ENDOSCOPIC BILIARY SPHINCTEROTOMY

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Results, Complications and Contra-Indications

ENDOSCOPISCHE BILIAIRE SPHINCTEROTOMIE
Resultaten, Complicaties en Contra-Indicaties

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Promotor	:	Prof. Dr. H.E. Schütte
Promotor	:	Prof. J.H.P. Wilson
Overige leden	:	Prof. Dr. J. Jeekel
		Dr. K. Huibregtse
		Drs. M. van Blankenstein

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To the memory of my parents

To Ria and Niels and Michiel

CONTENTS

Chapter 1

THE SCOPE OF THE THESIS

In 1986 the departments of Radiology and Internal Medicine II/Gastroenterology initiated a prospective study of therapeutic endoscopic retrograde cholangio-pancreatography (TERCP). The project was designed to obtain information which could be used to evaluate immediate and medium-term results and complications of endoscopic biliary and pancreatic interventions. During a three-year period 1362 consecutive patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) were included, and a large amount of information gathered in a standard, prospective fashion. This information was then used to answer specific questions or solve specific problems, most of which concerned cutting the papilla of Vater during TERCP to improve access to the common bile duct or main pancreatic duct.

The main aim of the work reported in this thesis was therefore to evaluate the results of endoscopic biliary sphincterotomy in patients with common bile duct obstruction due to malignancy or stones, with and without cholangitis, and patients suspected of biliary dyskinesia. The studies focussed especially on complications due to the intervention.

A general introduction and a review of the literature is given in chapter 2. Chapter 3 describes the patients and the protocol used for the therapeutic ERCP study.

In chapter 4 the problems encountered during endoscopic stenting in patients with malignant obstruction of the mid or distal common bile duct and/or the papilla are assessed.

Chapter 5 describes the complications observed in patients after endoscopic papillotomy (= endoscopic sphincterotomy) for common bile duct stones and how to prevent them.

In chapter 6 the risk factors influencing complications of sphincterotomy in patients with cholangitis due to common bile duct stones are assessed.

Follow-up results of endoscopic papillotomy in patients suspected of having a functional disorder of the papilla are described in chapter 7.

Patients with a history of Billroth II gastrectomy present special problem when they have to undergo sphincterotomy. A technique to succesfully perform sphincterotomy in these patients is described in chapter 8.

Finally the results and complications of endoscopic papillotomy presented in the previous chapters are discussed and summarized.

Chapter 2

GENERAL INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) was first described in 1970 by *Oi*[1] and *Takagi et al.*[2]as a method in the diagnosis of pancreatic cancer. In 1973 the technique was introduced in the University Hospital Rotterdam as a joint venture of the departments of Internal MedicineII/Gastroenterology and Radiology. In the following years the indications for ERCP rapidly expanded to include suspected pancreato-biliary disease which could not be evaluated adequately by conventional methods.

In 1974 a new dimension was added to ERCP procedures by the introduction of endoscopic papillotomy (EP), first reported by *Classen* and *Demling* and *Kawai et al.*[3,4]. Shortly after their publication this technique was introduced in our hospital. ERCP could now not only be used for diagnostic purposes, but also to treat patients with obstruction of the common bile duct or main pancreatic duct.

Endoscopic cutting of the papilla of Vater was initially intended to manage common bile duct stones in patients with increased surgical risk and made it possible to remove the bile duct stones without general anesthaesia. In the following years the indications for endoscopic sphincterotomy gradually increased.

The papillotomy technique developed further with the introduction of precut or needle-knife papillotomy, which made it possible to enter the common bile duct (CBD) without initial selective cannulation, by means of an incision into[5] or just above[6] the papilla.

A combined percutaneous endoscopic approach was first reported by *Mason* and *Cotton* [7] to avoid precutting in patients in whom endoscopic cannulation of the bile duct appears impossible. This involves introduction of a cannula into intrahepatic bile ducts through the abdominal wall. The papilla is thus approached percutaneously and dilated by balloons. The sphincterotome is advanced into the CBD as the deflated balloon is withdrawn.

In 1989 the wire-guided sphincterotomy[8,9] became widely accepted as a means to avoid precut papillotomy in cases where selective cannulation of the common bile duct was difficult.

One of the main indications for ERCP is in the diagnosis and relief of obstruction of the bile ducts. Obstructive jaundice due to gallstones or a malignant tumor compressing or growing into the common bile duct is associated with jaundice, pruritus, malabsorption and a risk of secondary infection. Many patients with obstructive jaundice are elderly, and surgical solutions are associated with a high morbidity and mortality.

Endoscopic bile duct drainage was first accomplished externally in 1976, by means of a nasobiliary tube[10]. Three years later the implantation of an endoprosthesis in the bile duct, for internal decompression, was first reported[11,12].

At that time there were no large-channel duodenoscopes available and only a size 7 French stent could be inserted into the bile duct. These fine-bore endoprostheses gave initial relief of the jaundice with a low morbidity and mortality in comparison to laparotomy, but tended to become clogged. In 1981, after technical modifications, larger-bore catheters, up to 10 French could be placed using a duodenoscope with a 3.7 mm channel[13,14]. Clogging appeared to be less a problem with the larger-bore stents, resulting in better drainage. At present the so-called jumbo duodenoscopes are used. They have an even larger working channel of 4.2 mm.

To cannulate the sphincter and to introduce a large-bore stent, papillotomy or sphincterotomy usually has to be performed. As shown in Table 1, in larger series the morbidity and mortality of endoscopic sphincterotomy varies between 2%-10% and 0%-2%, respectively. However, retrospective and multicenter series are prone to underreporting especially the late complications[19]. Many publications do not report success rates or discuss the contra-indications for papillotomy. We therefore examined the success rate of endoscopic drainage in patients with a malignant obstruction of the mid or distal common bile duct or the papilla. One of the main purposes of this study was to identify contra-indications for endoscopic sphincterotomy with stent insertion. The results of this investigation are reported in chapter 4.

Table 2.1 Results of endoscopic sphincterotomy in some large series

Reference	No. of patients	Success (%)	Morbidity (%)	Mortality (%)
Shakoor et al. [15]	1.367	99%	6.2%	0.1%
Sherman et al. [16]	423	99%	6.9%	1.7%
Huibregtse et al. [17]	987	98%	2.2%	-
Leese et al. [18]	394	98%	10.4%	0.8%

The problem of underreporting of complications, including late complications of sphincterotomy, was approached in our study by using a protocollized registration of the endoscopical findings and procedures and including both immediate and delayed complications based on standard definitions and, where possible, objective criteria. A study of the complication rate of papillotomy related to the endoscopic procedure in patients with normal gastric anatomy and common bile duct stones is reported in chapter 5.

In 1877 *Charcot* described the triad "fever", "chills" and "right upper quadrant pain"[20], which is considered to represent the clinical manifestation of partial or complete obstruction of the biliary system complicated with cholangitis and sepsis.

Cholangitis can be purulent and non-purulent. When pus is present in the biliary tree this condition is called suppurative cholangitis, which is usually fatal unless biliary decompression is performed[21,22]. There is still some discussion as to the timing of biliary decompression, and the success rate and incidence of complications following biliary decompression by the endoscopic route. We therefore examined all patients undergoing ERCP for cholangitis associated with gallstones. We paid special attention to the clinical history as a means of guiding management, and the timing of biliary decompression, in relation to the onset of cholangitis and the response to conservative management prior to drainage. As will be seen in chapter 6, based on the literature and on our own findings we present a practical endoscopic approach for patients presenting with clinical cholangitis, which includes the early installation of a nasobiliary drain in selected cases with severe cholangitis.

One problem relatively frequently encountered by endoscopists is that of the patient who presents with a history suggestive of biliary tract pain, but who does not have visible common bile duct stones. With obvious common bile duct stones at ERCP, papillotomy and stone removal are the standard procedure. However in the case of the patient without definite stones, the endoscopist has to decide whether the patient will benefit from papillotomy or not.

Clinical or biochemical evidence of cholestasis or pancreatitis can theoretically be helpful.

Since *Opie's* article in 1901[23], the relationship between acute pancreatitis and gallstones has become firmly established. *Acosta et al.*[24-26] and *Kelly et al.*[27-29] have reported gallstone migration as being of most importance in the genesis of acute pancreatitis. Calculi were present in the faeces of 85-90 per cent of the patients following an attack of acute gallstone pancreatitis (AGP). Many small size gallbladder stones were usually found in patients with AGP[24-29], but small stones might be missed, or might even have passed into the duodenum, with temporary obstruction.

Dilatation of the common bile duct has been used often as a criterium of recent biliary obstruction. *Osborne and associates*, however, determined that the size of the common bile duct of patients with AGP, on operative cholangiograms, was independent of the presence of choledochal calculi[30].

Other causes of attacks of epigastric pain associated with cholestasis or pancreatitis are spasm, fibrosis or inflammation of the sphincter of Oddi[31,32].

In 1887, *Ruggero Oddi* described in detail the muscle anatomy of the papilla of Vater[33] and suggested one year later, that jaundice may have a functional origin due to the contraction of the ampullary sphincter muscle. In 1977 a manometric technique has been presented by which pressures of the sphincter of Oddi, common bile duct, pancreatic duct and duodenum can be recorded at ERCP examination[34].

In patients with unexplained biliary tract pain sphincter of Oddi manometry has been recommended to select patients who might benefit from endoscopic

papillotomy[35-38]. However, this technique is not available in many centers where ERCP and sphincterotomy are performed. We therefore examined patients suspected of having biliary stones, in whom stones were not detectable in the common bile duct at ERCP, to try to identify criteria which would help to select patients with attacks of upper abdominal pain, in whom endoscopic sphincterotomy is justified without previous sphincter of Oddi manometry. The results of this study of endoscopic papillotomy in patients presenting with biliary tract pain but without visible common bile duct stones are presented in chapter 7.

Patients who have undergone gastric surgery can present special technical problems to the endoscopist. Standard techniques for patients with a normal stomach and duodenum cannot be used in patients with a Billroth II gastrectomy. Precut papillotomy was formerly the initial method to cut the papilla in patients with a Billroth II stomach resection. In 1980 the *Soehendra* papillotome[39], which can be pushed through the papilla into the CBD in patients with Billroth II stomach resection was introduced. Subsequent sphincterotomy, however, is usually more difficult to control than the standard papillotomy. In general, a standard EP cannot be performed after a Billroth II stomach resection because the papilla is approached endoscopically from the opposite direction as compared with the normal anatomy, with the cutting wire of the Classen-Demling type sphincterotome directed caudally towards the pancreas. In chapter 8 a new technique is presented in which needle-knife papillotomy is performed along a previously placed thin (1.8 mm) stent in the common bile duct. This technique seems to have some advantages above the previously described methods.

Endoscopic management of biliary and pancreatic duct obstruction has become highly popular during the past 15 years, as a preferred alternative to surgical drainage in almost all patients and to percutaneous drainage in many. As with all new forms of treatment, systematic evaluation of the results are essential to guide the use of the therapy and to identify areas for further improvements[40].

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Chapter 3

MATERIAL AND METHODS

The aim of the study was to evaluate the immediate and medium term results and complications of endoscopic biliary interventions. Before and during ERCP various factors which might influence the results and the complication rate of the procedure, were recorded in a protocol, as follows:

Before ERCP
Immediately before each ERCP the clinical history, including the timing of the complaints and previous upper abdominal surgery, was obtained from the patient. In addition, a separate registration was made of the course in time, from the date of the first complaint of the patient to the date of the ERCP, in order to record the delay caused by the patient, the general practitioner, the referring specialist and the appointment delay for ERCP.

The results and the timing of the physical examination, the laboratory findings including the coagulation status and the blood culture results, the findings of previous imaging and the conservative management before ERCP were obtained from the medical records that were routinely present at ERCP. In addition the previous radiographs of the patients were routinely present at the time of ERCP and a copy of the letter of the referring specialist was obtained.

During the ERCP
The following data were collected:

- It was noted whether or not prophylactic antibiotics had been administered 1 hour before ERCP and/or antibiotics after ERCP including the type and the dose.
- The duration of the diagnostic and the therapeutic part of the ERCP.
- The endoscopical findings during duodenoscopy.
- The type and amount of contrast material used.
- Data concerning the sphincterotomy procedure were recorded, as follows:
    a. the location: common bile duct and/or pancreatic duct.
    b. the use of precut and/or standard papillotomy.
    c. precut after cholangiography ("therapeutic precut") or without intra-ductal contrast material ("diagnostic precut").
    d. the size of the sphincterotomy was estimated using the volume of water-filled balloon that could just be pulled through the papillotomy orifice.
- The presence of bile duct stones was recorded in the following way:
    a. the location: extra-hepatic and/or intra-hepatic.

b. number of stones and the size of the largest extra- and/or intra-hepatic bile duct stone including the enlargement factor by reference to the known diameter of the endoscope.
c. similar to a and b, the situation after stone extraction procedure.
d. whether or not a nasobiliary drain or a stent had been inserted.

- Data concerning endoprosthesis insertion:
  a. location and type of the stent.
  b. in case of failed stent insertion: the reason.
- Complications during the ERCP:
  a. the type of complication: bleeding, perforation, retroperitoneal air leakage, parenchymal extravasation of contrast material.
  b. cause of the complication (cannulation including the type of cannula used, precut papillotomy or standard sphincterotomy, stone extraction or perforation by a guide wire).
  c. immediate treatment of the complication.

Follow-up after the ERCP

The information obtained from the general practitioner:
At three months' and 1 year follow-up the general practitioner was sent a questionnaire with the following possibilities for the clinical condition of the patient:
(1) Without complaints, (2) Improvement of the complaints, compared with prior to ERCP, (3) Unchanged complaints, (4) Worsened complaints, and (5) When the patient had died, the date and the cause.

In addition more precise information was requested about which complaints were still present.

The information obtained from the referring specialist:
At 3 months' and 1 year follow-up the discharge letter after ERCP was requested. In addition a questionnaire was sent for specific information about the complications after ERCP including the dates and the management. The following complications were to record separately: delayed bleeding, pancreatitis, cholangitis, cholecystitis, sepsis, abscess, (recurrent) jaundice, and gallstone ileus.

When the patient had died, in the meantime, the physician was asked for the cause and the results of autopsy.

Up to three months' follow-up information was obtained in all consecutive patients analyzed in this series.

During the 3 years of the study (1987-1990) all patients undergoing a therapeutic ERCP in the University Hospital Rotterdam-Dijkzigt were included in the study.

As all patients were examined by one of three endoscopists and one of two radiologists, and standard forms were used immediately before and during the investigation, no patients were lost from the study. In total 1.362 patients were investigated. The results of studies of subpopulations of the entire group are presented in the following chapters.

Chapter 4

MALIGNANT COMMON BILE DUCT OBSTRUCTION: FACTORS INFLUENCING THE SUCCESS RATE OF ENDOSCOPIC DRAINAGE

[1] J. Boender, [1] G.A.J.J. Nix, [1] H.E. Schütte, [1] J.S. Laméris, [2] M. van Blankenstein, and [2] J. Dees

[1] Department of Diagnostic Radiology and [2] the Department of Internal Medicine II. University Hospital Rotterdam-Dijkzigt, Rotterdam, The Netherlands

Endoscopy 1990; 22: 259-62.

4.1 Summary

The problems encountered in draining the bile ducts endoscopically in 148 patients with malignant obstruction of the mid or distal common bile duct and/or the papilla were assessed. Endoscopically visible extrinsic invasion of the papilla by a malignancy in the pancreatic head, with or without duodenal stenosis, appeared to be the major reason for the failure to insert a stent. The larger a tumor in the pancreatic head the greater the chance of invasion of the papillary region. This appeared to be evident for tumors restricted to the non-uncinate region of the pancreatic head. We would recommend primary percutaneous biliary drainage or surgery when the size of a proven malignancy restricted to the non-uncinate region of the pancreatic head is 5 cm or more, or when diagnostic duodenoscopy reveals extrinsic invasion of the papilla of Vater, or severe duodenal involvement with stenosis.

4.2 Introduction

Endoscopic insertion of biliary stents or sphincterotomy are accepted procedures for palliative treatment of patients with malignant obstruction of the common bile duct (CBD). Endoscopic insertion of endoprostheses, however, is unsuccessful in about 10-20% of these cases (1-5). The reasons for failure to insert an endoprosthesis have received relatively little attention.

The purpose of this investigation was to assess the difficulties that are encountered when endoscopic attempts are made to insert an endoprosthesis in a case of malignant obstruction of the mid and distal CBD and the ampullary region.

4.3 Material and Methods

Between March 1987 and September 1988 endoscopic drainage, either by the insertion of an endoprosthesis or by sphincterotomy, was attempted in 148 patients with a malignant stricture in the mid or distal portion of the CBD, or the papilla of Vater. Cases with high-level obstructions of the CBD, involving the hilum of the liver were excluded.

The mean age of the patients was 71 years, with a range of 23 to 90 years. None of the patients had had previous bile duct drainage or gastric surgery.

The following malignancies appeared to be responsible for the CBD obstructions: pancreatic carcinoma (83), metastatic disease (26), gallbladder carcinoma (14), carcinoma of the papilla of Vater (12), duodenal carcinoma (7), and cholangio-carcinoma of the mid or distal CBD (6).

Among these 148 tumors, 76 primary pancreatic head cancers, 13 cases of metastatic disease, and 2 cases of a distal cholangio-carcinoma had caused a stricture of the intra-pancreatic portion of the CBD. Among these 91 tumors, 8 primary pancreatic carcinomas and 1 case of metastatic disease were located in the uncinate lobe of the pancreas. In 82 patients the tumor mass was restricted to the non-uncinate region of the pancreatic head. In 89 patients (60%) the diagnosis was confirmed histologically or cytologically. In the remaining patients the diagnosis was made on the basis of radiological signs and the clinical course of the process.

The ERCP technique used and the diagnostic criteria have been described elsewhere[6,7]. In all cases the duodenal wall was additionally coated with contrast material during the procedure.

The diameters of the tumors in the pancratic head were determined on the radiograph by measuring the largest distance between the stenotic areas on cholangio-/pancreaticography and the impressions or the invasion of tumor on duodenography (Fig. 1-4). The true diameter of the tumor was then calculated by measuring the diameters on the radiographs, multiplied by the true diameter of the duodenoscope used (10.2 mm), and divided by the measured diameter of the duodenoscope on the radiograph, adjacent to the tumor in the pancreatic head. The average enlargement factor calculated was 1.5.

4.4 Results

The tumor was visualized on ERCP in 89% of the cases and drainage of bile was possible in 80% (Table 1). In those cases in which the tumor was not closely related to the orifice of the CBD, for example tumors of the pancreatic body, the gallbladder, and the CBD itself, optimal visibility and drainage was achieved.

The endoscopic findings that influence the success of diagnostic ERCP, and subsequent insertion of an endoprosthesis and drainage of bile are presented in Table 2.

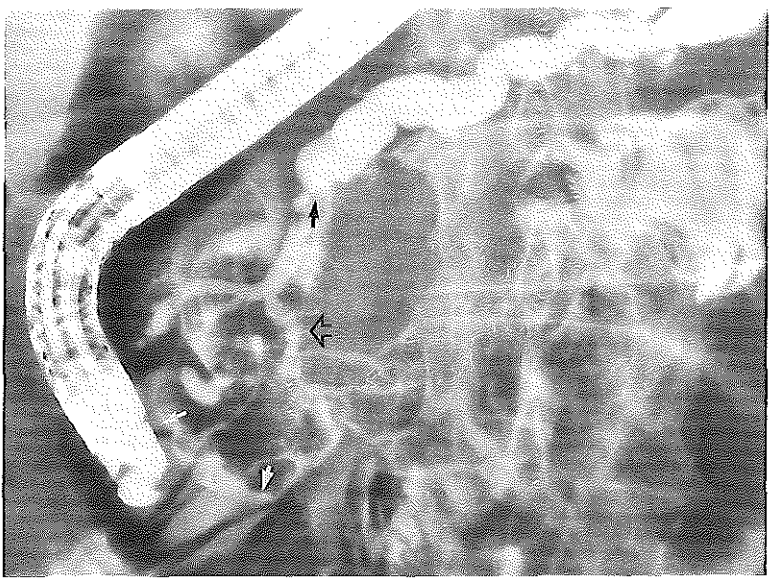

Figure 1: Non-uncinate primary pancreatic head carcinoma (closed arrows), diameter a good 4 cm, with endoscopically visible extrinsic invasion of the papilla. Normal uncinate duct (open arrow). Retrograde cholangiography and endoscopic stent insertion failed.

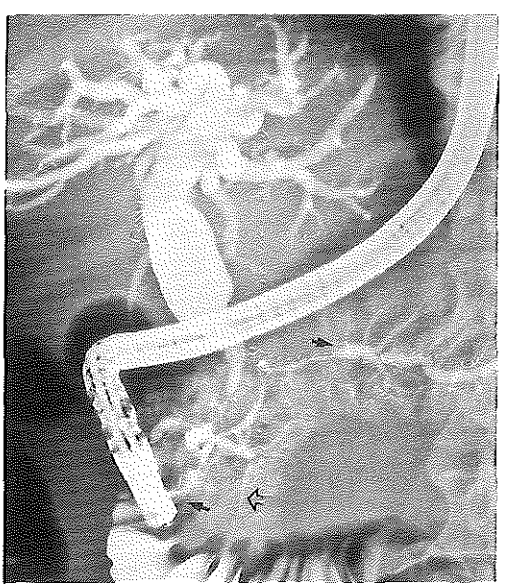

Figure 2: Metastases of an ovarian carcinoma in the non-uncinate region of the pancreatic head with a largest diameter of 6 cm (closed arrows). Normal uncinate duct (open arrow), with endoscopically visible invasion of the papilla; stent insertion failed. There is a small contrast medium extravasation directly behind the papilla.

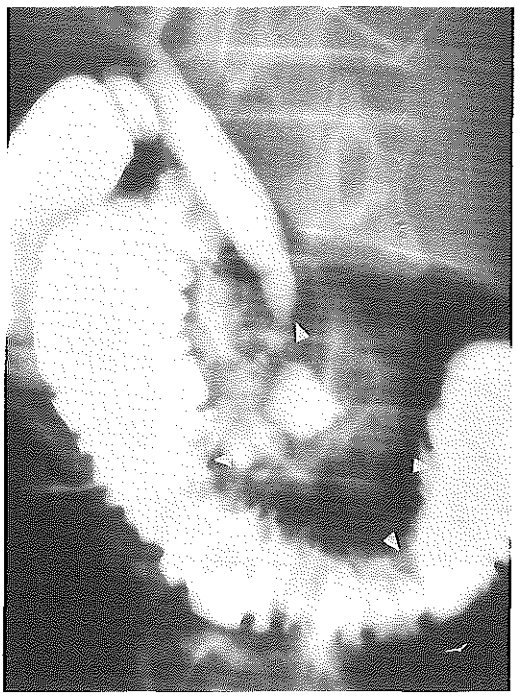

Figure 3: Carcinoma of the uncinate lobe of the pancreatic head, diameter 6 cm (closed arrows). Normal papilla, successful endoscopic stent insertion.

Figure 4: Carcinoma of the uncinate lobe of the pancreatic head, diameter 7 cm. Duodenal invasion (closed arrows) and proximal stenosis of the CBD (open arrow). The papilla was normal; endoscopic stent placement succeeded.

Endoscopically visible invasion of the papilla of Vater by a tumor in the pancreatic head, was the most important cause of failure to insert a stent (success rate 13% in 23 such cases). However, in cases of primary carcinoma of the papilla, bile drainage by means of a large papillotomy, was successful in all patients.

In Table 3, the primary carcinomas, metastases and cholangiocarcinomas located in the pancreatic head, and not in the uncinate lobe of the pancreas, are subdivided in accordance with the true maximal diameter of the tumor. The corresponding rates of successful drainage and the percentage of endoscopically visible, extrinsic invasion of the papilla are presented.

The nine tumor masses in the uncinate lobe of the pancreatic head were large, in three of these the tumor diameter was between 4.5 and 5.5 cm, in the other six between 5.5 and 7 cm. In the 9 cases of uncinate tumors, extrinsic duodenal invasion was observed distal to the papilla on hypotonic duodenography. In 8 patients with tumors in the uncinate region, the papilla appeared to be normal on endoscopy, and the insertion of the endoprosthesis was uneventful. In the remaining case, the papilla was involved in the duodenal wall invasion, and the planned stent insertion failed.

Extrinsic papillary invasion was diagnosed more often on hypotonic duodenography, also in patients in whom only a prominent papillary region was seen during endoscopy. In the latter patients, in whom extrinsic invasion of the papilla was not visible endoscopically, cannulation of the bile ducts and stent insertion succeeded in most cases.

Table 4.1 Causes of malignant bile duct obstruction and the success rates of diagnostic ERCP and endoscopic bile drainage in 148 patients

Cause of CBD obstruction	Number	Successful diagnostic ERCP	Successful endoscopic bile drainage
Duodenal cancer	7	6 (86%)	5 (71%)
Papillary cancer	12	12 (100%)	12 (100%)
Pancreatic head cancer	76	66 (87%)	57 (75%)
Pancreatic body cancer	7	7 (100%)	7 (100%)
Gallbladder cancer	14	14 (100%)	13 (93%)
Cholangiocarcinoma	6	6 (100%)	6 (100%)
Metastases involving the CBD	26	20 (77%)	18 (69%)
Total	148	131 (89%)	118 (80%)

Table 4.2 Endoscopic findings in 148 patients undergoing diagnostic ERCP and endoscopic bile drainage, and the success rates of these procedures

Endoscopic findings	Number	Successful diagnostic ERCP		Successful endoscopic drainage	
Normal	70	69	(99%)	66	(94%)
Juxtapapillary diverticulum	8	8	(100%)	8	(100%)
Prominent papillary region	13	11	(85%)	10	(77%)
Local extrinsic invasion of the duodenal wall not involving the papilla	15	15	(100%)	14	(93%)
Extrinsic invasion of the duodenal wall including the papilla	23	10	(43%)	3	(13%)
Duodenal tumor involving the papilla	7	6	(86%)	5	(71%)
Papillary tumor	12	12	(100%)	12	(100%)

Table 4.3 Relationship between diameter, endoscopic stent insertion, and endoscopically visible extrinsic invasion of the papilla in 82 cases of (non-uncinate located) tumors in the pancreatic head

Largest true tumor diameter	Number	Endoprosthesis successful (%)		Endoscopically visible papillary invasion (%)	
1-2 cm	6	6	(100%)	-	(- %)
2-3 cm	20	19	(95%)	2	(10%)
3-4 cm	30	24	(80%)	5	(17%)
4-5 cm	15	7	(47%)	5	(33%)
5 cm or more	11	2	(18%)	10	(91%)
Total	82	58	(71%)	22	(27%)

4.4 Discussion

In our hospital, high-level malignant obstructions of the CBD, involving the hilum of the liver, are often treated by percutaneous transhepatic insertion of exo- or endoprostheses, either for drainage or drainage and local irradiation of Klatskin tumors. Endoscopic insertion of endoprostheses seems to incur a high risk of early cholangitis in up to 40% of the cases[8,9], and insertion of multiple endoprostheses is usually difficult and time consuming[10].

In the case of a malignant CBD obstruction due to a tumor in the pancratic head, failure of endoscopic stent insertion is usually ascribed to an inability to cannulate the papilla or to insert a guide wire through a tight stricture, or to duodenal encasement by tumor growth[1,2,9,12]. *Soehendra* and *Grimm* reported difficulties in endoscopic stent placement in cases of malignant prepapillary CBD obstruction due to infiltration of the papilla by the tumor[10].

Failure of stent insertion in our cases is also clearly related to invasion and stricture of the papilla of Vater and the distal CBD by tumors located in the pancreatic head. Even small tumors in the pancreatic head may affect these parts when they are located adjacent to the papilla (Table 3). But, in all probability, the larger the pancreatic head tumor, the greater will be the likelihood of its invading the papilla.

Malignant tumors in the uncinate region of the pancreas bulge on the caudal side of the pancreatic head, and excentric to the CBD, and are consequently usually large before they involve the CBD, with the papilla still normal in most cases. This is of practical significance. Tumors of the uncinate lobe measuring up to 7 cm often had not invaded the papilla; this probably explains why endoscopic bile drainage was often uneventful in these cases. However, when the malignant lesion is restricted to the non-uncinate region of the pancreatic head and measures 5 cm or more, the papilla will most likely be invaded and endoscopic drainage unsuccessful (Table 3). In these cases, and if extrinsic papillary invasion is seen during diagnostic duodenoscopy, we would recommend primary surgery or PTBD. The choice between PTBD and gastroenterostomy with biliodigestive anastomosis depends on the age and clinical condition of the patient and the presence of duodenal obstruction[5].

In most centers, the patients with severe malignant duodenal involvement by a tumor in the pancreatic head are treated by palliative surgery, which is decided upon at the time of initial ERCP[2,5,9]. Our material includes five patients with extensive malignant duodenal invasion with stenosis by tumors in the pancreatic head. Stent insertion failed in all these cases. This is in agreement with our policy to refer these patients for palliative surgery.

The likelihood of successful endoscopic stent insertion is more than 90% when the tumor does not invade the papilla of Vater. This also applies in the cases in which the tumor invades the duodenum locally, but does not invade the papilla.

The 12 carcinomas of the papilla itself were all recognized endoscopically by the polypoid, fleshy and fragile enlargement of the papilla. In conformance with the literature, endoscopic bile duct drainage by means of a large papillotomy or stent

insertion without a preliminary sphincterotomy, was relatively easy in these cases[13,14,15].

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Chapter 5

ENDOSCOPIC PAPILLOTOMY FOR COMMON BILE DUCT STONES: FACTORS INFLUENCING THE COMPLICATION RATE

[1]J. Boender, [1]G.A.J.J. Nix, [2]M.A.J. de Ridder, [3]M. van Blankenstein, [1]H.E. Schütte, [3]J. Dees, [3]J.H.P. Wilson

[1] Department of Diagnostic Radiology; [2] Institute of Epidemiology and Biostatistics; and [3] Department of Internal Medicine II, University Hospital, Rotterdam-Dijkzigt, Rotterdam, The Netherlands.

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5.1 Abstract

In a prospective study, the complications observed in 242 consecutive patients after endoscopic sphincterotomy for common bile duct stones were recorded over a period of up to three months. Patients with previous gastric surgery, papillotomy, or additional pancreato-biliary disease other than gallbladder stones were excluded. The overall complication rate was 14%, 74% of these complications being moderate or severe.

The complication rate due to cholangitis was higher in (1) the group with retained stones following complete papillotomy and without biliary drainage and (2) the group with failed precut papillotomy and drainage after cholangiography, both compared to patients with successful drainage (75% vs. 2.6%: $p < 0.001$ and 40% vs. 2.6%: $p = 0.001$ respectively).

Both pancreatitis and retroperitoneal air leakage occurred in 1.7% of cases. They were more frequently observed in patients with a smaller diameter (< 10 mm) in the distal common bile duct (5.6% vs. 0%: $p = 0.007$ for pancreatitis, and 2.8% vs. 1.2%: n.s. for perforation) and especially following precut papillotomy (13.0% for pancreatitis and 8.7% for perforation), which had to be performed more often in these patients.

Bleeding following sphincterotomy was relatively frequent when the papilla was located at the lower rim of or inside a diverticulum, compared to patients without a diverticulum (16.2% vs. 2.7%: $p = 0.004$ and 26.7% vs. 2.7%: $p < 0.001$ respectively). When the papilla was located inside diverticula, both the rate of perforation and bleeding increased following precut papillotomy, compared with

standard papillotomy only (33% vs. 0%: n.s. and 33% vs. 22%: n.s.). At present we consider it to be a contraindication for precut papillotomy when the papilla is located inside a diverticulum.

5.2 Introduction

Most reports describing the complication rate associated with the endoscopic extraction of common bile duct (CBD) stones focus on a limited number of risk factors. Risk factors include (a) failed endoscopic biliary drainage (EBD) following endoscopic papillotomy (EP); (b) the presence of acute cholangitis; (c) the use of a precut or needle-knife papillotomy (NKP); and (d) the diameter of the CBD. The aim of this study is to evaluate the complication rate in patients undergoing EP for CBD stones in relation to all of these risk factors except the presence of cholangitis prior to EP. In addition, the effects of the location of a juxtapapillary diverticulum (JPD), of the age, of the presence or absence of the gallbladder, and of the estimated size of the papillotomy on the complication rate of EP are also evaluated.

5.3 Patients and Methods

Patients

Between March 1987 and November 1989 all 1362 patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) were included in a prospective study with the aim of evaluating the immediate and medium-term complications of diagnostic and therapeutic ERCP. This study includes the 242 consecutive patients who underwent EP for CBD stones but had not had previous gastric surgery, papillotomy, or additional pancreatobiliary disease such as cholangitis, pancreatitis, or liver parenchymal disease. Two patients, who were found to have CBD stones during subsequent laparotomy, were excluded from the study because the papilla was hidden deep within a JPD and inaccessible to endoscopic instrumentation.

Of the 242 patients, 156 were female and 86 male, the mean age being 70 years (range 32-97). Prior to EP, 238 patients had symptoms with an average duration of nine months (range eight days to 10 years). The remaining four patients had incidentally detected episodes of disturbed liver function tests without symptoms. The clinical features of the 242 patients are presented in Table 1.

Methods

Patients with jaundice received 1 g amoxycillin intravenously, one hour prior to ERCP. None of the patients were emergency cases, and anticoagulant drugs,

Table 5.1 Clinical features of the patients

Clinical features	Patients (Σ = 242) n	%
Upper abdominal pain	224	93
Nausea and/or vomiting	174	72
Jaundice	127	52
Previous cholecystectomy	92	38

Table 5.2 Subdivision of the risk factors used for statistical analysis

Risk factors analyzed	Subdivision
Papillotomy procedure	Standard EP Precut
Endoscopic biliary drainage	Successful drainage Failed drainage Failed therapeutic precut Failed diagnostic precut
Diameter of the distal CBD	≥ 10 mm < 10 mm
Location of the papilla related to a JPD	Without JPD Outside Lower rim Inside
Gallbladder	In situ Previous cholecystectomy
Size of the papillotomy	< 4 ml 4 ml > 4 ml
Age	≥ 60 years < 60 years

CBD: Common bile duct; EP: endoscopic papillotomy; JPD: juxtapapillary diverticulum.

including salycilates, were stopped for at least one week before and after the papillotomy. Before EP, bleeding time, platelet count, prothrombin time, and activated partial thromboplastin time were routinely measured. Correction of the coagulation status to normal values, using intravenous administration of vitamin K was performed in two patients with jaundice and in one case with discontinued anticoagulant treatment; no further abnormalities were found.

Deep cannulation of the CBD was defined as indicating that the tip of the cannula had completely passed the ampullary region and was fully inserted into the CBD.

Sphincterotomy was, whenever possible, performed using the standard method[1]. The visible intramural portion of the CBD (the longitudinal fold) was usually only incised, and major transverse folds were not dissected. Precut papillotomy was carried out after a failed standard EP (therapeutic precut) or after a failed cholangiography (diagnostic precut). The precut knife used was the Olympus KD-11Q. The precut knife was inserted into the papilla[2] or just above it[3]. An incision about 3 mm deep and 3-5 mm long, was made in the 11-12-o'clock direction. If access to the bile duct was not achieved, the incision was extended for another 2-3 mm, and if cannulation of the bile duct was still not possible, a slight deepening of the incision was made. Precutting was completed using standard EP in the same session or, if cannulation of the papilla was still not possible (failed precut), a reexamination was arranged a week later, at which time the biliary orifice was usually clearly visible.

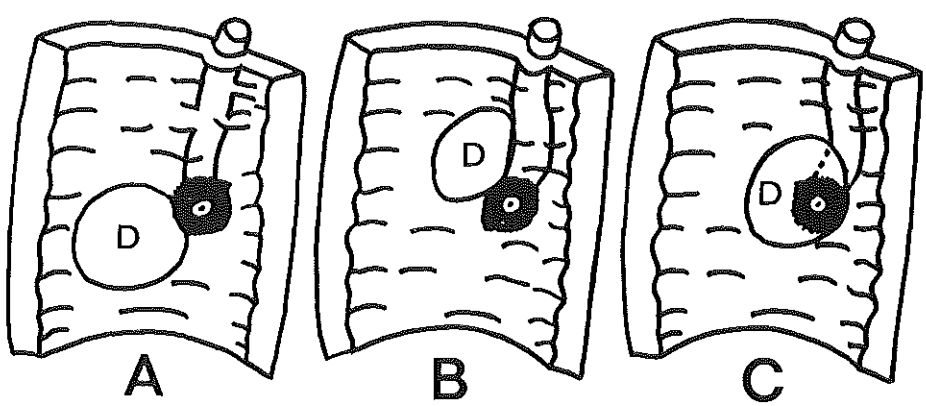

Figure 1: The location of the papilla in relation to a diverticulum (D).
a.: "Outside". The papilla and longitudinal fold outside the diverticulum.
b.: "Lower rim". The papilla at the lower rim of a juxtapapillary diverticulum.
c.: "Inside". The papilla on the inner wall of a diverticulum.

The endoscopic findings, therapeutic procedures, and acute complications were recorded during the ERCP. The location of the papilla in relation to a juxtapapillary diverticulum was divided into three groups, as shown in Figure 1. The diameter of the distal CBD, proximal to the ampulla, was measured on the radiograph and corrected for magnification with reference to the known diameter of the endoscope. Endoscopic biliary drainage was considered to have been successful if the CBD was completely stone-free or, in the case of residual stones, if it was possible to introduce a nasobiliary drain into the CBD with the tip proximal to the residual stone or stones without it dislodging. Drainage was considered to have failed if CBD stones were retained after completed sphincterotomy and there was no biliary drainage. The size of the papillotomy was estimated using the volume of a water-filled balloon that could just be pulled through the papillotomy orifice.

The risk factors were subdivided as indicated in Table 2. All of the complications except cholecystitis occurred at the time of EP, or within five days after EP and before the first cholecystectomy after EP had been performed. Bleeding was classified as moderate when conservative management - local epinephrine (1: 10.000 solution) injection[4] or blood transfusion, or both - was sufficient to control immediate or delayed bleeding following EP; and as severe when surgery was needed to stop bleeding. Pancreatitis was considered to be present when upper abdominal pain was combined with a serum amylase level in excess of 1000 IU/l. Pancreatitis was classified as moderate when it could be controlled conservatively and without residual abnormalities, such as pseudocysts. In all other cases pancreatitis was classified as severe.

Cholangitis following EP was classified as mild in the presence of fever, leucocytosis, and obstructive liver function disturbances, and as moderate when it was associated with sepsis. Both mild and moderate cholangitis responded rapidly to antibiotics, which were adjusted in relation to blood culture results in patients with sepsis.

If there was uncertainty about the presence of retained stones, a check cholangiogram was usually made during the procedure. The radiographs made during the procedure were interpreted before removing the endoscope, and additional films in an antero-posterior direction were taken routinely following difficult instrumentation, and whenever there was any doubt about the presence of retroperitoneal air leakage. Retroperitoneal air leakage was detected early in all cases, and managed with nasobiliary drainage and nasogastric suction, nothing by mouth, intravenous fluids, and antibiotics.

Of these complications, only one, a delayed bleeding, occurred after hospital discharge (two days) and four days after uneventful EP and stone removal.

Three months after each ERCP in the study period, a questionnaire was sent to the patient's general practitioner and referring specialist. The general practitioner was asked to indicate the patient's clinical condition and remaining complaints.

Table 5.3 Success rate of standard EP in relation to various risk factors

Presence of a JPD and the location of the papilla	Diameter of distal CBD	Number	Standard EP n	%	
Without JPD	≥ 10 mm	102	85	83	
	< 10 mm	45	31	69	p = 0.048
	All	147	116	79	
With JPD Papilla outside	≥ 10 mm	30	27	90	
	< 10 mm	13	9	69	n.s.
	All	43	36	84	
With JPD Papilla lower rim	≥ 10 mm	28	25	89	
	< 10 mm	9	6	67	n.s.
	All	37	31	84	
With JPD Papilla inside	≥ 10 mm	11	7	64	
	< 10 mm	4	2	50	n.s.
	All	15	9	60	n.s.
All patients	≥ 10 mm	171	144	84	
	< 10 mm	71	48	68	p = 0.004
Total		242	192	79	

CBD: common bile duct; EP: endoscopic papillotomy; JPD: juxtapapillary diverticulum; n.s: not significant.

The referring specialist was to record any complications following the EP, including the timing, treatment, and course. In addition, the patient's discharge letters were obtained. The follow-up information was obtained in all patients, apart from five who had died within three months of EP from other causes than pancreatobiliary disease, giving a mean follow-up period of 12 weeks, with a range of 20 days to 14 weeks. The risk factors were statistically analyzed, initially using univariate analysis and then by multivariate logistic regression.

Table 5.4 The achievement of endoscopic biliary drainage and associated complications

		Bleeding			Retroperi-toneal leakage	Pancreatitis			Cholangitis			All Complications		Mortality
	n	mod.	sev.	all		mod.	sev.	all	mild.	mod.	all	n	%	
Successful drainage	227	12	2	14	3	3	-	3	6	-	6	26	11	-
Failed drainage	4	-	-	-	-	-	-	-	1	2	3	3	75	-
Failed therap. prec.	5	1	-	1	-	-	1	1	2	-	2	4	80	1*
Failed diagn. prec.	6	-	-	-	1	-	-	-	-	-	-	1	17	-

* = Pancreatitis

5.4 Results

Endoscopic Cholangiography and Sphincterotomy at First Attempt

Immediate cholangiography was achieved in 222 patients (92%), in 209 of them after a deep cannulation of the CBD and in 192 cases (79%) followed by a standard EP. Precut papillotomies were performed in 50 patients, 20 of which involved diagnostic precuts and 30 of which involved therapeutic precuts. In 39 patients, the precut papillotomy was completed during the same procedure, using standard EP.

The correlation between the success rate of standard EP following cholangiography and the diameter of the distal CBD and presence and location of a JPD is presented in Table 3. The frequency of successful standard EP following cholangiography was significantly higher in the group in which the diameter of the distal CBD was 10 mm or more as compared with the group in which it was less than 10 mm (χ^2 : $p = 0.004$).

Table 5.5 Presence and location of JPDs and complications

Complication	Location of the papilla related to a JPD	n	Σ	%
Bleeding	Without JPD	4	147	2.7
	Outside	1	43	2.3
	Lower rim	6	37	16.2
	Inside	4	15	26.7
Pancreatitis	Without JPD	2	147	1.4
	Outside	2	43	4.7
	Lower rim	-	37	-
	Inside	-	15	-
Retroperitoneal leakage	Without JPD	2	147	1.4
	Outside	-	43	-
	Lower rim	-	37	-
	Inside	2	15	13.3
Cholangitis	Without JPD	5	147	3.4
	Outside	3	43	7.0
	Lower rim	3	37	8.1
	Inside	-	15	-
Total	Without JPD	13	147	8.8
	Outside	6	43	14.0
	Lower rim	9	37	24.3
	Inside	6	15	40.0

JPD: juxtapapillary diverticulum.

Endoscopic Biliary Drainage (EBD) and Further Procedures

EBD at first attempt succeeded in 227 patients (94%), as follows:

- Completely stone-free bile duct in 218 patients.
- Retained CBD stone or stones and a nasobiliary drain (NBD) which was located correctly and did not dislodge in nine patients. One complication due to (mild) cholangitis was recorded among these nine patients during nasobiliary drainage.

These 227 patients are recorded in Table 4 under "successful drainage".

Following completed sphincterotomy, three patients had residual CBD stones without an NBD and in one patient the NBD dislodged after initial correct installation. These four patients appear in Table 4 under "failed drainage". Six diagnostic and five therapeutic precut EPs initially failed. One week later, sphincterotomy with standard EP and stone evacuation was achieved in 10 of 11 patients without further complication. The remaining patient died of acute pancreatitis following therapeutic precutting.

Endoscopic evacuation of the CBD stones was achieved in 237 patients (98%), 218 of these being at first attempt. Further procedures for evacuation of residual CBD stones were performed without complication and included: shock wave therapy with nasobiliary drainage (two patients) and surgery (2 patients).

Acute Cholangitis at Follow-Up

Univariate analysis of all possible risk factors indicated two factors as being significant:

1. The papillotomy procedure: precut EP compared with standard EP results in an odds ratio (OR) of 3.4 ($p = 0.049$).
2. Failed drainage compared with successful drainage (OR 110.5, $p < 0.001$) and failed therapeutic precut compared with successful drainage (OR 24.6, $p = 0.001$).

In patients with a failed diagnostic precut, no complications due to cholangitis were found. The overall significance of the factor biliary drainage was below the 0.001 level. These factors remain significant when corrected for age, diameter, presence, and location of a JPD or the size of the papillotomy. In a model involving the papillotomy procedure and drainage, only drainage remains as a significant factor.

Complications related to the drainage procedures are listed in Table 4. Complications due to cholangitis occurred between 24 and 72 hours after failed drainage or failed therapeutic precut.

Bleeding Following Sphincterotomy

Univariate analysis of all the risk factors indicated that the location of a JPD was the only significant factor. Compared with patients without a JPD, the bleeding rate was not increased in patients with a location "outside", but increased significantly in the group with the location "lower rim" (OR 6.9, $p = 0.004$) and the

group with "inside" (OR 13.0, $p < 0.001$). The overall p-value for location was 0.001. These factors remain significant when adjusted for sphincterotomy procedure, age, diameter, drainage, and size of the papillotomy. The complications related to the location of a JPD are presented in Table 5.

Table 5.6 Relationship between CBD size and complications

Complication	size of the distal CBD	n	Σ	%
Bleeding	≥ 10 mm	10	171	5.8
	< 10 mm	5	71	7.0
Pancreatitis	≥ 10 mm	-	171	-
	< 10 mm	4	71	5.6
Retroperitoneal leakage	≥ 10 mm	2	171	1.2
	< 10 mm	2	71	2.8
Cholangitis	≥ 10 mm	7	171	4.1
	< 10 mm	4	71	5.6
Total	≥ 10 mm	19	171	11.1
	< 10 mm	15	71	21.1

CBD: Common bile duct

Table 5.7 Precutting versus standard EP in relation to complications

Complication	Papillotomy procedure	n	Σ	%
Bleeding	Standard EP	10	192	5.2
	Precut	5	50	10.0
Pancreatitis	Standard EP	1	192	0.5
	Precut	3	50	6.0
Retroperitoneal leakage	Standard EP	-	192	-
	Precut	4	50	8.0
Cholangitis	Standard EP	6	192	3.1
	Precut	5	50	10.0
Total	Standard EP	17	192	8.9
	Precut	17	50	34.0

EP: endoscopic papillotomy

Retroperitoneal Air Leakage

Retroperitoneal leakage was found only in four patients, all after precut EP (Fisher's exact test: $p = 0.002$). In the 50 patients with precut EPs, none of the other risk factors had any significant influence. Two retroperitoneal leakages were found in six patients with the papilla located inside a JPD. Compared with the patients without a JPD and precut EP, the odds ratio was 7.25 ($p = 0.080$).

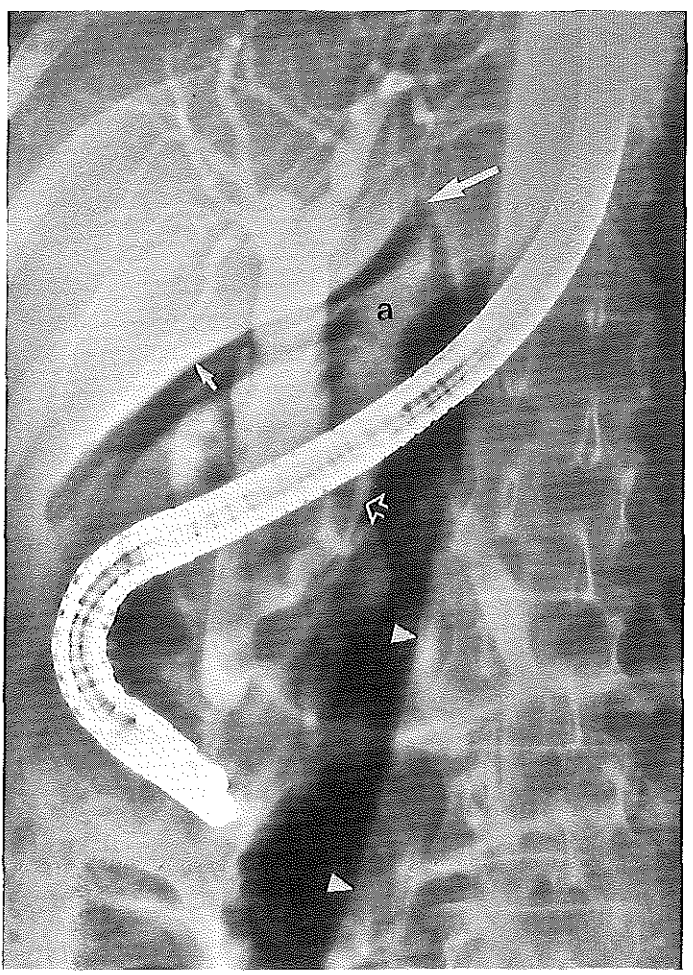

Figure 2: Perforation during therapeutic precut papillotomy. Retroperitoneal gas is outlining the adrenal gland (a), the lower border of the right liver lobe (arrow), the upper pole of the right kidney (open arrow), the lateral border of the right psoas muscle (arrowheads) and the medial segment of the extraperitoneal subdiaphragmatic tissue (large white arrow).

Pancreatitis at Follow-Up

Univariate analysis of all the possible risk factors pointed to three significant factors:

1. The sphincterotomy procedure: precut EP compared with standard EP (OR = 12.2, p = 0.032).
2. Failed therapeutic precut compared with successful drainage (OR = 18.7, p = 0.020). Pancreatitis did not occur in patients with failed drainage and a failed diagnostic precut.
3. Pancreatitis was found only in patients with a distal CBD diameter less than 10 mm (Fisher's exact test: p = 0.007).

In a model involving the factors drainage plus a sphincterotomy procedure, drainage had no influence (OR = 4.5, p = 0.259), while the papillotomy procedure did appear to have an influence (OR = 10.4, p = 0.058). Complications related to the diameter of the distal CBD and the sphincterotomy procedure are presented in Tables 6 and 7.

Presence or Absence of the Gallbladder

At the time of the EP procedure, 150 patients had their gallbladder in situ. At follow-up, 20 patients underwent elective cholecystectomy, and two patients died with an intact gallbladder, giving a median follow-up with gallbladder in situ of 79 days, with a range of 10 days to 14 weeks. Five patients (4%) developed cholecystitis from 20 to 42 days after EP, with an average of 36 days. All five patients recovered, three of them following cholecystectomy and two with conservative treatment. Complications other than cholecystitis were not related to the presence or absence of the gallbladder.

All Complications

Univariate analysis of all the risk factors indicated that the following risk factors were significant: 1) the papillotomy procedure; 2) endoscopic biliary drainage; and 3) the location of a JPD. These factors remained significant in a multivariate analysis involving all the risk factors. The figures are presented in Table 8.

5.5 Discussion

Without biliary drainage, CBD stones retained after endoscopic papillotomy were an important cause of complications due to cholangitis. This corresponds to the findings in the literature[5-8]. The same mechanism might explain two cases of cholangitis seen in five patients following failed therapeutic precutting and the absence of cholangitis seen after a failed diagnostic precut EP in six patients. When biliary drainage fails, any delay in achieving an alternative biliary drainage increases the risk of septic complications, especially when a CBD stone is left impacted distally [9]. Alternative drainage, either percutaneous or surgical, should be

performed within a few hours in these patients in order to avoid cholangitis. Surgery carries a relatively high mortality risk (up to 40%) in patients with acute cholangitis[10] which, in general, correlates with the severity of disease[11]. When cholangitis has already developed in the case of retained CBD stones after a completed sphincterotomy, we would prefer immediate percutaneous drainage, which in experienced hands has led to significant improvement in about 95% of patients with cholangitis[12], especially when finer catheters are used[13]. Using this method, definitive treatment was achieved after stabilization of the patient's clinical condition[12,13], in all 16 patients without additional surgical mortality[12].

Table 5.8 Risk factors that had a significant influence on the complication rate

Risk factors	Univariate OR	p-value		Multivariate OR	p-value	
Papillotomy:						
standard EP	1.0			1.0		
precut EP	4.8	< .001		4.9	.001	
Drainage:						
successful	1.0			1.0		
failed	23.2	.007		34.8	.007	
failed ther. prec.	11.6	.009	.002	5.9	.098	.005
failed diag. prec.	1.5	.696		.28	.321	
Diverticulum:						
Without	1.0			1.0		
Outside	1.7	.330		3.1	.072	
Lower rim	2.8	.034	.010	4.3	.015	.006
Inside	6.9	.001		9.4	.002	

EP: endoscopic papillotomy; OR: odds ratio

An increased complication risk due to cholangitis following EP has been reported in patients with cholangitis prior to EP[5,7]. Such patients were excluded from our material.

It is generally accepted that precut or needle-knife papillotomy (NKP) is a valuable adjunct to standard EP, but should be used only by the very experienced endoscopist and when there is a clear-cut need for diagnosis and therapy[14-18]. Complication rates following sphincterotomy have been reported to decrease with increasing endoscopic experience[19,20].

. Our results are in accordance with those of authors reporting a clearly increased complication rate with NKP when compared with standard EP[14,15,21]. *Sherman et al.* [22] reported a considerable complication risk with EP for a small diameter common

bile duct, but this was not related to the use of NKP, which was usually (63%) performed over a previously placed pancreatic stent. In our series, pancreatitis and retroperitoneal air leakage following EP were more frequently found in patients with a distal CBD diameter of less than 10 mm, especially following NKP, which was often performed in these patients. Retroperitoneal perforation was detected immediately in all four patients, and conservative management was successful in all [23]. However, when detection is delayed for more than eight hours, surgical management has been advocated[21]. In four patients with a dilated CBD, the indication for NKP was an impacted CBD stone at the ampulla. One of these four patients had moderate bleeding following EP, but stone evacuation was successful in all of them, and no further complications were recorded[24].

In 17 of 30 patients, a therapeutic precut papillotomy could have been avoided if the guide wire of a wire-guided papillotome had been introduced through the cannula into the CBD after difficult deep cannulation. After withdrawal of the cannula, the wire-guided papillotome[25,26] can be inserted, and this procedure is at present routinely used whenever full insertion of the cannula into the CBD is not easily achieved.

The estimated size of the sphincterotomy had no significant influence on the complication rate, but the size of the papillotomy was adjusted to the length of the longitudinal fold and major transverse folds were not dissected.

A classification of JPD variants has been made in a Russian study. EP was considered to be contraindicated in patients with the papilla on the floor of the JPD, and it was not performed when the papilla was located on the lower semicircumference of the diverticular orifice with the longitudinal fold running radially on the diverticular wall[27].

In a series of 227 patients with, and 447 patients without a JPD, *Vaira et al.*[28] reported an increased failure rate for cannulation and EP in patients who had a JPD. The complication rates were not significantly different. Morbidity and mortality of EP due to bleeding was 4.0%/0.9% with a JPD and 3.1%/0.2% without a JPD. In our series, these figures are 11.6%/0% and 2.7%/0%, respectively.

In our series, hemorrhage was managed by local adrenalin injection[4] immediately after cutting, and this controlled immediate bleeding in 8 of 11 patients. In one patient, additional transfusion was needed, and in two patients local adrenalin and transfusion failed to control bleeding following EP and urgent surgery with suturing of the arterial bleeding point was performed. The remaining four hemorrhages were delayed, by one to four days after uneventful EPs, and all were successfully controlled after transfusion.

Of interest was our finding that hemorrhage following standard EP and precut EP appeared to be related to a location of the papilla on the lower rim of the diverticular orifice or inside a JPD, with the longitudinal fold bordering the diverticular wall. *Vaira et al.* made a subdivision of 17 patients with the papilla inside the JPD. Two of these patients had undergone a failed sphincterotomy, but

the complication rate was not increased. When EP failed, a combined percutaneous-endoscopic technique was used. This might explain the high complication rate among these patients in our series: precut papillotomy was performed when deep cannulation of the papilla was not possible due to a location within a JPD. The direction of the longitudinal fold was difficult to assess, and precutting resulted in a high complication rate.

In patients with failed standard endoscopy alone, a combined percutaneous-endoscopic approach has been described[29-31]. A major cause of failed standard EP in patients with benign disease was the location of the papilla inside a JPD, preventing deep cannulation of the CBD[31-34]. Larger series describing the combined procedure for sphincterotomy in benign disease have reported success rates, with procedure-related morbidity and mortality varying from 83 to 100%, 11 to 18%, and 0%, respectively[32-34]. However, despite these occasionally good results, capsular puncture adds risks that are not associated with endoscopic therapy (35). In patients with the papilla located inside diverticula, we consider the combined percutaneous-endoscopic procedure to be indicated when it is performed by experts in endoscopy and interventional radiology [32-34,36] and only after standard EP by an experienced operator has failed on two attempts[32,34,36] and in the presence of contraindications to surgery[32-34].

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Chapter 6

ENDOSCOPIC SPHINCTEROTOMY AND BILIARY DRAINAGE IN PATIENTS WITH CHOLANGITIS DUE TO COMMON BILE DUCT STONES

[1] J. Boender, [1] G.A.J.J. Nix, [2] M.A.J. de Ridder, [3] J. Dees, [1] H.E. Schütte, [3] H.R. van Buuren, [3] M. van Blankenstein

[1] Department of Diagnostic Radiology, [2] Institute of Epidemiology and Biostatistics and [3] Department of Gastroenterology. University Hospital Rotterdam-Dijkzigt, Rotterdam, The Netherlands.

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6.1 Abstract

Objectives: In a prospective study, we analyzed 95 consecutive patients undergoing endoscopic papillotomy (EP) for cholangitis due to common bile duct (CBD) stones; our purpose was to evaluate the risk factors influencing the complication rate due to cholangitis, with special attention to the clinical history. *Methods:* Patients with previous gastric surgery or EP were excluded. Complications subsequent to sphincterotomy were recorded over a 3-month period. *Results:* In patients with persistent cholangitis before EP, the risk for complications due to cholangitis increased with increasing delay between the onset of cholangitis and biliary drainage. In patients with a good response to antiobiotics before EP, the delay in biliary drainage did not influence the risk of complications. After complete CBD stone removal, the morbidity (42% vs. 4%, $p = 0.001$) and the mortality (8% vs. 0%, NS) due to cholangitis were much higher in 12 patients with progressive cholangitis for > 3 days before biliary drainage, compared with 73 cases who had experienced a good response to antibiotics before EP and/or early drainage (< 3 days) after the onset of cholangitis. Two patients with advanced cholangitis and septic shock at the time of EP died < 12 hours after completed sphincterotomy with CBD stone removal. Three patients with retained CBD stones and failed biliary drainage after EP experienced disastrous morbidity (100% vs. 9%, $p < 0.01$) and mortality (67% vs. 1%, $p < 0.01$) due to cholangitis, compared with 85 patients without retained CBD stone(s). *Conclusions:* We recommend emergency biliary drainage in all patients presenting with calculous cholangitis who are severely ill with continuous fever for several days. Emergency nasobiliary

drainage without EP or after a limited EP may be a safer treatment in patients with (impending) septic shock. We believe that a more conservative approach is justified in patients presenting with symptoms of mild cholangitis, restricting emergency biliary drainage for those who do not respond rapidly (< 24 h) to antibiotics. Further emergency surgical or percutaneous biliary drainage should be performed immediately on patients in whom CBD stones are retained, after EP and drainage fails, especially if a stone is left impacted distally.

6.2 Introduction

In patients with calculous cholangitis, several initial procedures have been advocated as better alternatives to emergency surgery, namely, endoscopic sphincterotomy and stone removal, endoscopic nasobiliary drainage (NBD) with or without EP, and percutaneous transhepatic biliary drainage (PTBD). Patients who have cholangitis before endoscopic papillotomy (EP) have an increased risk of septic complications[1]. The aim of our study was to evaluate the rate of septic complications after EP that are related to the type of biliary drainage procedure and to the clinical history of patients with cholangitis due to common bile duct (CBD) stones.

6.3 Materials and Methods

Patients

Between March 1987 and November 1989, all 1.362 patients undergoing ERCP in our hospital were included in a prospective study with the aim of evaluating the immediate and medium-term complications of diagnostic and therapeutic ERCP.

Patients who had undergone previous gastric surgery or endoscopic papillotomy, or who had additional pancreato-biliary disease, except gallbladder stones, were excluded from this study. There remained 95 patients, 50 women and 45 men, mean age 76 yr (range 49-92 yr). Eighty percent of them were referred from other hospitals; the investigators had no influence on their management before ERCP. The clinical features of these 95 patients are presented in Table 1. In 33 patients, organisms were cultured from the blood (sepsis). The cultured organisms were *Escherichia coli* in 24 patients, *Streptococcus faecalis* or *Klebsiella* in each of two patients, *Proteus* in one, and *Enterobacter* in another. Three patients had blood cultures with *E. coli* and either *Proteus* or *Morganella morgani* or *S. faecalis*. Positive blood culture was associated with acute suppurative cholangitis (ASC) in three patients. In eight cases, purulent material was seen in the bile (ASC) by the endoscopist after sphincterotomy, without sepsis.

Table 6.1 Clinical features of the patients

Clinical Features	No. of patients (%)	
Upper abdominal pain	86	(91)
Jaundice	74	(78)
Fever (> 38 C)	95	(100)
Fever and chills	65	(68)
Positive blood culture(s)	33	(35)
Purulent bile (ASC)	11	(12)
Hypotension and mental confusion	4	(4)
Previous cholecystectomy	22	(23)
Concurrent disease	46	(48)

ASC: acute suppurative cholangitis

6.4 Methods

The clinical history of each patient with the timing and outcome of the various diagnostic tests, including the laboratory findings, were recorded before ERCP. During ERCP, the endoscopic findings, procedures, and complications were recorded. Three months after each ERCP, information about the clinical condition and possible complications was collected from questionnaires to the referring physician and general practitioners. When necessary, additional information was obtained from the medical records.

All patients had received parenteral broad-spectrum antibiotics before EP, usually a broad-spectrum penicillin plus an aminoglycoside; in cases of severe cholangitis and sepsis, additional intravenous fluid was administered. Antibiotics were continued until the symptoms of cholangitis had subsided.

Response to antibiotics prior to EP was classified good when the clinical signs of cholangitis had clearly improved rapidly (< 24 h) and did not recur. Otherwise cholangitis was classified as persistent.

Endoscopic biliary drainage was classified as delayed when attempted > 3 days after the onset of persistent cholangitis independent of the timing of antibiotic

treatment. The overall delay in each patient was the total of the delay caused by the patient, the general practitioner, and the referring physician.

After full insertion of the cannula into the CBD, a volume of at most 40 ml of dilute contrast material was gently injected into the CBD before EP. After decompression of the bile ducts, additional contrast medium was injected when the segmental intrahepatic bile ducts had not yet opacified, with a diagnostic balloon catheter. However, when the CBD and the segmental intrahepatic bile ducts had been visualized, the injection of contrast medium was stopped routinely to avoid further increase in ductal pressure with the associated increasing risk of sepsis due to cholangiovenous reflux of the infected bile.

The diameter of the distal CBD was measured on the radiograph and corrected for magnification by means of the known diameter of the endoscope.

In all patients, endoscopic cholangiography was followed by sphincterotomy during the same procedure. Sphincterotomy was intially attempted by the standard method[2] and, when necessary, a precut papillotomy was performed[3]. Large sphincterotomies were made; the visible intramural portion of the CBD was usually incised, but major transverse folds were not dissected. The size of the sphincterotomy was checked using a water-filled balloon. A balloon with a volume of 3 ml could be pulled through the papillotomy in all cases.

The presence of acute suppurative cholangitis was established by finding frank pus or turbid bile containing debris under pressure at the time of sphincterotomy.

If there was uncertainty about the presence of retained CBD stones after EP, a check cholangiogram was made during the procedure. Residual sludge and/or minor stone fragments that were obviously smaller than the diameter of the distal CBD and the papillotomy orifice were not classified as retained CBD stones. In the case of retained CBD stones after papillotomy, biliary drainage was considered successful if a nasobiliary drain was introduced into the bile ducts with the tip proximal of the residual stone(s) and was not dislodged before definitive therapy.

Cholangitis after EP was classified as mild in the presence of fever, leukocytosis, and obstructive liver function tests and negative blood culture(s), moderate when associated with positive blood culture (sepsis) and severe when septic shock developed. In patients with sepsis, antibiotic therapy was adjusted in accordance to the bloodculture results.

Statistical analysis was carried out with multivariate logistic regression, the χ^2 test, and, where necessary, Fisher's exact test (FE). The analyzed risk factors in patients without retained CBD stones are presented in Table 2.

Table 6.2 Analyzed risk factors in patients without retained CBD stones

Analyzed Risk Factors	Subdivision (No of Patients)	
No of days between onset of cholangitis and papillotomy	continuous 1-24 days, average 8.5 days	
Cholangitis prior to EP	Good response to AB Persistent cholangitis	(60) (25)
Sphincterotomy procedure	Standard EP Precut EP	(68) (17)
Diameter of the distal CBD	≥ 10 mm < 10 mm	(65) (20)
Blood culture results	Positive Negative	(30) (55)
Purulent bile (ASC)	With Without	(9) (76)
Gallbladder	In situ Previous resection	(68) (17)
Age	≤ 70 years > 70 years	(19) (66)
Concurrent disease	With Without	(41) (44)

CBD: common bile duct; EP: endoscopic papillotomy; ASC: acute suppurative cholangitis; Good response to antibiotics (AB): clinical signs of cholangitis had improved < 24 h and did not recur.

6.5 Results

Endoscopic Biliary Drainage and Subsequent Procedures

Standard EP succeeded in 76 patients (80%); in 19 cases (20%), precut papillotomy was performed before completion by means of standard EP during the initial procedure.

The results of subsequent CBD stone clearance and/or biliary drainage are presented in Table 3.

Table 6.3 Complications related to the biliary drainage results

Drainage procedure	N	Complications due to Cholangitis after EP Mild	Mod.	Sev.	All (%)	Mortality
Complete CBD stone clearance	85	4	2	2	8 (9%)	1 (1%)
Retained stones and nasobiliary drainage	7	-	-	-	-	-
Retained CBD stones without drainage	3	-	1	2	3 (100%)	2 (67%)

CBD: common bile duct; EP: endoscopic papillotomy; ASC: acute suppurative cholangitis; Mild: (increased) fever, leukocytosis and obstructive liverfunction tests with negative blood culture(s); Mod.: Mild plus positive blood culture; Sev.: if septic shock developed; Mortality: fatal septic shock.

Nasobiliary drainage failed in three patients with retained CBD stones after EP, the parenteral antibiotic treatment was continued in all. Two (both without previous sepsis, ASC or delayed biliary drainage) developed sepsis < 24h after EP. Of these two patients, one recovered after emergency surgery during which CBD stones were removed, and the other died from septic shock after 3 days of conservative management. The third patient had hypotension and mental confusion due to refractory cholangitis with sepsis during the 9 days before EP and died < 12 h after NBD was placed with the tip distal to a large retained CBD stone. These three patients experienced enormously increased morbidity (100% vs. 9%, χ^2 : p = 0.0015) and mortality rates (67% vs. 1%, χ^2 : p = 0.0023) due to cholangitis, compared with 85 patients in whom CBD stones were completely cleared.

Of the 7 patients with retained stones and NBD, six had had a good response to antibiotics before EP, and the remaining patient had experienced persistent cholangitis during the 4 days before biliary drainage, without sepsis or ASC. No complications due to cholangitis were recorded in these seven patients after EP, compared with eight complications due to cholangitis after complete removal of the CBD stones in 85 cases (0% vs. 9%, NS).

Further procedures for the evacuation of retained CBD stones included: endoscopic stone removal at second attempt (two patients), extracorporeal shock wave therapy after NBD (four patients), surgery (one patient), and stent insertion after failed shock wave therapy in 1 patient; all without complication.

Morbidity due to Cholangitis in Cases Without Retained CBD Stones

Exact logistic regression of all possible risk factors presented in Table 2 failed to show one single factor to be of significant influence in 85 patients with complete CBD stone removal. As shown in Figure 1, the risk for complications due to cholangitis in 25 patients with persistent cholangitis before EP increased with increasing delay before EP. In 60 patients with a good response to antibiotics before EP, a delay in biliary drainage had no influence on the risk of complications.

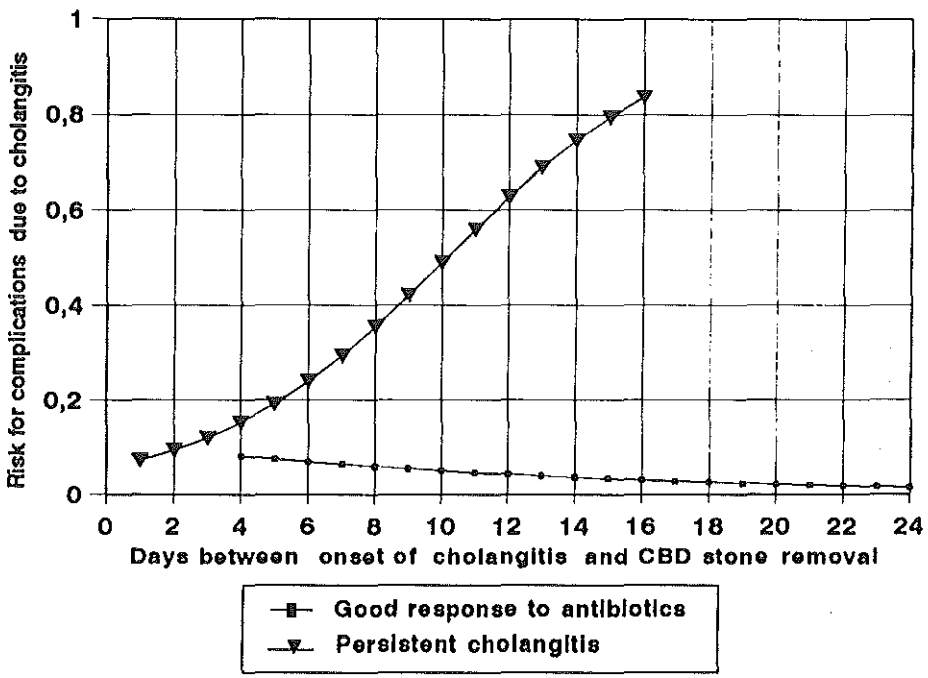

Figure 1: Risk for complications due to cholangitis after complete CBD stone removal related to the delay in biliary drainage and the presence or absence of persistent cholangitis at the time of sphincterotomy.

Among 25 patients with cholangitis that had not (yet) responded to antibiotics at EP, 13 patients were drained early (< 72 h after the onset of cholangitis) by emergency ERCP. A positive blood culture was present in only three of them, and, in all, the bile was without purulent material. No complications due to cholangitis were seen after EP in these 13 patients, compared with three mild complications due to cholangitis in 60 patients with a good response to antibiotics but biliary drainage > 3 days after the onset of cholangitis (NS).

However, the 12 patients in whom the antibiotic treatment had failed and cholangitis had persisted for > 3 days before EP were found to have a higher morbidity due to cholangitis (42% vs. 5%, FE : $p = 0.002$) and a higher rate of

septic complications (33% vs. 0%, FE : p = 0.0005), compared with the 60 patients with a good response to antibiotics and drainage > 3 days after the onset of cholangitis). The results are presented in Table 4.

Table 6.4 Results of early and delayed biliary drainage in 85 cases without retained CBD stones, with response to antibiotics in patients drained > 3 days after onset of cholangitis

Timing of Biliary Drainage with Response to Antibiotics	Sepsis and/or ASC	N	Complications due to Cholangitis after EP Mild	Mod.	Sev.	All (%)
Early drainage (< 3 days after the onset of cholangitis)	With	3	-	-	-	-
	Without	10	-	-	-	-
Bad response to antibiotics with persistent cholangitis for > 3 days prior to drainage	With	8	-	1	2*	3 (38%)
	Without	4	1	1	-	2 (50%)
Good response to antibiotics and drainage > 3 days after onset of cholangitis	With	27	1	-	-	1 (4%)
	Without	33	2	-	-	2 (6%)

* = One patient had a fatal septic shock. ASC: acute suppurative cholangitis; Good response to antibiotics: clinical signs of cholangitis improved < 24 h and did not recur; Mild: (increased) fever, leukocytosis and obstructive liver function tests with negative blood culture(s); Mod.: Mild plus positive blood culture; Sev.: if septic shock developed.

Reasons for Delay of Endoscopic Biliary Drainage

Biliary drainage was delayed for ≥ 72 h after the onset of persistent cholangitis in 14/95 patients, for the following reasons:

In six patients, cholangitis appeared to have been present for several days before the patient came under medical care. This advanced cholangitis did not respond rapidly to antibiotic therapy, and EP was performed within 2 days after the start of conservative management. In two patients, septic shock occurred < 24 h

after EP, which was fatal in one patient in whom endoscopic biliary drainage failed. In another patient, cholangitis failed to improve rapidly after successful drainage.

In eight patients, clinical cholangitis had persisted for more than 3 days under antibiotics. In one patient without upper abdominal pain, the cause of the infection was initially misdiagnosed. In the other patients, initial minor improvement of the symptoms had lead to an extension of the conservative approach which delayed the necessary biliary drainage. One of these patients developed fatal septic shock < 24 h after successful drainage. Two other patients experienced sepsis after successful endoscopic biliary drainage, but both recovered under conservative management.

Severe Sepsis with Mental Confusion and Hypotension

Four patients with positive blood culture had mental confusion and hypotension (systolic blood pressure < 100 mm Hg) before EP. Initial conservative management, including intravenous antibiotics and fluids, had been successful in 2/4 cases. In the other two patients, the cholangitis and sepsis were progressive, and both died within 12 h, after successful stone extraction in one case and after failed stone removal and biliary drainage in the other, from septic shock with multiple organ failure.

Presence of the Gallbladder

Seventy-three patients still had their gallbladder at the time of EP. During the follow-up period, elective cholecystectomy was performed in 10 patients, and three died with an intact gallbladder. The average follow-up time after EP in patients with a gallbladder was 76 days, range 1 day to 13 wk. Four patients (5%) developed cholecystitis from 6 days to 10 wk after EP and recovered after surgery or conservative treatment. No other complications were related to the presence of the gallbladder.

Other Complications

The following complications other than described above were recorded after papillotomy: four patients had hemorrhage immediately after sphincterotomy that was successfully controlled by local epinephrine (1 : 10,000 solution) injection; one patient had delayed bleeding, 2 days after EP, which was managed by blood transfusion. One patient developed a pancreatitis and one had retroperitoneal leakage which was recognized at ERCP. All patients recovered on conservative management and without additional signs of cholangitis. Including the 11 complications due to cholangitis, the overall procedure-related morbidity and mortality in 95 patients was 19% and 3.2% respectively. Two more patients died from other disease (heart failure and pneumonia), resulting in an overall mortality of 5.3% at 3-month follow-up.

6.6 Discussion

Emergency surgery for acute cholangitis carries a mortality up to 40%[4,5] which, in general, correlates with the severity of disease[6]. Following surgical treatment of acute suppurative cholangitis a lower mortality has been reported in patients who were operated upon within 24 h after admission or clinical deterioration compared to those with progressive cholangitis operated after some delay[7-9]. Urgent endoscopic stone extraction has been advocated for patients with acute cholangitis who fail to show an early response to conservative management, with early surgery reserved for those who do not improve following sphincteromy. Recurrent cholangitis following EP was usually associated with a failure to clear all CBD stones after sphincterotomy[10-13].

Our results confirm the literature findings that retained CBD stones after EP without biliary drainage are an important cause of septic complications following sphincterotomy[1,10-13]. When there is doubt about the presence of retained stones after control cholangiography, we insert a nasobiliary drain that provides both drainage and the opportunity to repeat cholangiography the next day, when overprojecting intestinal contrast material and excessive air has disappeared. We also use the nasobiliary drain to flush out residual small stone fragments and bile sludge. When NBD fails in cases of stones retained after EP, immediate alternative biliary drainage, either surgical or percutaneous, is indicated, especially when a CBD stone is left impacted distally.

There was no uniform policy as to the timing of ERCP in relation to the clinical course as a result of the fact that 80% of our patients were referred from other institutions. The best results were found in the 13 patients who were drained early, without awaiting the effect of conservative management. This is in accordance with the clinical pattern of cholangitis. Approximately 15% of patients with acute cholangitis and/or biliary sepsis do not respond to intravenous fluids and antibiotics, and biliary sepsis progresses and/or acute suppurative cholangitis develops, which is usually fatal if prompt biliary decompression is not performed[4,14]. In our study, two out of four patients, presenting with impending septic shock, had not responded rapidly to initial antibiotic management, and both patients became progressively hypotensive and mentally confused and died within 12 h after emergency endoscopic papillotomy and CBD stone extraction. When initial conservative management fails, the increased delay in biliary drainage will increase the risk for septic complications. This is of great importance in patients with severe calculous cholangitis and (impending) septic shock.

A number of authors have advised NBD with[15,16] or without[17,18] previous sphincterotomy or PTBD [19,20] before definitive therapy in cases of severe acute cholangitis.

In a randomized study, *Lai et al.*[16] reported a significantly higher mortality after emergency surgery than after initial emergency endoscopic NBD in 82 patients with severe acute cholangitis. In the endoscopic-drainage group, definitive therapy

was performed after NBD, which was successful in all 41 patients, without complications.

Leung et al.[21] reported favorable results of urgent endoscopic NBD in 105 patients not responding to conservative management for cholangitis, both with and without previous EP. In patients with coexisting coagulopathy, rapid decompression of the bile ducts was obtained by NBD only. The overall mortality was 4.7%. Among those patients in shock, two died, of the four who underwent drainage more than 72 h after admission, compared with three deaths among 38 who underwent drainage within 72 h.

In 42 patients with acute cholangitis, *Pessa et al.*[20] reported a 5% mortality and a 7% complication rate after initial PTBD with a 22-gauge "skinny needle". Deaths (two patients) were limited to the group of 12 patients presenting in septic shock and occurred within 8 h after admission. Definitive therapy, including surgery in 16 cases, was performed after resolution of sepsis without further mortality.

Our data showed that seven patients with NBD and retained stones did at least as well as those in whom stones where removed at first attempt.

However, the use of NBD and PTBD has been challenged. *Himal* and *Lindsay*[10] reported death due to sepsis in all 4 patients undergoing NBD and in one of three patients after PTBD, after failed repeated endoscopic sphincterotomy in patients with cholangitis. However, this treatment would appear to have been delayed too long, because all seven patients in the NBD-PTBD group were considered too ill to undergo surgery. Surgery had been successful in 10 of 11 patients after failed initial papillotomy.

In a series of 49 patients with calculous cholangitis, *Kiil et al.*[22] concluded that NBD was disappointing, mainly because the drains were frequently removed by the patients themselves. Insertion of an endoprosthesis, with or without a sphincterotomy, was preferred in case of retained CBD stones and settled cholangitis in 90%.

In our study, two patients with (impending) septic shock and failed initial conservative management died after completed EP and CBD stone removal. In these instances, it seems likely that an immediate and less agressive and time-consuming approach is indicated in the form of emergency endoscopic NBD without or after a limited sphincterotomy[15-18,21], which can be performed even at the intensive care unit[23]. NBD should be checked repeatedly in these patients, because the risk of dislodgment, especially by a confused patient, appears to be the main problem with nasobiliary catheters[22,24]. Definitive therapy can be performed after NBD subsequent to resolution of the clinical cholangitis.

In conclusion, our results support endoscopic biliary drainage as the initial procedure in patients with cholangitis due to CBD stones. Immediate biliary drainage, as opposed to initial conservative management, will avoid the increasing risk of septic complications in the patients with a bad response to antibiotics. An emergency approach is of greater importance when the presenting clinical cholangitis is more advanced and severe. We would advise immediate NBD

without or after limited sphincterotomy in patients presenting with (impending) septic shock due to calculous cholangitis with sepsis. However, in patients presenting with symptoms of mild calculous cholangitis, a more conservative approach may be justified. In these patients, elective biliary drainage can be performed after a good response to antibiotics and emergency biliary drainage reserved for those not responding rapidly (< 24 h) to antibiotics. Every effort should be made to avoid retained CBD stones after papillotomy without biliary drainage, which, especially when a CBD stone is left impacted distally, requires immediate surgery or percutaneous transhepatic biliary drainage.

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Chapter 7

ENDOSCOPIC PAPILLOTOMY IN BILIARY TRACT PAIN AND FLUCTUATING CHOLESTASIS WITH COMMON BILE DUCT DILATATION AND SMALL GALLBLADDER STONES

[1] J. Boender, [2] M. van Blankenstein, [1] G.A.J.J. Nix, [2] J.H.P. Wilson and [2] J. Dees

From the [1] Department of Diagnostic Radiology and the [2] Department of Internal Medicine II, University Hospital Rotterdam-Dijkzigt, Rotterdam, The Netherlands.

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7.1 Abstract

In patients suspected of having functional disorders of the papilla it is often difficult to establish the indications whether or not to perform endoscopic papillotomy (EP). We report on thirty-two consecutive patients referred for endoscopic retrograde cholangiopancreatography who all had longstanding biliary tract pain and episodes of liver enzyme elevation indicating cholestasis. Further features were: 1) a dilated common bile duct (CBD) after cholecystectomy (n = 11) or 2) a dilated CBD without or with larger (> cystic duct diameter) gallbladder stones (n = 6) or 3) multiple small gallbladder stones, with a normal or dilated CBD, in patients with signs of acute gallstone pancreatitis or in whom elective cholecystectomy was not indicated (n = 15).

No CBD stones, organic obstruction or other disorders were found in these patients. Without further diagnostic procedures, EP was routinely performed. The laboratory (up to 3 months) and clinical findings (2 to 4 years follow-up) showed improvement in all patients undergoing EP. We conclude that immediate EP appears justified in these selected patients.

7.2 Introduction

In patients suspected of having sphincter of Oddi (SO) dysfunction various tests have been advocated which are sometimes time consuming, expensive and dangerous and their value has therefore been challenged. Episodic biliary tract pain in patients without detectable CBD stones or organic obstruction can be caused

also by the recurrent passage of small gallbladder stones through the cystic duct and the SO. Therefore, the aim of our study was to evaluate if immediate endoscopic papillotomy (EP) following diagnostic ERCP is justified in selected patients who have long-standing episodic right upper abdominal or epigastric pain associated with fluctuating elevation of liver function tests (LFT) indicating cholestasis, but without detectable CBD stones or organic obstruction.

7.3 Patients and Methods

Patients

Between March 1987 and July 1989 1200 patients with evidence of biliary and/or pancreatic disease underwent ERCP at our institution. CBD stones were found in 375 of them. In the same period 32 patients were examined who all had: A) long-standing attacks of right upper abdominal or epigastric pain and B) episodes of disturbed LFT, especially elevated bilirubin, alkaline phosphatase and amino-transferase levels one of which was at least two times abnormal on two separate occasions *and* C) *one* of the following features according to which they were divided into 3 groups:

Group 1: Eleven post-cholecystectomy patients with a dilated CBD, suspected of having SO dysfunction:

There were 9 women and 2 men, mean age 66 years (range 41-85). The mean duration of symptoms was 600 days (range 45-2200). Cholecystectomy had been performed 4-32 years prior to EP (mean 13 years). The onset of complaints was at least 200 days after cholecystectomy. The abnormal LFT's were associated with fluctuating elevated serum amylase in 3 and a history of episodic mild jaundice in 4 patients. Cannulation of the SO and/or insertion of the papilotome into the CBD was difficult due to SO spasm in 9/11 patients. Between the pain attacks LFT's normalized in 7 patients and improved (at least 50% decrease within the abnormal range) in 4 cases.

Group 2: Six patients with a dilated CBD and a normal gallbladder (3 cases) or cholecystolithiasis with larger (> cystic duct diameter) stones (3 cases).

These patients were suspected of having SO dysfunction although the episodic passage of a small gallbladder stone could not be completely excluded. There were 2 women and 4 men. The age ranged from 48-78 years (mean 67). Average duration of symptoms was 600 days (range 60 days- 4 years). The abnormal LFT's were associated with an elevated serum amylase in 3 and episodic mild jaundice in 4 patients. During instrumentation SO spasm was encountered in 2/6 cases. Between the pain attacks LFT's normalized in 3 and improved in the other 3 patients.

Group 3: This group consisted of fifteen patients with multiple small stones in the gallbladder who were suspected of having recurrent stone passage through the cystic duct and the SO.

There were 8 women and 7 men, mean age 67 years (range 31-90). The diameter of the cystic duct varied from 4-7 mm on the radiograph (average 5 mm). The mean duration of symptoms was 50 weeks (range 6 weeks-3 years). The abnormal LFT's were associated with an elevated serum amylase in 9 patients and 4 of them also had clinical signs of acute pancreatitis. Episodic jaundice was present in 8 patients. Cannulation of the CBD was difficult, due to SO spasm, in only 2/15 patients. Between the pain attacks normal LFT's were found in 9 and improvement of LFT's in 6 patients.

Stones were defined as small when the diameter was less than the diameter of the cystic duct, in general < 5 mm on the radiograph. In these patients neither CBD stones nor organic obstruction were detectable on endoscopic cholangiography and a normal endoscopic appearance of the papilla was found. The borders of both the biliary and pancreatic part of the SO were smooth on the radiographs and the ability of the SO to contract and relax was confirmed in all cases by means of fluoroscopy. After EP a balloon catheter was introduced high up into the CBD, the balloon inflated and retracted through the open papilla. The outflowing bile and contrast material was inspected endoscopically and no stones nor sludge were seen. Patients were otherwise excluded.

In general there was no history of alcohol abuse, drugs, viral hepatitis or extrabiliary disease which could explain the abnormal LFT or upper abdominal pain. The episodic attacks of right upper abdominal or epigastric pain radiated to the back or shoulder in 23/32 and were associated with nausea and/or vomiting in 25/32. In all three groups elevations of the LFT's, were related to the pain attacks and LFT's returned to normal within one week after the attacks. The pancreatic duct and the intra-hepatic bile ducts were routinely opacified during ERCP and found to be normal or slightly dilated. Ultrasound was performed in all cases prior to ERCP and showed no pathology other than cholecystolithiasis or gallbladder sludge and/or a CBD dilatation.

Methods

The maximum diameter of the CBD was measured on the radiograph after the injection of a small amount of contrast medium and corrected for magnification by reference to the known diameter of the endoscope[1]. We considered the CBD dilated when the corrected maximum diameter of the CBD was > 8 mm with the gallbladder in situ[1,2] and > 10 mm after cholecystectomy[1,2,3]. The diagnostic procedure to detect CBD stones is described elsewhere[4].

The 3 months and 1 year follow-up information was obtained from the referring physicians and general practitionars by means of questionaires and additional study of the medical records. Two years after the last ERCP the follow-up was

completed by contacting all general practitionars of the patients in order to evaluate the clinical condition at that time and possible interventions in the meantime.

7.4 Results

Group 1: Post-cholecystectomy patients with a dilated CBD (n = 11):
Papillotomy was performed in all. One patient developped clinical signs of pancreatitis one day after EP and another had retroperitoneal air leakage following EP. Both recovered with conservative treatment.

Group 2: Patients with a dilated CBD and either a stone-free gallbladder or larger gallbladder stones (n = 6):
Papillotomy was performed in all. No complications were encountered in these patients. The follow up results of group 1 and 2 are presented in Table 1.

Table 7.1 Follow-up results after EP in patients with biliary tract pain and episodic abnormal LFT and a dilated CBD but without small gallbladder stones. Norm. = normal, Impr. = improved.

Patients	Lab. findings		Clinical condition after					
	3 months		3 months		1 year		2-4 years	
	Norm.	Impr.	Norm.	Impr.	Norm.	Impr.	Norm.	Impr.
Post-chole-cystectomy (11 cases)	8	3	9	2	10	1	9	2
Gallbladder in situ (6 cases)	5	1	5	1	6	-	6	-

Group 3: Patients with multiple small stones in the gallbladder with a normal or dilated CBD (n = 15):
EP was not performed in 2 cases. In 1 patient EP failed. The other was a 31 year old patient in whom elective cholecystectomy was considered the appropiate therapy but was refused by the patient. In one case emergency surgery was necessary 10 days after the EP because of a gallbladder empyema. In 3 cases, with signs of acute gallstone pancreatitis (AGP) at the time of EP, the clinical condition improved rapidly after EP and elective cholecystectomy was performed within 6 weeks in 2 cases and 4 months after EP in the remaining patient. In these cases both the clinical condition and the laboratory findings were normal at follow-up.

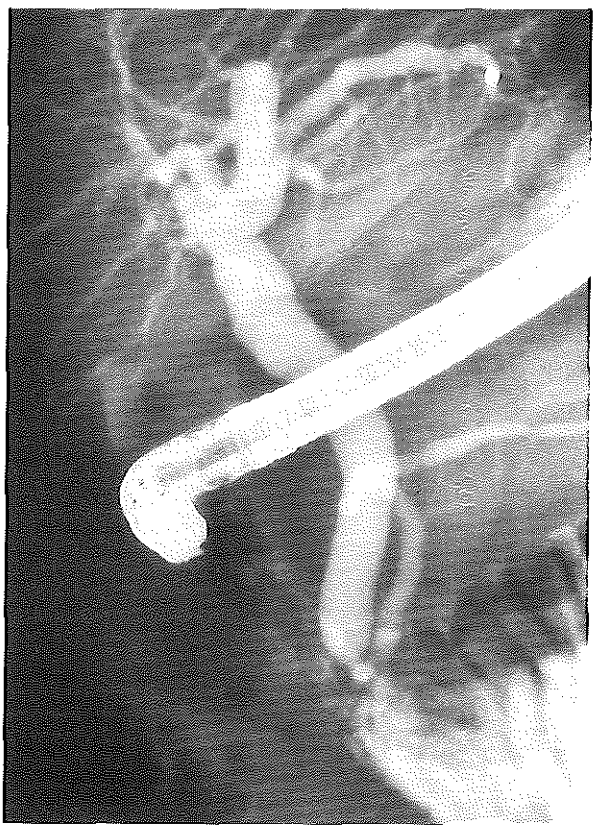

Figure 1: Post-cholecystectomy patient with a dilated CBD.

One patient had a delayed bleeding 2 days after EP but recovered following blood transfusion. Two patients died after 2 and 2.5 years follow-up, from other disease, but remained free of biliary complaints until death. One of the 2 patients, in whom EP was not performed, underwent emergency EP at 2 years follow-up for a severe attack of AGP. Subsequently his clinical condition and laboratory findings normalized. This patient was categorized as worsened in Table 2. The findings of group 3 at follow-up are shown in Table 2.

In Tables 1 and 2 the laboratory findings were classified as improved in those patients in whom the LFT's showed a decrease of at least 50% within the abnormal range at the time of hospital discharge. No further LFT's were obtained in these cases as they remained free of complaints. Clinical findings were classified improved when symptoms, ascribed to the biliary tract, had not completely resolved and minor symptoms remained. In the remaining patients findings were either normal (normal LFT or free of complaints) or unchanged (unchanged abnormal LFT or complaints).

Table 7.2 Follow-up results after ERCP with (n = 9) or without (n = 2) EP in patients with biliary tract pain and episodic abnormal LFT and multiple small stones in the gallbladder in whom the gallbladder was still present after follow-up. Norm. = normal, Impr. = improved, Unch. = unchanged, Wors. = worsened.

Patients	Laboratory findings			Clinical condition after						
	3 months			3 months		1 year		2-4 years		
	Norm.	Impr.	Unch.	Norm.	Impr.	Norm.	Impr.	Norm.	Impr.	Wors.
With papillotomy,										
Dilated CBD (5 patients)	3	2	-	4	1	4	1	4	1	-
Normal CBD (4 patients)	3	1	-	4	-	4	-	4	-	-
Without papillotomy,										
Normal CBD (2 patients)	-	-	2	-	2	-	2	-	1	1

7.5 Discussion

Endoscopic papillotomy is an accepted procedure for CBD stones[5]. In the absence of CBD stones episodic biliary tract pain can be caused by functional disorders of the SO[6]. These functional disorders include papillary stenosis[7,8] and papillary dyskinesia or dysfunction[9-11]. Most post-cholecystectomy patients may show a fusiform narrowing of the intra-ampullary portion of the CBD due to increased contraction of the SO suggesting papillary stenosis[7] but the fluoroscopic visualization of subsequent relaxation virtually excludes a fixed, fibrotic stenosis.

When in patients suspected of having sphincter of Oddi dysfunction or stenosis biliary tract pain is associated with 1) abnormal LFT's indicating cholestasis on two or more occasions and 2) a dilated CBD and 3) delayed drainage of contrast during ERCP beyond 45 minutes, EP is considered to be indicated[6,7,10,11]. But when biliary type pain occurs alone or combined with only one or two of the above mentioned criteria, manometric pressure measurements of the SO[12] have been recommended both in patients with[9,10,13,14] and without previous cholecystectomy [11,15] to select candidates for EP. Good overall results of EP are reported, in patients with unexplained post-cholecystectomy pain, when the basal SO pressure was elevated above 40 mm Hg[9,10,13,14]. In these and other studies satisfactory results of

Figure 2: Patient with a normal gallbladder and a dilated CBD.

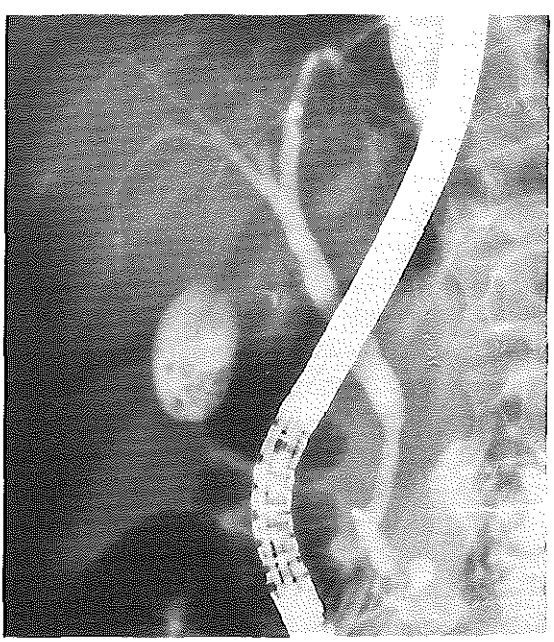

Figure 3: Patient with multiple small gallbladder stones and signs of AGP at the time of ERCP. The CBD is compressed in the intra-pancreatic part. A small juxtapapillary diverticulum is present.

EP were also found in patients with a dilated CBD[13,14] and/or delayed drainage of contrast material from the CBD (10,13,14,16). *Toouli et al.*[17], investigating 32 patients suspected of having SO dysfunction, found abnormal manometric results in 9/10 patients with associated abnormal LFT's versus only 6/22 cases with normal LFT's. All 6 patients with abnormal LFT and a dilated CBD had one or more manometric abnormalities. The validity of manometric investigation of the SO however has been challenged[16,18].

Roberts-Thomson et al.[18] offered no endoscopic treatment but simply reassured post-cholecystectomy patients without a previous history of jaundice, cholangitis or pancreatitis. If symptoms were severe, the authors started a trial of antispasmodic or antidepressant drugs. Bulk-forming agents were used in those with constipation. Symptoms improved in 234 of 304 patients (77%).

When biliary tract pain is associated with abnormal LFT's on two or more occasions but the CBD is not dilated and there are no multiple small stones in the gallbladder at ERCP or when there are potential causes of the abnormal LFT (i.e. drugs, liver parenchymal disease) further investigations are advisable. During ERCP, SO manometry[9-15] and delayed emptying of the CBD beyond 45 minutes[7,10,13,14,16] can be used to select patients for EP. However the observation of delayed biliary drainage beyond 45 minutes and SO manometry prolong the procedure and may inconvenience many patients. In addition, complications following SO manometry have been reported[19,20].

Our results suggest that manometry may be unnecessary and EP can be performed when long-standing biliary tract pain is combined with episodic abnormal LFT indicating cholestasis and a dilated CBD. This especially applies to post-cholecystectomy cases. A more conservative approach however, including the evaluation of biliary drainage, may still be wise in the smaller group with the gallbladder in situ and without small stones.

Restenosis of the papilla after EP was not encountered at follow-up in our patients although a rate of late SO restenosis up to 10% is reported in the literature in such cases[21]. Following EP a higher morbidity (16 versus 10%) and mortality (2 versus 1%) is reported in patients with presumed SO dysfunction as opposed to those undergoing EP for CBD stones[22,23]. In our series two of three complications, in 32 patients who underwent EP, occurred in the 11 post-cholecystectomy patients suspected of SO dysfunction. Patients with multiple small stones in the gallbladder may be regarded separately. In these cases the episodic upper abdominal pain and the transient changes in LFT, with or without elevated serum amylase, can be explained by the passage of small stones from the gallbladder through a normal sphincter of Oddi[24-27]. The CBD is often not dilated in these patients even in the presence of CBD calculi[21,24]. In such a situation we do not perform papillotomy and advise elective cholecystectomy when the CBD is normal and there are no signs of AGP[25,27,28]. We consider immediate papillotomy indicated in the presence of AGP[28-31] and when a high surgical risk is expected for other reasons (age, general

condition). Endoscopic papillotomy appeared benificial in these patients even when the diameter of the CBD was normal.

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Chapter 8

NEEDLE-KNIFE SPHINCTEROTOMY GUIDED BY A BILIARY ENDOPROSTHESIS IN BILLROTH II GASTRECTOMY PATIENTS

[1] H.R. van Buuren, [2] J. Boender, [2] G.A.J.J. Nix, [1] M. van Blankenstein

[1] Department of Gastroenterology and [2] the Department of Radiology, University Hospital Rotterdam-Dijkzigt, Rotterdam, The Netherlands.

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8.1 Abstract

A new technique for performing endoscopic sphincterotomy in patients with a Billroth-II gastrectomy is described. After selective bile duct cannulation a 0.35 mm guide wire is introduced through the cannula into an intra-hepatic bile duct. Using the same endoscope a thin (7 Fr) biliary endoprosthesis is positioned. After removal of the guide wire sphincterotomy is performed cutting the papilla in the proximal direction along the prosthesis with a diathermic needle. Thereafter the endoprosthesis is removed through the endoscope and further therapeutic procedures can be carried out. In a 3 years period this technique was successful in 18 of the 19 patients in whom it was attempted. In one patient the guide wire was withdrawn inadvertently and a non-guided needle-knife sphincterotomy was performed. There was one complication, a retroperitoneal leakage which settled with conservative treatment. In patients with a Billroth II anastomosis endo-prosthesis-guided sphincterotomy is a new and relatively easy procedure, which facilitates endoscopic interventions.

8.2 Introduction

In patients with a Billroth II anastomosis Endoscopic Retrograde Cholangio-pancreatography (ERCP) and subsequent endoscopic therapeutic interventions are associated with a number of specific problems[1]. These include troublesome intubation of the afferent jejunal loop, the presence of an entero-enteroanastomosis (Braun's anastomosis) and a long afferent jejunal loop, problems with identification

and cannulation of the papilla and the performance of a safe and adequate sphincterotomy while approaching the papilla from a distal direction[2].

Usually the standard sphincterotomy technique will result in an incorrect position of the (Classen-Demling type) sphincterotome, with the cutting wire directed caudally towards the pancreas[2]. To overcome this problem a number of techniques[3-5] and sphincterotomes[3,4,6,7] have been described. However, none are feasible or successful in all cases. More recently guided techniques, using a nasobiliary drain[8] or a cannula[10] have been reported. The obvious advantage of these techniques is that blind cutting or exploration is avoided and sphincterotomy is a controlled procedure under direct vision. A disadvantage of these guided techniques is that removal and subsequent reintroduction of the endoscope are required, which is particularly unattractive in patients in whom the papillary region was reached with difficulty. We report here our initial experience with a guided technique using an endoprosthesis. This procedure is relatively easy and does not require removal of the endoscope.

8.3 Endoprosthesis guided sphincterotomy technique (Figures 1, 2 and 3)

The forward viewing endoscope is positioned near the papilla of Vater and the common bile duct is cannulated. A 0.35 mm guide wire is advanced through the catheter into the common bile duct or, preferably, into a hepatic duct. The catheter is then removed and a thin endoprosthesis (Microvasive®; diameter 7 French; length 7 or 12 cm according to the anatomy of the common bile duct) is positioned into the common bile duct, using a 1.8 mm pusher. For this purpose the guiding catheter of a standard endoprosthesis set can be used. The guide wire is removed and a needle-knife sphincterotome is introduced. The papillary roof is carefully cut in the proximal (towards the blind end of the afferent loop) direction along the stent, with multiple short incisions. We used the Olympus PSD-10 electrosurgical device, with alternate cutting at 40 Watts and coagulation at 20 Watts. The endoprosthesis is gradually exposed, thus confirming that the sphincterotomy is being made in the correct direction. The length of the incision is mainly a matter of experience. To assess whether a sufficient opening has been achieved a balloon catheter can be introduced along the prosthesis. A 3-ml balloon, diameter when inflated 12 mm, which can easily be pulled into the duodenum indicates an adequate sphincterotomy. Also, bile appearing in the sphincterotomy orifice suggests that the incision is of sufficient length. The endoprosthesis can then be caught with a snare or basket and removed through the endoscope. Alternatively the prosthesis is withdrawn from the bile duct and left in the jejunum where it can be picked up at the end of the procedure. Throughout the procedure the position of the endoscope is maintained.

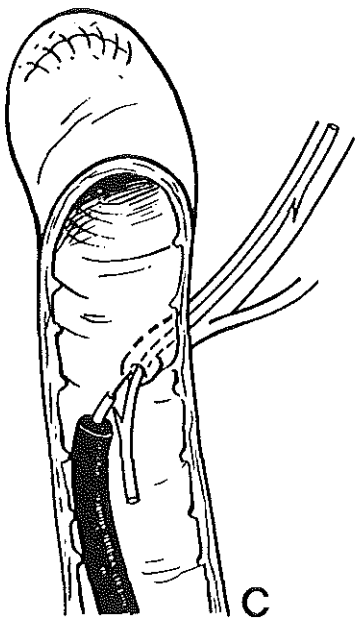

Figure 1: Drawing illustrating the technique of endoprosthesis-guided sphincterotomy in patients with Billroth II gastrectomy. Endoprosthesis in position; start of sphincterotomy using a needle-knife sphincterotome. The papillary roof is cut in the proximal direction, starting at the papillary orifice and following the endoprosthesis.

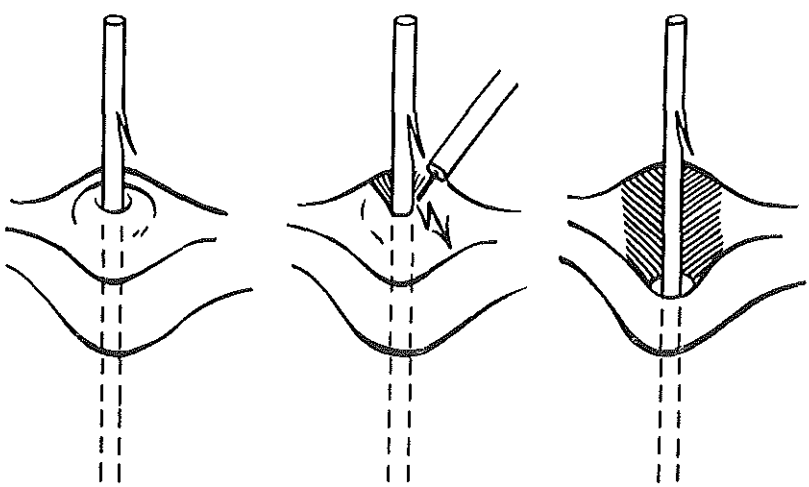

Figure 2: Schematic representation demonstrating the actual sphincterotomy. Incisions with the needle-knife follow, and gradually expose, the intrapapillary part of the endoprosthesis.

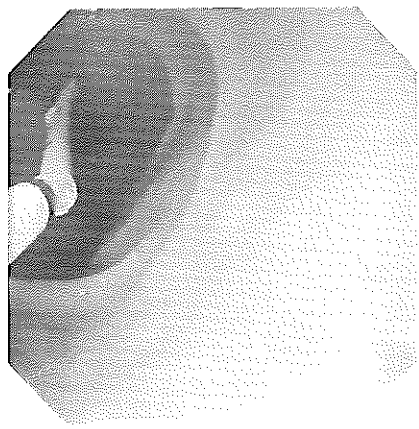

Figure 3: Endoscopic pictures showing the technique of endoprosthesis guided sphincterotomy.

A. A guide wire has been inserted and the cannula been removed.
B. Catheter pushing the endoprosthesis into the common bile duct.
C. First incision, starting at the orifice of the papilla.
D. Nearly completed sphincterotomy. Intrapapillary part of endoprosthesis becomes exposed.
E. Completed sphincterotomy. Visualization of the distal common bile duct. A balloon catheter has been introduced for stone removal.

8.4 Patients

Between January 1990 and January 1993 1549 ERCP's were performed in our hospital; 83 (5%) of these procedures were performed in 63 patients with a Billroth II anastomosis. In all these patients forward viewing endoscopes (Olympus Gif Q10, Gif Q20 and Gif Q200) were used. A total of 48 sphincterotomies were attempted, using the Soehendra sphincterotome[6] in 8 patients, a needle-knife sphincterotome in 16 patients, both a Soehendra and needle-knife sphincterotome in 5 and the endoprosthesis technique in 19 patients. The mean age of these patients was 75 years.

The endoprosthesis technique was developed and initially explored by one of the authors (MvB). After the first positive experiences the technique was gradually adopted by the other endoscopists. In 1990 26 percent of the sphincterotomies in B-II patients was performed using the endoprosthesis technique and in 1992 this percentage had increased to 70 percent. During this period, no specific a priori criteria were used to decide whether a patient would have a sphincterotomy using the endoprosthesis technique, the choice being left to the preference of the endoscopist.

8.5 Results

The endoprosthesis technique was employed in 19 patients. In one patient a previously inserted nasobiliary drain was used as a guide for performing the sphincterotomy. In one patient the guide wire was withdrawn inadvertently and a non-guided sphincterotomy was performed. An adequate sphincterotomy was accomplished in the other 18 patients without significant difficulties. Details of further therapeutic and diagnostic interventions are given in the table. Following the procedure in 4 patients it was possible to introduce the Q-endoscope into the bile duct; in 2 of them stones were removed under direct vision. There was one complication in a 64-year old man who developed signs of retroperitoneal leakage during the procedure. This settled within a few days with conservative treatment (nill per mouth, parenteral broad-spectrum antibiotics) and the patient was discharged from hospital 1 week later.

In the 29 patients in whom other sphincterotomy techniques were used an adequate sphincterotomy was eventually performed in all. In three of these patients a second ERCP was required to complete the sphincterotomy. One patient had a fatal cardiac arrest during the ERCP, without evidence to suggest a relation with sphincterotomy. In three other patients non-fatal complications were noted: two retroperitoneal perforations and one major bleeding.

Table 8.1 Endoprosthesis guided needle-knife sphincterotomy after Billroth II gastrectomy. Patients and results.

Patients	
- number	19
- sex	13 male
- age (mean, range in years)	75 (62-88)
Indication for sphincterotomy	
- removal of bile duct stones	16
- malignant bile duct stricture	2
- sphincter of Oddi dysfunction	1
Results	
- procedure attempted	19
- successful procedure	18
Complications	
- retroperitoneal leak	1
Additional procedures	
- stone removal	13
- insertion endoprosthesis	2
- insertion nasobiliary drain	8
- biopsies papilla	1

8.6 Discussion

The guided sphincterotomy technique using an endoprosthesis here described is attractive for a number of reasons. The sphincterotomy is performed under direct vision of the cutting device, in this case the needle-knife sphincterotome. The presence of a clear guide, indicating where and how deep to cut, is another important feature with regard to the safety of the procedure. Finally, the step-wise incision technique further contributes to a well controlled procedure. This contrasts with other techniques which require unguided or blind cutting, such as the fistula[3] and needle-knife[5] techniques, or which may be more difficult to perform and to control e.g. sphincterotomy with the push-type (Sohma)[3] or Soehendra[6] sphincterotomes.

Previously other groups have reported a guided sphincterotomy technique using a nasobiliary drain[8,9] or a special cannula[10]. Successful sphincterotomies were reported in all 63 patients, and both groups considered the guided procedure safer and more elegant than other techniques. However, both these techniques require

removal and reinsertion of the endoscope, which is time consuming and may be a major disadvantage in patients with a problematic approach to the papilla.

Needle-knife sphincterotomy is an option when either selective bile duct cannulation or the use of special B-II sphincterotomes fail. However, this procedure carries a recognized increased risk of complications, and alternatives should be used whenever possible[11,12]. Guided sphincterotomy is likely to be more safe than alternative, unguided procedures as found by *Sherman et al.*[13], who performed precut sphincterotomy over a previously placed small calibre stent when introduction of a standard sphincterotome had failed. Although not explicitely stated, their series probably only included patients with a normal anatomy. The complication rate of precut papillotomy, using this stent technique in 63% of the precut cases, was slightly lower than in the group who had undergone a standard sphincterotomy. The authors attributed this surprising result, at least partly, to the safety of the stent guided precut technique. In all our patients endoprosthesis guided sphincterotomy was accomplished within a single endoscopic procedure, with one complication in 19 patients (5.7 %), compared with 32 endoscopic procedures and a complication rate of 10% (3/29) in the 29 patients who underwent sphincterotomy using another technique. In our opinion this experience does not allow to draw conclusions with regard to the success- and complication rate of the endoprosthesis technique, mainly because our study was non-controlled and the groups undergoing one, or a combination, of the several sphincterotomy procedures were small.

Our favourable results may be explained by our preference for using forward-viewing endoscopes in patients with gastro-jejunal anastomoses. Especially introduction of the afferent loop and finding the correct route in jejunal entero-enteroanastomoses is much easier with these endoscopes. During the last three years failure to reach the papilla occurred in only 5 of the 64 (8%) B-II patients: caused by failure to enter the afferent loop in one patient, by a very long afferent loop in one patient and by jejunal entero-enteroanastomoses in three patients. Usually, once the endoscope is in position just below the papilla, cannulation of the bile duct is feasible. Selective bile duct cannulation may be easier with a forward-viewing endoscope because the endoscope and the cannula are in line with the common bile duct[1]. In our experience the lack of an elevator in forward viewing endoscopes is of only slight disadvantage, and not a main factor in determining the success rate of cannulation and subsequent procedures. Recently we have started to use an oblique-viewing endoscope (Olympus GifK20) in patients with B-II anastomoses, and we found that this endoscope improves visualization of the papilla. Moreover, this endoscope is equipped with an elevator at the tip.

In B-II gastrectomy patients the superiority of one over other sphincterotomy techniques has not been reliably assessed, and up till now no clear standard technique has emerged, all authors tending to be content with their own technique. However, the relatively large number of techniques, in contrast to the fairly

standard technique in normal anatomy, indicates that none are completely satisfactory.

Our initial results suggest that endoprosthesis guided sphincterotomy constitutes a valuable addition to presently available techniques. It is a relatively easy procedure, not requiring special or expensive equipment and likely to be safer than alternative techniques. Since no second introduction of the endoscope is required the endoprosthesis technique has an advantage over previously reported guided techniques. The procedure is especially attractive once selective bile duct cannulation has been achieved. If it is impossible to introduce a guide wire one of the other available techniques can be used. In that situation we usually continue with non-guided needle-knife sphincterotomy[5].

8.7 References

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Chapter 9

SUMMARY AND CONCLUSIONS

This thesis describes, in a prospective study, the results observed in 517 patients after therapeutic endoscopic retrograde cholangiopancreatography (TERCP). Patients with previous gastric surgery had been excluded. The study included endoscopic papillotomy and biliary drainage for common bile duct stones, malignant obstruction of the common bile duct or a suspected functional disorder of the papilla of Vater. In addition a new technique is presented for performing sphincterotomy after a Billroth II stomach resection.

Chapter 1 describes the scope of the thesis.

Chapter 2 provides a general introduction and literature review of the technique, results and complications of TERCP.

In *chapter 3* the protocol used for the prospective study described in the Chapters 4-7 is presented.

In *chapter 4* the problems encountered during endoscopic drainage in 148 patients with malignant obstruction of the mid or distal common bile duct and/or the papilla were assessed.

A tumor was visualized on endoscopic retrograde cholangiopancreatography in 89% of the cases and drainage of the bile was possible in 80%.

Stent insertion failed in all 5 patients with extensive malignant duodenal invasion with stenosis by tumors in the pancreatic head. This is in agreement with the general policy to refer these patients for palliative surgery, without further endoscopic intervention.

The likelihood of successful endoscopic stent insertion is greater than 90% when a tumor does not invade the papilla of Vater or when there is a carcinoma of the papilla itself.

In 23 patients with an extrinsic invasion of the duodenal wall, including the papilla, by a tumor in the pancreatic head, stent insertion was successful in only 3 patients (13%). Difficulties in endoscopic stent placement in these cases have been reported too by Soehendra and Grimm.

A new finding was the correlation between the size of tumors restricted to the non-uncinate region of the head of the pancreas, and the chance of papillary invasion and failure to insert a stent.

On the basis of our findings, we recommend primary percutaneous biliary drainage or surgery when a proven malignancy restricted to the non-uncinate

region of the pancreatic head is 5 cm or more in diameter, or when diagnostic duodenoscopy reveals extrinsic invasion of the papilla of Vater, or severe duodenal involvement with duodenal stenosis.

In *chapter 5* the complications observed in 242 consecutive patients after endoscopic papillotomy for common bile duct stones were analyzed. Patients with previous gastric surgery, papillotomy, or additional pancreatico-biliary disease other than gallbladder stones were excluded.

The following risk factors which may influence the complication rate were analyzed: the papillotomy procedure, endoscopic biliary drainage, the diameter of the distal common bile duct, the location of the papilla in relation to a juxtapapillary diverticulum, the gallbladder, the size of the papillotomy, and the age of the patient. The risk factors were analyzed, initially by univariate analysis and then by multivariate logistic regression.

Immediate cholangiography was achieved in 222 patients (92%), in 209 of them after a deep cannulation of the common bile duct. In 192 cases cholangiography was followed by a standard papillotomy. Precut papillotomies were performed in 50 patients. A new finding was the significantly higher frequency of successful standard papillotomy following cholangiography in the group in which the distal common bile duct was 10 mm or greater in diameter, compared with the group in which the diameter was less than 10 mm (χ^2 : $p = 0.004$). The overall procedure related morbidity and mortality following papillotomy was 14% and 0,4%, respectively.

Pancreatitis and retroperitoneal leakage occurred in 1,7% of cases. They were more frequently observed in patients with a smaller diameter (< 10mm) of the distal common bile duct (5.6% vs. 0%: $p = 0.007$ for pancreatitis, and 2.8% vs. 1.2%: n.s. for perforation) and especially following precut papillotomy (13.0% for pancreatitis and 8.7% for perforation), which had to be performed more often in patients with a narrow distal common bile duct.

Retroperitoneal leakage was found only in four patients, all after precut papillotomy (Fisher's exact test: $p = 0.002$). In 17 of 50 patients a precut papillotomy could have been avoided if the guide wire of a wire-guided papillotome had been introduced through the cannula into the common bile duct after difficult deep cannulation. After withdrawal of the cannula, the wire-guided papillotome can be inserted, and this procedure is at present routinely used whenever full insertion of the cannula into the common bile duct is difficult to achieve.

Inadequate biliary drainage was the only remaining significant risk factor for acute cholangitis at follow-up. Corresponding to the findings in the literature retained common bile duct stones after completed sphincterotomy were the most important cause of complications due to cholangitis.

The group of patients with a failed precut papillotomy after successful cholangiography had a significantly higher risk for (mild) complications due to cholangitis, compared with the group with successful biliary drainage resulting in an odds

ratio (OR) of 24.6 ($p = 0.001$). This finding had not yet been reported in the literature. The same mechanism of successful cholangiography in patients with bile duct obstruction and without subsequent biliary drainage can explain this finding. In patients in whom both the cholangiography and the precut papillotomy failed, cholangitis was not observed. A conclusion from this part of the chapter is that after completed sphincterotomy with retained common bile duct stones and failed endoscopic biliary drainage, alternative biliary drainage should be performed within a few hours, especially when a stone is left impacted distally.

Of interest was our finding that the location of a juxtapapillary diverticulum appeared to be the only significant factor influencing bleeding following sphincterotomy. Compared with 147 patients without a juxtapapillary diverticulum, the bleeding rate following sphincterotomy increased significantly in 37 patients with the papilla located at the lower rim (OR 6.9, $p = 0.004$) and the 15 patients with the papilla located inside a diverticulum (OR 13.0, $p < 0.001$). When the papilla was located inside diverticula, both the rate of perforation and bleeding increased following precut papillotomy, compared with standard papillotomy only (33% vs. 0%, n.s., and 33% vs. 22%, n.s.). When the papilla is located inside diverticula a combined percutaneous-endoscopic procedure is advised when it is performed by experts in endoscopy and interventional radiology and only after standard papillotomy by an experienced operator has failed on two attempts and in the presence of contraindications to surgery.

In *chapter 6* ninety-five consecutive patients undergoing sphincterotomy for cholangitis due to common bile duct stones were analyzed with the aim to evaluate the risk factors influencing the complication rate due to cholangitis.

Cholangitis was classified as "mild" in the presence of fever, leukocytosis and obstructive liver function disturbances, "moderate" when associated with sepsis and "severe" when septic shock developed. Response to antibiotics was classified as good when the clinical signs of cholangitis had clearly improved within 24 hours and did not recur. Otherwise cholangitis was classified as persistent. Endoscopic biliary drainage was classified as delayed when attempted more than 3 days after the onset of persistent cholangitis independant of the timing of antibiotic treatment.

The following risk factors were analyzed: the number of days between the onset of cholangitis and papillotomy, the response to antibiotics prior to endoscopic retrograde cholangiopancreatography, the sphincterotomy procedure, the diameter of the distal common bile duct, the blood culture results, the presence of purulent bile, the gallbladder, the age of the patient, and the presence of concurrent disease.

Sphincterotomy could be completed in all patients during the initial procedure, in 19 patients after a precut papillotomy. Including the eleven complications due to cholangitis (three of these fatal), the overall procedure related morbidity and mortality in 95 patients was 19% and 3,2%, respectively.

Three patients with retained common bile duct stones after sphincterotomy, without (naso)biliary drainage, experienced a significantly higher morbidity and

mortality due to cholangitis, compared with 85 patients in whom the common bile duct stones were completely cleared (100% vs. 9%:$p < 0.01$ and 67% vs. 1%:$p < 0.01$, respectively).

Exact logistic regression of the analyzed risk factors failed to show up a single factor of significant influence in 85 patients with complete common bile duct stone removal. However, the risk for complications due to cholangitis in 25 patients with persistent cholangitis prior to papillotomy increased with increasing delay before papillotomy. In 60 patients with a good response to antibiotics before sphincterotomy a delay in biliary drainage had no influence on the risk for complications.

No complications due to cholangitis were seen in 13 patients with cholangitis which had not (yet) responded to antibiotics at the time of endoscopic retrograde cholangiopancreatography and who were drained early (less than 72 hours after the onset of cholangitis), compared with three mild complications due to cholangitis in 60 patients with a good response to antibiotics but biliary drainage more than 3 days after the onset of cholangitis (NS). However, the 12 patients in whom antibiotic treatment had failed and in whom cholangitis had persisted for more than 3 days before papillotomy, were found to have a higher morbidity due to cholangitis and a higher rate of septic complications, compared with the 60 patients with a good response to antibiotics and drainage beyond 3 days after the onset of cholangitis (42% vs. 5%: FE:$p = 0.002$ and 33% vs. 0%: FE:$p = 0.0005$, respectively).

Two patients with advanced cholangitis and septic shock at the time of papillotomy died within 12 hours after a completed sphincterotomy procedure.

Emergency biliary drainage is advised in all patients presenting with calculous cholangitis who are severely ill due to continuous fever for several days. In the patients with (impending) septic shock we advise an immediate and less agressive and time consuming approach in the form of emergency endoscopic nasobiliary drainage without or after a limited sphincterotomy. Favorable results have been reported using this method in patients with severe acute cholangitis when definitive therapy was performed after nasobiliary drainage. We consider a more conservative approach justified in patients presenting with symptoms of mild cholangitis, with emergency biliary drainage restricted for those not responding rapidly (< 24 hours) to antibiotics.

In *chapter 7* the follow-up results after endoscopic papillotomy of 32 selected patients suspected of having a functional disorder of the papilla were evaluated. In patients suspected of having a functional disorder of the papilla it is often difficult to establish indications whether or not to perform sphincterotomy. Initial conservative management has been recommended in postcholecystectomy patients without a previous history of jaundice, cholangitis or pancreatitis. Among other tests, sphincter of Oddi manometry and the evaluation of delayed biliary drainage beyond 45 minutes have been advocated for selecting patients for sphincterotomy.

A study was undertaken to evaluate whether immediate papillotomy following endoscopic retrograde cholangiopancreatography is justified in selected patients suspected of dysfunction of the sphincter of Oddi.

Subjects were 32 consecutive patients referred for endoscopic retrograde cholangiopancreatography, all of whom had longstanding biliary tract pain and episodes of liver enzyme elevation indicating cholestasis.

Further features were (1) a dilated common bile duct after cholecystectomy (n = 11), (2) a dilated common bile duct without gallbladder stones or with larger (greater than cystic duct diameter) gallbladder stones (n = 6), or (3) multiple small gallbladder stones with a normal or dilated common bile duct, in patients with signs of acute gallstone pancreatitis or in whom elective cholecystectomy was not indicated (n = 15).

No common bile duct stones, organic obstruction, or other disorders were found in these patients. The maximum diameter of the common bile duct was corrected for magnification by reference to the known diameter of the endoscope. The common bile duct was considered dilated when the corrected maximum diameter of the duct was > 8 mm with the gallbladder in situ and > 10 mm after cholecystectomy. Endoscopic papillotomy was routinely performed without further diagnostic procedures.

The laboratory findings (up to 3 months' follow-up) and clinical findings (2-4 years' follow-up) showed improvement in all patients undergoing sphincterotomy. Immediate papillotomy seems justified in these selected patients.

In *chapter 8* a new technique for performing endoscopic sphincterotomy in patients with a Billroth II gastrectomy is described. After full insertion of the cannula into the common bile duct a 0.35 mm guide wire is advanced through the cannula, as deep as possible, into the bile ducts. The cannula is then removed and a 7 French stent is pushed over the guide wire into the common bile duct. After removal of the guide wire a needle-knife papillotomy can be performed along the endoprosthesis and in the proximal direction (towards the blind end of the afferent loop). The technique is a variant of the already reported guided sphincterotomy technique using a nasobiliary drain or a special cannula into the common bile duct. However, when a thin stent in the common bile duct is used to guide the needle-knife papillotomy, a second introduction of the endoscope is not necessary.

The patients were not specifically selected for the endoprosthesis or one of the other techniques. In a three year period a total of 48 sphincterotomies were attempted in 63 patients with a Billroth II anastomosis. The procedures were performed using a Soehendra papillotome in 8 patients, a needle-knife sphincterotome in 16 patients, both procedures in 5 and the endoprosthesis technique in 19 patients. One procedure related complication was found in 19 patients using the endoprosthesis technique, compared with three in the 29 patients in whom the other techniques were used.

The inial results suggest that the endoprosthesis guided sphincterotomy is a valuable addition to the presently available techniques. However, in the future

further investigation can compare in more detail the results of the three different techniques for performing sphincterotomy in patients with a Billroth II stomach resection.

We conclude that endoscopic sphincterotomy of the common bile duct is an established tool in the management of various disorders obstructing the biliary tract, and for patients with a normal gastric anatomy a reasonable consensus seems to have been reached about the indications and contra-indications and the risks associated with the procedure.

SAMENVATTING EN CONCLUSIES

Dit proefschrift presenteert de analyse van een prospectief onderzoek, bij 517 patiënten, naar de resultaten en complicaties welke geobserveerd werden na therapeutische endoscopische retrograde cholangiopancreaticografie (TERCP). Patienten met een status na maagresectie waren uitgesloten. Het onderzoek omvatte de endoscopische papillotomie (= endoscopische sphincterotomie) en galgangdrainage bij galgangstenen, maligne obstructie van de ductus hepatocholedochus of de verdenking op een functionele stoornis van de papil van Vater. Tevens wordt een nieuwe techniek gepresenteerd voor het verrichten van een papillotomie bij een status na Billroth II maagresectie.

Hoofdstuk 1 beschrijft 't bestek van het onderzoek.

Hoofdstuk 2 is een algemene introductie en geeft een overzicht van de literatuur met betrekking tot de techniek, de resultaten en de complicaties van TERCP.

In *hoofdstuk 3* wordt het protocol besproken dat gebruikt werd voor het prospectieve onderzoek dat in de hoofdstukken 4 t/m 7 wordt beschreven.

In *hoofdstuk 4* worden de problemen geanalyseerd die zich voordeden tijdens de endoscopische galgangdrainage bij 148 patiënten met een maligne obstructie van het middelste of distale gedeelte van de ductus hepatocholedochus of van de papil van Vater.

Tijdens endoscopische retrograde cholangiopancreaticografie werd de tumor afgebeeld bij 89% van de patiënten en endoscopische galgangdrainage gelukte bij 80%.

Bij alle 5 patiënten met een maligne invasie en stenose van het duodenum door een tumor in de pancreaskop mislukte de endoprotheseplaatsing. Dit komt overeen met het algemene beleid om deze patiënten door te verwijzen voor palliatieve chirurgie zonder verdere endoscopische interventie.

De kans dat de endoscopische galgangdrainage slaagt bleek groter dan 90% indien een tumor niet ingroeide in de papil van Vater of indien het een tumor uitgaande van de papil zelf betrof.

Endoprotheseplaatsing gelukte slechts bij drie van de 23 patiënten (13%) waarbij de papil van Vater betrokken was in een extrinsieke invasie van de duodenumwand door een tumor in de pancreaskop. In dergelijke gevallen hebben Soehendra en Grimm ook problemen gerapporteerd bij de endoscopische endoprotheseplaatsing.

Een nieuwe bevinding bleek de correlatie tussen de omvang van tumoren gelegen in de non-uncinatus regio van de pancreaskop en de kans op papilinvasie en het mislukken van de endoprotheseplaatsing.

Op grond van onze bevindingen adviseren we primaire percutane galgangdrainage of operatief ingrijpen indien een bewezen maligniteit in de non-uncinatus regio van de pancreaskop een diameter van 5 cm of meer heeft, of indien bij duodenoscopie extrinsieke invasie van de papil van Vater, of ernstige duodenumaantasting met stenose zichtbaar is.

In *hoofdstuk 5* werden bij 242 achtereenvolgende patiënten de complicaties geanalyseerd die waargenomen werden na sphincterotomie voor stenen in de ductus hepatocholedochus. Uitgesloten werden patiënten met een status na maagoperatie, papillotomie of met een aandoening aan de pancreas of galwegen uitgezonderd galblaasstenen.

De volgende risicofactoren die het complicatiecijfer kunnen beïnvloeden werden geanalyseerd: de papillotomieprocedure, endoscopische galgangdrainage, de diameter van de distale ductus choledochus, de plaats van de papil ten opzichte van een juxtapapillair divertikel, de galblaas, de grootte van de papillotomie, en de leeftijd van de patiënt. De risicofactoren werden eerst geanalyseerd d.m.v. univariabele analyse en vervolgens d.m.v. multivariabele logistische regressie.

Cholangiografie gelukte meteen bij 222 patiënten (92%), bij 209 van hen na een diepe canulatie van de ductus choledochus. Bij 192 patiënten werd een standaardpapillotomie aansluitend aan de cholangiografie verricht. Bij 50 patiënten werd een precut papillotomie uitgevoerd. Een nieuwe bevinding betrof het significant hogere percentage standaardpapillotomieën na cholangiografie bij de groep met een distale galgangdiameter van 10 mm of meer vergeleken met de groep waarbij deze diameter minder dan 10 mm was (χ^2 : $p = 0.004$).

De aan papillotomie procedure gerelateerde morbiditeit was 14% en de mortaliteit 0.4%.

Na papillotomie werd zowel pancreatitis als retroperitoneale lekkage bij 1,7% van de gevallen geconstateerd. Beide complicaties werden vaker waargenomen bij patiënten met een smalle (< 10 mm) distale ductus choledochus (5.6% vs. 0%: $p = 0.007$ voor pancreatitis, en 2.8% vs. 1.2%: n.s. voor perforatie) en vooral na precut papillotomie (13.0% voor pancreatitis en 8.7% voor perforatie). Precut papillotomie moest ook vaker verricht worden bij patiënten met een smalle distale galgang.

Bij slechts vier patiënten werd een retroperitoneale lekkage geregistreerd, bij allen na precut papillotomie (Fisher's exact test: $p = 0.002$). Een precut papillotomie had vermeden kunnen worden bij 17 van de 50 patiënten indien, na een moeizame diepe canulatie, door de canule de voerdraad van een voerdraad-papillotoom was opgevoerd in de galgang. Na terugtrekken van de canule kan dan een voerdraad-papillotoom in de ductus choledochus geplaatst worden. Het gebruik van een

voerdraad-papillotoom wordt thans routinematig toegepast wanneer het invoeren van de canule in de galgang voorbij de papil veel moeite kost.

De enige overblijvende risicofactor voor het ontstaan van cholangitis tijdens het vervolgonderzoek bleek een onvolledige galgangdrainage te zijn. De belangrijkste oorzaak van complicaties door cholangitis bleken achtergebleven stenen in de ductus hepatocholedochus te zijn, na gecompleteerde papillotomie. Dit komt overeen met de literatuurbevindingen.

De groep patiënten waarbij precut papillotomie mislukte, na een geslaagde cholangiografie, bleek significant meer (milde) complicaties door cholangitis te hebben in vergelijking met de groep patiënten waarbij de galgangdrainage succesvol was, hetgeen resulteerde in een odds ratio (OR) van 24.6 ($p = 0.001$). Dit is een bevinding die nog niet in de literatuur werd beschreven. Hetzelfde mechanisme van een geslaagde cholangiografie bij galgangobstructie zonder daaropvolgende galgangdrainage kan deze bevinding verklaren. Indien zowel de cholangiografie als de precut papillotomie mislukt was, werd cholangitis niet waargenomen.

Uit dit deel van het hoofdstuk wordt geconcludeerd dat alternatieve galgangdrainage binnen enkele uren verricht behoort te worden indien na gecompleteerde papillotomie een steen in de ductus hepatocholedochus achterblijft en endoscopische galdrainage mislukt is. Dit geldt met name indien een steen inklemt in de distale ductus choledochus.

Een ook nog niet beschreven bevinding was dat de locatie van een juxtapapillair divertikel als enige factor een significante invloed heeft op het ontstaan van een bloeding na papillotomie. Vergeleken met 147 patiënten zonder een juxtapapillair divertikel was het percentage bloedingen na papillotomie significant hoger bij 37 patiënten waarbij de papil aan de onderrand van een divertikel gelegen was (OR 6.9, $p = 0.004$) en bij de 15 patiënten waarbij de papil binnen een divertikel lag (OR 13.0, $p < 0.001$). Bij een ligging van de papil binnen divertikels bleek zowel het percentage perforaties (33% vs. 0%: ns.) als bloedingen (33% vs. 22%: n.s.) toe te nemen na precut papillotomie vergeleken met alleen een standaardpapillotomie. Daarom wordt geadviseerd om bij een ligging van de papil binnen een divertikel en standaardpapillotomie twee keer vergeefs is geprobeerd door een ervaren endoscopist, een gecombineerde percutane-endoscopische benadering toe te passen wanneer operatief ingrijpen gecontra-indiceerd is.

In *hoofdstuk 6* worden bij 95 patiënten met cholangitis t.g.v. stenen in de ductus hepatocholedochus de risicofactoren geanalyseerd die van invloed zijn op het ontstaan van complicaties door cholangitis na papillotomie .

Cholangitis werd als "mild" geclassificeerd in de aanwezigheid van koorts, leucocytose en obstructieve leverfunctiestoornissen; als "matig" indien geassocieerd met sepsis; en als "ernstig" indien een septische shock optrad.

De reactie op antibiotica werd als "goed" geclassificeerd indien het klinische beeld binnen 24 uur duidelijk verbeterde en niet weer opvlamde. In de overige gevallen werd de cholangitis geclassificeerd als "persisterend".

Endoscopische galgangdrainage werd als "vertraagd" geclassificeerd wanneer deze meer dan drie dagen na het ontstaan van een persisterende cholangitis werd uitgevoerd, onafhankelijk van de aanvang van de antibiotische behandeling.

De volgende risicofactoren werden geanalyseerd: het aantal dagen tussen het begin van de cholangitis en papillotomie, de reactie op antibiotica voor de endoscopische retrograde cholangiopancreaticografie, de sphincterotomieprocedure, de diameter van de distale ductus choledochus, de resultaten van de bloedkweken, de aanwezigheid van pus in de gal, de galblaas, de leeftijd van de patiënt, en de aanwezigheid van een bijkomend ziekteproces.

Bij alle patiënten kon de papillotomie tijdens het eerste onderzoek worden afgerond, bij 19 patiënten in aansluiting aan een precut papillotomie.

Inclusief de 11 complicaties door cholangitis, waarvan er drie fataal bleken, bedroeg bij 95 patiënten de totale aan de procedure gerelateerde morbiditeit 19% en de mortaliteit 3,2%.

Drie patiënten met achtergebleven stenen in de ductus hepatocholedochus na papillotomie en zonder (naso)biliaire drainage ondervonden een significant hogere morbiditeit (100% vs. 9%: $p < 0.01$) en mortaliteit (67% vs. 1%: $p < 0.01$) door cholangitis vergeleken met de 85 patiënten bij wie alle stenen uit de ductus hepatocholedochus konden worden verwijderd.

Bij de 85 patiënten waarbij de galgangstenen volledig waren geëxtraheerd bleek bij exacte logistische regressieanalyse geen afzonderlijke risicofactor met een significante betekenis aanwezig te zijn. Daarentegen bleek bij 25 patiënten met een persisterende cholangitis voorafgaande aan de papillotomie de kans op complicaties door cholangitis groter te worden naarmate de wachttijd voor de papillotomie toenam. Bij de 60 patiënten die goed gereageerd hadden op de antibiotische behandeling voor papillotomie, bleek de wachttijd geen invloed te hebben op de kans op complicaties.

Dertien patiënten die (nog) niet hadden gereageerd op antibiotica ten tijde van de endoscopische retrograde cholangiopancreatografie en die vroegtijdig (binnen 72 uur na het begin van de cholangitis) gedraineerd werden, ondervonden geen complicaties door cholangitis. Dit was niet significant verschillend in vergelijking met drie milde complicaties door cholangitis bij 60 patiënten die meer dan drie dagen na aanvang van de cholangitis gedraineerd waren, maar goed gereageerd hadden op antibiotica.

Daarentegen ondervonden de 12 patiënten waarbij de conservatievé behandeling mislukte en de cholangitis meer dan 3 dagen voor de papillotomie persisteerde een hogere morbiditeit (42% vs. 5%: FE: $p = 0.002$) door cholangitis en een hoger percentage septische complicaties (33% vs. 0%: FE: $p = 0.0005$) vergeleken met de 60 patiënten die goed gereageerd hadden op antibiotica en meer dan 3 dagen na aanvang van de cholangitis gedraineerd werden.

Twee patiënten met een vergevorderde cholangitis en septische shock ten tijde van de papillotomie overleden binnen 12 uur na een gecompleteerde papillotomie.

Bij alle patiënten die opgenomen worden met calculeuze cholangitis en die ernstig ziek zijn t.g.v. continue koorts gedurende meerdere dagen adviseren wij spoedgalgangdrainage. Wanneer een (dreigende) septische shock bestaat wordt geadviseerd om direct endoscopische nasobiliaire drainage uit te voeren na een kleine of zonder papillotomie, hetgeen een minder agressieve en tijdrovende procedure is dan volledige papillotomie plus steenextractie. Bij patiënten met ernstige calculeuze cholangitis zijn goede resultaten beschreven met deze methode, waarbij de definitieve behandeling verricht werd na nasobiliaire drainage.

Een meer terughoudende benadering is gerechtvaardigd bij patiënten die opgenomen worden met een milde calculeuze cholangitis waarbij een spoedgalgangdrainage beperkt kan blijven tot diegenen die niet snel (< 24 h) reageren op antibiotica.

In *hoofdstuk 7* worden de resultaten beschreven van het vervolg onderzoek van 32 patiënten die geselecteerd werden op grond van verdenking op een functionele stoornis van de papil van Vater.

Indien patiënten verdacht worden van een functionele stoornis van de papil is het vaak moeilijk om te bepalen of sphincterotomie geïndiceerd is of niet. Bij post-cholecystectomie patiënten zonder een voorgeschiedenis van geelzucht, cholangitis of pancreatitis, wordt het aanbevolen om met conservatieve behandeling te beginnen. Voor de selectie van patiënten die in aanmerking komen voor papillotomie is o.a. drukmeting van de sphincter van Oddi en de evaluatie van de galgang-ontlediging aanbevolen. De galgangontlediging is dan vertraagd indien deze langer dan 45 minuten duurt.

Het in dit hoofdstuk beschreven onderzoek werd opgezet om na te gaan of bij bepaalde patiënten die verdacht worden van dysfunctie van de sphincter van Oddi, direct papillotomie verricht kan worden volgend op endoscopische retrograde cholangiopancreaticografie. De studie omvatte 32 opeenvolgende patiënten die verwezen werden voor ERCP en die allen al langere tijd pijnaanvallen in de rechter bovenbuik en/of epigastrio hadden, tezamen met periodiek verhoogde leverenzymen wijzend op cholestasis.

Verdere kenmerken waren (1) een gedilateerde ductus choledochus na cholecystectomie (n = 11), (2) een gedilateerde ductus choledochus zonder galblaasstenen of met grotere (groter dan de diameter van de ductus cysticus) galblaasstenen (n = 6), of (3) multipele kleine stenen in de galblaas bij een normaal brede of gedilateerde ductus choledochus bij patiënten met symptomen van een acute biliaire pancreatitis of bij wie electieve cholecystectomie niet geïndiceerd was (n = 15).

Bij deze drie groepen patiënten werden geen galgangstenen, organische obstructie of andere afwijkingen gevonden. Teneinde de maximale diameter van de ductus choledochus te bepalen werd de vergrotingsfactor gecorrigeerd door middel van de bekende diameter van de endoscoop. De ductus choledochus werd geacht verbreed te zijn wanneer bij een intacte galblaas de gecorrigeerde maximale diameter van de galgang meer dan 8 mm was, en na cholecystectomie, meer dan

10 mm. Zonder verdere diagnostische procedures werd de papillotomie routinematig verricht.

Bij alle patiënten die een sphincterotomie ondergaan hadden, waren zowel de laboratoriumwaarden (nacontrole t/m 3 maanden) als het klinisch beeld (nacontrole 2-4 jaar) verbeterd. Een directe papillotomie lijkt gerechtvaardigd bij deze patiëntenselectie.

In *hoofdstuk 8* wordt een nieuwe techniek beschreven voor het verrichten van endoscopische papillotomie bij patiënten met een status na Billroth II maagresectie. Nadat de canule in de ductus choledochus gebracht is wordt door de canule een voerdraad met een diameter van 0.35 mm opgevoerd en zo diep mogelijk in de galwegen geplaatst. Vervolgens wordt de canule verwijderd en een 7 French endoprothese over de voerdraad in de ductus choledochus geduwd. Na verwijdering van de voerdraad kan precut papillotomie verricht worden langs de endoprothese, gaande in proximale richting, naar het blinde uiteinde van de afferente lis.

Deze techniek is een variant op de reeds beschreven geleide sphincterotomietechniek waarbij gebruik gemaakt wordt van een nasobiliaire drain of een speciale canule in de ductus choledochus. De precut papillotomie op geleide van een dunne stent in de ductus choledochus heeft echter als grote voordeel dat het niet nodig is de endoscoop twee keer in te brengen.

De patiënten waren niet geselecteerd voor de endoprothese of een van de andere technieken. Over een periode van drie jaar werden, op een totaal van 63 patiënten met een B-II anastomose 48 sphincterotomieprocedures verricht. Bij acht patiënten werd gebruik gemaakt van de Soehendra papillotoom, bij 16 patiënten van een precut papillotoom, bij 5 beide procedures en bij 19 patiënten de endoprothesetechniek. Gebruikmakend van de endoprothesetechniek bij 19 patiënten werd 1 aan de procedure gerelateerde complicatie gevonden, vergeleken met drie complicaties bij de 29 patiënten bij wie andere technieken werden gebruikt.

Gezien de eerste resultaten lijkt de endoprothesegeleide precut papillotomie een welkome aanvulling op de bestaande technieken. In de toekomst kunnen de drie verschillende technieken voor het verrichten van een papillotomie bij een status na Billroth II maagresectie nader vergeleken worden.

Wij concluderen dat de endoscopische sphincterotomie een vaste plaats verworven heeft in de behandeling van galgangobstructie. Met name bij de patiënten met een normale anatomie van de maag lijkt na twee decennia een redelijke mate van overeenstemming bereikt over de indicaties en contra-indicaties en de risico's van de procedure.

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CURRICULUM VITAE

The author of this thesis was born in 1954 in Dordrecht. The secondary school (HBS-B) was completed in 1972, followed by a chemistry study in Utrecht, during 1 year. In 1980 he graduated at the Medical Faculty of the Erasmus University of Rotterdam. During a 16-month period he served as a medical officer at the Hague, followed by obtaining the certificate of Radiation protection, expertise level 3 at the IRI at Delft.

From 1982-1986 he was a resident at the department of Diagnostic Radiology (head Prof. K. Hoornstra). From 12-01-1986 till 12-01-1989 he worked part-time for the department of Radiology and part-time for the T.E.R.C.P-project which has resulted in this thesis. The T.E.R.C.P.-project was taken up by Dr. G.A.J.J. Nix (staff-member of the department of Radiology) and was carried out in co-operation with the department of Internal Medicine II/Gastroenterology (head Prof. J.H.P. Wilson). From 01-01-1990 he is working at the department of Diagnostic Radiology (head Prof. Dr. H.E. Schütte) as a staff-member.