, 85, 90, 95, 96, 98, 99, 103, 108, 109, 114, 117, 122]; one was probably a retrospective study with unclear data sources [26]; two were editorials [39, 45]; seven were reviews [6, 48, 66, 71, 84, 101, 107]; and four were textbooks [8, 91, 92, 97].

RESULTS

Acute Cholecystitis

Cholecystectomy is considered the preferred treatment of choice for patients with acute cholecystitis. The main issue in the literature [53, 55, 64, 110] is whether to intervene early (generally defined as a nonemergency operation performed while acute symptoms are present or within seven days of the onset of symptoms) or to delay the operation (generally viewed as an elective operation performed once acute symptoms have subsided or from two to three months after the initial episode). Table 3 contains a selection of recommendations regarding the use of cholecystectomy in acute cholecystitis.

Previous Diagnosis of Acute Cholecystitis or Recurrent Biliary Pain

The clinical classifications depicted in Fig. 1 are not used in the literature as a framework for making recommendations regarding operation. Therefore, we have culled from the literature statements regarding "chronic" cholecystitis or "chronic biliary tract disease" and summarized them in Table 4. In Table 5, we have grouped the relevant statements about cholecystectomy when authors have not specified acuteness or chronicity or have considered both together. As can be seen, the largest number of authors support early cholecystectomy for biliary tract disease and suggest that this policy might decrease the incidence of gallbladder cancer.

Common Bile Duct Obstruction

Table 6 summarizes statements in the literature regarding the surgical treatment of common bile duct obstruction. Cholecystectomy with choledocholithotomy is the treatment of choice [91, 92]. A major issue has been whether operative cholangiography is indicated routinely or selectively in patients having cholecystectomy for cholelithiasis. Although some authors still support selective cholangiography [21, 85, 95, 98], the consensus seems to favor

Table 3

RECOMMENDATIONS REGARDING CHOLECYSTECTOMY FOR PATIENTS WITH ACUTE CHOLECYSTITIS

Recommendation	Reference Number
GENERAL RECOMMENDATIONS	
I. Cholecystectomy is procedure of choice (if no contraindications):	5,16,22,30,33 39,91
A. In younger patients (<65 years old) with biliary tract diseases. Cholecystectomy might reduce the incidence of acute cholecystitis.	33,34
B. For acute, noncalculous cholecystitis in children (≤18 years old) as well as for others.	49,91
C. For the elderly (>65 years old) patient with acute cholecystitis.	36
II. Cholecystectomy is not necessarily advisable in every patient with gallstones, with acute or chronic symptoms.	27
RECOMMENDATIONS FOR EARLY CHOLECYSTECTOMY	
I. Early cholecystectomy is generally suggested:	
A. With no specified time limit between onset of symptoms and treatment.	7,31,47,54,55 69,80,99,110
B. With time specified between onset of symptoms and treatment.	
1. Within 3 days.	83,91,122
2. Preferably within 3 days.	39,58
3. Within 3 days in patients whose symptoms worsen.	71
4. Within 7 days.	55,64
C. If surgeon is familiar with procedure	2,9,44,69,110
1. and diagnosis is certain.	27,53,65,96
D. If patient is adequately prepared	2,5,30,39
1. and diagnosis is certain.	26,46,71
E. For "elderly" patients (usually defined as ≥50 years old).	12,34,44,71
F. For diabetic patients.	71,108
G. For patients with jaundice, elevated serum and urinary amylase.	55
RECOMMENDATIONS FOR DELAYING CHOLECYSTECTOMY	
I. Delayed cholecystectomy is generally suggested:	56,65
A. For older patients (over 60) who may have other debilitating diseases or on whom further diagnostic work-up is needed.	71
WHEN TO USE CHOLECYSTOSTOMY INSTEAD OF CHOLECYSTECTOMY	
I. Cholecystostomy is indicated:	
A. In difficult cases (e.g., poor-risk patients, inexperienced surgeon, or patient begins to worsen).	2,5,10,30,33 39,44,46,47,69
B. In older patients (≥65 years).	31,34,56
C. For the patient with an acutely inflamed gallbladder.	26

Table 4

RECOMMENDATIONS REGARDING CHOLECYSTECTOMY FOR PATIENTS WITH CHRONIC GALLBLADDER DISEASE OR CHOLECYSTITIS

Recommendation	Reference Number
UNSPECIFIED CHRONIC GALLBLADDER DISEASE OR SYMPTOMS	
I. Cholecystectomy may not be advisable for all patients with chronic symptoms.	27,41
II. Cholecystectomy may be advisable for patients without positive radiographic evidence, if diagnosis is clear and patient accepts surgical risks.	71
CHRONIC CHOLECYSTITIS OR CHOLELITHIASIS	
I. Cholecystectomy is generally recommended:	45,91
A. For prophylaxis following diagnosis.	71
1. As a chance of preventing carcinoma of the gallbladder.	24,42
II. Elective surgery is recommended:	
A. For diabetic patients.	91
B. For elderly patients (>60 years).	12,50

Table 5

RECOMMENDATIONS REGARDING CHOLECYSTECTOMY FOR PATIENTS WHOSE BILIARY TRACT DISEASE IS NOT CATEGORIZED

Recommendation	Reference Number
GENERAL RECOMMENDATIONS FOR BILIARY TRACT DISEASE	
I. Cholecystectomy is the definitive procedure.	34,71
II. Elective surgery tolerated well by older patients (>65 years old).	36
III. Early treatment may prevent complications later (e.g., acute episode):	26,33,34,35, 63,70
A. Particularly in older (>age 60) patients with symptomatic disease who may be spared gallbladder cancer.	12
B. In young patients (<18 years of age) except those with congenital heart disease or other serious illness.	49
RECOMMENDATIONS FOR CHOLELITHIASIS	
I. Cholecystectomy is the treatment of choice:	35,66,91,101,107
A. Not necessarily in all cases.	27,48
B. In patients with biliary colic and complications.	63
II. Elective ("early") cholecystectomy might prevent complications later.	36,117
A. The incidence of cancer, in particular, might decrease.	1,24,63,70,103, 109
B. Diabetics, especially when younger (<50 years), should have planned, prophylactic cholecystectomy.	108
III. Cholecystectomy may be predisposing factor in development of colon cancer in women.	60

Table 6

RECOMMENDATIONS REGARDING CHOLECYSTECTOMY FOR PATIENTS WITH COMMON BILE DUCT OBSTRUCTION

I.	For patients with stones in the common bile duct, choledocholithotomy with cholecystectomy and T-tube drainage is the treatment of choice [91,92]
II.	When cholangiography is not performed routinely during cholecystectomy, it should be done in any patient who has: [21,85,95,98]
	A. Palpable stones within the common bile duct
	B. Dilated common bile duct
	C. Significant jaundice or a definite history of jaundice
	D. Recurrent chills and fever suggestive of cholangitis and pancreatitis
III.	Consensus recommendation is for routine pre-exploration cholangiography [8]

routine pre-exploration use of cholangiography, primarily because negative duct explorations are thereby reduced from 70–75 percent to 30–35 percent [8]. If a selective policy is utilized, accepted criteria for cholangiography include palpable stones within the common bile duct, dilated common bile duct, significant jaundice or a history of jaundice, or recurrent chills and fever suggestive of cholangitis, and pancreatitis.

Asymptomatic Gallstones

Table 7 summarizes the statements made in the literature regarding the advantages and disadvantages of operating electively on patients with biliary tract disease whose only symptoms are dyspepsia or fatty food intolerance (which are nonspecific), or who are asymptomatic. The largest number of authors recommend cholecystectomy at the time of diagnosis, but no RCTs have been performed, and the single paper approaching the question by decision analysis reaches the opposite conclusion [84]. Although the methodology of this paper is unimpeachable, the literature on which many of the probabilities are based is the same as that which we have reviewed; it thus comes from many nonexperimental studies.

We also draw attention to the fact that despite the literature's support for cholecystectomy at the time of positive diagnosis, few operations for asymptomatic gallstones have been reported. (See "Pathological Findings" below.)

Table 7

RECOMMENDATIONS REGARDING CHOLECYSTECTOMY FOR PATIENTS WITH ASYMPTOMATIC GALLSTONES

	Recommendation	Reference Number
I.	Cholecystectomy is generally recommended for prophylaxis:	6,91,97
	A. At time of diagnosis.	34,35,68
	B. For persons age 40 to 70 years old with cardiovascular disease.	90
	C. For most diabetics.	108
II.	Prophylactic cholecystectomy is not favored because it causes a decrease in survival and incurs more costs than does expectant management.	84

Chapter 3

UTILIZATION

In 1980, cholecystectomy was performed on 20.5 persons out of every 10,000 residents of the United States. The procedure was performed more than twice as often for women (29.1 per 10,000) as for men (11.4 per 10,000). Among persons 15 years of age and older, the rate was 26.5 per 10,000 [78].

Table 8 shows the frequency of cholecystectomy in the four census regions of the United States during the years 1975 through 1980 [73–78]. As can be seen from this table, the rate of performing cholecystectomy remained fairly constant. It was lowest in the West and highest in the North Central region of the United States. The ratio of highest utilization rate (the North Central region) to the lowest (the Western region) in 1980 was 1.3.

Many studies [3] investigated the patterns of use of cholecystectomy across specific geographic regions. Of them, 13 provided frequencies of use of cholecystectomy that were based on "primary" data; the results are summarized in Table 9, which includes rates of use of cholecystectomy from 1962 to 1980 for various geographic regions both inside and outside the United States. The data are reported for different categories (e.g., males, females, the elderly, or a general adult population) and geographic areas of various sizes and types (e.g., whole countries, provinces, counties, or local health service areas). The data in the table indicate that the use of cholecystectomy varies 1.3 times across the census regions of the United States, 1.4 to 4.1 times across health service areas in the United States and provinces in Canada, and up to 7 times across the countries of the Western world.

Among the possible causes for these variations might be an imprecise understanding on the profession's part of the natural history of the disease itself. There are differences among physicians in interpreting or recognizing clinical signs and symptoms of gallbladder disease, for example, and disagreement on the usefulness and meaning of diagnostic tests [71, 79, 119]. Because there is difficulty establishing the diagnosis (e.g., relating symptoms to stones), there is disagreement about appropriate treatment [17, 112, 119]. Several researchers have suggested

Table 8

ANNUAL FREQUENCY OF CHOLECYSTECTOMY FOR THE UNITED STATES BY CENSUS REGIONS

	Frequency Per 10,000 Per Year				
Year	Northeast	North Central	South	West	High/Low
1980	20.6	22.4	20.8	17.4	1.3
1979	22.7	20.5	21.6	16.6	1.3
1978	21.2	22.3	19.3	17.6	1.3
1977	21.2	23.0	19.0	21.4	1.2
1976	22.6	24.0	18.3	19.2	1.3
1975	23.2	24.0	19.1	17.7	1.4

SOURCES: Refs. 73–78.

Table 9

FREQUENCY OF CHOLECYSTECTOMY IN VARIOUS GEOGRAPHIC AREAS

Reference	Years Studied	Geographic Region	Population	High Rate (Per 10,000)	Low Rate (Per 10,000)	High/ Low
NCHS Vital and Health Statistics, Series 13, 1982 (78)	1980	USA by 4 census regions	General	22.4	17.4	1.3
Cageorge, S.M., Roos, L.L., and Danzinger, R. G., 1981 (17)	1977	9 regions of Manitoba, Canada	Adults (25 years or older)	52.2	25.0	2.1
Stockwell, H., and Vayda, E., 1979 (100)	1974	49 counties in Ontario, Canada	General	20.7	10.7	1.9
Detmer, D.E., and Tyson, T.J., 1978 (23)	1973	8 health planning regions in Wisconsin	General	29.0	21.1	1.4
Wennberg, J.E., and Gittelsohn, A., 1975 (121)	1973	13 hospital service areas in Maine	General population of females	55.0	27.0	2.0
Roos, N.P., and Roos, L.L., 1981 (86)	1972 1971	4 rural hospital areas in Manitoba, Canada	Elderly (older than 65)	99.0	36.0	2.8
Vayda, E., Morison, M., and Anderson, G.D., 1976 (115)	1972 1970 1968	9 provinces in Canada	General	45.2 39.8 40.0	22.1 17.6 15.5	2.1 2.3 2.6
Wennberg, J., and Gittelsohn, A., 1973 (120)	1969	13 hospital service areas in Vermont	General	57.0	17.0	3.4
Vayda, E., and Anderson, G. D., 1975 (112)	1968	9 provinces in Canada	General population of: Males Females	 16.6 56.0	 4.3 26.8	 4.1 2.3
Vayda, E., 1973 (111)	1968 1967	Canada, England, and Wales	General population of: Males Females	 13.5 48.7	 2.7 7.0	 5.0 7.0
Bunker, J.P., 1970 (13)	1966 1965	USA, England, and Wales	General population of: Males Females	 9.5 27.3	 3.2 9.0	 2.9 3.0
Lewis, C.E., 1969 (57)	1965	11 regions of Kansas	Adults (older than 21)	42.3	12.1	3.5
Pearson, R.J.C., et al., 1968 (81)	1964 1962	1 selected region in England and Sweden	General population of: Males Females	 21.0 49.0	 3.0 7.0	 7.0 7.0

that the use of different indications for surgical treatment plays some part in the differing rates [13, 79, 111, 113, 114]. One group of investigators found that consultations prior to surgery appeared to reduce substantially the number of cholecystectomies [13]. Their interpretation of this observation was that the increased use of consultation sharpens the criteria for surgery and, therefore, results in a smaller number of operations in patients in whom indications might be equivocal.

Another factor that has been considered in explaining why use-rates vary is that the mix of patients [62, 121] may vary throughout the country, and higher surgical rates in some areas might be due merely to a larger number of patients actually needing surgery [71]. The

literature seems to suggest, however, that case-mix does not vary with surgical rate, and in fact, the case-mix pattern for low-surgery areas appears quite similar to that of high-surgery areas [86].

Consumer characteristics such as educational history, pain threshold tolerance, ethnic background, and place of residence have been the concern of several studies attempting to explain use-rates; unfortunately, their findings are often inconsistent. For example, one study suggests the importance of consumer behavior [120], while the findings of others oppose the hypothesis that consumer characteristics and behavior are important [17, 86, 119].

Reports on the effect of possible differences in access to care have also been mixed. One study found no consistent relationship between access to health care (i.e., difficulty seeing a doctor or not having a regular physician) and use-rates [86], but another, which focused on physicians' families (and families of other professional groups), determined that an informed or educated public with adequate access and supply does undergo more surgery [14].

The methods of payment and organization of health services have also been considered by several researchers as relevant to use-rates [13, 57, 61, 111, 112, 115, 119]. The general consensus seems to be that the method of payment is definitely related to whether or not surgery is performed. Having insurance, for example, appears to increase the use of physicians' services [13, 115], and when all else is held constant, more insured persons are associated with more elective surgery [115]. In addition, in the United States, fee-for-service groups are associated with a higher rate of cholecystectomy than are prepaid group practices [61].

The availability of physical and skilled resources has been considered in explaining use-rates. (Physical resources refer to hospital beds, and skilled resources refer to the number of physicians who have appropriate training to perform cholecystectomy.) One study found that over 50 percent of the variation in rates could be explained by the number of acute-care treatment beds and physicians [100].

A series of studies has focused on how the supply of physicians influences the number of cholecystectomies. At least one researcher has suggested that differences in rates might be due specifically to differences in the personnel who perform the surgery [111], and this proposition appears to be supported. At least four other studies have found a significantly positive correlation between the supply of surgeons and the surgery rate at all levels of surgical complexity [23, 112, 115, 120]. However, some inconsistencies do exist that might possibly invalidate the proposition. At least one study reported that specialists explained more of the variation in the use of cholecystectomy than did general practitioners [100], while another study indicated that greater numbers of operations were performed by general practitioners in high-rate areas [86]. We conclude that the number of hospital beds available to a defined population affects the rate of surgery, while the number of physicians performing the procedure probably does so as well [57, 111].

Finally, just as the literature has considered how patient characteristics might affect the use of cholecystectomy, one study [114] has addressed physician characteristics that might be associated with the use of the procedure. In particular, it made the observation that, when faced with hypothetical patients presenting with typical problems seen in practice, surgeons who were graduated after 1950 are less likely to operate than are surgeons who were graduated before 1950.

Chapter 4

EFFICACY

In this literature review, we looked for studies that would answer the question, "What are the benefits of cholecystectomy compared with alternative forms of treatment for patients with various signs or symptoms of biliary tract disease?"

We specified the major options available for treating each of five groups of patients (Fig. 1). We found that, although some of the options had been investigated for some groups of patients, many important issues had been addressed by inadequately designed studies or not at all.

CURRENT DIAGNOSIS OF ACUTE CHOLECYSTITIS

Considering patients with acute cholecystitis, three options for treatment are available. The first is immediate cholecystectomy (or occasionally cholecystostomy) usually defined as occurring within seven days of the onset of the patient's acute episode. The second is medical therapy (antibiotics and supportive care) followed by surgery a few weeks to months later, provided that a complication (e.g., perforation of the gallbladder) does not occur in the acute period, thus requiring an operation. The third option is to treat the patient medically and, if the patient recovers without developing a complication that requires surgery, to discontinue further treatment or attempt to dissolve the gallstones. If the patient has a recurrent attack, then the choice between cholecystectomy and medical therapy must again be made.

No experimental studies have been performed that compare a surgical approach (either early or delayed) with a medical approach (avoidance of surgery in acute cholecystitis unless forced to operate by a complication). The nonexperimental literature on this disease, however, strongly suggests that surgery of some type is the preferred treatment for patients with acute cholecystitis.

Four randomized, controlled trials (RCTs) have been conducted in university settings concerning the timing of gallbladder surgery in patients with acute cholecystitis [53, 55, 64, 110]. Among the authors' concerns was whether early surgery (variously defined) leads to misdiagnoses, to higher intraoperative and postoperative complication rates, and to differences in length of stay in the hospital and lost workdays. The hoped-for research designs of these RCTs are somewhat contaminated, it should be noted, because 5.8 percent of the patients originally assigned to the delayed surgery group needed cholecystectomy for a complication before the planned date, and 21 percent suffered another acute attack of cholecystitis, which also resulted in an early operation.

In general, for both the early and delayed surgical groups (see Table 10), the RCTs showed that the frequency of intraoperative complications was low, with the most common complication for early surgery being the inability to perform operative cholangiography (6.7 percent)[1] and the need for blood transfusions (4.3 percent). For patients having delayed surgery, the major intraoperative complication was also an inability to perform operative cholangiography (6.7 percent).

[1]Inability to perform operative cholangiography is not strictly a complication of surgery; some researchers do not believe it should be done routinely and would not include it in the calculations for operative complications.

Table 10

RESULTS FROM FOUR RANDOMIZED, CONTROLLED TRIALS OF EARLY AND DELAYED SURGERY FOR PATIENTS WITH ACUTE CHOLECYSTITIS

Factor	Early Surgery[a]	Delayed Surgery[b]
Refusal of surgery	0.90% (2/220)[c]	10.27% (23/224)
Misdiagnosis	3.18 (7/220)	2.68 (6/224)
Negative occurrences during waiting period		
Surgery required before selected date	—	5.80 (13/224)
Recurrent acute cholecystitis or other related problems (e.g., jaundice, peritonitis)	—	20.80 (31/149)
Myocardial infarction	—	0.67 (1/149)
Mortality	—	1.34 (2/149)
Total intraoperative complications	4.23 (6/142)	3.33 (3/90)
Tear of duodenal stump	1.25 (1/80)	0.00
Bleeding of portal vein in patient with earlier partial gastrectomy	1.25 (1/80)	0.00
Minor bile leak at cystic duct	1.25 (1/80)	2.67 (2/75)
Problems requiring blood transfusion	4.26 (2/47)	0.00
Inability to perform operative cholangiography	6.67 (1/15)	6.67 (1/15)
Postoperative mortality	0.00 (0/212)	1.56 (3/192)
Total postoperative complications	18.40 (39/212)	21.88 (42/192)
Wound problems	10.85 (23/212)	9.38 (18/192)
Infection (other than wound)	7.88 (10/127)	10.08 (12/119)
Retained stone	2.13 (1/47)	6.82 (3/44)
Pancreatitis	0.00 (0/80)	2.67 (2/75)
Ileus	1.25 (39/212)	4.00 (3/75)
Mean operation time (in minutes)		
Simple cholecystectomy	81.65	81.75
Cholecystectomy with common duct exploration	107.50	122.50
Mean hospital stay (in days)	11.65	21.92
Mean days lost from work	42.60	57.10

SOURCES: Refs. 53, 55, 64, 110.

[a]Often defined as an operation within one week of an acute episode of cholecystitis.

[b]Often defined as an operation after an acute episode of cholecystitis had subsided; about one to three months after the cessation of an acute episode.

[c]The numbers in the parentheses describe how the percentages for each factor were calculated. The numerator refers to the number of patients (e.g., two) who provided data on a given factor (refused surgery), and the denominator refers to the number of patients across all four RCTs (e.g., 220). Percentage totals may not equal 100 because not all studies or patients provided data for all factors, while some may have provided data on more than one.

In the four RCTs there was no mortality in the early surgery group, but a postoperative mortality of 1.6 percent (not significantly different) in the delayed group. Overall, about 18 percent of patients having early surgery had postoperative complications, with the most typical being wound problems (10.9 percent) including infection, hematoma, or dehiscence. Other events such as intra-abdominal abscess, subphrenic abscess, respiratory infection, prolonged discharge from the drainage tube, or prolonged fever, occurred 7.9 percent of the time. The percent of postoperative complications was slightly greater in the delayed surgery group (21.9 percent); 9.4 percent had wound problems, and 10.1 percent had other untoward events.

No significant differences could be found in the average operating time between early and delayed surgery (81.7 versus 81.8 minutes without common bile duct exploration; 107 and 122 minutes with common bile duct exploration). Significant differences were found, however, for the average number of days spent in the hospital: Patients who had early surgery spent 11.7 days in the hospital, while those who had delayed surgery spent 21.9 days. Lost workdays for early surgery averaged 42.6, while for delayed surgery the average was 57.1 days. The difference between the two averages was significant.

In summary, the four RCTs conducted in teaching hospitals demonstrate that early surgery is as safe as delayed surgery for acute cholecystitis, and patients having early surgery spend fewer days in the hospital and lose fewer days of work. It should be noted that the figures for hospital days and lost workdays are based largely on data from European studies; the U.S. figures are probably different. Also, it is not clear whether the same results would have been obtained if the surgery had been performed by the average surgeon in the average hospital.

PREVIOUS DIAGNOSIS OF ACUTE CHOLECYSTITIS OR RECURRENT BILIARY PAIN

Because the therapeutic alternatives for patients with a previous diagnosis of acute cholecystitis are the same as for recurrent biliary pain (and for asymptomatic gallstones), we shall discuss their efficacy together in this section. The only research literature in this area relates to the chemical dissolution of stones [20, 40, 51, 52, 88]. The management of gallstones with chenodeoxycholic acid has been studied in five RCTs [4, 19, 32, 93, 102]. Differing dosages (e.g., 750 mg and 1000 mg) and combinations of drugs (e.g., chenodeoxycholic acid and phenobarbital) were administered to asymptomatic and other patients with nonacute biliary tract disease in order to determine if gallstones could be partially or completely dissolved. Chenodeoxycholic acid appeared to be more effective in achieving partial dissolution of gallstones (between 30 and 40 percent) than in eliminating them (14 percent); overall partial or complete dissolution rates ranged from 40 percent to 57.9 percent. Some complications were associated with the use of chenodeoxycholic acid. The major ones were diarrhea (which appeared relatively easy to control by reducing drug dosage), slight increases in serum transaminase values, and 10 percent elevation of the serum cholesterol and low-density lipoproteins.

The effectiveness of managing gallstones with ursodeoxycholic acid has been investigated in two RCTs [72, 106]. A third trial [105] was conducted in 1982. In the first two studies, patients were given 150 mg or 650 mg of ursodeoxycholic acid or a placebo. In the third study, patients were given dosages of 250 to 300 mg, 600 mg, or 900 to 1000 mg. Partial dissolution was achieved in 27.7 percent and complete dissolution in 23.4 percent of the patients. It should be noted that the rate of complete dissolution was significantly higher in the third study conducted in 1982 than in the earlier studies, an outcome perhaps related to the larger doses used. The complications associated with ursodeoxycholic acid were transient elevation of serum transaminase and diarrhea.

Little is known about the frequency, pathogenesis, or management of gallstone recurrence. At present, the use of bile acids in the therapeutic range (375 mg/day) to treat recurrent stones is considered hazardous for lifelong use [94].

In summary, it appears that chemical therapy is not effective enough to be recommended as an alternative to surgical treatment for patients with gallstones. Side effects, the recurrence of stones, and changes in blood lipids limit its usefulness at the present time.

COMMON BILE DUCT OBSTRUCTION

When common-duct stones are known to be present preoperatively, there is no question that the treatment of choice is choledocholithotomy along with cholecystectomy. There has been disagreement on a different issue: whether cholangiography should be performed routinely during cholecystectomy in the absence of history of findings suggesting stones in the common duct. The majority of authors answer in the affirmative [8] because this procedure reduces the prevalence of choledochostomy from 65 to 29 percent, while increasing the prevalence of finding and removing common bile duct stones from 23 to 66 percent [91].

Nonetheless, some argue for a policy of selective cholangiography [85, 91, 98]. This recommendation is based on false negatives [21], false positives [95], and faith in non-radiographic criteria to select cases for choledochostomy.

In a non-jaundiced patient, the performance of a choledochostomy does not change the mortality of the cholecystectomy. If jaundiced patients are included (where there is no choice but to explore the common duct surgically), mortality for the dual operation is 1.2 percent versus 0.2 percent in the uncomplicated cholecystectomy [91]. Thus, this increase in mortality appears to be due to the presence of obstruction and jaundice, rather than the choledochostomy *per se*. Even in the non-jaundiced patient, however, there is a significant increase in post-operative morbidity and hospital stay if a choledochostomy is performed along with the cholecystectomy.

ASYMPTOMATIC GALLSTONES

In the absence of evidence to support the use of chemicals, the major efficacy question for patients with asymptomatic gallstones remains: What is the role of surgery? This question is still being debated, with the still unresolved issue being a comparison of the costs, risk, and benefits of no treatment. One must also consider the fact that the risk of surgery increases with age.

Autopsy investigations have revealed gallstones in 4 to 16 percent of patients who had not had symptoms of gallbladder disease [90]. (The autopsy incidence of gallstones has been described as being higher in Scandinavia and Central Europe than in the United States. In those regions, almost 50 percent of females and 30 percent of males autopsied between the ages of 10 and 99 years have been found to have gallstones.) Some investigators estimate, or have determined by follow-up studies, that from 13 percent to 38 percent of asymptomatic patients with stones will develop biliary symptoms or complications after 11 to 20 years [41, 63, 117]. One of these studies showed the mean annual probability for the development of biliary pain to be 2 percent during the first quintennium, 1.5 percent during the second, 0.5 percent during the third, and 0 percent during the fourth [41]. In most cases, the initial expression of gallstone disease is uncomplicated biliary pain. However, older people, who have gallstones more often than younger persons, are more likely to experience acute cholecystitis as the first late complication of a previously asymptomatic stone, and they are also more vulnerable to the potential complications of the surgery that is used to treat the condition.

At present, it is estimated that the patient's lifetime risk of developing cancer of the gallbladder if the gallstones are not surgically removed is 1 to 2 percent. This cancer is almost always fatal. Most researchers, however, do not believe that cholecystectomy is indicated solely as prophylaxis for gallbladder cancer because the projected numbers of operative deaths from the surgery and cancer deaths are similar [92]. In addition, patients without a gallbladder may suffer an increased risk of cancer of the right colon [116].

In summary, this review of the literature on the efficacy of treatment for biliary tract disease would permit the following conclusions: (1) If surgery is used in patients with acute cholecystitis, then an early rather than a delayed operation is preferred; (2) pharmacologic treatment to dissolve stones in patients with nonacute biliary tract disease is not warranted today; and (3) surgical treatment of patients with asymptomatic gallstones, although often recommended in the literature, is still not established as preferable to no treatment.

Chapter 5

PATHOLOGICAL FINDINGS

Pathologic entities found in the gallbladder of patients subjected to cholecystectomy include acute cholecystitis, chronic cholecystitis, empyema, perforation, cholecystoenteric fistulae, hydrops or benign or malignant tumors. In patients with stones in the common bile duct, cholangitis or pancreatitis may be found.

Chronic cholecystitis is a pathologic diagnosis made at the time the gallbladder is removed. It is characterized by a gallbladder wall that is thickened and rigid. About 85 to 95 percent of the time gallstones are present; conversely, almost all patients with gallstones, whether or not they have symptoms, have chronic cholecystitis on pathologic examination. In terms of clinical correlation, patients with chronic cholecystitis may have had acute cholecystitis, recurrent biliary pain, common duct obstruction, nonspecific symptoms such as dyspepsia or fatty food intolerance, or no symptoms at all.

McSherry and Glenn [67] report that, from September 1, 1932 through August 31, 1978, there were 11,808 patients operated on at the New York Hospital Cornell Medical Center for nonmalignant disease of the biliary tract. Chronic conditions were found in 9,461 (80.1 percent) and acute cholecystitis in 2,347 (19.9 percent).

Very few operations have been reported for patients who were asymptomatic but were found to have gallstones, despite the support of many authors (see "Indications" above) for this kind of surgery. This conclusion is based on data from major academic medical centers; we do not know if community hospitals perform similarly (i.e., operate on few patients for asymptomatic gallstones).

Acute and "chronic" cholecystitis have been observed without stones, although the incidence of acalculous inflammatory disease is difficult to establish. For adults in the United States, it is perhaps between 5 and 10 percent [91]. Possible causes include anatomic conditions such as kinking, fibrosis, and obstruction of the cystic duct due to tumor or anomalous vessels; thrombosis of major blood vessels producing ischemia and gangrene; spasm or fibrosis of the sphincter of Oddi in patients with a common channel with or without associated pancreatitis; systemic diseases such as diabetes mellitus and collagen disease; or a specific infection such as typhoid fever, actinomycosis, or parasitic infection.

Chapter 6

COMPLICATIONS

DATA SOURCES

The complications of cholecystectomy can be summarized for 6,951 patients who were operated on for acute cholecystitis and 12,235 for other specified reasons. In 3,526 one could not tell for what indication surgery had been performed. Data come from one text [92] and 40 articles: four randomized, controlled trials (RCTs) [53, 55, 64, 110]; one prospective study [10]; and 35 retrospective studies with clearly defined sources of information [2, 3, 5, 11, 18, 27, 29–31, 33–38, 43, 44, 46, 47, 50, 54, 56, 65, 67, 68, 80, 83, 87, 89, 90, 96, 108, 114, 116, 122].

RESULTS

Table 11 presents data on the complications of cholecystectomy for acute cholecystitis. The mortality was 2.6 percent, while 5.5 percent of the patients suffered a postoperative wound infection. The rate of retained gallstones (in the cystic or common duct) was 1.3 percent. Respiratory infection affected 4.8 percent of all patients. The average length of hospital stay was 15.7 days, and days lost from work averaged 51 days.

Table 11

COMPLICATIONS OF CHOLECYSTECTOMY ACCORDING TO THE INDICATION FOR THE OPERATION

Complication	Indication for Operation		
	Acute Cholecystitis	Other than Acute Cholecystitis	Unspecified Indication
Mortality (%)	2.6 (N=6,951)	0.9 (N=12,335)	1.4 (N=3,526)
Wound infection (%)	5.5 (N=3,344)	4.2 (N=626)	3.6 (N=2,928)
Respiratory infection (%)	4.8 (N=3,133)	12.0 (N=626)	2.8 (N=2,432)
Retained stones (%)	1.3 (N=2,352)	No data	No data
Mean length of hospital stay (in days)	15.7 (N=1,690)	13.3 (N=626)	8.5 (N=1,425)
Mean days out of work	51.1 (N=283)	No data	No data

SOURCES: Refs. 2, 3, 5, 10, 18, 27, 29–31, 33–38, 43, 44, 46, 47, 50, 53–56, 64, 65, 67, 68, 80, 83, 87, 89, 90, 92, 96, 108, 110, 114, 116, 122.

NOTE: Numbers in parentheses are numbers of patients who were examined for the complication.

The studies of cholecystectomy for acute cholecystitis suggest that age was an important predictor of mortality. One study of 250 patients over a 15-year period, for example, found that when cholecystectomy was performed for patients with acute cholecystitis who were over sixty, the average mortality was 2.9 percent, while for those below sixty, it was 0.7 percent [46].

The mortality of elective cholecystectomy for patients with a biliary tract problem other than acute cholecystitis was 0.9 percent [11]; when cholecystectomy was accompanied by choledochostomy, the mortality rate rose to 2.9 percent. As can be seen from Table 11, patients without acute cholecystitis had fewer (4.2 percent) wound infections than did those with acute cholecystitis (5.5 percent). Fewer wound infections might be expected with a primarily elective procedure in a healthy individual, but the greater number of respiratory problems in this group is difficult to explain. Perhaps the criteria used to establish the presence of respiratory infections varied considerably among the studies. Not surprisingly, the mean length of hospital stay was lower in patients with chronic problems (13.3 days) than for those with acute cholecystitis (15.7 days).

Table 11 also contains data that are difficult to interpret because they are from studies in which cholecystectomy was performed on patients with cholelithiasis, but no information is given as to the indication for surgery. Relatively good outcomes (as reflected by such factors as low rates of infection and short hospital stays) suggest that most of these cholecystectomies were probably performed electively for patients without acute cholecystitis at the time of surgery.

Finally, one study compared mortality from cholecystectomy in diabetics with that in nondiabetics [108]. Mortality was noted to be five times higher in diabetics; and among patients aged 51 to 65 years, mortality from this operation in diabetics was almost twenty times that in nondiabetics (19 percent versus 1.1 percent). Mortality in both groups was contributed almost exclusively by those patients over 50 years of age who were admitted for emergency management of acute complications of cholelithiasis. In contrast, negligible risk was found in diabetic and nondiabetic patients who sought elective, planned management of cholelithiasis by cholecystectomy.

Chapter 7

COSTS

DATA SOURCES

Six references were used to provide information about costs of performing cholecystectomy. Three were retrospective studies with clear data sources [18, 29, 118], two were probably retrospective with unclear or unspecified sources [28, 59], and one was a review [84].

RESULTS

Although the literature about the cost of cholecystectomy is sparse, some important facts emerge. One is that the cost is considerable. Corlette [18] studied 100 consecutive patients who underwent cholecystectomy with only minor complications in 1980. The typical postoperative stay for this group of patients in a small (165-bed) community hospital in Massachusetts was under four days, and the total charges (including surgeon's and anesthesiologist's fees) were just over $2,000. Lindgren and colleagues [59] measured the charges for elective cholecystectomies in 1955, 1965, and 1975 in Sweden. They found that the average length of stay decreased by 25 percent between 1955 and 1965, and by the same amount again between 1965 and 1975, but that there was no significant decrease in charges between 1965 and 1975.

For patients with acute cholecystitis, the cost of early surgery is less than for delayed surgery. Fowkes and Gunn [29] compared the hospital charges for early and delayed cholecystectomy in patients with acute gallbladder disease in a British hospital. The operating time was the same for both. The average length of hospitalization in the delayed group (16.1 days) was significantly greater than in the early group (12.4 days). The hospital costs calculated on the basis of length of stay were 156 pounds cheaper (at 1977/78 prices) for early than for delayed cholecystectomy.

In another study, Wennberg, Bunker, and Barnes [118] estimated the expenditure per capita for cholecystectomy in the United States for 1975. The estimate was computed as the surgical exposure per capita multiplied by the average charge per surgical case. The charges included surgeon's fees and were based on data provided by the Maine Health Data Service for 1975. The researchers calculated an average expenditure of $941 million for the United States; however, a greater than two-fold variation was projected when expenditures were estimated based on low rates of use ($630 million) or high rates ($1.477 billion).

Recognizing the large number of cholecystectomies that could be performed if an aggressive approach to diagnosing and removing asymptomatic gallstones were adopted, Fitzpatrick, Neutra, and Gilbert [28] estimated that if all persons in their fifties and sixties in the country were screened, about 368,000 cases of gallstones would be found. If all these patients underwent surgery, an additional expenditure of $1.1 billion (1972 dollars) would result. (Information assembled in 1983, and examined by a decision-analysis method, suggests that no benefit would accrue to the health of this country's population from this policy [84].)

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ANNOTATED BIBLIOGRAPHY

First Author	Year of Publication	Article Rating[a]	Topics Covered					
			Indications	Utilization	Efficacy	Pathological Findings	Complications	Costs
1. Appleman	1963	C-1	•					
2. Archibald	1979	C-1	•				•	
3. Baraldi	1980	C-1					•	
4. Bateson	1978	A			•			
5. Becker	1957	C-1	•				•	
6. Binder	1978	F	•					
7. Bodvall	1967	C-1	•					
8. Bolton	1981	G	•		•			
9. Brandstaetter	1976	C-1	•					
10. Bremner	1974	B	•				•	
11. Boquist	1972	C-1					•	
12. Broden	1980	C-1	•					
13. Bunker	1970	C-1		•				
14. Bunker	1974	D		•				
15. Bunker	1973	E		•				
16. Burnett	1958	C-1	•					
17. Cageorge	1981	C-1		•				
18. Corlette	1980	C-1					•	•
19. Coyne	1975	A			•			
20. Danzinger	1972	C-2			•			
21. Deitch	1982	B	•		•			
22. DePriest	1979	C-1	•					
23. Detmer	1978	C-1		•				
24. Diehl	1981	C-1	•					
25. Donaldson	1982	E	•					
26. du Plessis	1973	C-2	•					
27. Essenhigh	1966	C-1	•				•	
28. Fitzpatrick	1972	C-2						•
29. Fowkes	1980	C-1					•	•
30. Gagic	1975	C-1	•				•	
31. Gardner	1973	C-1	•				•	
32. Gerolami	1977	A			•			
33. Glenn	1976	C-1	•				•	
34. Glenn	1981	C-1	•				•	
35. Glenn	1980	C-1	•				•	
36. Glenn	1955	C-1	•				•	
37. Glenn	1963	C-1					•	
38. Glenn	1968	C-1					•	
39. Glenn	1963	E	•					
40. Goldstein	1975	F			•			
41. Gracie	1982	C-1			•			
42. Gupta	1980	C-1	•					
43. Haff	1969	C-1					•	
44. Hargreaves	1967	C-1	•				•	
45. Hess	1977	C-1	•					
46. Hilton	1970	C-1	•				•	

ANNOTATED BIBLIOGRAPHY—continued

First Author	Year of Publication	Article Rating[a]	Topics Covered					
			Indications	Utilization	Efficacy	Pathological Findings	Complications	Costs
47. Hinchey	1965	C-1	•				•	
48. Hoey	1979	F	•					
49. Holcomb	1980	C-1	•					
50. Ibach	1968	C-1	•				•	
51. Iser	1975	C-1			•			
52. Isselbacher	1981	F			•			
53. Jarvinen	1980	A	•		•		•	
54. Klingensmith	1966	C-1	•				•	
55. Lahtinen	1978	A	•		•		•	
56. Lee	1958	C-1	•				•	
57. Lewis	1969	C-1		•				
58. Lindahl	1969	C-1	•					
59. Lindgren	1979	C-2						•
60. Linos	1981	C-1	•					
61. LoGerfo	1979	C-1		•				
62. Luft	1979	C-1	•	•				
63. Lund	1960	C-1	•		•			
64. McArthur	1975	A	•		•		•	
65. McCubbrey	1959	C-1	•				•	
66. McSherry	1981	F	•					
67. McSherry	1980	C-1				•	•	
68. Meyer	1967	C-1	•				•	
69. Mitchell	1982	C-1	•					
70. Mitmaker	1964	C-1	•					
71. Naitove	1978	F	•	•				
72. Nakagawa	1977	A			•			
73. NCHS Vital & Health Stat. Series 13, #31	1977	C-1		•				
74. NCHS Vital & Health Stat. Series 13, #37	1978	C-1		•				
75. NCHS Vital & Health Stat. Series 13, #41	1979	C-1		•				
76. NCHS Vital & Health Stat. Series 13, #55	1981	C-1		•				
77. NCHS Vital & Health Stat. Series 13, #60	1981	C-1		•				
78. NCHS Vital & Health Stat. Series 13, #64	1982	C-1		•				
79. Opit	1974	C-1		•				
80. Payne	1969	C-1	•				•	
81. Pearson	1968	C-1		•				
82. Piehler	1978	F		•				

ANNOTATED BIBLIOGRAPHY—continued

First Author	Year of Publication	Article Rating[a]	Topics Covered: Indications	Utilization	Efficacy	Pathological Findings	Complications	Costs
83. Raine	1975	C-1	•				•	
84. Ransohoff	1983	F	•					•
85. Reasbeck	1981	C-1	•		•			
86. Roos	1981	C-1		•				
87. Ross	1975	C-1					•	
88. Ruppin	1982	C-1			•			
89. Salleh	1974	C-1					•	
90. Sato	1974	C-1	•		•		•	
91. Schwartz	1979	G	•		•	•		
92. Schoenfield	1982	G	•		•		•	
93. Schoenfield	1981	A			•			
94. Shaffer	1985	F			•			
95. Skillings	1979	C-1	•		•			
96. Sokhi	1973	C-1	•	•			•	
97. Spiro	1977	G	•					
98. Stark	1980	C-1	•		•			
99. Stefanini	1974	C-1	•					
100. Stockwell	1979	C-1		•				
101. Thistle	1973	F	•					
102. Thistle	1973	A			•			
103. Thorbjarnarson	1959	C-1	•					
104. Thorbjarnarson	1960	C-1	•					
105. Tint	1982	A			•			
106. Tokyo Cooperative Gallstone Study Group	1980	A			•			
107. Tondelli	1979	F	•					
108. Turrill	1961	C-1	•				•	
109. Vaittinen	1970	C-1	•					
110. van der Linden	1970	A	•		•		•	
111. Vayda	1973	C-1		•				
112. Vayda	1975	C-1		•				
113. Vayda	1982	F		•				
114. Vayda	1981	C-1	•	•			•	
115. Vayda	1976	C-1		•				
116. Vernick	1980	C-1			•		•	
117. Wenckert	1966	C-1	•		•			
118. Wennberg	1980	C-1						•
119. Wennberg	1977	C-1		•				
120. Wennberg	1973	C-1		•				
121. Wennberg	1975	C-1		•				
122. Wright	1960	C-1	•				•	

[a]Key: A = Randomized, controlled trial
B = Prospective, non-RCT design
C-1 = Retrospective study
C-2 = Probably retrospective study with unclear/unspecified data source(s)
D = Survey
E = Editorial
F = Review
G = Textbook

PART II

INDICATIONS AND APPROPRIATENESS RATINGS

Robert H. Brook, David H. Solomon, Rolla Edward Park

Chapter 8

METHODS

The indications and ratings for cholecystectomy reflect the findings of a nine-member panel of physicians who rated indications twice.[1] The initial ratings of appropriateness were made individually and without group discussion. The second round of ratings followed a structured method that was based on procedures often used to bring people closer to consensus or agreement.

The panelists were chosen because of their clinical expertise, community influence (in professional organizations, for example), and diversity of geographic location, with all four major census regions represented. Also, the panelists were selected to represent academic and community medicine and different specialties. There were one family physician, two internists, two general surgeons, three gastroenterologists, and one radiologist.

INITIAL INDICATIONS LIST

Physicians on the project staff compiled the initial list of indications, using as guides the literature review and the advice of other expert physicians. The indications categorized patients in terms of their symptoms and history. We attempted to compile a list that was detailed, comprehensive, and manageable. We tried to make the indications detailed enough so that patients presenting with a particular indication would be reasonably homogeneous, in the sense that doing the procedure would be equally appropriate (or inappropriate) for all of them. We tried to make the list comprehensive enough so that all indications for doing the procedure that might arise in practice would be included. At the same time, we tried to keep the list short enough so that all of the indications could be rated by the panelists within a reasonable length of time.

INITIAL RATINGS

We sent literature reviews, rating forms, and instructions to the panelists. The literature review gave all panelists equal access to a central core of relevant literature. The rating form listed 48 indications for each of four patient categories (older and younger patients, with and without diabetes) and provided space for an appropriateness rating on a scale of one to nine. Figure 2 shows one page from the initial rating form.

The instructions asked the panelists to rate the appropriateness of each indication using their own best clinical judgment (rather than their perceptions of what other experts might say), and considering an average group of patients presenting to an average U.S. physician who performed the procedure. "Appropriate" was defined to mean that the expected health benefit (i.e., increased life expectancy, relief of pain, reduction in anxiety, improved functional capacity) exceeded the expected negative consequences (i.e., mortality, morbidity, anxiety of

[1]For a complete explanation of the panels and rating process, see R. E. Park, A. Fink, R. H. Brook, et al., *Physician Ratings of Appropriate Indications for Six Medical and Surgical Procedures*, The Rand Corporation, R-3280-CWF/PMT/HF/RWJ, 1986. A shorter version appears in *American Journal of Public Health*, July 1986.

```
+-------------------------------+
|     Appropriateness Scale     |
|     (For All Age Groups)      |
|     ---------------------     |
|      1 2 3 4 5 6 7 8 9        |
|                               |
|1 = extremely inappropriate    |
|5 = equivocal (neither clearly |
|    appropriate nor clearly    |
|    inappropriate)             |
|9 = extremely appropriate      |
+-------------------------------+
```

	Rating of Appropriateness (Circle One)
I. Patients Less than 55 and Nondiabetic	
A. Cholecystectomy is indicated in patients who are either asymptomatic or have vague symptoms (such as heartburn, belching, fatty food intolerance, flatulence, vague abdominal discomfort) if:	
1. Nonvisualized gallbladder (single dose) is present	1 2 3 4 5 6 7 8 9
2. Nonvisualized gallbladder (double dose) is present	1 2 3 4 5 6 7 8 9
3. Free gallstones in gallbladder are present	1 2 3 4 5 6 7 8 9
4. Stone in common duct	1 2 3 4 5 6 7 8 9
B. Cholecystectomy is indicated in patients with one or two attacks of biliary colic if:	
1. Nonvisualized gallbladder (single dose) is present	1 2 3 4 5 6 7 8 9

Fig. 2—Initial form used by panelists to rate the appropriateness of indications for cholecystectomy

anticipating the procedure, pain produced by the procedure, time lost from work) by a sufficiently wide margin that the procedure was worth doing. Extremely appropriate indications should be rated 9, equivocal indications (neither clearly appropriate nor clearly inappropriate) should be rated 5, and extremely inappropriate indications should be rated 1. The panelists were encouraged to modify and supplement the indications list to make it more complete and clinically relevant. As a result, the list and rating forms were revised for the second round of rating. The new list subdivided each indication into four comorbidity categories (no, low, medium, and high).

PANEL MEETING

The gastrointestinal panel met for two and one-half days in Santa Monica during February 1984. After brief preliminaries, panelists spent about two hours discussing and rerating indications for cholecystectomy. (The remainder of the meeting was spent reviewing and rerating indications for upper gastrointestinal endoscopy.) The discussion was led by the physician who was primarily responsible for developing the initial indications list. He was assisted by other physicians and social scientists on the project staff.

During the discussion of the indications, the panelists had in front of them printouts that summarized the initial ratings. Figure 3 shows one page from the printout.

By looking at the printout, the panelists could see the distribution of initial ratings. The numbers above the 1-to-9 rating line show how many panelists assigned each rating. For example, four panelists assigned a rating of "1," four assigned a "2," and one assigned a "3" to the first cholecystectomy indication in Fig. 3. Each panelist received a different printout; the distribution of ratings was the same on all reports, but the caret (^) below the rating line showed the initial rating assigned by that particular panelist. For example, the panelist whose printout is shown in Fig. 3 rated the first indication "2," the second indication "5," the third indication "7," and so on. This procedure preserved the confidentiality of individual panelists' ratings while allowing each panelist to see his own rating in relation to a distribution of the entire group's ratings. The indications list was revised during the discussion. The changes tailored the indications so that they better fit clinically relevant categories. Of the original 48 indications, 33 were unchanged; the remainder were revised. The final list contained 49 indications.

ANALYSIS OF THE APPROPRIATENESS RATINGS

For each indication, the median was used to measure the central tendency of the nine panelists' ratings and the mean absolute distance from the median to measure the dispersion of the ratings. These measures are well-suited, we believe, to the appropriateness scale.

Our 1 through 9 scale is an ordinal scale. It ranks excess of benefit over risk (including negative values when risks exceed benefit). A 9 is always more appropriate than an 8, and an 8 is always more appropriate than a 7. But risk-benefit levels are not specified for each point on the scale, so that a difference between a 9 and an 8 is not necessarily the same as the difference between an 8 and a 7. This suggests that we should avoid measures like means and standard deviations that treat intervals as though they were equal.

Our scale does have some characteristics of an interval scale, however. The center of the scale (5) is well-anchored at the point where risk equals benefit. Although the ends (1 and 9)

CHOLECYSTECTOMY PATIENTS (COMORBID CONDITIONS)

	Nondiabetic >=55 Years Old	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
A. Cholecystectomy is indicated in patients who are either asymptomatic or have vague symptoms (such as heartburn, belching, fatty food intolerance, flatulence) if:					
1. Nonvisualized gallbladder (single dose) is present	4 4 1 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
2. Nonvisualized gallbladder (double dose or intravenous cholangiography or hepatobiliary imaging diacetic acetate) is present	2 2 3 1 1 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
3. Free gallstones in gallbladder are present	2 2 1 1 3 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
4. Stone in cystic duct	1 2 1 3 2 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
5. Stone in common duct	1 2 6 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
B. Cholecystectomy is indicated in patients with one or two attacks of biliary colic if:					
1. Nonvisualized gallbladder (single dose) is present	3 2 2 1 1 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
2. Nonvisualized gallbladder (double dose or intravenous cholangiography or hepatobiliary imaging diacetic acetate) is present	1 2 1 4 1 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
3. Free gallstones in gallbladder are present	1 6 1 1 1 2 3 4 5 6 7 8 9 ^	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9

Fig. 3—The form used to summarize appropriateness ratings for cholecystectomy and to rate indications a second time

are not precisely specified, they are anchored to some degree. At 1, risks exceed benefits by a sufficiently wide margin that the procedure should definitely not be done. At 9, it definitely should be done.

Second, it is now established that using interval measures on ordinal scales seldom has much effect on the results.[2] To shun interval measures entirely would throw away information. A four-point difference on our scale may not represent precisely four times as big a difference in the excess of benefit over risk as a one-point difference, but it almost certainly represents a bigger difference than one point. A strictly ordinal measure would not distinguish between them.

Table 12 describes the average of the median ratings, the mean absolute deviation from the median, and the percent of agreement and disagreement in the panel's initial and final appropriateness ratings for cholecystectomy. The table shows that the ratings were lowered from an initial median of 6.28 to a final median of 4.76. The table also shows that the dispersion (the mean absolute deviation from the median) decreased slightly and insignificantly from 1.19 to 1.05 ($p>0.1$).

Table 12

MEDIAN RATINGS AND EXTENT OF AGREEMENT AND DISAGREEMENT ON APPROPRIATENESS RATINGS FOR CHOLECYSTECTOMY

Measure	Initial Ratings	Final Ratings
Number of indications	48	49
Panel median	6.28	4.76
Mean absolute deviation from median	1.19	1.05
Percent of agreement	43.8	53.1
Percent of disagreement	33.3	20.4

NOTE: See text for definitions of agreement and disagreement.

On what fraction of the indications did the panelists agree? Our preferred definition of agreement is that after discarding one extreme high and one extreme low rating, the remaining seven fall within any three-point range. Panelists' agreement increased from an initial 43.8 percent agreement to 53.1 percent, but this rise fell short of statistical significance.

On what fraction of indications did the panelists disagree? Our preferred definition of disagreement is that, after discarding one extreme high and one extreme low rating, at least one of the remaining seven ratings falls in the lowest three-point region (1 to 3) and at least one falls in the highest (7 to 9). Disagreement decreased from 33.3 percent initially to 20.4 percent after the conclusion of the rating process, although the decrease was not significant. On the whole, the amount of disagreement among the panelists was smaller for indications with very low or very high median ratings.

We urge caution in reviewing or using the indications. Since they apply to 1981, their relative appropriateness may have changed. Also, the overall median value of 4.8 across all indications is a meaningless number. The median does not tell us anything about the extent to which cholecystectomy is appropriately used in practice; to determine this, one must collect data on the actual distribution of indications for which cholecystectomy is performed.

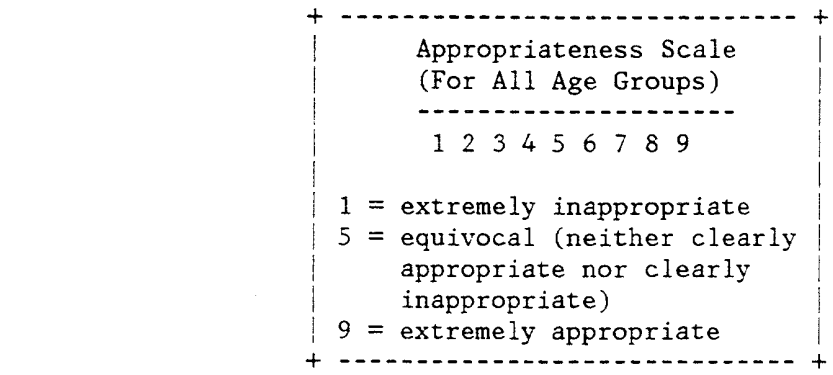
We provide these indications for research and educational purposes only; they are not suitable as prescriptions for current practice or as a basis of regulation.

[2]See, for example, L. Moses, J. D. Emerson, and H. Hosseini, "Analyzing Data from Ordered Categories," *The New England Journal of Medicine*, August 1984, pp. 442–448.

Chapter 9

RESULTS

The following is the final list of rated indications for cholecystectomy; Fig. 4, preceding the list, provides a plan for reading the ratings. To read the table, note that the first indication for cholecystectomy is for patients who are either asymptomatic or who have vague symptoms, if a nonvisualized gallbladder (single dose) is present. This indication was rated for patients with no, low, medium, and high comorbidity. Comorbidity was defined as clinical problems, conditions, or alterations in health other than those due to the index condition for which the patient is under clinical consideration. The table shows that for patients with no comorbidity, the indication was rated "1" by eight panelists and "2" by one; the median rating was 1; the dispersion was 0.1; and panelists agreed on the rating according to our preferred definition of agreement.



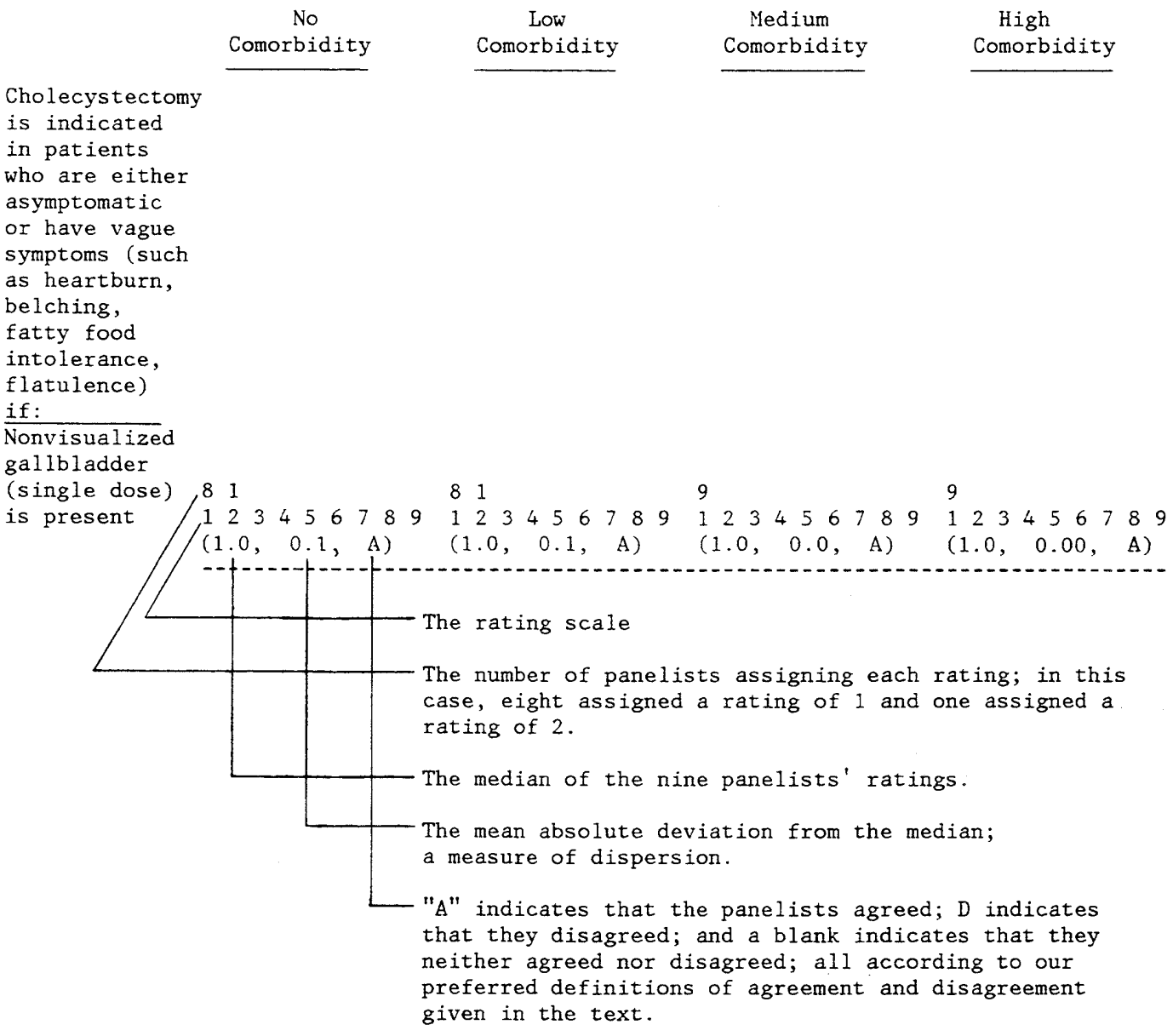


Fig. 4—A key to reading the final results of appropriateness ratings for each indication for cholecystectomy

CHOLECYSTECTOMY PATIENTS

	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
A. Cholecystectomy is indicated in patients who are either asymptomatic or have vague symptoms (such as heartburn, belching, fatty food intolerance, flatulence) if:				
1. Nonvisualized gallbladder (single dose) is present	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.1, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.1, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
2. Nonvisualized gallbladder (double dose or intravenous cholangiography or hepatobiliary imaging diacetic acetate) is present	3 1 1 2 2 1 2 3 4 5 6 7 8 9 (3.0, 1.4,)	3 2 1 2 1 1 2 3 4 5 6 7 8 9 (2.0, 1.2,)	4 2 3 1 2 3 4 5 6 7 8 9 (2.0, 0.8, A)	5 4 1 2 3 4 5 6 7 8 9 (1.0, 0.4, A)
3. Free gallstones in gallbladder are present	3 1 1 1 2 1 1 2 3 4 5 6 7 8 9 (5.0, 2.3, D)	3 2 1 1 1 1 1 2 3 4 5 6 7 8 9 (4.0, 2.1, D)	3 3 1 1 1 1 2 3 4 5 6 7 8 9 (3.0, 1.4,)	3 5 1 1 2 3 4 5 6 7 8 9 (2.0, 0.8, A)
4. Stone in common duct	1 1 7 1 2 3 4 5 6 7 8 9 (9.0, 0.8,)	1 1 1 1 5 1 2 3 4 5 6 7 8 9 (9.0, 1.3,)	2 1 1 3 2 1 2 3 4 5 6 7 8 9 (8.0, 2.1, D)	2 1 1 2 2 1 1 2 3 4 5 6 7 8 9 (7.0, 2.4, D)
B. Cholecystectomy is indicated in patients with one or two attacks of biliary colic if:				
1. Nonvisualized gallbladder (single dose) is present	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.3, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.1, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
2. Nonvisualized gallbladder (double dose or intravenous cholangiography or hepatobiliary imaging diacetic acetate) is present	1 1 2 4 1 1 2 3 4 5 6 7 8 9 (8.0, 1.2, A)	1 1 1 3 3 1 2 3 4 5 6 7 8 9 (7.0, 1.2,)	1 1 3 1 3 1 2 3 4 5 6 7 8 9 (5.0, 1.2,)	2 3 1 2 1 1 2 3 4 5 6 7 8 9 (3.0, 1.1,)
3. Free gallstones in gallbladder are present	2 3 4 1 2 3 4 5 6 7 8 9 (8.0, 0.7, A)	1 3 3 2 1 2 3 4 5 6 7 8 9 (8.0, 0.8, A)	1 2 1 5 1 2 3 4 5 6 7 8 9 (7.0, 0.9, A)	1 2 2 2 2 1 2 3 4 5 6 7 8 9 (4.0, 1.1,)
4. Stone in common duct	9 1 2 3 4 5 6 7 8 9 (9.0, 0.0, A)	1 8 1 2 3 4 5 6 7 8 9 (9.0, 0.2, A)	1 4 4 1 2 3 4 5 6 7 8 9 (8.0, 0.7, A)	1 1 3 1 3 1 2 3 4 5 6 7 8 9 (7.0, 1.8,)

CHOLECYSTECTOMY PATIENTS

	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
C. Cholecystectomy is indicated in patients with 3 or more attacks of biliary colic if:				
1. Nonvisualized gallbladder (single dose) is present	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.4, A)	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.4, A)	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.3, A)	7 2 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)
2. Nonvisualized gallbladder (double dose or intravenous cholangiography or hepatobiliary imaging diacetic acetate) is present	1 1 2 5 1 2 3 4 5 6 7 8 9 (9.0, 1.2, A)	1 4 1 3 1 2 3 4 5 6 7 8 9 (7.0, 1.3, A)	1 3 1 1 2 1 1 2 3 4 5 6 7 8 9 (6.0, 1.7,)	1 1 2 1 3 1 1 2 3 4 5 6 7 8 9 (5.0, 1.8,)
3. Free gallstones in gallbladder are present	3 6 1 2 3 4 5 6 7 8 9 (9.0, 0.3, A)	3 2 4 1 2 3 4 5 6 7 8 9 (8.0, 0.8, A)	2 2 2 1 2 1 2 3 4 5 6 7 8 9 (7.0, 1.2,)	1 2 2 2 2 1 2 3 4 5 6 7 8 9 (5.0, 1.6, D)
4. Stone in common duct	9 1 2 3 4 5 6 7 8 9 (9.0, 0.0, A)	1 8 1 2 3 4 5 6 7 8 9 (9.0, 0.2, A)	1 1 3 4 1 2 3 4 5 6 7 8 9 (8.0, 1.0,)	1 1 1 2 2 2 1 2 3 4 5 6 7 8 9 (7.0, 1.8,)
D. Cholecystectomy is indicated in patients with an old history of acute cholecystitis 6 mo to 2 yr ago if:				
1. Nonvisualized gallbladder (single dose) is present	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.1, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
2. Nonvisualized gallbladder (double dose or intravenous cholangiography or hepatobiliary imaging diacetic acetate) is present	1 1 2 2 1 1 1 1 2 3 4 5 6 7 8 9 (5.0, 1.9, D)	1 1 2 2 2 1 1 2 3 4 5 6 7 8 9 (5.0, 1.8, D)	1 6 1 1 1 2 3 4 5 6 7 8 9 (3.0, 1.1,)	2 4 1 1 1 1 2 3 4 5 6 7 8 9 (2.0, 1.2,)
3. Free gallstones in gallbladder are present	1 2 1 1 3 1 1 2 3 4 5 6 7 8 9 (7.0, 2.1,)	1 2 1 2 2 1 1 2 3 4 5 6 7 8 9 (7.0, 2.0,)	1 4 2 1 1 1 2 3 4 5 6 7 8 9 (3.0, 2.0, D)	2 3 3 1 1 2 3 4 5 6 7 8 9 (2.0, 1.9,)
4. Stone in common duct	1 8 1 2 3 4 5 6 7 8 9 (9.0, 0.1, A)	2 7 1 2 3 4 5 6 7 8 9 (9.0, 0.4, A)	1 1 1 3 3 1 2 3 4 5 6 7 8 9 (8.0, 1.7,)	1 1 1 1 2 2 1 1 2 3 4 5 6 7 8 9 (7.0, 2.0, D)

CHOLECYSTECTOMY PATIENTS

	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
E. Cholecystectomy either early or delayed is indicated in patients with acute cholecystitis within past 6 mo if:				
1. Gallstones are present in the gallbladder (no other findings)	1 2 6 1 2 3 4 5 6 7 8 9 (9.0, 1.0, A)	1 4 4 1 2 3 4 5 6 7 8 9 (8.0, 1.1, A)	1 1 3 2 2 1 2 3 4 5 6 7 8 9 (7.0, 1.3,)	1 1 1 1 1 2 2 1 2 3 4 5 6 7 8 9 (6.0, 1.9, D)
2. Gallstones and a complication are present (empyema, pancreatitis, stone in common duct, jaundice, hydrops, fistula, gallstone ileus)	9 1 2 3 4 5 6 7 8 9 (9.0, 0.0, A)	1 8 1 2 3 4 5 6 7 8 9 (9.0, 0.1, A)	2 2 5 1 2 3 4 5 6 7 8 9 (9.0, 0.7, A)	1 2 1 2 3 1 2 3 4 5 6 7 8 9 (8.0, 1.2,)
3. In absence of gallstones (either in gallbladder or ducts) or any complication such as empyema or perforation, but in presence of a nonvisualizing gallbladder	1 1 4 1 2 1 2 3 4 5 6 7 8 9 (7.0, 1.2,)	1 1 2 4 1 1 2 3 4 5 6 7 8 9 (7.0, 1.2, A)	1 1 1 4 1 1 1 2 3 4 5 6 7 8 9 (5.0, 1.3, D)	1 2 2 1 1 1 1 1 2 3 4 5 6 7 8 9 (3.0, 1.7,)
4. In absence of gallstones or complication (e.g., gallbladder normal or test of gallbladder function was not done)	3 1 2 2 1 1 2 3 4 5 6 7 8 9 (3.0, 1.6,)	4 1 1 2 1 1 2 3 4 5 6 7 8 9 (2.0, 1.7,)	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.1, A)	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.7, A)
F. Cholecystectomy is indicated in patients who are asymptomatic or have vague symptoms:				
1. With adenomyomatosis a) and gallstones	3 1 1 1 1 1 1 1 2 3 4 5 6 7 8 9 (4.0, 2.6, D)	3 2 1 1 1 1 1 2 3 4 5 6 7 8 9 (3.0, 2.3, D)	4 1 1 1 1 1 1 2 3 4 5 6 7 8 9 (2.0, 2.0,)	5 1 1 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.6,)
b) without gallstones	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.8, A)	5 3 1 1 2 3 4 5 6 7 8 9 (1.0, 0.6, A)	7 2 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.1, A)

CHOLECYSTECTOMY PATIENTS

	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
2. With cholesterolosis ("cholesterol polyps") a) and gallstones	3 1 1 1 2 1 1 2 3 4 5 6 7 8 9 (4.0, 2.3, D)	3 2 1 2 1 1 2 3 4 5 6 7 8 9 (3.0, 1.9,)	4 1 1 2 1 1 2 3 4 5 6 7 8 9 (2.0, 1.7,)	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.0,)
b) without gallstones	5 3 1 1 2 3 4 5 6 7 8 9 (1.0, 1.2, A)	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.9, A)	5 2 1 1 2 3 4 5 6 7 8 9 (1.0, 0.6, A)	7 1 1 2 3 4 5 6 7 8 9 (1.0, 0.3, A)
3. Porcelain gallbladder	1 5 1 2 1 2 3 4 5 6 7 8 9 (3.0, 0.8, A)	2 2 3 2 1 2 3 4 5 6 7 8 9 (3.0, 1.1,)	3 4 1 1 1 2 3 4 5 6 7 8 9 (2.0, 0.8, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)
4. Limey (milk of calcium) bile	3 1 3 1 1 1 2 3 4 5 6 7 8 9 (3.0, 1.9, D)	3 2 2 1 1 1 2 3 4 5 6 7 8 9 (2.0, 1.7,)	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.3,)	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.7, A)
5. With a "floating" gallbladder (no gallstones)	8 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	8 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	8 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	8 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
6. With a phrygian cap (no gallstones)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
7. Very large gallstones (> 2 cm diameter)	1 1 3 1 1 1 1 1 2 3 4 5 6 7 8 9 (3.0, 1.9, D)	2 2 1 1 1 1 1 1 2 3 4 5 6 7 8 9 (3.0, 2.0,)	4 3 1 1 1 2 3 4 5 6 7 8 9 (3.0, 1.4,)	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.0, A)
G. Cholecystectomy is indicated in patients with jaundice (asymptomatic)				
1. With common duct stone or dilated common duct	9 1 2 3 4 5 6 7 8 9 (9.0, 0.0, A)	1 1 7 1 2 3 4 5 6 7 8 9 (9.0, 0.4, A)	1 1 1 1 3 2 1 2 3 4 5 6 7 8 9 (8.0, 1.4,)	1 1 2 2 1 2 1 2 3 4 5 6 7 8 9 (6.0, 2.0, D)
2. With gallstone but neither dilated common duct nor common duct stone	2 2 1 1 2 1 1 2 3 4 5 6 7 8 9 (3.0, 1.7,)	3 2 2 1 1 1 2 3 4 5 6 7 8 9 (2.0, 1.6,)	5 1 2 1 1 2 3 4 5 6 7 8 9 (1.0, 1.0, A)	5 4 1 2 3 4 5 6 7 8 9 (1.0, 0.4, A)
3. Without evidence of gallstones or duct stones	6 2 1 1 2 3 4 5 6 7 8 9 (1.0, 0.4, A)	7 2 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)

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	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
Ha. Cholecystectomy is indicated in patients with chronic or acute recurring pancreatitis not ascribed to alcohol and:				
1. No gallstones, or stones in cystic or common bile duct	6 2 1 1 2 3 4 5 6 7 8 9 (1.0, 1.2,)	6 1 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.0,)	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.7, A)	8 1 1 2 3 4 5 6 7 8 9 (1.0, 0.2, A)
2. Gallstones but no stones in common bile duct	1 1 2 1 4 1 2 3 4 5 6 7 8 9 (8.0, 1.8,)	1 1 1 2 4 1 2 3 4 5 6 7 8 9 (7.0, 1.9,)	1 2 1 1 1 2 1 1 2 3 4 5 6 7 8 9 (6.0, 2.2, D)	3 1 1 1 1 2 1 2 3 4 5 6 7 8 9 (3.0, 2.4, D)
3. Stones in common bile duct	1 8 1 2 3 4 5 6 7 8 9 (9.0, 0.1, A)	1 1 1 6 1 2 3 4 5 6 7 8 9 (9.0, 0.8, A)	1 2 1 1 4 1 2 3 4 5 6 7 8 9 (8.0, 1.9,)	1 2 1 2 3 1 2 3 4 5 6 7 8 9 (8.0, 2.6, D)
Hb. Cholecystectomy is indicated in patients with acute pancreatitis not ascribed to alcohol and:				
1. No gallstones, or stones in cystic or common bile duct	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
2. Gallstones but no stones in common bile duct	4 2 2 1 1 2 3 4 5 6 7 8 9 (2.0, 2.2, D)	5 1 1 2 1 2 3 4 5 6 7 8 9 (1.0, 2.0, D)	6 1 2 1 2 3 4 5 6 7 8 9 (1.0, 1.6,)	6 2 1 1 2 3 4 5 6 7 8 9 (1.0, 1.4,)
3. Stones in common bile duct	1 3 1 1 3 1 2 3 4 5 6 7 8 9 (6.0, 2.1,)	1 1 3 1 3 1 2 3 4 5 6 7 8 9 (5.0, 2.3, D)	1 1 1 2 1 2 1 1 2 3 4 5 6 7 8 9 (5.0, 2.2, D)	2 1 1 2 2 1 1 2 3 4 5 6 7 8 9 (5.0, 2.3, D)
Ia. Cholecystectomy is indicated in patients with chronic or acute recurring pancreatitis and heavy alcohol intake and:				
1. No gallstones, or stones in cystic or common bile duct	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)

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	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
2. Gallstones but no stones in common bile duct	3 2 3 1 1 2 3 4 5 6 7 8 9 (5.0, 2.3, D)	3 2 1 1 1 1 1 2 3 4 5 6 7 8 9 (4.0, 2.1, D)	4 1 1 1 1 1 1 2 3 4 5 6 7 8 9 (2.0, 1.9,)	6 1 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.2,)
3. Stones in common bile duct	1 2 6 1 2 3 4 5 6 7 8 9 (9.0, 0.4, A)	1 1 1 1 5 1 2 3 4 5 6 7 8 9 (9.0, 1.1,)	2 2 2 1 2 1 2 3 4 5 6 7 8 9 (7.0, 1.7,)	1 2 1 2 1 2 1 2 3 4 5 6 7 8 9 (6.0, 2.3, D)
Ib. Cholecystectomy is indicated in patients with acute pancreatitis and heavy alcohol intake and:				
1. No gallstones, or stones in cystic or common bile duct	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
2. Gallstones but no stones in common bile duct	4 1 1 1 1 1 1 2 3 4 5 6 7 8 9 (2.0, 1.7,)	4 2 1 1 1 1 2 3 4 5 6 7 8 9 (2.0, 1.2,)	6 1 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.7, A)	7 1 1 1 2 3 4 5 6 7 8 9 (1.0, 0.3, A)
3. Stones in common bile duct	2 2 1 1 1 2 1 2 3 4 5 6 7 8 9 (6.0, 2.8, D)	2 2 1 1 1 2 1 2 3 4 5 6 7 8 9 (5.0, 3.0, D)	4 1 1 2 1 1 2 3 4 5 6 7 8 9 (2.0, 2.9, D)	5 1 2 1 1 2 3 4 5 6 7 8 9 (1.0, 2.6, D)
J. Cholecystectomy is indicated in patients with an asymptomatic cholecystoenteric fistula	2 2 3 1 1 1 2 3 4 5 6 7 8 9 (5.0, 1.7,)	2 3 3 1 1 2 3 4 5 6 7 8 9 (3.0, 1.4,)	5 3 1 1 2 3 4 5 6 7 8 9 (1.0, 1.6, A)	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.3, A)
K. Removal of gallbladder at time of surgery for other condition if:				
1. Gallbladder has stones and symptoms compatible with gallbladder disease	1 2 2 1 3 1 2 3 4 5 6 7 8 9 (7.0, 1.2,)	1 1 1 1 3 2 1 2 3 4 5 6 7 8 9 (7.0, 1.7,)	2 1 1 1 2 1 1 1 2 3 4 5 6 7 8 9 (5.0, 2.3, D)	3 1 3 1 1 1 2 3 4 5 6 7 8 9 (5.0, 2.2, D)
2. Gallbladder has stones but no symptom compatible with gallbladder disease	1 2 2 1 1 1 1 1 2 3 4 5 6 7 8 9 (4.0, 2.1, D)	2 1 1 1 2 1 1 1 2 3 4 5 6 7 8 9 (4.0, 2.2, D)	3 2 2 1 1 1 2 3 4 5 6 7 8 9 (2.0, 2.0, D)	5 2 1 1 1 2 3 4 5 6 7 8 9 (1.0, 1.7,)

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	No Comorbidity	Low Comorbidity	Medium Comorbidity	High Comorbidity
3. Gallbladder is without stones	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)	9 1 2 3 4 5 6 7 8 9 (1.0, 0.0, A)
L. Cholecystectomy is indicated in salmonella carriers	2 1 1 5 1 2 3 4 5 6 7 8 9 (9.0, 1.2,)	1 1 4 1 2 1 2 3 4 5 6 7 8 9 (7.0, 1.3,)	1 2 1 1 2 2 1 2 3 4 5 6 7 8 9 (5.0, 2.1, D)	5 1 1 2 1 2 3 4 5 6 7 8 9 (1.0, 2.0, D)