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Severe and Fatal Complications After Diagnostic and Therapeutic ERCP: A Prospective Series of Claims to Insurance Covering Public Hospitals

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Background and Study Aims: Increasing numbers of patients are undergoing endoscopic retrograde cholangiopancreatography (ERCP) prior to laparoscopic cholecystectomy, and more departments and doctors are performing ERCP, while new data from large prospective series have documented the risks of both diagnostic and therapeutic ERCP. The establishment in Denmark of a Patient Insurance Association, which has covered injury caused during investigation and treatment in public hospitals since July 1992, has made it possible to collect and analyze a large prospective series of ERCP complications for which compensation has been claimed.

Patients and Methods: Thirty-nine consecutive claims for compensation due to complications after ERCP occurring between 1 July 1992 and 31 December 1996 were investigated. Case notes were reviewed, along with laboratory reports and radiographs. The complications were classified according to the international consensus.

Results: Claims for compensation were made in 39 cases from 25 hospitals. The indication for ERCP was appropriate in 31. Precut papillotomy for access had been performed in seven. The severity of the complications was mild in one patient, moderate in three patients, severe in 24, and fatal in nine; in two cases, the severity was not classifiable. The complications were: pancreati-

tis in 23 patients (seven cases fatal, one of which had involved a precut procedure), bleeding in two, perforation in nine (six had a precut procedure, one died), and other reasons in five (including one fatal case). Among the nine fatal cases, cannulation had not been achieved in two and the endoscopic retrograde cholangiogram was normal in four, one of whom underwent a sphincterotomy. One patient with a previous adenoma had an endoprosthesis removed, developed gangrenous cholecystitis afterward, and died. Thirty patients were eligible for compensation. The rejected cases included mild and moderate pancreatitis, a case of fatal hemorrhagic pancreatitis in which the patient had refused blood transfusion, and one patient who had pancreatitis prior to ERCP.

Conclusions: ERCP, even for diagnostic purposes, may be associated with very serious and even fatal complications. The use of the precut procedure for access should still be considered dangerous. Other means of investigating the bile ducts should be developed. If endoscopic ultrasonography and magnetic resonance cholangiography prove to have the same diagnostic value as ERCP, which must be considered the gold standard for visualizing the ducts today, they might replace ERCP as the primary investigation in patients with an intermediate or low risk of bile duct stones; this would reduce the numbers of patients exposed to the risks of ERCP.

Introduction

During the first decade in which the laparoscopic technique was used, the rate of cholecystectomy in the Western world increased, and the numbers of patients undergoing preoperative endoscopic retrograde cholangiopancreatography (ERCP) also increased [1]. New data documenting the

complication rates of ERCP have emerged. Large prospective case series covering university departments, general hospitals and private practice have found overall complication rates of 5-6% after diagnostic ERCP [2], and 4-10% after endoscopic sphincterotomy (EST) [3-5]. Severe complications have occurred in 0.4% after diagnostic procedures [6], and in 0.05-1.6% after therapeutic procedures [3-6]. Fatal complications are reported in 0.07-0.1% after diagnostic ERCP [2], and in 0.1-0.4% after therapeutic ERCP [3-6]. There is no correlation between risk and co-morbid status [2, 4].

The relative infrequency of severe and fatal complications makes it difficult to identify risk factors. The introduction of a public insurance system providing compensation for injury after treatment in public hospitals (ERCP is only offered in the public setting in Denmark), has made it possible to analyze a large consecutive series of cases in which claims for compensation were made.

Patients and Methods

The Danish Patient Insurance Act

The Patient Insurance Act was passed by the Danish Parliament in 1991 and came into effect on 1 July 1992. The general purpose of this patient insurance scheme is to ensure that patients can receive indemnification for the consequences of medical injury, even when the injury is not caused by negligent examination or treatment methods. Emphasis is laid on whether the injury, viewed in retrospect, could have been avoided, or whether the injury, although unavoidable, clearly exceeds the risk that a patient has to accept [7]. The patient or relatives have to file the claim with the Patient Insurance Association (PIA), which reviews the claim and obtains the information and evidence necessary to make a decision.

The Patient Insurance Act specifies four ways in which a patient can demand compensation for an injury covered under the mandatory insurance scheme:

- Paragraph 2.1.1. If there is reason to believe that an experienced specialist in the field in question would have acted differently and thereby avoided the injury.
- Paragraph 2.1.2. If the injury is caused by defects or failure of the equipment or instruments used for the examination or treatment.
- Paragraph 2.1.3. If subsequent evaluation shows that the injury could have been avoided by using another available treatment modality, which from a medical point of view would have been equally effective for treating the patient.
- Paragraph 2.1.4. In spite of the fact that an injury was unavoidable, the patient can be indemnified if the injury caused by an examination or treatment is rare and disproportionate to the initial disease.

The claimant or the insurance company involved can appeal against the Association's decisions to the Patient Injury Appeals Board. Between 1 July 1992 and 31 December 1996, the PIA received a total of 6058 notified claims.

ERCP Complications Claimed

All claims relating to complications associated with ERCP procedures performed between 1 July 1992 and 31 December 1996 were identified. All the information was reviewed, including the advice given to the PIA by the medical experts. Information about the indications, technical details of the ERCP, and the course after the procedure was derived from the case notes. Indications were consid-

ered appropriate, for example, in cases of documented bile duct stones prior to endoscopy, jaundice with dilated ducts, or gallstone pancreatitis, but were regarded as questionable in cases in which the indication was stated to be resolved jaundice with currently normal liver function tests, or pain without ultrasonographic or biochemical signs of bile duct pathology or stones. The complications were classified according to the criteria suggested by Cotton et al. [8] (Table 1). The total number of ERCPs per year was derived from the National Board of Health's In-Patient Registry. Rulings concerning compensation were recorded for cases in which the proceedings had been concluded.

Table 1 Classification of the severity of complications [8]

Severity	Definition
Mild	Complication requiring hospital admission or prolongation of a planned admission for up to three days
Moderate	4-10 days' hospitalization, including further endoscopic or radiological intervention if necessary
Severe	More than 10 days' hospitalization, or a need for surgical intervention or intensive care
Fatal	Death attributable to the procedure within 30 days, or longer with continuous hospitalization

Results

Claims

Compensation was claimed by 39 patients (28 women) (Table 2). The median age at the time of ERCP was 47 years (interquartile range 40-61 years, range 19-81 years). Two cases were not classifiable according to the international consensus (one tooth injury, and one case of Hashimoto thyroiditis secondary to contrast exposure). Four were mild or moderate, while 24 were severe, and nine fatal. The indication for ERCP was appropriate in 31 cases (Table 3). The most frequent complication was post-ERCP pancreatitis, which occurred in 23 cases (Table 4). Nine patients suffered perforations. Six of these underwent a needle-knife papillotomy (NKP) ("precut") for access, and one pa-

Table 2 Annual number of endoscopic retrograde cholangiography (ERCP) procedures in Denmark, and claims for compensation relative to the severity of the complication [8]. ERCP figures kindly provided by the National Board of Health in Denmark

Year	ERCPs	Not classifiable	Mild	Moderate	Severe	Fatal
1992	3155		1		3	
1993	4239			1	6	2
1994	4850	1		1	4	
1995	4657	1		1	4	5
1996	5471				7	2
Total		2	1	3	24	9

Severe and Fatal Complications After ERCP

Table 3 Appropriateness of the indication for ERCP and severity of the complication after ERCP [8]

	Not classifiable	Mild	Moderate	Severe	Fatal
Appropriate indication	2	1	3	20	5
Questionable indication				4	4

Table 4 Specification of complications, use of needle-knife papillotomy (NKP) for access, and outcome

Complication	n	NKP	Fatal
Pancreatitis	23	1	7
Bleeding	2	0	0
Perforation	9	6*	1
Other	3**	0	1
No complication	2***	0	0

*Including one patient with prior Billroth II surgery.
 ** One patient with back pain after ERCP under general anesthesia, one with Hashimoto's thyroiditis, and one case of cholecystitis (fatal).
 *** One patient with tooth injury investigated by a dentist three months later, and one patient who had uneventful ERCP twice, due to a stone being missed at the first ERCP.

Table 5 Patients, indications, specification of the ERCP procedure, and cause of death in nine fatal cases

Sex, Age	Indication	Diagnostic or therapeutic ERCP	Precut	ERCP	Cause of death	Autopsy finding
F 49	Pain for 6 y Suspected SOD Normal LFTs and US	Diagnostic	-	Normal BD Moderate PD changes	Pancreatitis, multiple organ failure	-
F 37	Resolved jaundice (normal LFTs) US: stones in gallbladder	Diagnostic	-	Normal BD and PD Difficult cannulation	Pancreatitis	Severe pancreatitis
F 61	Elevated LFTs and pain	Therapeutic	-	Normal BD and PD, EST was done	Hemorrhagic pancreatitis and anemia	-
M 61	Resolved jaundice	No access, bleeding, monopolar coagulation	+	PD normal, BD not cannulated	Pancreatitis	BD stones
F 66	Elevated LFTs Pain for 10 y	Diagnostic	-	Normal BD and PD	Pancreatitis, renal failure	-
F 49	Elevated LFTs Dilated CBD	Diagnostic	-	Dilated BD, no stones, PD normal	Pancreatitis	GB cancer
F 61	Jaundice (hepatocellular pattern) US: normal	No BD cannulation	+	BD not cannulated, PD normal, PD injection several times	Perforation, abscess, renal failure	Perforation, hepatitis A
M 74	Control ERCP after endoscopic resection of villous adenoma 9 months earlier	Diagnostic	-	No adenoma, no BD stricture, PD not cannulated	Peritonitis due to gangrenous cholecystitis	No adenoma recurrence
F 29	Pancreatitis Elevated LFTs US: no stones	Diagnostic	-	BD stones on review postmortem, PD normal	Pancreatitis, multiple organ failure	BD stones impacted in papilla

BD: bile duct; F: female; GB: gallbladder; LFTs: liver function tests; M: male; PD: pancreatic duct; SOD: sphincter of Oddi dysfunction; US: ultrasonography

tient, in whom cannulation failed, died. In one of the six cases in which NKP was used, cannulation with a guide wire was used prior to the choice of NKP. The nine fatalities (listed in Table 5) included seven patients with pancreatitis. Six of the fatal cases involved only a diagnostic ERCP.

Compensation

Thirty patients were eligible for compensation, but three cases were below the minimum amount for compensation (then DKK 20000, corresponding to US\$ 3000). Four patients received compensation according to the "specialist criterion" (Paragraph 2.1.1) for the following reasons: no indication for ERCP; NKP without prior attempts at alternative cannulation techniques; NKP at the 12-o'clock and 6-o'clock position; and an overlooked pneumoperitoneum on the final radiograph and no stenting or other drainage procedure in spite of residual bile duct stones.

Twenty-six patients received compensation according to the relative rarity and seriousness of the complication (Paragraph 2.1.4), while compensation was not awarded in one fatal case of hemorrhagic pancreatitis, in which the patient refused blood transfusion due to religious beliefs.

Compensation was not awarded for any of the mild complications. Other rejected cases not mentioned above were four cases of post-ERCP pancreatitis; one case in which two ERCPs were needed to clear the ducts; one in which newly diagnosed diabetes was not likely to have been caused by ERCP; one of tooth injuries diagnosed three months later; and one of severe pancreatitis at the time of ERCP. The case of Hashimoto's thyroiditis was thought to have been caused by the Isopaque amine contrast used, and compensation was awarded because of the rarity of this complication.

Discussion

Only a few studies have described the rates and severity of complications after ERCP in a broader community setting. Prospective collection of data on individual cases requires a considerable extra effort, which may explain why the available data mostly originate from large and academic centers focused on outcomes research. In such centers, the level of expertise is usually high, so that it can be assumed that the rate and distribution of adverse effects may not be representative of the endoscopic community in general. Given the significant number of claims in the PIA, analysis of a larger series of severe complications from a broad community setting has become possible.

In the present series, the PIA awarded compensation to a large number of patients who would otherwise have had to bear the burdens of ERCP injuries themselves. The no-fault nature of the PIA's insurance scheme, and the fact that physicians are not personally involved in the claims resolution process, makes the physicians less reluctant to admit that an adverse event has occurred. Physicians are therefore more likely to inform their patients about the possibility of obtaining compensation.

Fortunately severe and fatal complications occur infrequently. Recent reports on therapeutic ERCP have focused on specific procedures such as EST and factors related to specific patients and procedures. In a multicenter study with 30 days of follow-up after EST [4], the most frequent

patient-related risk factor for complications was sphincter of Oddi dysfunction. Of those who underwent EST for sphincter of Oddi dysfunction, 21.7% sustained complications. Sphincter of Oddi dysfunction is much more frequently diagnosed in the United States than in other parts of the world; possible explanations for this might be the fact that patients are often diagnosed with irritable bowel syndrome in other countries, and/or the less frequent use of manometry in many other countries. In the present study, some of the patients with normal findings at ERCP and an indication of pain and slightly elevated liver function tests might have had sphincter of Oddi dysfunction, but manometry was not performed in any of these cases.

The distribution of the grades of severity of complications in large, prospectively collected series after diagnostic or therapeutic ERCPs in the United States is approximately: 59% mild complications, 32% moderate, 7% severe, and 2% fatal [2,3,9]. If the previously reported complication rates (Table 6) can be extrapolated to the present setting with approximately 5000 procedures per year, an estimated 50 severe and fatal cases per year might be expected – or even more, since the previously published rates originate from expert academic centers. It may therefore be assumed that even more complications may have occurred than those claimed with the PIA.

The indications and risks of precut techniques for access have been debated and emphasized in the literature, textbooks, and at postgraduate endoscopy courses for almost ten years [10]. Recently, recognized centers with a high level of expertise have reported immediate cannulation rates of 67–88% after NKP (increasing to 93–99% when successful cannulation at repeated ERCP is included), and complications in 11–12% without fatalities [11,12]. Guide wire manipulation of the fresh papillotomy site caused perforations in some cases [11]. Recently, two major centers have both published 44% rates of NKP (as a percentage of all papillotomies) [12,13]. Other experts, however, found that NKP was necessary for access in only 3–5% [14]. Vandervoort and Carr-Locke [14], reflecting on the fact that both multiple failed cannulation attempts (more

Table 6 Overall complication rates and numbers of severe and fatal complications in large prospective case series of diagnostic or therapeutic endoscopic retrograde cholangiopancreatography

First author, ref.	Year	Setting	Procedure(s)	ERCPs	Complications		
					%	Severe (n)	Fatal (n)
Cotton et al. [2]	1994	1 university dept.	Diagnostic only	1 949	5.5	9	5
Cotton et al. [3]	1998	7 university depts.	EST for stones	1 921	5.8	1	0
Freeman et al. [4]	1996	11 university depts., 6 private clinics	EST (all indications)	2 347	9.8	38	10
Davis et al. [5]	1997	4 university depts., 44 other	EST in rel. to LC	780	9.6	3	0
Maie et al. [6]	1994	2 university depts.	All therapeutic	4 589		45	5
Present study	1995–96	33 public hospitals	All procedures			10	7

EST: endoscopic sphincterotomy; LC: laparoscopic cholecystectomy

than 15 or 20) and NKP are independent risk factors for post-ERCP pancreatitis, noted that the question of whether access papillotomy should be used either as a last resort, or quite early in order to reduce the morbidity of multiple cannulations, is as yet unresolved. Dorais et al. [15] randomly assigned 25 patients (of 237) in whom cannulation was not achieved within 12 minutes to either NKP or additional persistent cannulation attempts for a further 15 minutes, and found no significant differences in the success rates (64% and 73%), bleeding rates (14.2% and 9%), or rates of post-ERCP pancreatitis (7 and 9%), although there was a trend toward longer cannulation times in cases of failed NKP [15].

Alternatively, the papilla can be „de-roofed“ using an Erlangen-type precut papillotome [16]. Using this instrument in 123 prospective patients in whom standard cannulation was unsuccessful, Binmoeller et al. achieved cannulation in 91% at the first attempt and in 100% on a repeat attempt. The overall complication rate was 5.3% [16].

The endoscopist's and unit's total yearly ERCP volumes are important risk factors that need to be taken into consideration for the study period, during which the use of ERCP may have expanded to more hospitals with the introduction of laparoscopic cholecystectomy. Freeman et al. found that centers whose endoscopists performed more than one EST per week had significantly fewer difficult cannulations (>15 attempts required): 7.1% versus 14.6% in low-volume centers ($P < 0.001$), as well as significantly fewer pancreatic duct injections, failures of biliary access or drainage after EST, fewer hemorrhages, fewer severe complications (0.9% versus 2.3%, $P < 0.01$) and fewer overall complications (8.4% versus 11.1%, $P < 0.03$) [4]. A volume of one EST or less per week increased the risk of bleeding significantly in the multivariate analysis, but did not increase the risk of post-ERCP pancreatitis [4]. Analyzing the outcomes of ERCP and EST in the context of laparoscopic cholecystectomy, Davis et al. [5] found that gastroenterologists with a lifetime experience of less than 200 ERCPs had significantly lower success rates for EST (82%) than more experienced colleagues (99–100%), regardless of setting. The local availability of ERCP also influences selection. In high-volume ERCP centers (more than 200 ERCPs per year), more patients scheduled for laparoscopic cholecystectomy underwent preoperative ERCPs (up to 45%) than in low-volume centers (10–15%) [1].

The issue of training has been studied prospectively by Jowell et al. [17]. To achieve cannulation of the bile duct in more than 80% of cases, more than 160 ERCPs were required. Including other ERCP procedures, it was found that at least 180 ERCPs were required before the fellows could be considered competent in ERCP. This number is higher than generally recommended previously on empirical grounds. It should be taken into consideration that the data in the study by Jowell et al. were obtained in the United States, where „advanced endoscopy fellows“ are exposed

to higher numbers of ERCPs within a limited time-span than in Scandinavian countries, and are supervised during the entire procedure in every single case, partly for reimbursement and judicial reasons. Thus, in a less intensively supervised training system, even higher numbers might be required to obtain competence.

The frequent occurrence of complicated cases in which access was attempted using NKP without prior attempts using alternative techniques, except in a single case, underlines the necessity for providing continuous information and offering courses teaching modern techniques in the present community. However, the rate of NKP use amongst patients who did not develop complications is not known.

The relatively frequent occurrence of patients with normal findings in the present study suggests that the indications for ERCP might be made more strict. Selection of patients with a low or intermediate probability of stones, based on history or clinical impression alone, may result in too many patients without stones presenting at the time of ERCP, with too many patients consequently being exposed to the risks of the procedure. Simple scoring models for optimized identification of patients with bile duct stones can be used [18].

Magnetic resonance cholangiopancreatography (MRCP) in patients with a low or intermediate risk of choledocholithiasis may be useful for selection for therapeutic ERCP, provided that it has a sufficiently high diagnostic specificity and sensitivity, even in patients with non-dilated ducts [19]. This can only be evaluated in prospective comparative blinded studies with sufficiently large numbers of patients. Until such studies have been performed, ERCP must be regarded as the gold standard for detecting bile duct stones, since endosonography, which has a sensitivity for stones that is at least as good as ERCP [20], is not generally available.

The present data document the risks of serious and fatal complications after ERCP, even for purely diagnostic procedures, and show that precut papillotomy may be dangerous. It is worrying that the material includes a substantial number of patients who had normal findings at cholangiography. In general, it might be speculated that centralization in centers with a high level of expertise might result in stricter selection and probably avoidance of some of the complications associated with the cannulation technique used. The issues of indications and techniques in ERCP must also be emphasized in training and postgraduate courses. In younger patients with a low or intermediate probability of stones, the options of surgery with intraoperative cholangiography and duct clearance should also be investigated further in prospective studies.

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Twenty-Four-Hour Serum Amylase Predicting Pancreatic Reaction After Endoscopic Sphincterotomy

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Background and Study Aims: Acute pancreatitis is still the most common complication after endoscopic sphincterotomy (ES) and cholangiopancreatography (ERCP). The aim of this study was to detect the time when the peak of serum amylase was predictive for postprocedure pancreatitis or long-lasting severe hyperamylasemia, in order to plan the follow-up of patients.

Methods: Serum amylase activity was measured in a prospective series of 409 consecutive patients after ES, immediately before ES and two, four, eight and 24 hours thereafter; the two, four and eight-hour data were compared with those at 24 hours and with the outcome. Evaluation was done separately for the 198 cases with pancreatic duct opacification and for the 202 cases at high risk for postprocedure pancreatitis.

Results: Twenty-four hours after ES, amylase was still more than five times the upper normal limit in 26 patients, associated with pancreatic-like pain in 19 of them (mild/moderate pancreatitis) and asymptomatic

in the remaining seven (long-lasting severe hyperamylasemia). There was a significant difference at all sampling times between the 26 patients with 24-hour severe hyperamylasemia and those with the lower level. Although the sensitivity of amylase measurement in detecting pancreatitis was highest at eight hours, in practice the four-hour assessment appears a reliable predictor. Almost all patients with serum amylase levels more than five times the upper normal limit at four, eight and 24 hours had had pancreatic duct opacification. In contrast, patient-related risk factors for postprocedure pancreatitis did not play a significant role in the present series.

Conclusions: Serum amylase assessment four hours after ES is a reliable, cost-effective follow-up and minimizes the likelihood of underestimating the risk of postprocedure pancreatic reaction. It should be recommended particularly in out-patients and when pancreatic duct opacification has occurred.

Introduction

After endoscopic sphincterotomy (ES) and endoscopic cholangiopancreatography (ERCP) an asymptomatic increase in serum amylase is common, occurring in up to 70% of cases [1-3]. Amylasemia generally peaks 90 minutes to four hours after the procedure [4,5] and resolves within 48 hours, so it can be considered clinically insignificant and there is normally no need for hospital treatment. However, postprocedure acute pancreatitis may develop in 1-6% of cases [6-9]; patient-related as well as procedure-related risk factors have been shown to further raise the incidence of such complications [8,9]. In some cases, the

complication may be delayed up to 12 hours after the endoscopic procedure [7,10].

The early recognition of patients who are likely to develop postprocedure pancreatitis is highly desirable, on the one hand to plan prolonged follow-up in hospital and an early therapeutic approach, either to reduce the risk of pancreatitis or to attenuate its course, and on the other hand to avoid unnecessary hospital admission when ES and ERCP are performed as an outpatient procedure.

Up till now, postprocedural assessment of the enzyme profile and symptoms regarding the risk of pancreatitis has not been systematically studied, so that their reliability still remains questionable.

The aim of this study was therefore to assess the 24-hour serum amylase pattern after ES in order to detect the time when the peak of the enzyme was predictive for pancreati-