NIH State-of-the-Science Conference on Endoscopic Retrograde Cholangiopancreatography (ERCP) for Diagnosis and Therapy

January 14–16, 2002
William H. Natcher Conference Center
National Institutes of Health
Bethesda, Maryland

Sponsored by:

♦ National Institute of Diabetes and Digestive and Kidney Diseases ♦ Office of Medical Applications of Research ♦

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Introduction

The National Institutes of Health (NIH) is convening a State-of-the-Science Conference on Endoscopic Retrograde Cholangiopancreatography (ERCP) for Diagnosis and Therapy on January 14–16, 2002.

ERCP is a procedure that physicians use to diagnose and treat problems in the liver, gallbladder, bile ducts, and pancreas. It combines the use of X-rays and an endoscope—a long, flexible, lighted tube. The physician inserts the endoscope in a patient's mouth and guides it down through the esophagus and into the stomach and small intestine. ERCP allows the physician to look inside these organs and also to send dye to the bile and pancreatic ducts, thereby making them visible on an X-ray.

ERCP first came into use about 30 years ago and has been applied to the diagnosis and management of a variety of gastrointestinal disorders. However, the value of ERCP relative to other means for diagnosing and treating these diseases has not been firmly established.

This NIH State-of-the-Science Conference has been convened to examine the current state of knowledge regarding the use of ERCP in clinical practice and to identify directions for future research. Specifically, the conference will explore the following key questions:

- What is the role of ERCP in gallstone disease?
- What is the role of ERCP in pancreatic and biliary malignancy?
- What is the role of ERCP in pancreatitis?
- What is the role of ERCP in abdominal pain of possible pancreatic or biliary origin?
- What are the factors determining adverse events or success?
- What future research directions are needed?

During the first day-and-a-half of the conference, experts will present the latest ERCP research findings to an independent, non-Federal panel. After weighing all of the scientific evidence, the panel will draft a statement addressing the key questions listed above. The panel's draft statement will be presented to the conference audience on the final day of the conference.

General Information

Conference sessions will be held in the Natcher Conference Center, NIH, Bethesda, MD. Sessions will run from 8:30 a.m. to 5:30 p.m. on Monday, from 8:30 a.m. to 12 p.m. on Tuesday, and from 9 a.m. to 11 a.m. on Wednesday. The telephone number for the message center is (301) 496-9966; the fax number is (301) 480-5982.

Cafeteria

The cafeteria in the Natcher Conference Center is located one floor above the auditorium on the main floor of the building. The cafeteria is open from 7 a.m. to 2 p.m. and serves breakfast and lunch.

Sponsors

The lead agencies for this conference are the National Institute of Diabetes and Digestive and Kidney Diseases and the NIH Office of Medical Applications of Research. Supporting agencies include the National Cancer Institute and the U.S. Food and Drug Administration.

Continuing Medical Education Credit

The NIH/FAES is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

The NIH/FAES designates this educational activity for a maximum of 13.5 hours in category 1 credit towards the AMA Physician's Recognition Award. Each physician should claim only those hours of credit actually spent in the educational activity.

Statement of Interest

Each speaker presenting at this conference has been asked to submit documentation outlining all outside involvement pertaining to the subject area. Please refer to the chart in your participant packet for details.

Agenda

Monday, January 14, 2002

8:30 a.m. Opening Remarks
Allen M. Spiegel, M.D., Director
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health

8:40 a.m. Charge to Panel
Susan Rossi, Ph.D., M.P.H., Deputy Director
Office of Medical Applications of Research, Office of the Director
National Institutes of Health

8:50 a.m. Conference Overview and Panel Activities
Sidney Cohen, M.D., Panel and Conference Chairperson, Director
Research Programs, Division of Gastroenterology and Hepatology
Jefferson Medical College, Thomas Jefferson University

I. Overview

9:00 a.m. Overview of the Role of ERCP in the Management of Diseases of the Biliary Tract and the Pancreas
David L. Carr-Locke, M.D., M.A., F.R.C.P., F.A.C.G., D.R.C.O.G.
Director of Endoscopy
Gastroenterology Division
Brigham and Women's Hospital

II. Role of ERCP in Common Bile Duct Stones

9:20 a.m. Epidemiology and Natural History of Common Bile Duct Stones and Prediction of Disease
Sum P. Lee, M.D., Ph.D., Professor and Head
Division of Gastroenterology, Department of Medicine
University of Washington

9:40 a.m. Use of MRCP Versus ERCP in the Diagnosis of Common Bile Duct Stones
Ann S. Fulcher, M.D., Director, Abdominal Imaging Section
Department of Radiology
Medical College of Virginia, Virginia Commonwealth University

9:55 a.m. Endoscopic Ultrasonography (EUS) in Bile Duct Stones: How Does It Compare to ERCP?
Michael V. Sivak, Jr., M.D., Chief
Gastroenterology
University Hospitals of Cleveland

Monday, January 14, 2002 (continued)

II. Role of ERCP in Common Bile Duct Stones (continued)

10:10 a.m. Therapeutic Role of ERCP in the Management of Suspected Common Bile Duct Stones
David L. Carr-Locke, M.D., M.A., F.R.C.P., F.A.C.G., D.R.C.O.G.
Director of Endoscopy
Gastroenterology Division
Brigham and Women's Hospital

10:25 a.m. Surgical Management of Common Bile Duct Stones
Joseph B. Petelin, M.D., F.A.C.S., Clinical Associate Professor
General and Telescopic Surgery, Department of Surgery
University of Kansas School of Medicine

10:40 a.m. Evidence-Based Assessment of Diagnostic Modalities in Common Duct Stones
David Mark, M.D., M.P.H., Senior Scientist
BlueCross BlueShield TEC Evidence-based Practice Center
BlueCross BlueShield Association

11:00 a.m. Discussion

12:00 p.m. Lunch

III. Role of ERCP in Pancreatic and Biliary Malignancy

1:00 p.m. Epidemiology and Natural History of Pancreatic and Biliary Tract Malignancies
Dominique Michaud, Sc.D., Investigator
Nutritional Epidemiology Branch
National Cancer Institute, National Institutes of Health

1:20 p.m. Diagnostic and Therapeutic Uses of ERCP in Pancreatic and Biliary Tract Malignancies
Robert H. Hawes, M.D., Professor of Medicine
Gastroenterology, Digestive Disease Center
Medical University of South Carolina

1:40 p.m. Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) in Pancreatic and Biliary Tract Malignancies
Pablo R. Ros, M.D., M.P.H., Professor of Radiology
Harvard Medical School
Executive Vice Chair and Associate Radiologist-in-Chief
Department of Radiology
Brigham and Women's Hospital

Monday, January 14, 2002 (continued)

III. Role of ERCP in Pancreatic and Biliary Malignancy (continued)

1:55 p.m. Surgical Intervention in Pancreatic and Biliary Malignancies
Steven M. Strasberg, M.D., Ph.D., Pruett Professor of Surgery and Head, Hepatobiliary Pancreatic Surgery
Department of Surgery
Washington University

2:10 p.m. Evidence-Based Assessment of the Approaches to Pancreatic and Biliary Tract Malignancies
Carole Redding Flamm, M.D., M.P.H., Associate Director
BlueCross BlueShield TEC Evidence-based Practice Center
BlueCross BlueShield Association

2:25 p.m. Discussion

IV. Role of ERCP in Pancreatitis

3:05 p.m. Epidemiology, Natural History, and Predictors of Disease Outcome in Acute and Chronic Pancreatitis
Peter A. Banks, M.D., Professor of Medicine
Harvard Medical School
Director, Clinical Gastroenterology Service
Division of Gastroenterology
Brigham and Women's Hospital

3:20 p.m. Role of ERCP in Acute Pancreatitis
Richard A. Kozarek, M.D., Chief
Section of Gastroenterology
Virginia Mason Medical Center

3:35 p.m. Role of ERCP and Other Endoscopic Modalities in Chronic Pancreatitis
Glen A. Lehman, M.D., Professor of Medicine and Radiology
Department of Medicine, Indiana University Medical Center
Indiana University School of Medicine

3:50 p.m. The Role of Ultrasonography and Computed Tomography in Pancreatitis
Mary Ann Turner, M.D., Section Chief
Abdominal Imaging, Division of Diagnostic Radiology
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4:05 p.m. Surgical Intervention in Pancreatitis
Howard A. Reber, M.D., Professor
Department of General Surgery, School of Medicine
University of California, Los Angeles

Monday, January 14, 2002 (continued)

IV. Role of ERCP in Pancreatitis (continued)

4:25 p.m. Evidence-Based Assessment of ERCP in Pancreatitis
David Mark, M.D., M.P.H., Senior Scientist
BlueCross BlueShield TEC Evidence-based Practice Center
BlueCross BlueShield Association

4:40 p.m. Discussion

5:30 p.m. Recess—Panel Meets in Executive Session

Tuesday, January 15, 2002

V. Role of ERCP in Abdominal Pain of Suspected Pancreatic or Biliary Origin

8:30 a.m. Overview of Differential Diagnosis of Abdominal Pain
Anthony N. Kalloo, M.D., F.A.C.P., Associate Professor of Medicine
Director of Endoscopy
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The Johns Hopkins Hospital, The Johns Hopkins University

8:45 a.m. What Is the Role of ERCP in the Setting of Abdominal Pain of Pancreatic or Biliary Origin?
Stuart Sherman, M.D., Professor of Medicine and Radiology
Department of Medicine, Indiana University Medical Center
Indiana University School of Medicine

9:05 a.m. There Is No Role for ERCP or EUS in Unexplained Abdominal Pain of Pancreatic or Biliary Origin
Pankaj J. Pasricha, M.D., Professor of Medicine and Anatomy and Neurosciences, and Chief
Division of Gastroenterology and Hepatology
University of Texas Medical Branch at Galveston

9:20 a.m. Discussion

Tuesday, January 15, 2002 (continued)

VI. Balancing Risks and Benefits

9:45 a.m. Income and Outcome Metrics Needed for Objective Evaluation
Peter B. Cotton, M.D., F.R.C.P., Director
Digestive Disease Center
Medical University of South Carolina

10:05 a.m. What Are the Complications (Adverse Events) of ERCP?
Martin L. Freeman, M.D., Associate Professor of Medicine
University of Minnesota Medical School
Gastroenterology Division, Department of Medicine
Hennepin County Medical Center

10:25 a.m. What Are the Determinants of Success in Utilization of ERCP in the Setting of Pancreatic and Biliary Diseases?
Glen A. Lehman, M.D., Professor of Medicine and Radiology
Department of Medicine, Indiana University Medical Center
Indiana University School of Medicine

10:45 a.m. Evidence-Based Assessment of Adverse Effects of ERCP
Carole Redding Flamm, M.D., M.P.H., Associate Director
BlueCross BlueShield TEC Evidence-based Practice Center
BlueCross BlueShield Association

11:00 a.m. Discussion

12:00 p.m. Recess—Panel Meets in Executive Session

Wednesday, January 16, 2002

9:00 a.m. Presentation of Consensus Statement

9:30 a.m. Public Discussion

11:00 a.m. Panel Meets in Executive Session

1:00 p.m. Press Conference

2:00 p.m. Adjournment

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Abstracts

The following are abstracts of presentations to the NIH State-of-the-Science Conference on Endoscopic Retrograde Cholangiopancreatography (ERCP) for Diagnosis and Therapy. They are designed for the use of panelists and participants in the conference and as a reference document for anyone interested in the conference deliberations. We are grateful to the authors for their participation and for supplying these summaries.

Abstracts for the following presentations do not appear:

Evidence-Based Assessment of Diagnostic Modalities in Common Duct Stones—David Mark, M.D., M.P.H.

Evidence-Based Assessment of the Approaches to Pancreatic and Biliary Tract Malignancies—Carole Redding Flamm, M.D., M.P.H.

Role of ERCP and Other Endoscopic Modalities in Chronic Pancreatitis—Glen A. Lehman, M.D.

Surgical Intervention in Pancreatitis—Howard A. Reber, M.D.

Evidence-Based Assessment of ERCP in Pancreatitis—David Mark, M.D., M.P.H.

Evidence-Based Assessment—Carole Redding Flamm, M.D., M.P.H.

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Overview of the Role of ERCP in the Management of Diseases of the Biliary Tract and the Pancreas

David L. Carr-Locke, M.D., M.A., F.R.C.P., F.A.C.G., D.R.C.O.G.

As we enter the fourth decade of endoscopic retrograde cholangiopancreatography (ERCP) and its related techniques and reflect on what has been achieved in its evolution, a number of technological, clinical and research milestones can be identified along with the experts and their teams who developed them. They showed the practicing gastroenterologist how to learn, perfect and apply the wide range of therapeutic modalities encompassed by the ERCP umbrella today. ERCP has grown from a limited esoteric procedure performed by a few to a mainstream modality for diagnosis and treatment of a very wide variety of benign and malignant ampullary, biliary and pancreatic disorders. It has taken surprisingly long to subject some of the applications of endoscopic therapy of biliary and pancreatic disease to the same scientific evaluation as alternative treatments, define patient populations and their associated risk profiles and to understand how positive, negative and unplanned treatment outcomes are determined by patient, technical and physician influences. Training requirements for physicians wishing to acquire and maintain the necessary skills needed to perform high quality ERCP have been defined but remain a contentious area in endoscopic practice and education.

ERCP is currently involved in the management of (1) bile duct stones, (2) benign and malignant inflammatory and neoplastic biliary obstruction, (3) benign and malignant pancreatic neoplasia, (4) acute and chronic pancreatitis, (5) bile duct injuries, (6) pancreatic duct disruption and pseudocyst, (7) benign and malignant diseases of the major and minor papilla, (8) pain syndromes considered to be of pancreatic, biliary or sphincter of Oddi origin, (9) certain congenital and acquired hepatic conditions affecting the biliary tract, (10) bleeding suspected of being of hepatic, biliary or pancreatic origin and (11) infection of a suspected hepatic, biliary or pancreatic source. This wide range of indications has grown with clinical experience based on empirical judgement, case reports, case series, prospective studies and randomized controlled trials. The precise role of ERCP in these varied clinical settings has not, however, always been well characterized in terms of difficulty, success, associated morbidity risk, overall outcome and patient satisfaction in comparison with the most suitable alternatives, which are often surgical.

Choice of ERCP in the continuum of patient care and management of specific conditions requires analysis and synthesis of “incomes” (pre-procedure influences from patient characteristics and co-morbidities, cognitive and technical skills of the endoscopist, the nature of the pathology to be treated and ethical circumstances), “withincomes” (ERCP techniques to be used, intra-procedure findings and unexpected events, degree of success and difficulty) and “outcomes” (technical and clinical success, adverse events, need for further intervention, patient satisfaction and recovery) for an individual together with supportive evidence from the literature. Past research has allowed us to reach the current level of ERCP usage with considerable benefit to our patients, but definition of risk-benefit has been lacking and is desirable in all of the settings in which ERCP is applicable. Future research, whether carefully performed prospective or retrospective analyses of databases, cohort studies or randomized controlled trials, must

concentrate on precise definition of patient populations, cost-benefit and risk-benefit in order to clarify the role of ERCP in the setting being tested.

This landmark NIH-sponsored conference will address many of these issues and clarify where the science of ERCP has come from, is now and will be. The innovators who gave us the technique of endoscopic sphincterotomy began a new era of minimally invasive therapy well ahead of the surgical revolutions of more recent years, and the pioneers who followed expanded these methods to provide the tools with which to treat our patients with biliary and pancreatic disease successfully, safely and efficiently. Personally, I hope that the recognition of importance of the practice of ERCP techniques that this conference will impart will assist in the development of additional research planning and training programs and provide strong evidence for agencies to make appropriate decisions regarding funding and reimbursement.

Epidemiology and Natural History of Common Bile Duct Stones and Prediction of Disease

Sum P. Lee, M.D., Ph.D.

More than 98% of all biliary tract disorders are in some way related to biliary concretions. Stones are most commonly found in the gallbladder, and 15% of the population harbors stones in the gallbladder, which necessitates 675,000 cholecystectomies per year. The fiscal burden of gallstone disease has been estimated to be at least $6 billion, which exceeds the sum total for chronic liver disease and cirrhosis ($1.6 billion), chronic hepatitis C ($0.8 billion), and diseases of the pancreas ($2.2 billion). Gallstones are related to genetic and environmental factors. It is more common in Native Americans and South Americans and is related to female gender (and multiparity), age, central obesity, hypercholesterolemia, diabetes, dietary constituents, and physical activity. Gallstones can pass through the cystic duct to become intrahepatic or extrahepatic stones. In some clinical situations, bile duct stones can develop as primary intrahepatic or extrahepatic bile duct stones without involving the gallbladder. Primary bile duct concretions are much more common in patients of Asian descent compared with those of European descent.

Choledocholithiasis, or stones in the common bile duct, mostly originate from the gallbladder and are found in 8–18% of patients with symptomatic gallstones. Coexistent gallbladder and common duct stones are correlated with increasing age, Asian descent, chronic inflammatory conditions (primary sclerosing cholangitis [PSC], AIDS, or parasites), and possibly hypothyroidism.

Choledocholithiasis may present in any of the following ways: (1) biliary colic, (2) jaundice, (3) cholangitis, or (4) pancreatitis. The last three of these may appear in all possible combinations. For example, although pain may be the only symptom in some, it may be accompanied by jaundice in others. Pancreatitis may develop without symptoms referable to the biliary system, or it may be accompanied by jaundice or cholangitis. Other much less common complications include hepatic abscesses, secondary biliary cirrhosis, and portal hypertension. Common bile duct stones are covered by a biofilm of bacteria. The sessile adherent bacteria reside in a sealed off microenvironment and are quiescent. When the stone obstructs the bile duct or ampulla of Vater, cytokines, probably from epithelial cell origin, activate these bacteria to the planktonic and virulent forms. Obstruction by stones is often accompanied by bacterial sepsis because of the activation of the bacterial biofilm in stones. Malignant obstruction without stones is much less likely to result in sepsis. Cholangitis should be viewed as a medical emergency. In patients with acute pancreatitis who also harbor gallbladder stones, the incidence of common bile duct stone has been reported to be as high as 78% in those requiring urgent surgery. Many stones will pass spontaneously into the duodenum in a matter of hours.

Predictions of coexistent common bile duct stone in the context of gallbladder stone include the use of clinical, biochemical, and imaging modalities. A history of cholangitis or pancreatitis, age, an elevation of serum bilirubin, aspartate transaminase (AST), and alkaline

phosphatase are independent positive predictors. Ultrasonography is not a sensitive and specific diagnostic tool for the presence/absence of common duct stone. The caliber of the common bile is a useful predictor. A number of imaging techniques can be used: magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography (EUS), computerized tomography (CT), or IV cholangiogram with tomography. In a patient with gallbladder stones prepared for elective cholecystectomy or a patient with known gallbladder stones presenting with acute pancreatitis, when should the common bile duct be imaged or therapeutic intervention be considered, remain areas of active investigation.

References

American Gastroenterological Association. The burden of gastrointestinal diseases. 2001.

Onchen J, Brazer SR, Eisen GM, et al. Predicting the presence of choledocholithiasis in patients with symptomatic cholelithiasis. Am J Gastroenterology 1996; 91: 762–767.

Sekijima J, Lee SP. Gallstones and cholecystitis. In: Textbook of internal medicine. Kelly WN (ed). Lippincott-Raven, 1997. Third Edition, p. 807–814.

Use of MRCP Versus ERCP in the Diagnosis of Common Bile Duct Stones

Ann S. Fulcher, M.D.

Magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) are both useful tools for evaluating biliary and pancreatic ductal disease. Although ERCP has long been considered the standard of reference for evaluating the biliary tract and pancreatic duct, MRCP is assuming a larger role as a rapid, accurate, and non-invasive alternative to diagnostic ERCP. During the past several years, radiologists and nonradiologists alike have shown a keen interest in MRCP and its clinical applications. Technical refinements, such as fast MR sequences that allow for imaging of the entire biliary tract and pancreatic duct in a single breathhold, have resulted in marked improvement in the quality and diagnostic yield of MRCPs.[1] As the quality of MRCPs has improved, the clinical applications of this technique have expanded such that MRCP is now replacing diagnostic ERCP in many instances. One clinical application of MRCP lies in the detection of common bile duct (CBD) stones.

In order for MRCP to gain acceptance as an alternative to diagnostic ERCP in the detection of choledocholithiasis, the sensitivity and specificity of MRCP must at least equal those of ERCP in this setting. However, the determination of the sensitivity and specificity of ERCP in the diagnosis of choledocholithiasis is difficult, since ERCP is considered the standard of reference for CBD stone detection. In an analysis of 72 patients studied with intraoperative cholangiography and ERCP, Frey et al. found a sensitivity of 90% and a specificity of 98% for ERCP in the setting of choledocholithiasis.[2]

Early studies focusing on the role of MRCP in the detection of CBD stones yielded sensitivities ranging from 81–92% and specificities ranging from 91–100%.[3–5] However, technical advances resulting in improvements in signal-to-noise and spatial resolution and in minimization of motion artifacts have further enhanced the MRCP diagnosis of choledocholithiasis. Recent studies note sensitivities of 90–100%[6–8] and specificities of 92–100%, matching and, in most cases, exceeding those of ERCP. Positive predictive values range from 96 to 100%.[6–8]

Equally important as the sensitivity, specificity, and positive predictive value of MRCP is its negative predictive value that ranges from 96–100%.[6–8] Therefore, if an MRCP is interpreted as negative for common duct stones, then one can avoid the performance of a diagnostic ERCP in most cases. MRCP is particularly useful in the evaluation of patients with suspected gallstone pancreatitis, as many gastroenterologists are reluctant to perform diagnostic ERCP in the setting of ongoing acute pancreatitis. If MRCP is positive for CBD stones, then those patients can be triaged to therapeutic ERCP when deemed clinically appropriate. Alternatively, if MRCP is negative for CBD stones, then a diagnostic ERCP and its complications may be avoided.

MRCP is useful not only in detecting and excluding CBD stones, but also in determining their number, size, and location. MRCP detects stones as small as 2 mm.[3,6]

In order for MRCP to compare favorably with diagnostic ERCP, MRCP must provide depiction of the biliary tract not only in patients with ductal dilatation, but also in those with normal caliber ducts. Multiple studies have shown that MRCP allows for depiction of normal caliber and dilated extrahepatic bile ducts in their entirety in essentially all patients.[3,5,6] Fulcher et al. noted that complete depiction of the normal caliber extrahepatic bile was achieved in 35 of 35 control patients.[6] This degree of ductal depiction exceeds that of ERCP, since ERCP fails to opacify the ductal system in up to 10–20% of all attempts.[9]

In contrast to ERCP, MRCP is noninvasive. This represents a major advantage as complications occur in as many as 5% of patients undergoing diagnostic ERCP.[9,10] The most common ERCP-related complication is pancreatitis, which occurs in 3.6%–5.1% of diagnostic ERCPs.[10–12]

The major disadvantage of MRCP is that it does not provide access for therapeutic interventions as does ERCP.

In summary, since the first clinical application of MRCP over a decade ago, MRCP has emerged as a viable alternative to diagnostic ERCP in the setting of suspected choledocholithiasis. The utility of MRCP in this setting is related to its sensitivity and specificity, which equals or exceeds those of ERCP; its ability to provide complete depiction of normal caliber and dilated bile ducts; and its noninvasive nature. However, as the role of MRCP continues to evolve, not only must these factors be considered, but also its cost effectiveness in detecting and excluding CBD stones.

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Endoscopic Ultrasonography (EUS) in Bile Duct Stones: How Does It Compare to ERCP?

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An accurate, noninvasive, reliable, and safe method for bile duct imaging would be highly advantageous, particularly for patients with symptoms due to cholelithiasis when laparoscopic cholecystectomy is contemplated. In this clinical situation, the possibility of choledocholithiasis must always be considered, as choledocholithiasis dictates modification of the therapeutic plan. The suspicion for choledocholithiasis, based on clinical and biochemical parameters, ranges from low to high. For this diagnosis, the accuracy of currently available noninvasive imaging studies, with the possible exception of magnetic resonance cholangiopancreatography (MRCP), is unsatisfactory. Endoscopic retrograde cholangiopancreatography (ERCP) is relatively reliable and highly accurate in relation to computerized tomography (CT) and transabdominal ultrasonography (US), but ERCP is the most invasive of the available methods. EUS, a potential alternative, is relatively less invasive, with a risk of complications similar to that of upper endoscopy.

The systematic use of endosonography for diagnosis of choledocholithiasis was first reported by Edmundowicz et al.[1] in 1992. Since then, the results of eight prospective controlled trials (two from a single group; two multicenter),[2–9] and one retrospective study[10] have been reported. Although differing in design, all studies found EUS accuracy comparable to that of ERCP for the diagnosis and exclusion of choledocholithiasis. The echoendoscopes employed in all studies were radial scanning instruments, but comparable accuracy has been obtained with a linear scanning echoendoscope.[11]

One limitation of these studies is that cholangiography, either endoscopic retrograde (ERC) or intraoperative (IOC), was used predominantly as the reference standard for the presence or absence of stones. Although this was usually combined with endoscopic sphincterotomy (ES) and duct instrumentation, or surgical exploration of the duct, it is well-recognized that stones, especially if small, may be missed by cholangiography. Thus, the true sensitivity and negative predictive value of EUS, based on available data, are less certain. Nevertheless, it is clear that EUS is at least as sensitive and specific as ERCP for the diagnosis of choledocholithiasis.

A further limitation of most available studies is that, by design, bile duct stones were highly suspected in the patients enrolled.[2–5,9] Although endosonographers were usually blinded to the results of other imaging studies, they were aware of the inclusion criteria for the study. Thus, available data pertains mainly to situations where there is a reasonable probability stones are present. However, in the multicenter trial of Montario et al.,[7] EUS was compared to IOC in 240 patients with no clinical or biochemical evidence of choledocholithiasis, who were scheduled for cholecystectomy because of symptoms attributed to cholelithiasis. Patients were followed for 1 year. Although the sensitivity, specificity, positive and negative predictive values for EUS with respect to choledocholithiasis were excellent, IOC was in all respects significantly

better. Canto et al.[6] stratified patients into groups at high, moderate, indeterminate, and low risk for bile duct stones. The negative predictive value of EUS was high (91 to 100%) for patients in risk categories moderate, indeterminate, and low. Whereas ERCP is more likely to be beneficial when choledocholithiasis is probable, and the risks, therefore, justified, these investigators suggested EUS as the more appropriate test, based on risk and cost, when the index of suspicion for ductal stones is low or uncertain.

There are limited data regarding EUS versus MRCP for the diagnosis of choledocholithiasis. de Ledinghen et al.[9] obtained EUS and MRCP in 43 patients with suspected choledocholithiasis with ERC/ES or surgery as the reference standard. The sensitivity, specificity, positive predictive value, and negative predictive values for EUS were, respectively, 100%, 95.4%, 90.9%, and 100%. Corresponding values for MRCP were, respectively, 100%, 72.7%, 62.5%, and 100%.

Although US is the imaging method of choice for cholelithiasis, the question arises whether EUS alone would be satisfactory for evaluation of the gallbladder in patients undergoing endosonography because of a suspicion for choledocholithiasis. In the multicenter study of Chak et al.,[8] EUS was performed immediately before ERCP (separate endoscopists) in 36 patients with suspected gallstone-induced pancreatitis. EUS was highly accurate for the diagnosis of bile duct stones and also provided useful information concerning pancreatic inflammation. Moreover, US and EUS were also concordant with respect to gallbladder findings in 92% of patients.

The few technical limitations of biliary endosonography include stenotic upper gastrointestinal (GI) lesions and prior gastric resection. Imaging may be compromised by air in the bile duct (as might occur after ES), surgical clips, calcification in the pancreas, and the presence of a duodenal diverticulum. Perhaps the major technical problem, however, is the inability to adequately image the intrahepatic ducts.

Cholangiographic detection of small stones and/or sludge can be problematic, especially if the bile duct is dilated. Dense opacification may obscure small defects. Furthermore, it can be difficult to differentiate air bubbles, introduced inadvertently during ERCP, from small stones. Thus, stones may be missed or ES may be performed unnecessarily. High frequency catheter ultrasound probes are suitable for intraductal imaging.[12–14] Newer designs allow insertion over a guidewire.[13] In addition, small, inexpensive processors/display units are available for use with these probes, making the entire system highly portable and suitable for use in the ERCP procedure room. Because stones have specific ultrasonographic characteristics, intraductal ultrasound (IDUS) is technically simple and can be performed in a few minutes. Although data are limited, all studies show that IDUS in conjunction with ERC increases diagnostic accuracy by comparison to ERC alone.[12–14]

Although available data are sufficient to establish a role for EUS in the diagnosis and exclusion of bile duct stones, this imaging technique has not been widely adopted, despite the potential of EUS to improve the management of patients when choledocholithiasis is a possibility. This undoubtedly relates to issues of training, experience, and availability of EUS instrument systems. And while the concept of performing ERCP immediately if EUS demonstrates bile duct stones is attractive, for logistical and other reasons, this is possible in only a few endoscopy units.

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Therapeutic Role of ERCP in the Management of Suspected Common Bile Duct Stones

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Therapeutic endoscopic retrograde cholangiopancreatography (ERCP) was born with the introduction of endoscopic sphincterotomy (ES) in 1973, which transformed the therapeutic approach to biliary disease, especially the management of common bile duct (CBD) stones. Today, more than 150,000 endoscopic biliary sphincterotomies are performed annually in the United States. Patients with bile duct stones present with a variety of clinical problems, alone or in combination, namely, cholestasis, pain, cholangitis, pancreatitis, or as asymptomatic demonstration on imaging or operative cholangiography. It has become increasingly feasible, acceptable and supportable to treat patients in all these categories endoscopically.

In its infancy, endoscopic therapy was initially considered justifiable only in elderly post-cholecystectomy patients with recurrent or retained CBD stones who were at high risk of serious complications from open surgical CBD exploration or re-exploration. At that time, few endoscopy centers could offer the techniques, and criticisms by surgical experts were common. Adolescence witnessed the impressive successes of ES and stone extraction methods in this high-risk group and, because of an expansion of units offering endoscopic therapy, the low level of associated complications and a strong patient preference, many centers were persuaded to widen their indications for the procedure to include younger post-cholecystectomy patients, and, later, a range of patients with gallbladders for whom CBD stones were the principal clinical problem. Much of this occurred in the absence of any comparative trial data to aid decisionmaking and, indeed, there was such enthusiasm for endoscopic therapy that the establishment of randomized trials became difficult. Nevertheless, the wisdom of maturity dictated that, as they are essential to settle arguments about relative morbidity and mortality risks in different patient populations and the bias of selection for treatment by endoscopic or surgical means, such prospective studies were forthcoming and have provided a sound basis on which to triage patients.

Concomitant with the developments of wider clinical application has been the evolution of endoscopic techniques to reduce stone size and facilitate endoscopic removal. These comprise mechanical lithotripsy, laser lithotripsy and electrohydraulic lithotripsy (EHL). There was a growing appreciation that maintaining biliary drainage was imperative following any endoscopic intervention and could be achieved by nasobiliary tube or endoprosthesis. Many lithotripsy techniques can also be applied through percutaneous choledochoscopy, which may be the only endoscopic option if the per-oral route is denied or fails.

The endoscopist is now faced with the referral of a number of clearly defined groups of patients with confirmed or suspected bile duct stones for whom endoscopic therapy may be optimal compared to alternatives:

- Severe cholangitis with or without cholelithiasis
- Severe gallstone pancreatitis
- Symptomatic CBD stone(s) with pain, abnormal liver enzymes/bilirubin or obstructive jaundice (with positive or suspicious imaging)
- Post-cholecystectomy retained stone(s)
- Post-cholecystectomy, stone(s) shown on intraoperative cholangiography
- Gallbladder in situ, variable risk factors for surgical CBD exploration and a questionable need for cholecystectomy

The availability of endoscopic therapy has significantly influenced surgical decisionmaking in the era of laparoscopic cholecystectomy when bile duct stones are suspected or confirmed and the technique of ERCP with ES can be conveniently performed pre- or post-operatively. When the expertise of laparoscopic CBD stone extraction is available, however, its use is cost-effective compared to therapeutic ERCP in patients undergoing cholecystectomy.

Risk factors can be identified in all patients with CBD stones, allowing decisions to be made in favor of one or other mode of therapy. Documentation of such factors and how they influence outcome from different treatments needs to be examined in relation to endoscopic therapy and its surgical alternatives. Such factors may confer lower as well as higher-than-average risk from endoscopic intervention.

There are expert endoscopy centers with a greater than 99% bile duct clearance rate for bile duct stones, yet there are many circumstances in which an integrated team approach must involve two or all of the disciplines of gastroenterology, radiology, and surgery in order to plan an empirically safe and successful strategy.

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Surgical Management of Common Bile Duct Stones

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Overview

Choledocholithiasis occurs in approximately one in ten patients who have cholelithiasis. Despite suggestions by some authors that the incidence of common bile duct (CBD) stones is decreasing, data from clinical series in which intraoperative imaging (cholangiography or ultrasonography) is routinely practiced continues to demonstrate an 8 to 15% incidence of CBD stones.[1]

Surgical management of CBD stones at the time of cholecystectomy, with a success rate of $\geq$ 90%, was well established as the standard of care for the treatment of CBD stones in the era of open cholecystectomy (1882–1988).[2] Soon after the introduction of laparoscopic cholecystectomy (LC) in 1985 in Germany and in 1988 in the United States, LC replaced open cholecystectomy as the "gold standard" for the treatment of gallbladder stones. It was unclear at that time, however, whether a laparoscopic solution to CBD stone management was feasible, safe, practical, and cost-effective.[3,4] Fortunately, developments during the last decade have allowed us to answer those questions in the affirmative. The feasibility of laparoscopic common duct exploration (LCDE) was demonstrated in 1990, and since that time numerous techniques have been developed.[5] The rapid evolution of LCDE has resulted in success rates of $\geq$ 90% in numerous large series, just as in the pre-laparoscopic era. Additionally, the patient benefits associated with LC—decreased pain, shorter length of stay (LOS), and more rapid return to full activity—are preserved with LCDE.[6–9]

Techniques

Laparoscopic choledocholithotomy may involve the application of a number of technical maneuvers. These include administration of glucagon and flushing of the ductal system, dilatation of the distal common bile duct and flushing, balloon catheter manipulation and stone retrieval, basket manipulation and stone retrieval—with or without fluoroscopic guidance, choledochoscopic manipulations, and intraoperative lithotripsy.[5–10] In keeping with the minimally invasive theme, less invasive techniques are generally used before more invasive techniques. All of these techniques presuppose that intraoperative imaging has been performed, whether or not preoperative ductal evaluation (chemical, radiographic, or endoscopic retrograde cholangiography [ERC]) has been used to evaluate or treat the common duct pathology prior to that time.

The feasibility of laparoscopic biliary drainage procedures has also been documented. These maneuvers include intraoperative antegrade or retrograde sphincterotomy, and choledocho-enterostomy. While the latter is employed primarily for obstructive neoplastic disease, intraoperative sphincterotomy has been used for some cases of choledocholithiasis.[11]

Intraoperative sphincterotomy, however, has not been widely adopted because of the logistics of bringing a second team of endoscopists with their equipment and staff into an already crowded operating room.

Most laparoscopists have generally preferred the transcystic route for ductal exploration when it is feasible. In most series, it is successful in 80 to 90% of cases.[9,17,18] In some authors' experience, Franklin for example, the type and size of the ductal stones dictate the need for a transductal approach in approximately 90% of cases.[19] As discussed above, there are well-defined criteria that should lead a surgeon to one or the other approach.

Patient Management

There are three situations that the clinician may encounter with the patient who harbors CBD stones: those in whom the stones are documented preoperatively, those in whom the stones are found intraoperatively, and those in whom stones are present postoperatively. It is well established that the third situation is best treated with endoscopic retrograde cholangiopancreatography and extraction with or without sphincterotomy (ERCP ± S), so this will not be discussed here.

In the first situation, the clinician must decide whether to attempt ductal stone treatment, ERC ± S before the operation or to proceed directly with LC and LCDE.[15] ERC ± S is successful in clearing the common duct in 70% to > 90% of cases.[12–14] Similarly, LCDE is successful in clearing the duct in 70% to > 90% of cases as well.[5–11] In the early 1990s, however, when preoperative ERCP ± S was used quite liberally for patients suspected of having CBD stones, a normal exam was documented in 40 to 60% of cases.[4,12,14] So, almost half of these exams were unnecessary. Moreover, these patients were exposed to the added morbidity and mortality for ERC ± S, which has been reported as high as 5–19% and 1.3%, respectively.[15,16]

Numerous authors have suggested that the choice of clearance method should be based on the local availability of expert endoscopists capable of a high degree success with ERC ± S, the availability of laparoscopic and choledochoscopic equipment, the surgeon's own expertise in laparoscopic surgery, and the general condition of the patient.[5–11]

When CBD stones are discovered intraoperatively, the surgeon either proceeds with LCDE and converts the case to open common bile duct exploration (CBDE) and choledocholithotomy or leaves the stones in place for subsequent ERC ± S. The rationale for leaving the stones in place and not proceeding directly with open CBDE was developed in an attempt to maintain the minimal invasiveness and morbidity of the laparoscopic approach in the treatment of CBD stones.

Although any of these alternatives is acceptable, the latter two are more costly, and open CBDE is associated with increased morbidity. Therefore, it would seem wise in most situations, if the surgeon is properly trained, to attempt LCDE, unless the patient's condition warrants termination of the anesthetic as soon as possible. If LCDE is unsuccessful or not attempted, then the decision regarding conversion to open CBDE versus postoperative ERC ± S will depend on

the local availability of expert endoscopists. That is to say, if expert endoscopists are not readily available, then conversion to open CBDE should be considered.

These considerations are illustrated in Figure 1.

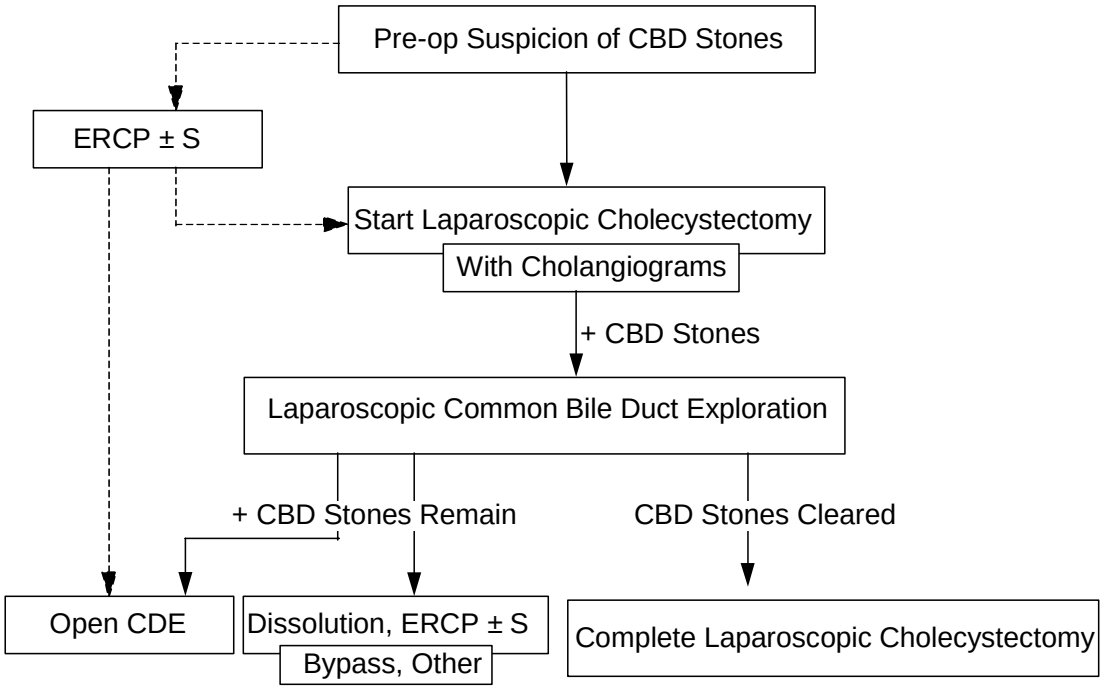

Figure 1. Protocol for Management of Common Bile Duct Stones

Results

Thousands of successful LCDEs have been reported since the introduction of LC in the late 1980s. During this time, techniques have evolved that enhance the likelihood of success of the procedure. In experienced hands, successful ductal clearance rates exceed 90%.[5,6,10,11,14,17–19] Morbidity rates have been low in these series, 8–10%. Mortality has occurred in less than 1% of patients. An overview of the results of some larger series is shown in Table 1.

Laparoscopic choledocholithotomy takes longer than straightforward LC. The mean operative times (in minutes) for some of the larger series are given here: DePaula,110; Petelin, 120; Phillips, 136; Franklin, 150; Millat, 140; Lezoche, 128; Gigot, 170–219; Rhodes, 55 (basket only). Assuming that the mean operative time for LC is less than 1 hour, it appears that LCDE adds approximately 1 hour or more to the procedure time.

Table 1. Results of Laparoscopic Common Bile Duct Exploration

Surgeon	Year	Total LCDE Cases	Transcystic Route	%	Choledochotomy Route	%	Total Successful Clearance	%	Mortality	%
Petelin	1991	22	20	91	1	5	19	86	0	0.0
Shapiro	1991	16	15	94	1	6	16	100	0	0.0
Hunter	1992	20	20	100	0	0	17	85	0	0.0
Petelin	1993	77	75	97	2	3	74	96	1	1.3
Fielding et al.	1993	21	20	95	1	5	17	81	0	0.0
Fletcher	1993	12	12	100	0	0	8	67	0	0.0
DePaula	1994	119	107	90	12	10	108	91	1	0.8
Phillips et al.	1994	120	111	93	9	8	112	93	1	0.8
Dion et al.	1994	59	18	31	41	69	52	88	0	0.0
Ferzli et al.	1994	24	13	54	11	46	24	100	0	0.0
SAGES Study	1994	226	188	83	38	17	210	93	1	0.4
Franklin	1995	113	2	2	111	98	112	99	1	0.9
Phillips et al.	1995	162	145	90	17	10	150	93	1	0.6
Rhodes et al.	1995	129	94	73	35	27	119	92	0	0.0
Millat et al.	1995	115	80	70	35	30	100	87	0	0.0
Lezoche et al.	1996	100	67	67	33	33	96	96	1	1.0
Motson et al.	1996	60	46	77	14	23	56	93	0	0.0
EAES Study	1996	82	42	51	40	49	68	83	1	1.2
Petelin	1996	197	173	88	24	12	189	96	1	0.5
Drouard et al.	1997	161	60	37	101	63	148	92	0	0.0
Millat et al.	1997	236	134	57	102	43	208	88	1	0.4
Gigot et al.	1997	92	62	67	30	33	77	84	2	2.2
Rhodes et al.*	1998	40	28	70	12	30	30	75	0	0.0
Lezoche et al.	1998	161	109	68	52	32	157	97	1	0.6
Franklin et al.	1998	148	3	2	145	98	140	95	1	0.7
DePaula	1998	181	147	81	34	19	170	94	1	0.6
Petelin	1998	243	206	85	37	15	235	97	1	0.4

Note: Some authors are listed more than once to show series evolution over time.
*This series is reported from a different institution with other associates. No choledochoscopic methods were used.

Whereas the LOS for LC is generally less than 24 hours, the LOS for patients undergoing LCDE ranges from 1.3 to 7 days, depending on the severity of the disease, co-morbid factors, access route, whether or not a T-tube was placed, and whether or not a biliary enteric anastomosis was created. For transcystic LCDE, the mean length of stay is 1.5 days in many large series. LOS for LCDE via choledochotomy is generally longer than that for the transcystic approach.

Morbidity associated with LCDE occurs in approximately 8 to 10% of patients and includes those problems typically associated with general surgery and laparoscopy: nausea, diarrhea, ileus, ecchymosis, atelectasis, fever, phlebitis, urinary retention, urinary tract infection, wound infection/inflammation, biliary leak, dislodged T-tube, sub-hepatic fluid collection, pulmonary embolus, and myocardial infarction. It is generally found that the incidence of complications is less with a laparoscopic approach than an open approach to CBD stones.

Summary

Since 1990, surgeons throughout the world have developed a comprehensive laparoscopic solution to the problem of CBD stones. The success rate among accomplished laparoscopists approaches 90% or better. This compares favorably with treatment expectations in the pre-laparoscopic era and addresses Perissat's challenge, which is, "We must move towards a management policy . . . which prevents patients from needing a dangerous and debilitating second operation . . . (i.e. ERC ± S)."[20]

Unfortunately, most surgeons in America do not currently employ a laparoscopic approach to the treatment of CBD stones. This presents significant costs (nearly double) to the patients and the health care system.[21]

Biliary tract surgeons practicing in this era should have the ability to treat all benign biliary tract pathology laparoscopically in one setting, not requiring a series of patient manipulations.

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Epidemiology and Natural History of Pancreatic and Biliary Tract Malignancies

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Pancreatic cancer is the fifth leading cause of cancer-related death in the United States and will result in an estimated 28,900 deaths in 2001.[1] In comparison, biliary tract cancer is rare, accounting for approximately 4,300 deaths per year.[2] The progression of pancreatic and biliary tract cancer often occurs without early symptoms, and diagnosis takes place late in the natural history of the disease. Consequently, both types of cancers have dismal survival rates, and treatment has little to no effect on prolonging the lives of these patients.

The majority of pancreatic cancer arises in the exocrine pancreas.[3] In the United States, incidence rates among men are approximately 1.3 times those among women, and blacks have 1.6 times the rates of whites. Incidence increases exponentially with age after 30 years old, and 80% of all cases are diagnosed between the ages of 60 and 80. Although pancreatic cancer incidence varies widely around the world, comparisons are challenging due to inconsistencies in diagnostic accuracy. However, industrialized nations appear to carry a higher burden of pancreatic cancer than less developed nations.

In the past two decades, epidemiological studies examining pancreatic cancer have been plagued with methodological issues associated with studying a highly fatal disease, thereby hindering our understanding of the etiology of pancreatic cancer. Nevertheless, studies have consistently shown that tobacco smoking increases the risk of pancreatic cancer. Strong evidence also supports the association between pancreatic cancer and two medical conditions—chronic pancreatitis and diabetes mellitus. Given that these conditions are often present numerous years prior to the cancer diagnosis, they should be considered as etiologically relevant.[4] A series of recent studies indicates that obesity may be an important risk factor for pancreatic cancer.[5–9] Other potential lifestyle risk factors include dietary factors such as meat and glycemic load, and physical activity.[7–8]

Biliary tract cancer can arise in the gallbladder or extrahepatic bile ducts. Gallbladder cancer is the most common of the two types and occurs more frequently in women than in men. In contrast, extrahepatic bile duct cancer is seen more frequently in men. Although biliary tract tumors are relatively uncommon in the United States, certain ethnic groups, notably American Indians and Hispanic Americans, have substantially higher rates than the rest of the population. Gallstone disease is the most important risk factor for gallbladder cancer, increasing the risk by at least threefold. Due to the rarity of biliary tract tumors, diagnostic difficulties, and high mortality, other risk factors for this cancer are not well established. Among the potential risk factors are cholecystitis, biliary tract infections, reproductive factors, ulcerative colitis, family history, and obesity.

Given the important epidemiologic dissimilarities of pancreatico-biliary cancers, correct classification is critical to improve the quality of epidemiologic studies. A better understanding

of the underlying causes of these deadly cancers will provide new leads for early detection, treatment, and prevention.

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Diagnostic and Therapeutic Uses of ERCP in Pancreatic and Biliary Tract Malignancies

Robert H. Hawes, M.D.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has an established role in the diagnosis and treatment of pancreatobiliary malignancies. Its role has been expanded with the advent of ancillary techniques, such as intraductal ultrasound (IDUS) for staging, cholangiopancreatoscopy for diagnosis, and the recent introduction of photodynamic therapy (PDT) for the treatment of cholangiocarcinoma. The principle role of ERCP has been in the palliation of malignant obstructive jaundice, and this has been accomplished by the placement of plastic, or more recently, expandable metal stents. This paper will review the clinical utility of ERCP in pancreaticobiliary malignancies and will explore its role compared to alternative techniques.

Role of ERCP in the Diagnosis of Pancreatobiliary Malignancies

ERCP has become the primary technique for obtaining direct cholangiography and pancreatography. Percutaneous transhepatic cholangiography (PTC) is an alternative technique but is limited to imagining the biliary tree and is felt to be more invasive and carry higher risk when compared to ERCP. The indications for PTC are failed ERCP and altered anatomy preventing successful ERCP—Bilroth II and Roux-Y choledochojejunostomy. Direct cholangiopancreatography is quite a sensitive technique in detecting the presence, level, and extent of obstruction in the biliary system and pancreas. Experience with the interpretation of cholangiopancreatography can lead to a relatively accurate diagnosis as to the presence or absence of malignancy.

More recently, an alternative technique of magnetic resonance cholangiopancreatography (MRCP) has emerged, and with respect to determining the presence or absence, level, and extent of biliary and pancreatic obstruction, studies would suggest that MRCP approaches the accuracy of ERCP (Soto 1996, Hall-Craggs 1993). Accuracy of ERCP is dependent on the experience of the endoscopist, while MRCP is dependent on the sophistication of the MR machine, technique, and software. From a purely diagnostic perspective, MRCP and ERCP are relatively equivalent in their ability to diagnose pancreatobiliary cancers.

The actual diagnosis of malignancy must be established by tissue acquisition. There are basically 4 techniques used to obtain cytology or biopsy at the time of ERCP—(1) forceps biopsy, (2) needle aspiration, (3) bile or pancreatic juice aspiration, and (4) brush cytology. From a technical perspective, bile or pancreatic juice cytology and cytologic brushings are the easiest samples to obtain. Forceps biopsy and needle aspiration cytology generally require a

sphincterotomy in order to achieve access to the biliary tree or pancreas. Individually, forceps biopsy has the highest yield, and needle aspiration fluid cytology probably has the lowest yield (Iitsuka 1984, Howell 1992, Kubota 1993). Several studies have suggested that the overall diagnostic accuracy can be increased by increasing the variety of samples. For example, the combination of needle aspiration, brush cytology, and forceps biopsy has greater accuracy than needle aspiration plus brush cytology, brush cytology plus forceps biopsy, or needle aspiration plus forceps biopsy, and these combinations are better than any single sampling technique (Jailwala 2000).

From a technical standpoint, many practitioners wish to avoid performing sphincterotomy, and, therefore, needle aspiration and forceps biopsies are not routinely performed. In general, brush cytology will be the only tissue sample taken in most cases of pancreatobiliary strictures (Foutch 1990).

Ancillary Procedures for Diagnosis of Pancreatobiliary Malignancy

Just as direct inspection of the gut mucosa with flexible endoscopy has proved more sensitive than barium contrast studies in the diagnosis of gut malignancies, so it is likely that direct inspection of the pancreatobiliary tree would improve our diagnostic potential over cholangiopancreatography (Seo 2000, Kim 2000). Up to now, industry has been unable to produce simple, reliable, and inexpensive optical catheter systems that permit direct inspection of the biliary and pancreatic epithelium to improve the diagnosis of biliary and pancreatic strictures. Some reports have emerged suggesting that direct inspection of pancreatic or biliary strictures using ultrathin endoscopes can aid in the differential diagnosis between malignant and benign biliary stricture—the vascular pattern is apparently different (Kim 2000) in these two entities. At this time, experience is very preliminary; because of the general unavailability of babyscopes or optical catheters, this is not a procedure that is routinely performed.

Some very preliminary work is beginning with performing “optical biopsies.” These utilize spectroscopic data obtained by passing a laser light or bright light down flexible catheters (Mike Wallace—personal communication). These systems are currently most widely employed in the gastrointestinal tract and bronchial tree but may find application in the future in the biliary tree and pancreas.

The Role of ERCP in the Therapy of Pancreatobiliary Malignancies

The primary consequence of malignancies arising from the pancreas or biliary tree is obstructive jaundice. It is widely appreciated that relief of obstructive jaundice improves symptoms, quality of life, and survival. Despite the introduction of endoscopic stenting in the late 1970s, it was not until the mid-1990s that we began to see formal outcomes studies assessing the efficacy of endoscopic stenting in terms of quality of life. Three studies were published in the mid-1990s, and all showed improvement in quality of life measures after endoscopic stenting (Sherman 1996, Luman 1997, Ballinger 1994). Though all three studies had methodologic problems, a consistent conclusion from all of them was that endoscopic stenting in malignant obstructive jaundice relieved symptoms and improved quality of life compared to the time before stenting. There are three competing techniques for relief of jaundice associated with

pancreatobiliary malignancies: (1) percutaneous transhepatic cholangiography with drainage, (2) surgical bypass, and (3) endoscopic stenting.

There have been relatively few studies to compare these competing techniques. In the mid-1980s, plastic stents were the only available technology to relieve jaundice in an obstructed biliary tree. These could be placed endoscopically or transhepatically. One randomized trial was performed and showed a significantly lower complication rate and higher success rate for endoscopic stenting (Speer 1987). This trial has not been repeated since the advent of expandable metal stents, which would likely improve the results with percutaneous placement.

It is extremely difficult to successfully complete studies that compare surgical to endoscopic treatments. One study did randomize patients with malignant obstructive jaundice (unresectable for cure) to surgical versus endoscopic palliation (Smith 1994). The interpretation of this study is somewhat complex, but as one might guess, surgical palliation has a higher immediate complication rate and a longer initial hospitalization but provides longer term palliation without need for reintervention. Regrettably, economic factors were not analyzed, but in two other studies—one a decision analysis model and the other a retrospective cost analysis—endoscopic stenting was shown to be more cost-effective (Raikar 1996, Brandabur 1998).

Over the last 15 years, gastroenterology training programs have succeeding in training a sufficient number of gastroenterologists to perform a standard therapeutic ERCP, which includes sphincterotomy and stent placement. As a result of the general availability of this technique in most communities combined with the perception that endoscopic stent placement is less invasive than surgical bypass or percutaneous drainage, endoscopic stenting for the palliation of malignant obstructive jaundice has become the standard. Exceptions include young patients who are explored with the hope of cure but ultimately require palliation alone and patients with altered anatomy preventing successful ERCP.

In the late 1980s, expandable metal stents became available to endoscopists, and following their introduction, a number of studies compared expandable metal stents to plastic stents for the palliation of jaundice due to malignancy (Davids 1992, Prat 1998). These trials have been relatively uniform in their findings and demonstrate that patency of metal stents is significantly longer than plastic stents, but despite the longer patency, 50% of patients undergoing metal stent placement required reintervention due to current biliary obstruction. Economic analyses have been relatively rudimentary but highlight the balance between the high up front costs for metal stent placement versus the lower rate of reintervention (thus avoiding the costs of repeat ERCP). In clinical practice, if the life expectancy of the patient is $\leq$ 4 months or the patient has not been completely evaluated as to their resectability, plastic stents are placed (Yeoh 1999). If at the time of the index ERCP, patients are known to have metastatic disease and are felt to have a life expectancy greater than 4 months, metal stents are generally considered to be more appropriate. Further studies are needed to measure predicted survival when patients present with unresectable malignant obstructive jaundice.

Photodynamic Therapy for Cholangiocarcinoma

Until recently, palliation via stenting was the only endoscopic treatment available for palliation of patients with malignant obstructive jaundice. Recently, we have seen the introduction of photodynamic therapy as a potential treatment both for the destruction of the primary tumor as well as the palliation of jaundice. In 1998, Ortner et al published their experience using PDT in 9 patients with non-resectable bismuth type III and IV cholangiocarcinomas, who had failed endoprosthesis placement. Patients underwent intravenous application of hematoporphyrin derivative Photofrin II (QLT Phototherapeutics, Vancouver, British Columbia) and then underwent intraluminal photoactivation via ERCP. In this small study, bilirubin levels had decreased significantly, and quality of life indices improved dramatically. The 1-year survival rate was 77% in these patients with advanced cancer with a median survival time of 439 days. This technique was then applied to a larger number of patients (21 patients) with cholangiocarcinoma, and again the bilirubin decreased, and the Karnovsky index improved significantly. The introduction of photodynamic therapy as an adjunct to endoscopic stenting appears to be a promising alternative approach to patients with cholangiocarcinoma. To date, single arm studies have been encouraging, but the efficacy must be further tested by completing randomized multicenter studies.

In summary, endoscopic placement of a plastic stent is considered standard for palliation of patients with malignant obstructive jaundice. Selected patients undergo surgical bypass or percutaneous transhepatic stent placement. Expandable metal stents have been introduced, but their longer mean patency rate is offset by substantially higher costs for the stent. The primary disadvantage of endoscopic palliation is the high rate of reintervention required for recurrent jaundice. Areas for further study include the following:

- Development of the “ideal” stent—one that will predictably remain patent for the duration of the patient’s survival
- More predictable measures of survival at the time of presentation
- Development of new endoscopic techniques that would bypass obstruction rather than require the need for stent, thus avoiding recurrent obstruction (endoscopic choledochoduodenostomy or hepaticogastrostomy)
- Further development of techniques that effectively relieve jaundice but also deliver therapy to the primary tumor

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Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) in Pancreatic and Biliary Tract Malignancies

Pablo R. Ros, M.D., M.P.H.

With the advent of multislice (multidector) CT (MS-CT) and breath hold pulsing sequences in MRI, these two cross-sectional imaging techniques are poised to play an even more important role in the management of patients with pancreatic and biliary malignancies. In this presentation, we review the state-of-the science of these two techniques applied to the study of the pancreas and biliary tract. We will not review magnetic resonance cholangiopancreatography (MRCP) since it is discussed elsewhere.

With the advent of MS-CT, the visualization of small abdominal organs and structures (such as the pancreas and the biliary tree) has dramatically improved. First, MS-CT allows fast, thin-section scanning of the abdomen with routine 1 to 1.5 mm sections. This results in scans demonstrating an exquisite anatomic detail and, therefore, allowing the detection of minute neoplasms and anatomical structures, such as minor vessels or lymph nodes. Secondly, MS-CT allows multiphasic vascular enhancement with early and late arterial phases as well as venous phase of enhancement. Thirdly, MS-CT allows isovolumetric reconstructions, allowing the visualization in any plane (even curved planes) of the pancreatic duct, biliary tree, and both arterial and venous vascular structures (CT-arteriography and venography). Therefore, MS-CT has become a superb tool for detection of small neoplasms, increasing the overall diagnostic accuracy (differentiating pancreatitis from neoplasm, and characterizing the different neoplasms), and finally as an able tool to assess resectability of pancreato-biliary tumors. We'll discuss the key findings in pancreatic adenocarcinoma, cystic neoplasms (serous and mucinous cystadenoma and cystadenocarcinoma), other exocrine neoplasms, and islet cell tumors.

In the biliary tree, MS-CT makes CT-cholangiography a viable alternative to MRCP. It also makes the detection of sub-centimeter extrahepatic cholangocarcinomas possible, refining the diagnosis of klatskin tumor and intrahepatic cholangiocarcinoma.

The role of MRI continues to be complementary to CT in pancreatic and biliary malignancies, once MRCP is excluded. However, due to the higher contrast resolution of MRI (particularly post gadolinium enhancement), it is able to depict occasionally small pancreatico-biliary tumors undetected by CT.

Finally, positron emission tomography **(**PET) and PET-CT hold the promise to play a key role in the evaluation of pancreatico-biliary malignancies, improving both detection and staging.

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Surgical Intervention in Pancreatic and Biliary Malignancies

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Introduction

Patients with pancreatic and biliary malignancies may have a surgical procedure for the purposes of diagnosis, staging, palliation, or intended curative resection of these malignancies. Endoscopic retrograde cholangiopancreatography (ERCP) may be used in such patients for diagnosis, for preoperative decompression of obstructed bile ducts, or for definitive palliation of inoperable patients. Although preoperative decompression by ERCP is commonly performed, this procedure is controversial. Unresectable patients may be palliated by ERCP or operative decompression; there is no consensus on which is the better option. I will discuss the roles of surgery and the areas of controversy in regard to ERCP from the perspective of a hepatic, pancreatic, and biliary (HPB) surgeon.

Surgery in Diagnosis

Surgery is rarely needed for diagnosis. Furthermore, preoperative tissue diagnosis is not required in those patients, whose clinical picture is compatible with a diagnosis of malignancy and who are fit for surgery. However, when the diagnosis of malignancy is doubtful or when the patient is not a surgical candidate, a tissue diagnosis is desirable. Percutaneous computerized tomography (CT)-guided or ultrasound (US)-guided biopsies or EUS directed biopsies are the first choice in these patients. Occasionally, these will fail to provide a diagnosis, either because of inaccessibility or insufficient tissue. We have shown that laparoscopic US-guided biopsy, which can supply multiple core biopsies of the pancreas, is very useful in such patients.[1]

Surgery in Staging

Many patients with hepatobiliary and pancreatic malignancies come to laparotomy after conventional preoperative testing with undetected liver or peritoneal metastases. Surgeons from the Massachusetts General Hospital[2] and the Royal Infirmary in Edinburgh[3] introduced laparoscopic staging in an attempt to lessen the incidence of unneeded laparotomies due to this cause. They reported that laparoscopy was an effective method of detecting metastases that were not apparent after standard preoperative imaging. For instance, in the case of pancreatic carcinoma, about 35% of staging laparoscopies were positive for previously undetected metastatic cancer.[2,3] Others, including our group, subsequently published studies confirming the value of staging laparoscopy in HPB malignancies.[4,5]

Examination of the abdomen by laparoscopic ultrasound was introduced as an adjunct to laparoscopy, since it can see abnormalities below the surface of structures and thereby detect intrahepatic metastases, involved lymph nodes, and vascular invasion by tumor. The Edinburgh group demonstrated that this technique increased the yield of laparoscopic staging of liver and pancreatic tumors.[3] Again, our experience and that of others supported their prior findings.[4,5] We recently showed that the utility of staging laparoscopy is diagnosis dependent.[6] In patients with cancer of the head of the pancreas, metastatic disease or vascular invasion was discovered frequently by laparoscopy (22%), whereas in ampullary/duodenal cancer, it was never found. The laparoscopic findings in cancer of the head of the pancreas had an important influence on treatment decisions, while in cancer of the ampulla/duodenum, laparoscopy had no effect on clinical decisions.[6] Laparoscopy also substantially influenced treatment of gallbladder cancer; in other tumor types, results were intermediate. Laparoscopic ultrasonography was valuable in cancer of the head of the pancreas.[6]

The value of staging laparoscopy is also dependent on the belief that endoscopic palliation is superior to operative palliation. In some major HPB centers, this is not accepted; all patients considered operable after conventional staging receive a laparotomy, and if found to be inoperable at that time, palliative surgical bypasses are performed.

Surgery for Palliation

The standard therapy for patients who are not operative candidates is endoscopic stenting of the bilary tree to relieve jaundice. The competing therapy is surgical “double bypass,” i.e., bilo-enterostomy and gastroenterostomy. One randomized controlled trial (RCT) performed in over 200 patients has compared these therapies.[7] Technical success was achieved in 94 surgical and 95 stented patients, with functional biliary decompression obtained in 92 patients in both groups. In stented patients, there was a lower procedure-related mortality (3% vs 14%, $p = 0.01$), major complication rate (11% vs 29%, $p = 0.02$), and median total hospital stay (20 vs 26 days, $p = 0.001$). Recurrent jaundice occurred in 36 stented patients and 2 surgical patients. Late gastric outlet obstruction occurred in 17% of stented patients and 7% of the surgical group. Despite the early benefits of stenting, there was no significant difference in overall survival between the two groups (median survival: surgical 26 weeks; stented 21 weeks; $p = 0.065$). The authors concluded that endoscopic stenting and surgery are effective palliative treatments, with the former having fewer early treatment-related complications and the latter fewer late complications. This study is the basis for selecting stenting over operative bypass. It has been criticized for having a high surgical morbidity and mortality rate. Additional confirmatory RCTs are highly desirable.

One criticism of endoscopic stenting is that it does not deal with the issue of gastrointestinal obstruction, which affects 10–20% of patients with pancreatic cancer. The counter-argument is that duodenal stenting or laparoscopic gastroenterostomy is available for those patients that develop obstruction after stenting—i.e., open surgery is rarely needed. An overriding factor in decision making is the life expectancy in unresectable cases of pancreatic cancer.

Surgical Resection With Curative Intent

The Whipple procedure is the standard operation for pancreatic and low bilary tumors. In the past, it was an operation associated with high morbidity and mortality. Mortality has fallen steeply in high volume HPB centers, at which mortality rates are usually 1–2% (Table 1). Nonetheless, most Whipple procedures in the United States are still performed outside tertiary care centers, and there the mortality rate remains over 15%. The main morbidity is fistula after pancreaticojejunostomy, but as we have shown (Table 1), this can be lowered to about 1.5% with the most modern techniques. The quality of life after the procedure is excellent when patients without recurrent cancer are assessed at one year after surgery.[8]

Clinical Effectiveness of the Whipple Procedure: Five-year survival for ampullary, bile duct, and duodenal malignancies, which have been respectable since the inception of pancreaticoduodenectomy, have remained largely unchanged in recent years. These rates range between 20–45%, and ampullary and duodenal cancers appear to have the best prognosis. In contrast, the results for adenocarcinoma of the head of the pancreas have been extremely poor in the past. In 1987, Gudjonsson reviewed more than 50 case series, published from 1949 to 1986, containing 2,400 pancreaticoduodenectomies performed for pancreatic cancer. He estimated the 5-year survival in resected cases at 4%.[9] Gudjonsson's figures were estimates that depended on some unproven assumptions and may have been slightly pessimistic, but were not much lower than results in many case series in which complete data were available. Recently, however, three large case series have reported 5-year actuarial survival rates of about 20%.[10,11] Results were even better in patients with small tumors or with negative lymph nodes, reaching 40% 5-year survival in some subgroups.[10,11] Not all recent series have realized such results.[12,13]

A continuing area of controversy is the use of ERCP in the preoperative period. Several randomized controlled trials dating back to the 1970s have shown the lack of benefit of preoperative decompression in jaundiced patients. Most authorities agree that diagnostic ERCP is not needed in patients with a typical history of periampullary malignancy associated with CT findings of a mass in the head of the pancreas, yet stenting prior to surgical referral in operable patients of this type is still common. A recent study showed an increased incidence of wound infection in stented than in operated patients. There is also a small but undesirable rate of pancreatitis, which delays the operation or makes it more difficult.[14]

Table 1. Rates of Pancreatic Fistulas, Intra-abdominal Abscesses, and Anastomotic Failures After Pancreaticojejunostomy

Publication	Data Years	Site	Fistula Definition	Number of Patients	Chronic Pancreatitis (%)	Fistulas (%)	Abscesses (%)	Anastomotic Failure (%)§	Reoperations %)	Mortalities (%)
Yeo et al. 2000	1998–2000	Johns Hopkins	A	211	21(10)	21(10)	14(7)	25(17)	13(6)	1(0.5)
Buchler et al. 2000	1993–1999	Bern Switzerland	B	331	133(40)	7(2.1)	4(1.2)	11(3)	13(4)	7(2.1)
Gouma et al. 2000	1997–1999[a]	Netherlands	C	151	NS	8(5)	5(3)	13(8)	12(8)	1(0.7)
Brooks et al. 2000	1993–1998[a]	NYU	A	111	6(5)	15(14)	2(2)	17(16)	NS	0
Grobmeyer et al. 2000	1994–1998	Cornell	A*	59	3(6)	10(17)	3(6)	13(23)	1(2)	2(3.4)
Bottger et al. 1999	1985–1997	Mainz Germany	D	221	18(8)	18(8)	12(5)	30(13)	19(9)	7(3)
Rios et al. 1998	1983–1996[a]	Charleston SC	E	98	27(28)	13(13)	1(1)	14(14)	NS	1(1)
Sato et al. 1998	1992–1997	Fukuoka Japan	F	62	7(11)	9(15)	2(3)	11(18)	2(3)	1(2)
Castillo et al. 1995	1991–1994	Mass Gen Hospital	E	237	62(26)	16(8)	10(4)	26(12)	3(1)	1(0.8)
Howard		Toledo OH	C	56		0	3(5)	3(5)		
Ohwada et al.	1992–1999	Maebashi Japan	G	100	8(8)	4(4)	1?(1)	5(5)	3(3)	2(2)
Strasberg et al.	1996–2000	Washington University, St Louis	A	126	16(13)	2(1.6)	2(1.6)	4(3)	1(0.8)	1(0.8)

A. Johns Hopkins Group Definition: Greater than 50-ml amylase-rich fluid (more than threefold elevation above upper limit of normal in serum) per day through the surgically placed drains on or after postoperative day 10 or pancreatic anastomosis disruption demonstrated radiographically. A* has substantially the same definition with slight variation.
B. Secretion or 30 ml or more of amylase rich drainage fluid (5,000 units) per day for more than 10 days
C. Not specifically defined
D. Amylase concentration in drainage fluid of >2,000
E. “High" amylase drain output after day 7—"high" not defined
F. "High" amylase drainage or radiological demonstration. High not defined
G. Drainage of fluid with amylase concentration greater than 3 times normal or radiological demonstration
§ Anastomotic Failure = fistulas + intra-abdominal abscesses
[a] Latest reported period taken

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Epidemiology, Natural History, and Predictors of Disease Outcome in Acute and Chronic Pancreatitis

Peter A. Banks, M.D.

Acute Pancreatitis

The incidence of acute pancreatitis per 100, 000 inhabitants per year varies considerably throughout the world. Recent data suggest that the incidence is comparatively low in England and the Netherlands (perhaps 5–10 per 100,000), is somewhat higher in Scotland and Denmark (approximately 25–35 per 100,000 inhabitants), and is still higher in the United States and Finland (approximately 70–80 per 100,000 inhabitants). The incidence appears to be increasing, but this data may reflect improved methodology of diagnosis and more accurate record keeping.

The natural history of acute pancreatitis is a reflection of the two most important determinants of severity: pancreatic necrosis and organ failure. Approximately 15% of patients with acute pancreatitis develop pancreatic necrosis, with a mortality of 15–20%. The remainder develop interstitial pancreatitis, with a mortality of 1–3%. Half of the deaths in necrotizing pancreatitis occur within the first 7 to 14 days and are mainly due to the development of multiple organ failure. The remaining patients die at a later stage, usually as a result of infected necrosis. Organ failure occurs in approximately 5–10% of patients with interstitial pancreatitis and is usually the cause of death. Hence, research in the future to decrease mortality of acute pancreatitis must be directed to methods that prevent or eliminate organ failure and to methods that prevent or provide more effective treatment of infected necrosis.

Predictors of disease outcome are usually sought within the first few days and preferably at admission. A high Apache II score at admission (≥ 8) is generally considered to be a predictor of severe disease. Additional factors that are available at admission that provide some prognostic information include age and obesity. In general, older individuals have a worse prognosis than younger people, as do individuals who are very obese. Laboratory tests that have been shown to have prognostic significance include hematocrit and creatinine. Hemoconcentration (reflective of intravascular volume depletion) appears to correlate with the development of pancreatic necrosis; the absence of hemoconcentration at admission suggests a more benign course. Renal failure at admission, as evidenced by a serum creatinine > 2 mg/dl in the experience of some investigators has also indicated a worse prognosis. Finally, in necrotizing pancreatitis, the development of multisystem organ results in a mortality of 30–50%.

Chronic Pancreatitis

The incidence of chronic pancreatitis appears to be in the range of 3–10 per 100,000 inhabitants in many parts of the world. The most important medical problems associated with chronic pancreatitis include abdominal pain, steatorrhea, and diabetes mellitus. In addition, in

recent years, chronic pancreatitis has been shown to be a premalignant condition. Two important etiologies are alcohol and tropical pancreatitis. The cause of the latter condition remains elusive. In addition, some families are predisposed to chronic pancreatitis (hereditary pancreatitis) because of cationic trypsinogen gene mutations. Many patients with idiopathic pancreatitis have been found to have mutations of the cystic fibrosis gene.

The natural history of chronic pancreatitis varies considerably and may differ among the various etiologies. A great deal of attention has been paid to the natural history of pain in chronic pancreatitis. In some parts of the world, pain has been shown to diminish and even to cease completely over time, but this has not been the general experience. The natural history of pain does not appear to be influenced by the development of severe functional abnormalities (steatorrhea and diabetes) nor by the development of severe structural changes (pancreatic calcification or severe pancreatic ductal abnormalities). When chronic pancreatitis is caused by alcohol, abstention may in selected instances be helpful in ameliorating pain. The role of endoscopic procedures to eliminate pain requires additional study. While several reports have suggested that endoscopic procedures are effective in relieving pain, thus far there have been no randomized prospective trials of endoscopic procedures designed to eliminate pancreatic stones and/or decrease ductal dilatation. The role of surgical procedures to eliminate pain also requires additional study. While many surgical series have reported decrease and at times elimination of pain following decompression of a dilated pancreatic duct (lateral pancreaticojejunostomy) or removal of the head of the pancreas when most of the inflammation occurs in this area (Whipple procedure), surgical procedures have also not been subjected to randomized prospective trials. Similarly, techniques to relieve pain, such as celiac plexus block and thoracoscopic splanchnic nerve interruption, require further study.

Steatorrhea caused by deficiency in pancreatic enzyme secretion can usually be treated successfully with the use of pancreatic enzymes. Diabetes mellitus can usually be well controlled with the use of insulin among compliant patients. Additional problems—such as development of a pancreatic pseudocyst, stenosis of the common bile duct, ascites secondary to pancreatic ductal disruption, and gastrointestinal bleeding from a variety of sources—can usually be treated successfully with a variety of techniques, including radiologic, endoscopic, and surgical methods. It remains difficult to diagnose pancreatic carcinoma that develops in association with chronic pancreatitis.

In addition to the above complications, prognostic factors in chronic pancreatitis include narcotic addiction, alcoholism, cirrhosis of the liver, and smoking. Mortality of patients with chronic pancreatitis has been shown to be 3.6 times higher than that of patients without chronic pancreatitis.

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Role of ERCP in Acute Pancreatitis

Richard A. Kozarek, M.D.

Caused primarily by gallstones and alcohol in the adult U.S. population, acute pancreatitis is associated with considerable morbidity and mortality rates of approximately 5–10%, usually as a consequence of sepsis or multi-organ failure.[1,2]

ERCP interaction in acute pancreatitis has primarily been one of cause and effect.[3] In other words, there is a variable incidence of acute pancreatitis following the performance of ERCP thought to be the consequence of sphincter edema or spasm, rupture of small ductules and pancreatic acini, or due to the direct toxicity of the contrast agent used.

It is a homeopathic tenet: "Like cures like." Thus, it may be deep-seated homeopathic insecurities that enjoin practitioners to treat acute pancreatitis with endoscopic retrograde cholangiopancreatography (ERCP), a major etiology of iatrogenic disease.

By far and away, the major interaction between ERCP and acute pancreatitis has been in the setting of presumptive biliary pancreatitis, in which there is concern for an impacted or ball-valving common bile duct stone.[4] While there is debate about the likelihood of a persistent stone based upon common bile duct (CBD) diameter, biochemical abnormalities, and the presence or absence of concomitant cholangitis, there is little debate that 1/3–2/3 of patients with persistent gallstones develop a second attack of acute pancreatitis, usually within months.[1] Nor is there debate that cholecystectomy or endoscopic biliary sphincterotomy, which disconnects the pancreaticobiliary orifices in most patients, can preclude these subsequent attacks.[2] Historically, the major debate in the endoscopic treatment of acute gallstone pancreatitis has been "Does it ameliorate or exacerbate the disease?" There are four prospective trials in the literature that have attempted to address this issue.[5–8]

British Study. In this seminal study by Neoptolemos et al., 121 patients with acute pancreatitis and gallstones documented ultrasonographically were randomized to conservative treatment or ERCP and sphincterotomy (ES) if indicated, within 72 hours of hospital admission.[5] In the ERCP group, ductal stones were found in 25% of the patients with mild disease and 63% of individuals with severe disease. Although performance of ES did not change outcomes in patients with mild disease, there were statistically significant reductions in complications and hospitalization time in the endoscopically treated group.

Hong Kong Study. A second prospective, randomized trial of ERCP-ES versus conservative management was published by Fan et al.[6] Of 195 patients included in the trial, CBD stones were found in 65%. In patients in whom stones were found and endoscopically treated, there were statistically fewer complications than the conservatively managed group (16% vs 33%), and there was a trend towards lower mortality (5% vs 9%) in the urgent endoscopy group as a whole. This trend was magnified in individuals with severe disease (morbidity 54% vs 13%; mortality 22% vs 12%).

Polish Study. To date published only in abstract form, this study prospectively looked at 280 patients with acute biliary pancreatitis, all of whom had urgent ERCP-ES within 24 hours of admission.[7] Excluding the 75 patients who were treated for an impacted stone, patients were randomized to undergo ES or conventional therapy. Those treated endoscopically had a statistically significant reduction in both complications (17% vs 36%) and mortality (2% vs 13%). This study has been the only one to suggest that ERCP-ES is beneficial in mild as well as severe disease.

German Study. In contrast to the other single center studies outlined above, this was a 22 institution multicenter trial, which also excluded patients who had either jaundice or cholangitis.[8] Randomizing 238 patients with suspected biliary pancreatitis to either conservative treatment or ERCP-ES within 72 hours, 58 of the 126 patients randomized to endoscopy had CBD stones, as did 13 of 20 patients initially randomized to the control group. Not only did endoscopy fail to ameliorate the disease process in this study, but patients undergoing ERCP had a higher incidence of respiratory failure and more severe complications. This study has been criticized for the design, the randomization process, and the fact that 19 of the centers contributed less than 2 patients per year to the trial.

With the weight of the above mentioned studies suggesting a role for urgent ERCP-ES in at least a subset of patients with acute biliary pancreatitis, the debate now focuses on what the subset should be. From a personal perspective, I undertake endoscopic evaluation in any patient with severe disease, jaundiced patients, those who experience an in-hospital exacerbation, and patients with smoldering disease. The latter are often the result of a pancreatic disruption, an event that occurs not only in pseudocysts, but also in high amylase pleural effusions, pancreatic ascites, and pancreaticocutaneous fistulas resulting from the percutaneous drainage of peripancreatic fluid collections.[9] These disruptions are also present in many cases of severe pancreatic necrosis. Undertaking ERCP in these settings not only attempts to define the etiology of the pancreatitis (biliary stone, variant anatomy, chronic pancreatitis), but also the anatomic consequence (stenosis or leak) prolonging the course. ERCP also entails placement of pancreatic prostheses in some patients with amenable anatomy and an ongoing ductal disruption. As such, our group, as well as others, have shown that transpapillary placement of pancreatic prostheses beyond a ductal disruption can resolve some pancreatic pseudocysts as well as cases of refractory pancreatic ascites and persistent pancreaticoenteric and pancreaticocutaneous fistulae.[9]

More recently, as one component of a multidisciplinary team approaching extremely ill patients with pancreatic necrosis (computerized tomography [CT] severity index [CTSI] ≥ 6), we have noted that 75% of these patients have ductal disruption on the basis of a high amylase/volume percutaneous fistula or by direct pancreatography at ERCP. The latter procedure is controversial and raises concerns about pancreatitis exacerbation or iatrogenic infection of the necrosis. Nevertheless, the placement of pancreatic prostheses to control the ductal disruption, in conjunction with endoscopic or percutaneous drainage of amenable fluid collections, and surgery in a subset of patients whose central pancreatic necrosis leaves them with a disconnected gland syndrome have been associated with an 11% mortality in our institution. This figure, historically, should approximate 30% in patients with a CTSI ≥ 6. Although it is impossible to define the individual roles played by this multidisciplinary approach, it is the author's distinct opinion that treatment of an ongoing ductal disruption often short circuits the inflammatory process by removing continued enzymatic insult to the necrotic area.

In summary, ERCP plays a distinct role in the very ill patient with acute biliary pancreatitis, may be useful in defining the etiology of "idiopathic" relapsing pancreatitis, and has a potential role in the delineation and treatment of a pancreatic disruption in a subset of patients.[10] While accepted in the subacute state (e.g., pancreatic ascites and high amylase pleural effusions, pancreaticocutaneous fistulae), its role in necrotizing pancreatitis is more controversial and requires additional study.

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The Role of Ultrasonography and Computed Tomography in Pancreatitis

Mary Ann Turner, M.D.

Non-invasive imaging of the pancreas and biliary tract with sonography (US) and computed tomography (CT) plays a major role in evaluation of patients with pancreatitis. US, CT and ERCP are all widely used tests but have different and specific roles. Compared to ERCP, which is invasive and is limited to depiction of biliary and pancreatic ductal anatomy, both US and CT are non-invasive and are capable of depicting not only ductal changes, but also pancreatic parenchymal abnormalities and peri-pancreatic involvement. Additionally, US and CT are useful in excluding other abdominal disorders that may mimic pancreatitis. US and CT are widely available, rapidly performed, and safe, have a high correlation with disease definition, and may serve to guide therapeutic needle aspiration or drainage of fluid collections. Compared to ERCP, US and CT require no sedation, have few patient limitations and, in the case of US, can be performed portably.

Imaging is generally not necessary in mild self-limited pancreatitis. CT is the single most widely used imaging technique and provides the most comprehensive evaluation in patients with suspected moderate or severe pancreatitis. Dynamic contrast-enhanced CT has high sensitivity and specificity for diagnosing moderate (77% and 98–100%) and severe (92% and 98–100%) pancreatitis. CT is used to confirm the diagnosis of pancreatitis, to define the extent of the disease, and to identify complications such as abscess or hemorrhage. CT is superior to US in assessing extrapancreatic structures and vascular and GI tract involvement and for diagnosing and quantifying pancreatic necrosis, which allows for prediction of disease severity. US is mainly used to exclude gallstones as an etiology and to follow up pseudocysts. US is also used to assess biliary obstruction, which may be due to stone, stricture or compression by pseudocyst or inflammatory mass. The role of ERCP has diminished as non-invasive imaging has improved. ERCP is reserved mostly for therapeutic procedures and when other tests are equivocal. ERCP is also useful in identification of ductal leaks or fistula and in precise depiction of complex or variant ductal anatomy.

In suspected gallstone pancreatitis, US is the diagnostic study of choice for the detection of stones in the gallbladder, with a sensitivity and specificity of 95–98%. US depicts stones in the bile ducts less readily, with a sensitivity of 25–90% (average 75%) and a specificity of 90–95%. Bile duct stones are identified with a 76–90% accuracy rate using conventional CT, with reports as high as 94% on unenhanced helical CT; however the generally accepted figure for identification of duct stones using CT is approximately 75%. This compares to a sensitivity of 80–90% and a specificity of 95–98% for ERCP.

In pancreatitis, US and CT readily demonstrate glandular size and contour, calcifications, pancreatic ductal dilatation and pseudocysts. Peri-pancreatic fluid collections, pancreatic necrosis, abscess, and hemorrhage are better seen with CT. Vascular complications such as splenic or mesenteric venous thrombosis or pseudoaneurysms may be identified with either US

or CT, however, CT is considered the more optimal study for demonstration of vascular abnormalities. US is less precise than are ERCP, MRCP or CT in depicting detailed ductal anatomy.

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Overview of Differential Diagnosis of Abdominal Pain

Anthony N. Kalloo, M.D., F.A.C.P.

The differential diagnosis of abdominal pain is a common but challenging problem facing physicians. It is a frequent cause of disability and absence from work, and it is the most common reason that a patient will seek consultatory services from a gastroenterologist. Abdominal pain is purely subjective and is heavily influenced by psychosocial factors. Furthermore, there is significant individual variability on the subjective experience of pain because of pathophysiological and neuroanatomical factors. The clinicians, therefore, must consider neuroanatomical, neurophysiological, pathophysiological, and psychosocial factors in the evaluation of abdominal pain.

Neuroanatomy of Abdominal Pain

There are three levels of neurons between the abdominal viscera and the cerebral cortex that mediate abdominal pain sensation. First-order neurons link viscera to the spinal cord, second-order neurons link the spinal cord to the brain stem, and third-order neurons travel from the brain stem to the cerebral cortex. Nociceptive stimuli are transmitted almost entirely by the sympathetic nervous system. First-order neurons first pass through an autonomic plexus usually associated with a major artery supplying the organs, such as the celiac artery. Second-order or postsynaptic neurons begin in the dorsal horn and cross at the midline to the contralateral side and then travel within the ventrolateral quadrant of the spinal cord upwards toward the brain stem. These neurons run in several pathways; such as the spinothalamic tracts. Third-order neurons go from the spinoreticular tracks to the frontal cortex and limbic system.

Neurophysiology of Abdominal Pain

There are three functional types of visceral nociceptors. The low-threshold, intensity-coding afferents are activated by normal physiologic activities and result in “normal sensations,” such as hunger and fullness. If the intensity of this type of input is significantly increased then the stimulus is perceived as pain. High-threshold class of visceral nociceptors responds only to intense visceral input and, therefore, results in pain sensation. These nociceptors predominate in the biliary tree. Finally, there are some nociceptors that appear to be activated only in response inflammation or tissue damage.

One of the paradoxes of pain is that similar visceral pathology may be associated with different degrees of pain in different patients. These phenomena are probably best explained by the gate-controlled theory of pain. This theory suggests that a stimulus is perceived as painful because of interacting factors at the site of the synapse within the spinal cord. The dorsal horn of the spinal cord is the site of the synapse between afferent neurons that carry nociceptive information, second-order neurons that relay to the brain stem, and interneurons that inhibit T-cell neurons. Furthermore, descending inhibitory systems that arise within the central nervous

system (CNS) when activated by a variety of factors also simulate the interneurons to inhibit T-cell firing. The balance of these excitatory and inhibitory forces determines the amount of nociceptive information that is transmitted to the brain.

Referred Pain

Referred pain refers to the perception of abdominal pain at a site that is remote from the location of the affected viscera. It is usually associated with cutaneous dermatomes, whose afferent nerve roots enter the same level of the spinal cord as those from the painful abdominal structure. For example, the biliary tree is innervated by visceral nerves that enter the spinal cord from T5 to T9. T5 to T9 also innervates region of the back, right shoulder, and right scalpel, and hence, pain from a biliary tree lesion may be referred to that area. Although the abdominal visceral afferent fibers terminate mainly in Laminar 1 and 5 of the dorsal horn, which is adjacent to the site where somatic nerves synapse, both sets of afferent inputs activate the same spinothalamic track neurons. This conversion-projection theory explains most features of referred pain.

Localization of Abdominal Pain

The ability to precisely locate their abdominal pain is often a frustrating experience for patients. There are several reasons for this phenomenon. First, there are relatively few afferent nerves leaving the viscera as compared to somatic organs such as the skin. Secondly, although there are few visceral afferent inputs to the spinal cord, a significant number of second-order neurons respond to stimulus. A phenomenon referred to as functional divergence, i.e., a small number of viscera afferent nerves stimulating a relatively great number of spinothalamic tract neurons, makes exact localization of pain difficult.

Because most abdominal viscera have embryologic origins as midline structures with bilateral symmetric innervations, most digestive tract pain is midline in location. In organs whose innervation is predominately one-sided, such as the kidneys, ureters, and ovaries, the abdominal pain is usually lateralized. A useful general rule of abdominal pain localization is to consider the embryologic origin of the organ. Organs that originate from the foregut, such as the distal esophagus, stomach, proximal duodenum, liver, biliary tree, and pancreas, are innervated by nerves from spinal segments T5 to T6 and T8 to T9, resulting in pain that is usually localized between the xiphoid and the umbilicus. Nerves whose origins are T2, T11 to L1, primarily innervate organs whose origin is from the midgut, such as the small intestine, appendix, extending colon, and proximal two thirds of the transverse colon. The location of abdominal pain from midgut origin is usually periumbilical. Finally, in organs whose embryologic origin is the hindgut, such as the distal one-third of the transverse colon, descending colon, and rectosigmoid, and whose innervation is from T11 to L1, the location of the pain is usually between the umbilicus and the pubis.

Diagnoses

Careful history and a detailed physical examination generally result in correct diagnosis. The differential diagnosis of possible causes of abdominal pain is listed in Table 1.

Table 1. Differential Diagnosis of Abdominal Pain

Thoracic Origin

1. Esophagitis/esophageal spasm
2. Myocardial ischemia
3. Myocarditis
4. Pneumonitis
5. Pulmonary embolism
6. Pneumothorax
7. Esophageal rupture

Neurogenic

1. Entrapment neuropathy of spine
2. Radiculitis: herpes zoster, spinal cord tumors
3. Tabes dorsales

Muscular-Skeletal Origin

1. Slipping rib syndrome
2. Surgical scar neuromas
3. Muscular contusions/ hematomas

Biliary Tract Origin

1. Biliary obstruction: stones, strictures, tumors, parasites, hemophilia, sphincter of Oddi dysfunction
2. Inflammatory: viral and toxic hepatitis, cholangitis, acute and chronic calculous and acalculous cholecystitis

Pancreas

1. Acute pancreatitis
2. Chronic pancreatitis
3. Neoplastic conditions of the pancreas

Small Intestine

1. Intermittent intestinal obstruction, intussusception
2. Abdominal wall hernia
3. Inflammatory bowel disease
4. Mesenteric ischemia

Colon

1. Inflammatory bowel disease
2. Mesenteric ischemia
3. Appendicitis
4. Diverticulitis
5. Colitis

Renal Origin

1. Pyelonephritis
2. Ureteral obstruction
3. Neoplastic disorders of the urogenital system

Gynecologic Origin

1. Endometriosis
2. Endometritis
3. Ovarian torsion
4. Uterine neoplasm
5. Ectopic pregnancy

Ischemic

1. Mesenteric ischemia/infarction
2. Polyarteritis
3. Splenic infarction
4. Torsion of gallbladder, spleen, testicle, omentum, appendix
5. Hepatic infarction
6. Tumor necrosis: hepatoma, uterine fibroid

Metabolic

1. Porphyria
2. Uremia
3. Diabetes mellitus
4. Adrenal insufficiency

Toxins

1. Heavy metal poisoning

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What Is the Role of ERCP in the Setting of Abdominal Pain of Pancreatic or Biliary Origin?

Stuart Sherman, M.D.

Endoscopic retrograde cholangiopancreatography (ERCP) is a commonly utilized technique for the evaluation and management of patients with anatomic evidence of pancreatic and/or bile duct obstruction. The role of ERCP in patients with pancreaticobiliary-type pain in the absence of obvious obstructive disorders of the pancreatic and bile duct (often referred to as suspected sphincter of Oddi dysfunction) is less clear.

Sphincter of Oddi (SO) dysfunction refers to an abnormality of SO contractility. It is a benign, noncalculous obstruction to flow of bile or pancreatic juice through the pancreaticobiliary junction. SO dysfunction (SOD) may be manifested clinically by pancreaticobiliary pain, pancreatitis, or deranged liver function tests. It is actually made up of two entities. SO dyskinesia refers to a primary motor abnormality of the SO, while SO stenosis refers to a structural alteration of the sphincter. Because it is often impossible to distinguish patients with SO dyskinesia from those with SO stenosis, the term SOD has been used to incorporate both groups of patients. In an attempt to deal with this overlap and also to determine the appropriate utilization of SO manometry, a clinical classification system has been developed for patients with suspected SOD and is based on clinical history, laboratory results, and ERCP findings.

The Rome II diagnostic criteria for SOD are episodes of severe, steady pain located in the epigastrum and right upper quadrant and all of the following: (1) symptom episodes last 30 minutes or more with pain-free intervals (2) symptoms have occurred on at least one occasion in the prior 12 months, (3) the pain is steady and interrupts daily activities, and (4) there are no structural abnormalities to explain symptoms. Laboratory abnormalities consisting of transient elevations of liver function tests, amylase, and lipase are present in less than 50% of patients.

Evaluation of patients with suspected SOD should be initiated with standard serum liver chemistries, serum amylase, and/or lipase, abdominal ultrasound and/or computerized tomography (CT) scan. The value of other noninvasive tests, such as ultrasonographic assessment of extrahepatic bile duct and main pancreatic duct diameter after secretory stimulation and quantitiative hepatobiliary scintigraphy, have not been clearly elucidated. Because of their associated risks, invasive testing with ERCP and SO manometry should be reserved for patients with clinically significant or disabling symptoms. In general, invasive assessment of patients for SOD is not recommended unless definitive therapy (sphincter ablation) is planned if abnormal sphincter function is found. The American Society for Gastrointestinal Endoscopy's (ASGE) appropriate use of gastrointestinal endoscopy guideline states that ERCP is generally not indicated in the evaluation of abdominal pain of obscure origin in the absence of objective findings that suggest biliary or pancreatic disease. In support of this guideline, Sherman and colleagues found ERCP alone to be of certain value in only 19 of

197 (9.6%) consecutive type III SOD patients; 13 of these patients had chronic pancreatitis. SO manometry was abnormal in 61% of these patients, prompting endoscopic sphincter ablation.

SO manometry, (most commonly performed in the setting of ERCP), is considered by most authorities to be the gold standard for evaluating patients for SOD, as it is the best predictor of outcome in type II and type III patients. Endoscopic sphincter ablation is currently the procedure of choice for sphincter of Oddi dysfunction. In a landmark study, Geenen and colleagues randomized 47 type II post cholecystectomy patients to biliary sphincterotomy or sham sphincterotomy. During a 4-year followup, 95% of patients with an elevated basal sphincter pressure benefited from the sphincterotomy. In contrast, only 30–40% of patients with an elevated sphincter pressure treated by sham sphincterotomy or with a normal pressure treated by endoscopic sphincterotomy or sham benefited from this therapy ($P<0.005$). The two important findings of this study were that SO manometry predicted the outcome from endoscopic sphincterotomy and that endoscopic sphincterotomy offered long-term benefit in type II biliary patients with SOD. Sherman and colleagues reported their preliminary results of a randomized study comparing endoscopic sphincterotomy, surgical biliary sphincteroplasty with pancreatic septoplasty to sham sphincterotomy for type II and III biliary patients. During a 3-year followup period, 69% of patients undergoing endoscopic or surgical sphincter ablation improved compared to 24% in the sham sphincterotomy group ($P=0.009$). There was a trend for type II patients to benefit more frequently from sphincter ablation than type III (13 of 16, 81% vs 11 of 19, 58%; $P=0.14$). In a third randomized study, 11 of 13 patients (85%) with an elevated basal sphincter pressure were improved at 2 years after endoscopic sphincterotomy, while 5 of 13 patients (38%) improved after a sham procedure ($P=0.041$).

Based on the current data, it appears that ERCP alone has little role in the evaluation of patients with pancreaticobiliary pain because of its low yield and high complication rate. When SO manometry is added to ERCP, the diagnostic yield is improved dramatically. The results of SO manometry appear to predict outcome from sphincter ablation in type II and III patients. SO manometry is highly recommended in type II patients and is mandatory in type III patients. The data indicates that the response rate and enthusiasm for sphincter ablation must be correlated with patient presentation and balanced against the high complication rates reported for endoscopic therapy of SOD.

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There Is No Role for ERCP or EUS in Unexplained Abdominal Pain of Pancreatic or Biliary Origin

Pankaj J. Pasricha, M.D.

Introduction and Nature of the Problem

The diagnosis of pancreatic or biliary disease in patients with "classic" clinical or biochemical features (e.g., steatorrhea, obstructive jaundice, elevated enzymes etc.) is usually straightforward. Invasive tests may not always be required with such patients, and when they are, the risk-benefit ratio is relatively easy to justify as a number of the underlying conditions may be amenable to specific palliative or curative therapy. By contrast, the subject of this discussion is a group of patients who present with the sole symptom of abdominal pain, suspected to be "pancreatobiliary" in origin. At the present time, this group represents one of the biggest challenges for diagnosis and treatment in clinical gastroenterology. Many of these patients will undergo a battery of tests, including endoscopic retrograde cholangiopancreatography (ERCP). It is the stated position of this paper that ERCP and endoscopic ultrasonography (EUS) are not helpful in these patients for reasons that will be presented in detail and that are summarized in the next few pages.

Careful analysis will reveal a set of assumptions implicit in the decision to request an ERCP or EUS in a given patient with abdominal pain of "suspected pancreatobiliary origin." These assumptions are listed in Table 1 and will now be critically examined.

Table 1. ERCP in Suspected Pancreatobiliary Pain
Underlying Assumptions

1.	Clinical criteria can reliably be used to indicate the presence of underlying pancreatic or biliary disease in the absence of positive information on other, more "objective" tests.
2.	ERCP and EUS can reliably detect subtle, morphological changes in the pancreatobiliary system.
3.	Morphological changes, when found, reliably correlate with the origin and intensity of pain.
4.	Finally, effective intervention exists for the newly diagnosed abnormalities.

Problems With Clinical Definition of "Biliary" or "Pancreatic" Pain

One of the many challenges facing the clinician in the consideration of these syndromes is the difficulty in the characterization of biliary or pancreatic pain, which, contrary to popular opinion, is often nonspecific and lacks any typical features. For instance, although many clinicians consider right upper quadrant pain as synonymous with biliary pain, "true" biliary pain is not always the classic right upper quadrant colic: In one experimental study using post-operative biliary distention in patients, the most common site of pain was epigastric or upper abdominal (36%); other sites included the right upper quadrant pain (18%), epigastric pain radiating to the back (11%), midline pain only (9%), unilateral back pain (7%), or no pain (19%).[1]

Another way to look at right upper quadrant pain and the specificity of its association with biliary pain was provided by another study from the United Kingdom.[2] These investigators studied 22 consecutive patients who had severe chronic right upper quadrant (RUQ) pain and had on an average had 3.5 consultations, 7.3 procedures, 1.7 operations, and more than 20 blood tests. Balloon distention of the esophagus, duodenum, jejunum, ileum, right colon, and left colon was performed. Reproduction of the patient's spontaneous RUQ pain was seen in 21/22 patients with distention of at least one site and in 12/22 patients with distention at two or more different sites.

In fact, experimental distension of the esophagus, duodenum, and jejunum results in pain that is very similar to that after distension of the bile ducts.[3] As far back as 1947, Chapman et al. studied patients with **established biliary or pancreatic pathology** and distended their esophagus, duodenum, jejunum, and biliary tree with air/fluid. The pain elicited by these maneuvers was then compared to the patients' description of their spontaneous clinical pain. Regardless of whether the patients had biliary or pancreatic disease, 80% of the patients could not distinguish between biliary or upper intestinal distention and reported that the experimental pain was similar to the clinical pain that they experienced.[4]

Problems With the Morphological Definition of Pancreatitis on ERCP and EUS: What Is the Gold Standard?

Pancreatic Disease. The sensitivity and specificity of ERCP for the diagnosis of chronic pancreatitis are often quoted to be in the range of 90% or higher. Unfortunately, the inability to safely and easily obtain pancreatic tissue has deprived the field of a convenient gold standard for comparison. Both EUS and ERCP have no difficulty in detecting gross pancreatic and biliary disease; however, these patients are also readily identified by clinical or noninvasive biochemical and/or imaging studies. In patients who present with abdominal pain only, ERCP and EUS appear to lack both sensitivity and specificity.[5]

Many such patients will be found to harbor so-called minor changes on pancreatography, such as mild irregularities in secondary and tertiary branches, leading to a label of chronic pancreatitis. However, it may be perilous to rely on such morphological changes alone to make a clinical diagnosis of pancreatic disease. To begin with, several studies have shown that such changes exist in many patients, particularly the elderly, in whom a variety of focal or diffuse

ductular abnormalities can be seen, without necessarily denoting disease or associated with any functional impairment.[6] In another study, ductograms were obtained at autopsy in 69 patients without known pancreatic disease, and endoscopists were asked to comment on the changes: 81% of the ductograms were interpreted as compatible with chronic pancreatitis (37% minimal, 31% moderate, and 11% severe).[7] Secondly, the diagnosis of chronic pancreatitis on initial ERCP may justify further invasive maneuvers, such as pancreatic stenting or sphincterotomy, which by themselves can lead to alterations in ductal morphology. This can also happen if the initial diagnostic ERCP is complicated by an attack of moderate or severe acute pancreatitis. In some patients, therefore, a well-intentioned attempt to establish a diagnosis of pancreatic disease may in fact become a self-fulfilling prophecy.

Apart from these issues of specificity, ERCP may also have limited sensitivity in this setting, particularly when dealing with the somewhat controversial entity of "minimal change" diseases, where changes of chronic pancreatitis may be widespread in the parenchyma and the periductular regions but appear to spare the collecting system itself, leading to a normal or equivocal pancreatogram. In such patients, chronic pancreatitis has been diagnosed either after examination of surgically resected specimens or by pancreatic function tests.[8] Although not part of this discussion, it is worth mentioning that functional pancreatic tests may fare only slightly better than pancreatography, with a sensitivity reported to be in the range of 80% or less, and do not correlate well with either pathological appearance or clinical manifestations.[5,9]

EUS has been reported to be equally sensitive as (if not more sensitive) than ERCP in the diagnosis of chronic pancreatitis.[10] In one study, the "yield" of EUS in patients with pain due to suspected pancreatic disease with no or minimal changes was reported to be nearly 80%.[11] However, as stated before, the true significance of these findings cannot be confidently established in the absence of histological correlation.

Biliary Tract Disease. Fortunately, most clinically significant biliary disease presenting with abdominal pain is accompanied by changes in conventional imaging or classic liver "function" tests, such as elevations in one of the hepatic aminotransferases or alkaline phosphatase. The exception here appears to be the so-called "functional" biliary pain, often used synonymously with biliary dyskinesia (see below).

Review of Studies. There are very few studies that have systematically and prospectively reported the yield of these tests in patients with unexplained abdominal pain. Axon et al. reported their experience in 1,005 ERCPs, of which 13 of 138 (14%) were for unexplained abdominal pain (suspected to be biliary in 58%, pancreatic in 30%, and unspecified in the rest).[12] The duct or ducts of interest were delineated by ERCP in 95% of patients. ERCP was negative in about 80% of patients; in the rest, the lesions found were bile duct stones in 10 patients, chronic pancreatitis in five, pancreatic carcinoma in one, peptic ulcer or duodenitis in four. None of the 10 patients with duct stones had normal ultrasound and normal alkaline phosphatase, and it can be argued that in the four patients with acid-peptic disease, a simple upper endoscopy would have sufficed. Thus, if these simpler tests had been performed prior to the exam, the yield of ERCP would have been less than 5%.

Discrepancy Between Pain and Morphological Changes

The third critical issue to be examined is the significance of morphological changes, even if they can be detected, particularly as it relates to pancreatic pain. Pain is undoubtedly not only the most important symptom of chronic pancreatitis, but also is the most frustrating and difficult to treat. Unfortunately, the mechanism of pain in pancreatitis is poorly understood, and there are few, if any, studies that attempt to explore the biology and pathogenesis of nociceptor sensitization in this condition. For many decades, investigators have focused on a possible anatomical cause of the pain, prompted by the appearance of an irregularly dilated duct (characteristic of many cases of chronic pancreatitis) as well as the finding of increased intraparenchymal and intraductal pressures in both humans and animal models of the disease.[13–18] The importance of pancreatic duct and intraparenchymal hypertension as a cause of pain has been attributed to inadequate ductal drainage, causing the pancreatic duct to dilate. However, pancreatic ductal dilatation can occur in the absence of pain, and pain can be present in the absence of ductal dilatation. Similarly, changes in ductal pressure correlate poorly, if at all, with either pain or its relief after ductal decompression.[19,20] Therefore, even if morphological changes are found in the pancreas, these are not necessarily responsible for the pain. They may at best be a marker for underlying chronic pancreatitis, but only if these changes are robustly abnormal.

As mentioned above, it is rare to see isolated abnormalities on cholangiography as a significant cause of biliary pain, except when dealing with biliary dyskinesia. This is a term that refers to both gallbladder dyskinesia and sphincter of Oddi dysfunction (SOD). ERCP, in the absence of any abnormalities in liver function tests (LFTs), has little, if any, role to play in the former. (The diagnosis is usually made on the basis of an abnormal ejection fraction on scintigraphy.) However, it is often advocated when SOD is suspected, usually along with an attempt to measure sphincter pressures. This remains an area of ongoing controversy, but it appears that again, the patients most likely to benefit from this procedure (and subsequent sphincterotomy) are those with persistently or intermittently abnormal “objective” signs, such as elevated liver enzymes or dilated bile ducts (the so-called type I and type II patients, according to the widely used Hogan-Geenen classification).[21] Unfortunately, despite two or more decades since its recognition, not much progress has been made in clarifying the role of SOD in the type III patient (presenting with pain alone), and the outcome after sphincterotomy, despite a positive manometric test, remains at best a toss-up and at worst no better than a placebo response.[22,23]

Lack of Effective Therapy

Even if the previous issues have been satisfactorily addressed and a diagnosis of underlying pancreatic or biliary disease has been made with reasonable confidence, the final, and perhaps most important, question remains to be answered: What can we do about the pain? The treatment of pain in chronic pancreatitis has been “strategically haphazard, ill directed, too often unsuccessful, and controversial.”[24] Despite a wide variety of approaches covering innocuous (enzyme therapy), minimally invasive (endoscopic decompression, nerve blocks), and highly aggressive (surgical decompression, pancreatectomy), no consensus has emerged, and no form of treatment can be considered satisfactory at the present time. While there are effective replacement strategies to deal with the endocrine and exocrine insufficiencies associated with

chronic pancreatitis, it is clear, therefore, that pain remains the "most disturbing" complication.[25] The multiplicity of treatment strategies and their limited efficacy is largely a reflection of our lack of understanding of the biology and pathogenesis of pain. Similar considerations apply to the type III patient with SOD, where sphincterotomy would not meet most criteria for an effective or safe therapy. There are those who remain in "hot pursuit" of any remaining muscle activity in these patients, but an impressive body of literature on patients with functional bowel pain clearly indicates that these conditions cannot be treated as simply disturbances of motility.

Conclusions and Directions for Research

It is hoped that a clear argument has been made not to generally endorse ERCP for patients with the only symptom of "suspected pancreatobiliary pain." That is not to say that such studies should not be done in the context of rigorously controlled clinical studies. Indeed, if anything, the brief review above has pointed out several areas of research, including those highlighted in Table 2.

Table 2. "Underserved" Areas of Research

1. Neurobiology of pancreatic and biliary pain
2. Animal models representing the spectrum of pancreatic disease that could be used to provide accurate histological correlation with imaging studies
3. Controlled trials on outcomes after pancreatobiliary interventions for various painful conditions
4. Development of "noninvasive" means of obtaining pancreatic tissue

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Income and Outcome Metrics Needed for Objective Evaluation

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The goal of this conference is to define the role of endoscopic retrograde cholangiopancreatography (ERCP) in the management of patients with known and suspected problems in the biliary tree and pancreas, to assist both practitioners and patients in making appropriate choices.

There are two fundamental questions: Firstly, what can ERCP offer? Secondly, how does that compare with available alternatives? It is difficult to generalize in either arena. There are huge variations in the types of patients and their presenting problems, the expertise of the operators, and the perspectives on possible outcomes (both good and bad). Furthermore, both ERCP and alternative techniques are evolving continuously.

This contribution concentrates on the first question: What does ERCP have to offer? This contribution discusses the metrics that must be considered when trying to make that evaluation in research projects or in a particular patient context.[1]

ERCP has both diagnostic and therapeutic potential. This fact can be beneficial clinically (reducing the number of procedures needed to achieve a clinical resolution), but adds complexity to the evaluation. Diagnostic and therapeutic aspects must be assessed separately, because their goals (and their determinants) are quite different. Yet they are not separate, because the therapeutic procedure requires a correct diagnostic assessment. Attempts at ERCP treatment may be poorly focused (or even never get started) if the diagnostic process is inadequate. Sometimes the intention of ERCP is clearly therapeutic (e.g., known bile duct stone). However, in many other cases (e.g., suspected sphincter of Oddi dysfunction or obstructive jaundice), the intent is initially diagnostic, with the possibility of proceeding to therapy if it appears to be indicated and technically possible. There is a range of contexts in which ERCP is considered (Table 1). Patients can usually be placed into one of these groups after standard clinical assessment and initial ultrasound (US)/computerized tomography (CT) imaging. Management algorithms must be generated and tested in those contexts.

Diagnostic ERCP

There are published figures for the sensitivity and specificity of ERCP in various diseases. Some of these reports are open to question, because ERCP is operator dependent, and there may be dispute about the gold standard (e.g., in early chronic pancreatitis). Diagnostic accuracy is important, but the true value of a diagnostic procedure (and its role) is not determined mainly by its performance characteristics in a specific disease, because we use diagnostic methods only in circumstances of clinical uncertainty, where there may be a long list of diagnostic possibilities. Except in rare circumstances, like acute cholangitis, ERCP is always preceded by other simpler and safer imaging methods like ultrasound or CT. Thus, we do not

Table 1. Clinical Contexts in Which ERCP Is Considered

Obstructive jaundice	Intermittent abdominal pain ± cholecystectomy (? sphincter dysfunction, ? pancreatitis, ? stone)
Abnormal liver function tests	Acute post surgery problems
Probable/known duct stones	Probable/known benign stricture
Chronic pancreatitis	Suspected papillary mass
Acute pancreatitis (? gallstones)	Suspected biliary or pancreatic mass
Complicated pancreatitis (necrosis/pseudocyst)	Stent service
Idiopathic (recurrent) pancreatitis	Other
Chronic pain (? pancreatitis, ? cancer)	

consider doing diagnostic ERCP in complete ignorance. Its contribution is measured by how far we can move from relative diagnostic ignorance to the truth (i.e., the difference between the posttest and the pretest probabilities). What difference does the procedure make in the patient's diagnostic journey? This evaluation must be extended, because (for ERCP) the goal is not only diagnostic. The question then becomes whether (and how much) the new diagnostic information changed the management plan (correctly). The **metrics** of diagnostic evaluation are simple. A list of the differential diagnoses (with associated probabilities) generated before and after the diagnostic phase of ERCP will show the magnitude of diagnostic change. This assumes some method for assessing ultimate diagnostic "truth." The contribution to patient care can be assessed only if the management plans are also defined before and afterwards, to demonstrate and measure the change.

The diagnostic role of ERCP is diminishing, due to developments in other technologies (CT and Magnetic Resonance (MR) particularly). This discussion will, therefore, focus more on the evaluation of therapeutic ERCP.

Therapeutic ERCP

The goal of therapeutic ERCP is to make patients "better" (i.e., reduce or eliminate disease and its effects), at acceptable cost. Outcome studies attempt to document that process. For outcomes to be understood or predicted for an individual patient, many details about that patient ("income" data), the likely quality of the intervention, and its costs must be known. The "therapeutic intervention equation" (Figure 1) includes all of the many elements that must be considered when trying to calculate therapeutic performance.

Patients vary in many ways (by age, sex, geography, disease, co-morbidities, and expectations). **Co-morbidities** are important for several reasons. They may aggravate the disease problem being treated (e.g., cholangitis may be worse in an immunocompromised patient). In addition, they may make intervention itself more hazardous. This risk may be general (e.g., respiratory deficit and sedation/anesthesia) or more specific (e.g., coagulation problems and sphincterotomy). The key co-morbidities may be different for different interventions (e.g., surgery or endoscopy), which would clearly affect the appropriate choice. The ASA (American Society of Anesthesiology) score (Table 2) is a useful, crude guide to overall co-morbidity and correlates reasonably well with cardiopulmonary risks involved in sedation/anesthesia, at least in

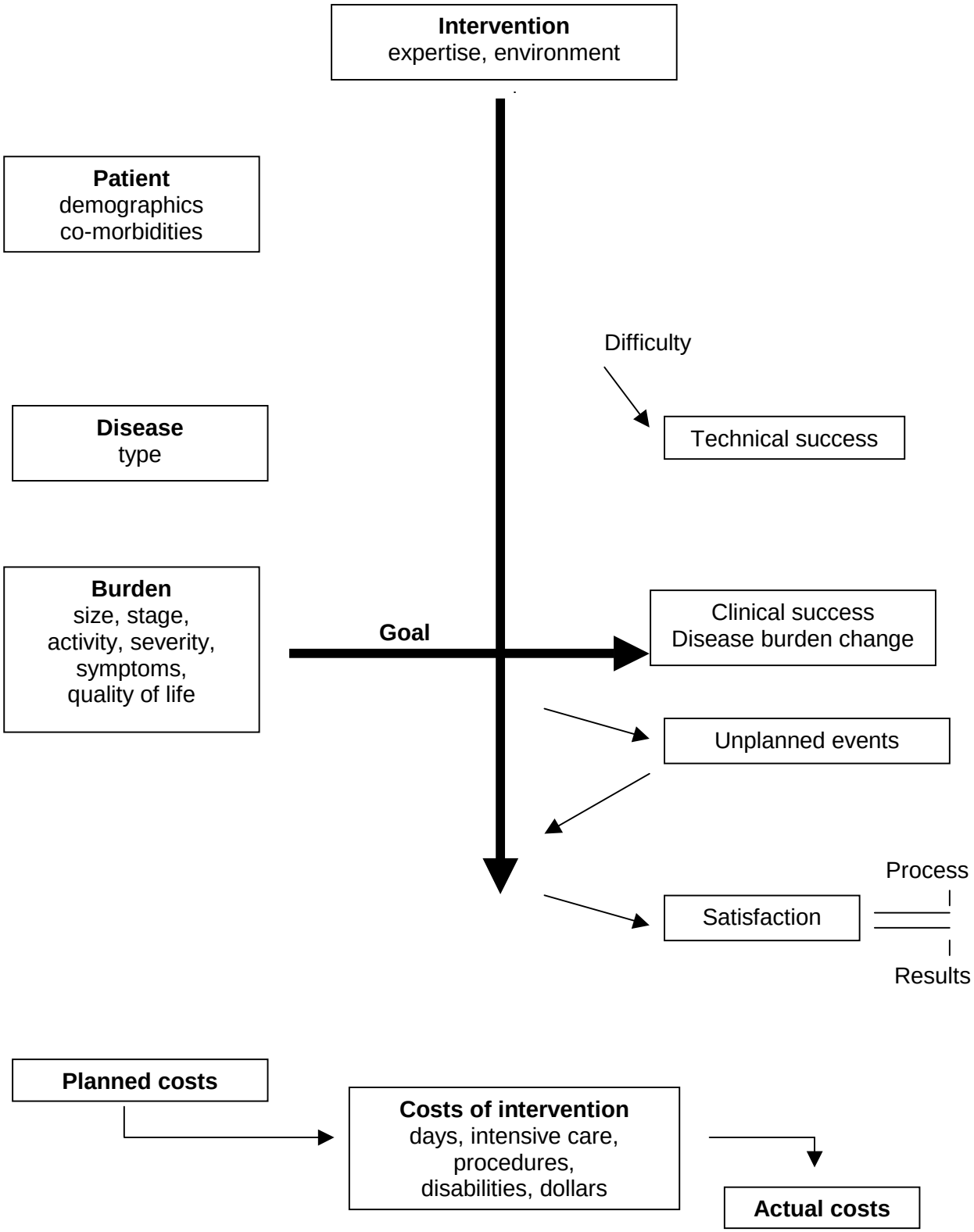

Figure 1. Data Elements for Evaluation of Therapeutic Interventions

Table 2. ASA Classification of Physical Status

1.	Healthy patient. This patient is physically, mentally, and biochemically healthy, apart from the symptoms or disease requiring endoscopic examination.
2.	Mild to moderate systemic disease. This patient will have a systemic disease, but little or no functional limitation. The disease may or may not be related to the indication for endoscopy. Examples include chronic bronchitis, mild heart disease, essential hypertension, diabetes, anemia, obesity, and extremes of age.
3.	Moderate to severe systemic disease. This patient will have some functional limitation, but the condition will not be incapacitating or life threatening. Examples include chronic lung disease or heart disease that limits activity, poorly controlled hypertension, angina, and diabetes with complications.
4.	Severe systemic disease. This patient will have a severe systemic disturbance that is incapacitating and poses a constant threat to life. Examples include congestive heart failure, persistent or unstable angina, pulmonary disease requiring oxygen, and advanced renal or hepatic dysfunction.
5.	Moribund. This patient is unlikely to survive 24 hours with or without urgent treatment.

surgery. However, these are not the commonest risks of ERCP procedures, where pancreatitis is dominant, and they are paradoxically more likely to occur in the young and healthy (i.e., ASA classes 1 and 2). In order to understand and then predict the risk of post-ERCP pancreatitis, more detailed factors need to be measured and studied. The consequence of these considerations is that the "income" data that need to be documented may vary according to the clinical context, as well as the type of intervention planned. While it might be ideal to collect all of the possibly relevant co-morbidity data on every patient (Table 3), this is a major documentation burden, so there has to be a compromise in practice (e.g., ASA score plus a few key specifics, such as coagulation status).

Diseases. Patients presenting for possible ERCP can carry a variety of different diseases, which may inflict many different burdens. Diseases may be described by several parameters (e.g., size, stage, indexes of activity and severity). The relevant **metrics** will vary. For many diseases (e.g., stones, tumors, cysts, strictures, and leaks), the precise size and site will affect the likely outcome (with and without treatment). Clinical severity is more important in disease syndromes such as pancreatitis and cholangitis. The **burden** of the disease is the effect it has on the individual patient (i.e., symptoms, expectation of survival, quality of life, and utilization of health care). Specific symptoms such as pain, fever and jaundice, should be easy to measure. Pain scoring should be standardized and include both intensity and frequency. There are numerous general quality of life instruments,[2] but only a few have been validated in the precise contexts of ERCP intervention.[3] Health care utilization is commonly measured by the number of needed consultations, emergency room visits, and hospitalizations. This combination of details (patient, disease, and its burden) constitute the "clinical problem" for which we may consider a therapeutic intervention.

Table 3. Co-morbidities/Endoscopy Alerts

1. Allergies
   - local anesthetic
   - iodine
   - IV contrast
   - antibiotics
   - latex
   - other
2. Pulmonary
   - dyspnea (grade)
   - lung disease (type)
   - pulmonary hypertension
   - thromboembolic disease (previous, active)
   - sleep apnea
   - lung resection
   - lung transplant
   - aspiration problem
   - stridor
   - tracheostomy
   - other
3. Cardiovascular
   - pacemaker
   - defibrillator
   - infarct < 3 mm
   - artificial heart valve
   - heart murmur
   - hypertension
   - heart failure (Class I–IV)
   - angina (Class I–IV)
   - rheumatic valve disease (asymptomatic, symptomatic)
   - previous endocarditis
   - periforal graft surgery < 1 yr
   - heart transplant
   - systemic-pulmonary shunt
   - dysrhythmia (asymptomatic, symptomatic)
   - peripheral vascular disease (claudication, amputation)
   - heart surgery
   - mitral valve prolapse
   - prior arrest
   - other
4. Metabolic
   - diabetes (insulin, oral, diet)
   - thyroid dysfunction)
   - hyperthyroid (controlled, uncontrolled, complications)
   - hypothyroid (controlled, uncontrolled, complications)
   - adrenal dysfunction (substituted, noncompensated)
   - morbid obesity
   - obesity surgery
   - other
5. Blood
   - anticoagulants
   - coagulopathy (controlled, uncontrolled)
   - immunosuppression (moderate, severe)
   - other
6. Cancer
   - lymphoma/leukemia (controlled, uncontrolled)
   - solid organ malignancy (previous, local, metastatic)
   - radiotherapy (previous, recent)
   - bone marrow transplant
   - other
7. Renal
   - renal failure (acute, chronic)
   - dialysis requirement (hemodialysis, peritoneal)
   - renal transplant
   - other

Table 3. Co-morbidities/Endoscopy Alerts (Continued)

8. Infection
   - HIV (asymptomatic, AIDS)
   - tuberculosis (TB) (quiescent, purified protein derivate (PPD)+, on treatment)
   - hepatitis B
   - hepatitis C
   - sepsis current
   - other
9. Musculoskeletal
   - spine instability/fixation
   - connective tissue disease
   - orthopedic implant
   - other
10. CNS
    - stroke (transient ischemic attack (TIA), resolved stroke, unresolved stroke)
    - dementia
    - seizures
    - psychosis
    - brain surgery
    - other
11. Liver
    - ascites
    - cirrhosis
    - transplant
12. Intervention challenges
    - unable to sign consent (age under 18, mental handicap)
    - unable to accept blood transfusion
    - other beliefs affecting care
    - prior difficulties with sedation/anesthesia
    - abdominal surgery within 30 days
    - pregnant

The intervention. The results of ERCP are influenced by the experience of the endoscopist and possibly by the procedure environment (location and team). The key metric here should be the documented expertise of the specific endoscopist, i.e., track record of technical and clinical success in context. Very little of that information is available currently, but there are recommendations that endoscopists should keep "report cards" containing some of this data.[4,5]

The results. The main goal of our interventions is to diminish the burden of disease, as previously described. Thus, the metrics are the change in these parameters attributable to the intervention. Unfortunately, this "clinical success" cannot be measured easily or quickly. Mature assessment often requires months or years of followup, which adds complexity and cost. There is another complicating factor: Who does the assessment? Research studies attempt to have objective endpoints, but they are often supervised by protagonists of a single technique, who may introduce bias, however unconsciously. We should insist on independent arbiters. Also, patients may differ from researchers, and among themselves, in their view of the outcome priorities. Some cancer patients may be concerned primarily with the chance of cure or longevity; others are concerned more with freedom from pain.

These difficulties explain why many studies of ERCP have focused more on "technical success," i.e., the simple ability to remove a bile duct stone or to place a stent. These are interesting (and important) metrics, but poor surrogates for clinical assessment. Regarding

technical success, we know that some procedures are much more difficult technically than others, a concept recently developed into a "degree of difficulty score."[6] An example is shown in Table 4. Documenting these variations is important when comparing results between centers or individuals.

The costs. The value of reducing disease/symptom burden by ERCP intervention cannot be assessed without considering the costs that are incurred and the patient's overall experience/satisfaction. Planned costs are the anticipated pain, anxiety, social disruption, and dollar costs of the procedure and surrounding events. Actual costs will be substantially greater if the procedure cannot be completed (resulting in another expensive procedure) or if there are unplanned, adverse outcomes (complications), requiring prolonged hospitalization and other interventions.

Documentation of **unplanned, adverse outcomes** (complications) remains a controversial and sensitive topic because of potential credentialing and medicolegal implications. However, we cannot complete the intervention equation unless we can document all of the unplanned events and their severity, as assessed by the extent of change in the plan of care (Table 5), with their associated costs. At some threshold of severity, an unplanned event becomes a "complication" in the sense that we now use that term. Until now, we have used the need for hospitalization as that threshold,[7] but this requires review and an up-to-date consensus.

Patient satisfaction with the process and its results can be measured with standard instruments.[4]

Balancing Benefits and Risks

We started by stating that there are two questions: What can ERCP offer? How does that compare with available alternatives? Compiling all of these metrics in individual patients and cohorts of similar patients should enable us to better study and understand the predictors of good and bad outcomes and thus improve our ability to give patients meaningful, personalized information, so that they can truly understand what ERCP can offer (i.e., real informed consent).

Table 4. Grades of Technical Difficulty at ERCP, Adopted From Schutz and Abbott[6]

	Diagnostic	Therapeutic
Standard (level 1)	Selective deep cannulation Diagnostic sampling	Standard sphincterotomy Stones < 10 mm Stents/nasobiliary drains for leaks and low tumors
Advanced (level 2)	Billroth II diagnostics Minor papilla cannulation	Stones > 10 mm Hilar tumor therapy Benign biliary strictures
Tertiary (level 3)	Manometry Roux-en-Y, Whipple intraductal endoscopy, biopsy	Billroth II therapeutics intrahepatic stones pancreatic endotherapy

Table 5. Unplanned Events (Complications)

1. Unplanned event occurred? no/yes

2. Timing (event first appears)
   - preprocedure
   - procedure
   - early recovery (< 4 hours)
   - late recovery (4–24 hours)
   - delayed (1–30 days)
   - late (>30 days)

3. Nature
   - Medication/sedation/anesthesia
     - — allergic reaction (antibiotic, contrast related, other _____)
     - — hypoxia (transient, prolonged)
     - — hypotension
     - — hypertension
     - — dysrhythmia (afib, af, heart block, ischemic changes, tachycardia, bradycardia
     - — hypoventilation
     - — wheezing
     - — drug interaction (details
     - — _____)
     - — neuropsychiatric reaction
     - — IV site problems
   - Equipment malfunction
     - — endoscope
     - — radiology equipment
     - — accessories
     - — diathermy
     - — implanted devices
   - Direct events
     - — endoscopic perforation
     - — sphincterotomy perforation
     - — snare/diathermy perforation
     - — dilator perforation
     - — duct penetration/dissection
     - — bleeding
     - — hemobilia
     - — pancreatitis
     - — biliary infection
     - — cholecystitis
     - — infection
     - — pseudocyst infection basket impaction
     - — peritonitis
     - — other
   - Indirect (non-GI) events
     - — pain ? cause
     - — fever ? cause
     - — renal
     - — neurological
     - — musculoskeletal
     - — pregnancy-related
     - — other

4. Details of events

5. Procedure
   - not started
   - stopped prematurely
   - completed

6. Changes in care plan
   - none
   - extra consultation
   - unplanned admission (days)
   - prolonged admission (days)
   - Intensive Care Unit (ICU) admission (days)

Table 5. Unplanned Events (Complications) (Continued)

7. Interventions
   - medical
     - naloxone
     - flumazenil
     - atropine
     - oxygen
     - transfusion
     - other
   - ventilation assistance
     - intubation
     - emergency code called
   - endoscopy _____
   - radiology imaging _____
   - radiology intervention _____
   - surgery _____
   - other intervention
8. Outcome
   - full recovery
   - permanent disability/loss of function _____
   - death date _____ (days after procedure _____)
9. Attribution event related to endoscopy?
   - yes
   - probably
   - no
   - uncertain

The second question—Is ERCP the best option?—can be answered only if other possible approaches (e.g., surgery, interventional radiology) have been subjected to equally stringent scrutiny. This requires the development and use of comparable metrics for evaluating these alternative methods—either in careful, objective cohort studies or through true randomization.

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What Are the Complications (Adverse Events) of ERCP?

Martin L. Freeman, M.D.

Complications, or adverse events, are deleterious events that result from but are not an inevitable consequence of a procedure. Events may range in severity from minor with spontaneous resolution to life threatening or fatal. Previous definitions of complications have included only overt events that require unplanned hospitalization or intervention and implied error or fault, while the more recent concept of "unplanned events" includes a de-stigmatized but broader scope of negative events, such as failure to complete a procedure. The rate of complications reported will vary depending on the definition used and the thoroughness of followup.

ERCP with or without sphincterotomy is associated with the highest rate of complications (2–20%) of any common gastrointestinal (GI) endoscopic procedure. Complications include pancreatitis, hemorrhage, perforation, infection, cardiopulmonary events, and miscellaneous others. In contrast to many surgical procedures, the risk of ERCP complications is generally not higher in patients who are older or have increasing numbers of co-morbid illnesses. Endoscopists performing higher volumes of ERCP have lower rates of overall complications and of severe complications.

Pancreatitis is the most common complication, occurring after 2–20% of ERCP, depending on a number of factors. Pancreatitis is usually defined as new or worsened abdominal pain associated with a rise in serum amylase to more than three times above normal and requiring unplanned hospitalization. Recent multicenter studies have shown that risk factors for pancreatitis after ERCP are related as much to the patient characteristics as to endoscopic technique. Risk factors for pancreatitis include indication of suspected sphincter of Oddi dysfunction, female gender, younger age, absence of jaundice, a history of previous post-ERCP pancreatitis, but do not include small bile duct diameter. Chronic pancreatitis is protective. Techniques associated with higher risk include difficult cannulation, repeated pancreatic duct contrast injections, balloon dilation of the biliary sphincter, and pancreatic sphincterotomy. Performance of biliary sphincterotomy or biliary therapy in general is not clearly linked to pancreatitis, although the use of "precut" techniques to access the bile duct is a risk factor in some studies involving less experienced endoscopists. Sphincter of Oddi manometry utilizing aspirating catheters does not appear to add independent risk. The placement of a pancreatic stent can reduce risk in selected circumstances. Pancreatitis after ERCP is managed as for any other etiology. A number of drugs under investigation shows promise to reduce or prevent post-ERCP pancreatitis.

Clinically significant hemorrhage occurs primarily after sphincterotomy (less than 2%) and is related to the presence of coagulopathy, use of anticoagulants, presence of acute cholangitis, bleeding at the time of sphincterotomy, and inexperience on the part of the endoscopist, but probably is not related to the use of aspirin or related drugs. Hemorrhage can usually be stopped by endoscopic intervention. Perforation is rare and may consist of guidewire

perforation, retroperitoneal perforation after sphincterotomy, both of which can usually be managed without surgery or bowel wall perforation. Cholangitis results primarily from inadequate drainage.

Because complications after ERCP, particularly pancreatitis, are most likely to occur in patients without definite biliary obstruction and because endoscopists with more experience have lower complication rates, principal strategies for reducing complications include avoidance of ERCP when the indication is equivocal and performance of ERCP by high-volume endoscopists.

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What Are the Determinants of Success in Utilization of ERCP in the Setting of Pancreatic and Biliary Diseases?

Glen A. Lehman, M.D.

There are many parameters which influence the ultimate success or failure of a diagnostic or therapeutic endoscopic retrograde cholangiopancreatography (ERCP) examination. Success may be categorized as complete (total) or partial. Further categorization may be (a) technical success and (b) disease resolution success. These two may be the same in post cholecystectomy common duct stone removal, where the patient is left stone free and presumably disease free for probably the remainder of his/her life. In contrast, common duct stone removal in a sclerosing cholangitis patient who also has strictures and cirrhosis is an entirely different picture. Successful stone removal would only be a small factor in ultimate disease treatment. This session will deal mostly with technical success, as if it is easier to quantitate.

1. Personnel Skill and Experience

ERCP is a relatively complex combined endoscopic/radiographic procedure, which, therefore, requires multiple skilled personnel. The success depends on the combined effort of all involved people, and one weak link may limit success. At a minimum, ERCP involves a physician, one endoscopy nurse for patient sedation and vital sign monitoring, and one nurse for managing guidewires, catheters, etc. Most centers use a radiology technician to aid in fluoroscopy/filming. Some centers include a radiologist to aid in fluoroscopy, exposing films, or film interpretation. Some centers add a nurse anesthetist or anesthesiologist.

Most endoscopists gain initial skills in a formal training setting.[1] Jowell et al.[2] have shown that at least 180 ERCPs are required before a biliary successful cannulation rate of 80% is achieved. Skills to remove uncomplicated bile duct stones and place stents in uncomplicated biliary strictures can be expected simultaneously. A multisociety Australian committee set minimal training standards at 200 total ERCPs with 80 therapeutic exams.[3] My personal experience is that it takes approximately 400–500 exams for a trainee to achieve a cannulation rate of 90% and be more fully proficient at most aspects of therapeutic ERCP, such as sphincter of Oddi manometry and pancreatic therapeutics.

Several reports show that increases in annual ERCPs performed correlates with greater success rate in biliary therapeutics and decreased overall complication severity and frequency.[4,5,6,7] Our group[8,9] has shown that second attempt ERCP has a greater than 95% success rate, even though an initially attempted ERCP failed at a smaller hospital. Therefore, centers with skilled physicians and a relatively large number of patients per year (greater than 500) can be expected to provide better quality service than smaller centers. Unfortunately, even many larger centers do not concentrate their ERCP experience, so that 500 cases may be divided among 5–10 endoscopists. We are unaware of studies correlating nursing skill and outcomes.

2. Aggressiveness

Technical success can be partially equated with successful ductal cannulation. If a cannulation attempt is failing, the use of precut sphincterotomy (a higher risk procedure if used by less experienced endoscopists) will likely increase cannulation success rates. Such aggressiveness may be at least partially offset by increased complications. Stenting the pancreatic duct decreases complication rates from precutting in some series.[6,10,11]

Good clinical judgment and informed consent are required to apply aggressiveness appropriately. Use of more aggressive technique should be limited to highly skilled/experienced endoscopists.

3. Patient Anatomic Disease Factors

Many postoperative and pathologic alterations of anatomy, such as duodenal diverticulum, Billroth II, tumors compressing/obstructing the bowel, make examinations more difficult. Large duct stones and tight tortuous bile duct strictures are difficult to treat. Roux-en-y choledochojejunostomies and Roux-Y gastrojejunostomies (especially with long limbs) are extremely difficult cases for ERCP. Long endoscopes of at least 160 cm are required. The prudent ERCP team should attempt cases commensurate with their expertise and available equipment. Understanding the appropriate alternatives (surgery, interventional radiology, etc.) is part of good clinical judgment. A detailed review of prior surgical operation notes is often required. Schutz, et al.[12] have published a grading scale to quantitate exam difficulty. Future publications quantitating success rates should include difficulty factor grading.

4. Equipment

ERCP has many technical components, including the endoscope, accessories, and radiographic equipment. Most experts agree that video endoscopic equipment (as opposed to fiber-optic) contributes to easier endoscopic teaching and ease of exam performance. Current generation endoscopes with greater flexibility, wider angles of view, better elevators, and larger accessory channels are clearly superior to older equipment. Large channel endoscopes are required to place plastic stents greater than 8 French. Appropriate radiographic visualization is essential to ERCP performance. Radiographic equipment used for ERCP varies greatly throughout the United States. Fine detail resolution, which is essential for quality viewing, varies greatly with small portable C-arm technology, old generation barium study units, and modern angiographic digital technology. No radiology equipment manufacturer that we are aware of makes a radiology suite specifically for ERCP. Most endoscopists have little radiology training and no hospital appointment on the radiology staff; therefore, equipment updates may be difficult to acquire. Multiple accessories (guidewires, catheters, stents, sphincterotomes, lithotriptors, etc.) may be required to succeed at ERCP. One size does not fit all, and having multiple devices available for a single case may be mandatory for success. Again, smaller facilities with limited inventory may not have the appropriate equipment for an individual examination.

5. Time

With increasing use of gastrointestinal endoscopy, endoscopists are often required to perform more procedures per day. This may limit the time available for complex cases. Similarly, reimbursement for endoscopic procedures continues to drop, thereby encouraging endoscopists to limit the time for individual exams. This lesser time commitment per exam may adversely affect success rates, especially for complex exams. Involvement of trainees adds time requirements and cost.[13]

6. Travel

Since skill and equipment are clearly less available at low volume hospitals, patients with diseases addressable by ERCP may need to choose alternative therapies (i.e., percutaneous, laparoscopic, or open surgical therapy), or the patient must travel to a center with these skills. The referral center[8,9] may be nearby or at a great distance in less populated, rural areas. Elderly patients, those with less financial resources, those with less family support, and those with near end-stage diseases may choose not to travel.

7. Sedation

While ERCP is done unsedated in some countries, the tolerance and success almost certainly are greater if the patient is sedated. Intravenous sedation/analgesia is the most common means of sedating for ERCP. Some centers use deep sedation with propofol and/or general anesthesia for most cases. Children often require general anesthesia. Such sedation adds time and cost to the procedure, although patient cooperation is increased.

8. Miscellaneous

Patient satisfaction is a desired endpoint. Attention to small detail may improve "success."

Patient concerns for a procedure often involve a variety of peripheral issues, including traffic flow to the endoscopy area, parking, waiting room comforts, waiting time, food facilities, secretarial scheduling, general politeness, intravenous (IV) site or blood drawing comforts, recovery room area, etc.

Summary

Optimizing factors that contribute to ERCP success continues to be a challenge, especially in low volume centers.

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