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Quality assurance of sphincterotomy: A prospective single-centre survey

Research Article

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Abstract: Quality assurance becomes an increasingly important part of clinical medicine and of the field of endoscopy. Endoscopic sphincterotomy is associated with a fairly high complication rate. We aimed to assess our quality of sphincterotomy for benchmarking by using a prospective electronic database registry, and to identify potential risk factors for post-interventional complications. Over 2 years, 471 sphincterotomies were performed in a single tertiary referral centre. Patient– and procedure-related variables were prospectively recorded with the support of a multi-centre international sphincterotomy registry. Multivariate analysis was performed. The overall post-interventional complication rate was 9.3%. Pancreatitis happened in 5.5%, bleeding in 2.1%, perforation in 1.3%, and cholangitis in 0.4%. In the multivariate analysis following variables remained highly significant and predictive for complications: 'papilla only in lateral view' (p=0.001), antiplatelet therapy (p=0.024), and opacification with contrast up to the pancreatic tail (p=0.001). The primary success rate of sphincterotomy was 95.1%. The rate of post-interventional pancreatitis did not differ significantly regardless of the presence of prophylactic pancreatic stent (p=0.56). The outcome of sphincterotomy in our centre matches with literature data. The extent of pancreatic duct opacification has an influence on the pancreatitis rate. Prevention of pancreatitis by inserting pancreatic stents is not confirmed.

Keywords: *ERCP • Sphincterotomy • Complication • Pancreatitis • Stent • Quality assurance*

1. Introduction

Since its initial description [1] 40 years ago, endoscopic retrograde cholangiopancreatography (ERCP) has evolved from a diagnostic to a predominately therapeutic procedure [2]. Endoscopic sphincterotomy (EST) is performed in order to remove pancreatic or biliary stones prior to the placement of stents through malignant or benign biliary strictures. It remains a cumbersome technique because it is known to be associated with a fairly high complication rate, even in the hands of experienced interventional endoscopists [3,4]. Therefore, a high level of quality should be one of the main goals of ERCP clinics.

Quality assurance becomes an increasingly very important part of modern clinical medicine and of the field of interventional endoscopy, like ERCP [5,6]. In 2006, a list of quality end-points for ERCP was proposed by the ASGE/ACG taskforce on the quality in endoscopy [7]. Surveys regarding quality assurance of ERCP and EST under real-life conditions may detect hidden deficits. This was reflected by a complete survey on the current quality of ERCP practise in the United Kingdom which showed quality deficiencies ranging from general unit organisation to consent practise, patient preparation, sedation, and ERCP outcome [8].

To the best of our knowledge, there is a lack of studies regarding quality assurance of EST in Switzerland. The objectives of our study were to assess our own quality of EST as an objective basis for benchmarking with other national and international ERCP clinics by using a prospective electronic database registry and to identify any of the assessed variables as potential risk factors of post-interventional complications of EST.

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2. Material and Methods

2.1. Interventional setting

Our centre is a high volume tertiary referral centre for endoscopic retrograde cholangiopancreaticographies (ERCPs) (>200 ERCPs/year) providing health service for a population of 500,000 in the northeastern part of Switzerland. We have been participating in the German Sphincterotomy Registry since 2005. The German Sphincterotomy Registry is a voluntary prospective multi-centre registry of endoscopic sphincterotomy for quality assurance with anonymous participation of clinics in Germany and Switzerland. The German Sphincteromy Registry is a project of the German Working Group of Clinical Gastroenterologists (ALGK) and is supported by the German Society of Digestive and Metabolic Diseases (DGVS). This publication is based on our Swiss data retrieved from the German Sphincteromy Registry.

All ERCPs with and without EST were performed by board-certified gastroenterologists assisted by one or two endoscopy nurses. Four operators were well-trained (>1000 ERCPs), while one operator was a trainee in ERCP (<50 ERCPs). During the examination, each operator could individually decide, on his discretion, whether to insert a prophylactic pancreatic stent or not. A prophylactic pre-interventional antibiotic (Ceftriaxone) was given routinely. The written informed consent was compulsory. The sedation was performed after good preoxygenisation under monitoring of blood pressure, heart rate, and oxygen saturation rate. Propofol was used routinely in all patients who did not have contraindications to this drug. In patients with contraindications to Propofol we used Midazolam (DormicumR) combined with Pethidin.

2.2. Assessment

All patients undergoing EST during ERCP between September 1, 2005 and August 31, 2007 were recorded in the sphincterotomy registry (inclusion rate of 100%).

There were two steps of assessments documented on two separate forms. The first form included demographics and any interventional data as the following: indication, type of sedation, anatomic circumstances, technique of sphincterotomy, extent and number of pancreatic duct opacification with contrast fluid, pancreatic stent insertion, primary success or failure of EST, and complications during intervention (data entered by the operator). The second assessment form recorded any post-interventional complication (follow-up form). The time period between intervention and follow-up was not strictly defined: hospitalised patients were followed up on the day of discharge by the gastroenterology ward physician. Outpatients (day-clinic) were followed up by the patient´s GP at the next appointment. Our study nurse recollected all follow-up forms (in- and outpatients) (follow-up rate: 100%) and entered these data in the electronic registry program. The appropriate Ethics Committee approval has been obtained for this research project.

2.3. Data analysis

Success and complications of EST were analysed with regard to a) indication, b) sedation, c) anatomic circumstances, d) technique of procedure (times and extent of opacification of the pancreatic duct; precut), and e) patient-related factors (e.g. age, ASA classification, antiplatelet therapy and/or anticoagulation).

Complications were classified in minor and major complications. Minor complications were defined as mild post-interventional pancreatitis and post-interventional cholangitis. Major complications were defined as moderate to severe pancreatitis, post-interventional bleeding, proven perforation, and any lethal complication. In order to clarify the term ´post-interventional pancreatitis` we used the definition introduced by Cotton et al. [9]. Post-interventional cholangitis was defined to be the combination of a newly diagnosed fever, a temperature >38.5°C, and raising cholestasis parameters. The definition for bleeding is composed of the following criteria: any transfusion of packed red cells or need for any post-interventional haemostasis. Bleeding immediately following EST was not recorded as complication. A perforation had to be proven using plain X-ray or computed tomography scans.

2.4. Statistical Analysis

Statistical analysis was performed using contingency tables. Pearson`s chi-square test was calculated in order to assess dependencies between categorical risk factors and complications of EST. In the case of ordered categories the Cochran-Armitage test for trend was used instead. P-values <0.05 were assumed to indicate statistical significance. All variables that showed univariate significant associations with complications including pancreatitis, cholangitis, bleeding, and perforation were entered into a logistic regression model (multivariate analysis).

Table 1. Overall and specific post-interventional complications of EST.

Complications	n (Percentage of 471 ESTs)	Percentage of complications
Mild/moderate pancreatitis	22 (4.7%)	50.00
Severe pancreatitis	4 (0.8%)	9.10
Bleeding	10 (2.1%)	22.72
Perforation	6 (1.3%)	13.63
Cholangitis	2 (0.4%)	4.55
Total	44 (9.3%)	100

3. Results

During the period of 2 years EST was performed in 512 of 822 ERCPs. Sphincterotomy of the minor papilla (3), septotomy of the pancreatic duct (20), multiple ESTs (8), and repeated ESTs in the same patient (10) were not recorded. Thus, 471 ESTs of the common bile duct were analysed (47.5% males; 52.5% females). The age of patients varied between 14 and 96 years (median 66 years). Regarding the state of general health (ASA classification [American Society of Anaesthesiology]), 31.8% of patients had ASA I classification, 46.9% ASA II, 17% ASA III, and 0.6% ASA IV.

Choledocholithiasis and malignancy of the pancreaticobiliary system were the two most common indications for EST, 51% and 22%, respectively. Other indications consisted of biliary pancreatitis in 11% and other in 16%. ´Sphincter of Oddi dysfunction´ (SOD) represented 2.1% of all indications.

Out of the total of 471 procedures, 10 ESTs were performed by the trainee (during 4 months in 2007). The other four operators performed between 20 and 165 ESTs within that time period.

The interquartile range of prospective post-interventional follow-up was 7 to 29 days (median 16 days).

3.1. Incidence of complications

In our study the rate of overall post-interventional complications was 9.3% (44/471) (Table 1). The most common post-interventional complications were pancreatitis (50%) and bleeding (22.72%) (Table 1). Major and minor complications happened in 4.2% and 5.1% of all ESTs, respectively. 4.7% of all patients (22/471 ESTs) suffered from mild/moderate post-interventional pancreatitis (Table 1). All patients with mild and moderate post-interventional pancreatitis were managed conservatively (fasting, volume therapy, no antibiotics) without intensive care. Only 0.8% (4/471 ESTs) of all patients (3 females, 1 male; median age 51 years [40-72]; three patients with ASA III, one patient with ASA I) suffered from severe post-interventional pancreatitis. In all cases, ERCP was described as difficult (two with precuts, all with staining of the pancreatic duct). In two cases, a prophylactic pancreatic stent was inserted. The median CRP was 260 mg/l (180-430), the median length of hospital stay was 18 days (10-60), and the median stay in intensive care unit was 8 days (5-28). One patient developed necrotizing pancreatitis. All patients survived.

The rate of overall complications varied between 3.5% and 12.5% among the operators but did not significantly differ between operators in general (p=0.292), or between the trainee and the experienced interventional endoscopists (p=0.923). The trainee had one moderate pancreatitis out of 10 procedures. The occurrence of pancreatitis varied between 0% and 10.7% among the other operators. No more than one cholangitis was observed per operator. Perforations varied between 0 and 5%.

13 patients (2.8%) died after EST, but these deaths were not related to the procedure itself (Table 2). Death was caused by either underlying end stage cancer disease or severe inflammatory disease (cholangiosepsis or severe biliary pancreatitis) that already existed beforehand (Table 2). In one case with treated cholangitis, a fulminant lung embolism happened 38 days after EST. In another patient with known liver cirrhosis, EST was performed to gain bile drainage suspecting cholangiocarcinoma. Later, the patient was diagnosed with hepatocellular carcinoma, developed liver failure with hepatorenal syndrome, and died. The death was not related to EST.

3.2. Univariate analysis

Complications were analysed with regard to various variables, including patient`s health state (ASA classification), antiplatelet therapy, anatomic circumstances, indication, sedation, precut, and opacification of the pancreatic duct. The main findings are shown in Tables 3 and 4. The variables ‘antiplatelet and heparin therapy,’ ‘papilla only in lateral view,’ and ‘precut’ were significantly associated with overall complication rates of EST (p=0.041, p=0.0005, and p=0.013, respectively) (Table 3).

Table 2. Cases of death not related to ERCP/EST.

No.	Age (y)	Sex m/f	ASA (0-IV)	Underlying condition	ERCP	Clinical course	Cause of death	Interval EST to death (d)
1	49	m	II	Severe biliary necrotizing pancreatitis	Needle-knife EST without intubation due to massive duodenal oedema		Multiorgan failure	5
2	49	m	III	Severe biliary necrotizing pancreatitis	EST	Intensive care unit Hemofiltration Rhythmogenic instability	Heart failure	9
3	56	m	III	Cholanciocarcinoma with multiple liver and pulmonary mets	EST and Cotton stent insertion in CBD		Sepsis	6
4	70	f	II	Acute biliary pancreatitis	EST; no stones	Severe necrotizing pancreatitis, abdominal compartment syndrome (laparotomy, decompression of small and large bowel)	Multiorgan failure	41
5	71	m	III	Suspicion of cholangiocarcinoma Known liver cirrhosis CHILD C	EST; intermittent intrainterventional bleeding with endoscopic hemostasis	Palliative care in decompensated liver cirrhosis; diagnosis of hepatocellular carcinoma after MRI re-evaluation	Liver failure with hepatorenal syndrome	10
6	75	m	III	Biliary sepsis; obstruction by multiple liver metastases (colonic cancer)	Successlessdrainage	PTC not performed due to fulminant metastases	Sepsis and malignancy	10
7	76	m	II	Cholangiosepsis	EST	Multiorgan failure	Sepsis	5
8	78 y	f	III	Biliary leakage after laparoscopic cholecystectomy with gangraenous cholecystitis	Precut and EST	Suspicion of duodenal perforation;Laparotomy showing necrotizing pancreatitis. Closure of cystic duct, drainage	Severe bronchopneumonia	23
9	79	m	III	Pancreatic carcinoma	EST and Cotton stent insertion in CBD	Planned Whipple-intraoperatively gastrojejunostomy (small bowel ileus)	Postoperative severe bilateral pneumonia with septic shock	11
10	79	f	II	Cholangiosepsis and cholecystitis with septic shock, cystoduodenal fistula	Precut, EST	Conservative treatment without intensive care unit (due to the age of the patient).	Sepsis with renal and respiratory failure	1
11	84	m	II	Endstage pancreatic head carcinoma	EST and metal stent insertion in CBD	Acute on chronic renal failure; no hemofiltration due to age and malignancy with poor prognosis	Malignancy	24

continued Table 2. Cases of death not related to ERCP/EST.

12	85	f	IV	Cholangiosepsis and cholecystitis	EST; stone retraction	Postsurgical resuscitation Multiorgan failure (intensive care unit)	Sepsis	1
13	85	f	III	Cholangitis (stones)	EST and stone retraction	Fulminant lung embolism	Lung embolism	38

A poorer state of health (ASA) was not associated with a higher complication rate (ASA I representing healthy individuals compared to ASA II and ASA III, p= 0.215 and p=0.986, respectively) (Table 3). Patients with pancreatobiliary malignancy as an indication for EST were not exposed to higher risk of overall complications than those with choledocholithiasis (p=0.459).

3.2.1. Pancreatitis

Singular opacification of the pancreatic duct within the caudal part of the pancreas was associated with a significantly increased risk of pancreatitis (p= 0.00008), whereas singular opacification of the duct limited to the pancreatic head or body had no significantly raised risk (p=0.461 and p=0.644, respectively) (Table 4). Opacification of the pancreatic duct within the pancreatic head more than two times and already twice within the body respectively was associated with the significant risk of pancreatitis (p=0.041 and p=0.009, respectively) (Table 4).

In 25.9% of all ESTs, a prophylactic pancreatic stent was inserted. The rate of post-interventional pancreatitis did not differ significantly (6.6% with a pancreatic stent versus 5.2% without; p=0.56). The number of pancreatic duct opacifications was significantly higher in ESTs with inserted pancreatic stents than in ESTs without stents (p for trend 0.011). In the entire group of patients, the pancreatic duct opacification was significantly more extensive (tail versus head) in ESTs with inserted pancreatic stents than in ESTs without (p=0.009). The comparison of patients with prophylactic pancreatic stent versus no stent in the subgroup that had pancreatic duct opacification, showed that the pancreatitis rate was slightly higher in the stent group (9.2% versus 7.7% in the non-stent subgroup). This difference was not statistically significant (p=0.7). The total number of cases was too low to calculate whether the extent or number of duct opacification would be significant.

There were significantly more patients under the age of 65 with pancreatitis than above the age of 65 (9.4% and 3.1%, respectively; p=0.004).

3.2.2. Bleeding

Statistically significant raised rates of bleeding were seen with the combination of antiplatelet and heparin therapy (p=0.007) and the situation that the papilla could only be viewed partially in a lateral view (p=0.00002).

In 7% of all EST, immediate bleeding following the procedure occurred. These bleedings were not recorded as complications since at the end of the examination they were stopped mostly by epinephrine injection. The incidence of post-interventional bleeding was 3-fold higher in cases with immediate bleeding than without (6.1% and 1.9%, respectively), but this finding was not statistically significant (p=0.11).

3.3. Multivariate analysis

All variables that showed univariate significant associations with complications including pancreatitis, cholangitis, bleeding, and perforation were entered into a logistic regression model (multivariate analysis). 'Papilla only in lateral view' remained highly significant (p=0.001) predictive for complications revealing an odds ratio of 24.0 (95%CI 4.4-131.2). The use of antiplatelet/heparine therapy was significant as well (p=0.024) and its risk for complications was estimated to be 2.7 fold (95%CI 1.1-6.4). Risk for complications of opacification up to the pancreatic tail remained significantly elevated (p=0.001) (odds ratio = 5.7, 95%CI 2.0-16.2) in the multivariate analysis. The precut failed to show a significant effect (p=0.41).

3.4. Success rate

The primary success rate of EST was 95.1%. Without the precut, the rate was 98.4% (Table 3). In Table 3 rates of successful EST are listed for all analysed variables. The primary success rate in cases with normal anatomy was 97.3%. The main reasons for failure were anatomic circumstances (e.g. Billroth II gastric resection and papilla in diverticula; success rate 66.6% and 88.2%, respectively) or a papilla, which could only be focused laterally (success rate 85.7%). The success rate was slightly lower in patients with malignancy of the pancreaticobiliary tract (91.3%) than in patients with

Table 3. Association between various variables and complications and primary success.

	Number of EST	Primary sucess	Complications	Pancreatitis	Bleeding	Cholangitis	Perforation
Total	471 (100%)	448 (95.1%)	44 (9.3%)	26 (5.5%)	10 (2.1%)	2 (0.4%)	6 (1.3%)
Health condition (ASA) +							
ASA I	150 (31.8%)	145 (96.7%)	17 (11.3%)	10 (6.7%)	3 (2.0%)	1 (0.7%)	3 (2.0%)
			reference	reference	reference		
ASA II	221 (46.9%)	211 (95.5%)	16 (7.2%)	10 (4.5%)	4 (1.8%)	0	2 (0.9%)
			p=0.215	p=0.396	p=0.896		
ASA III	80 (17%)	73 (91.2%)	9 (11.3%)	5 (6.3%)	2 (2.5%)	1 (1.3%)	1 (1.3%)
			p=0.986	p=0.909	p=0.808		
ASA IV	3 (0.6%)	3 (100%)	0	0	0	0	0
Heparin /antiplatelet							
none	414 (87.9%)	394 (95.2%)	34 (8.2%)	23 (5.6%)	7 (1.7%)	0 reference	4 (1.0%)
			reference	reference	reference		reference
antiplatelet	39 (8.3%)	38 (97.4%)	6 (15.4%)	1 (2.6%)	2 (5.1%)	2 (5.1%)	1 (2.6%)
			p=0.178	p=0.444	p=0.155	p=0.007	
heparin	13 (2.8%)	12 (92.3%)	2 (15.4%)	1 (7.7%)	0	0	1 (7.7%)
			p=0.413	p=0.757			p=0.033
antiplatelet and heparin	5 (1.1%)	4 (80%)	2 (40%)	1 (20%)	1 (20%)	0	0
			p=0.041	p=0.220	p=0.007		
Anatomy							
Normal anatomy	366 (77.7%)	356 (97.3%)	29 (7.9%)	19 (4.0%)	6 (1.6%)	1 (0.3%)	3 (0.8%)
			reference	reference	reference		reference
Abnormal anatomy	105 (22.3%)	92 (87.1%)	15 (14.9%)	7 (6.9%)	4 (3.9%)	1 (1.0%)	3 (3.0%)
			p=0.076	p=0.582	p=0.185		p=0.107
Papilla in diverticula	17 (3.6%)	15 (88.2%)	3 (17.6%)	0	1 (5.9%)	1 (5.9%)	1 (5.9%)
			p=0.210		p=0.218		p=0.052
Billroth II	3 (0.6%)	2 (66.6%)	0	0	0	0	0
Papilla only in lateral view	7 (1.5%)	6 (85.7%)	4 (57.1%)	2 (28.6%)	2 (28.6%)	0	0
			p=0.0005	p=0.022	p=0.00002		
Indication							
Choledocholithiasis	238 (50.5%)	231 (97.1%)	25 (10.5%)	13 (5.4%)	7 (2.9%)	2 (0.8%)	3 (1.3%)
			reference	reference	reference	reference	reference
Acute biliary pancreatitis	50 (10.6%)	44 (88%)	1 (2.0%)	0	0	0	1 (2.0%)
			p=0.073				
Malignant tumour	104 (22.1%)	95 (91.3%)	8 (7.6%)	6 (5.8%)	2 (1.9%)	0	0
			p=0.459	p=0.914	p=0.597		
Sphincter of Oddi dysfunction	10 (2.1%)	10 (100%)	2 (20%)	1 (10%)	0	0	1 (10%)
			p=0.414	p=0.572			p=0.041
Loss of bile stones with	24 (5.1%)	21 (87.5%)	5 (20.8%)	4 (16.6%)	0	1 (4.2%)	0
gallbladder in situ			p=0.192	p=0.056		p=0.154	
Other indications	68 (14.4%)	67 (98.5%)	8 (11.8%)	6 (8.8%)	1 (1.5%)	0	1 (1.5%)
			p=0.791	p=0.345	p=0.512		
Precut							
yes	75 (15.9%)	58 (77.3%)	13 (17.3%)	9 (12%)	1 (1.3%)	1 (1.3%)	2 (2.7%)
			p=0.013	p=0.007	p=0.586		p=0.159
none	382 (81.1%)	376 (98.4%)	28 (7.3%)	15 (3.9%)	9 (2.4%)	1 (0.3%)	3 (0.8%)
			reference	reference	reference		reference

+ *In 17 cases (3.6%) ASA classification was not stated.*

Table 4. Association between extensiveness of pancreatic duct opacification and general complication and pancreatitis.

Pancreatic duct opacification	Number	Complications	Pancreatitis
none	208 (44.2%)	12 (5.8%) reference	4 (1.9%) reference
Pancreatic head 1 x	55 (11.7%)	2 (3.6%) p=0.550	2 (3.6%) p=0.461
Pancreatic head 2 x	39 (8.3%)	4 (10.3%) p=0.334	1 (2.6%) p=0.798
Pancreatic head >2 x	20 (4.2%)	4 (20%) p=0.035	2 (10%) p=0.041
Pancreatic body 1 x	31 (6.6%)	3 (9.7%) p=0.438	1 (3.2%) p=0.644
Pancreatic body 2 x	25 (5.3%)	4 (16%) p=0.085	3 (12%) p=0.009
Pancreatic body >2 x	14 (3.0%)	3 (21.4%) p=0.046	3 (21.4%) p=0.0002
Pancreatic tail 1 x	6 (1.3%)	3 (50%) p=0.0009	2 (33.3%) p=0.00008
Pancreatic tail 2 x	14 (3.0%)	2 (14.3%) p=0.249	2 (14.3%) p=0.010
Pancreatic tail >2 x	20 (4.2%)	3 (15%) p=0.150	3 (15%) p=0.002
No statement	39 (8.3%)	4 (10.3%) p=0.334	3 (7.7%) p=0.057

Table 5. Complication rates of endoscopic sphincterotomy in literature.

Author	N	Data collection	Complications	Pancreatitis	Bleeding	Cholangitis	Perforation	Lethality	Mortality
Andriulli (Metaanal.) [2007]	16855	1977-2006	6.85%	3.47%	1.34%	1.44%	0.60%		0.33%
Barthet [2002]	658	1996-2000	7.70%	3.50%	1.20%	sepsis 1.2%	1.80%	0.90%	n.s
Freeman [1996]	2347	1992-1994	9.80%	5.40%	2.00%	1.50%	0.30%	0.40%	2.30%
Kapral [2008]	3132	2006	11.20%	5.20%	3.70%	1.90%	0.50%		0.10%
Loperfido [1998]	1827	1992-1994	5.40%	1.60%	1.10%	1.10%	1.50%	0.50%	1.40%
Rabenstein [1998]	438	1994-1996	7.50%	4.30%	2.30%	0.90%	0%	0.50%	6.40%
Sulz	471	2005-2007	9.30%	5.50%	2.10%	0.40%	1.30%	0.20%	2.80%
Wang [2009]	2691	2006-2007	7.92%	4.30%	1.41%	1.41%	0.26%		0.26%
Williams [2007]	5264	2004	5.10%	1.50%	0.90%	1.10%	0.40%		0.40%
Zinsser [1999]	861	1990-1994	15.70%	5.90%	3.50%	4.40%	0.60%	0.10%	n.s

choledocholithiasis (97.1%). Regarding the type of indication, a lower primary success rate could be found in patients with acute pancreatitis (88%).

4. Discussion

Quality assurance becomes an increasingly important part of modern clinical medicine and the field of interventional endoscopy, like ERCP [10,11]. In 2006, a list of quality end-points for ERCP was proposed by the ASGE/ACG taskforce on quality in endoscopy [7]. The impact of quality measurements on clinical routine in ERCP was reflected by Williams et al. [8], who reported the most complete survey on the current quality of ERCP practise in the United Kingdom. The survey revealed an important deficit in the overall quality of ERCP practise. Recently, a prospective nation-wide benchmarking project for ERCP was performed in Austria [6]. It is encouraging to improve fair and open-minded prospective quality assurance in ERCP on national and even international levels. To the best of our knowledge there are currently no published data regarding quality assurance and outcome assessment of EST in Switzerland. Therefore, we prospectively assessed the quality and outcome of EST at our tertiary referral centre to set an objective basis for benchmarking with other national and international ERCP clinics by using a prospective electronic database registry. The advantage of such a registry for other ERCP clinics would be an easy and objective comparison of databases.

The overall complication rate of 9.3% in our trial matches with those in various international trials varying between 5.1% and 15.7% (Table 5) [3,6,8,12-17]. The heterogeneity in reported rates of complications most likely reflects differences in patients` characteristics, endoscopists` skills and experience, and procedural complexity. For example, the number of patients with suspected SOD could influence the rate of post ERCP pancreatitis. In our study, the proportion of suspected SOD was very small (2.1%). The overall rate of pancreatitis was 5.5%. Cheng and co-workers [18] published an overall pancreatitis rate of 15.1% but their survey contained a high proportion of suspected SOD (33.9%). In previous prospective large-scale risk factor

studies, the proportion of SOD patients was usually less than 10% [3,19-23].

Differences in definitions of complications may also play a certain role. For example, Zinsser et al. [17] defined adrenaline injection in case of immediate peri-interventional bleeding as a complication, resulting in a higher rate of bleeding complications (3.5%). In contrast, immediate bleeding was not considered to be a complication in most other studies, including ours. Standardised definitions for complications would be preferable to compare results of different trials. Therefore, we referred to definitions proposed by Cotton et al. [9] regarding post-interventional pancreatitis.

A variety of patient-related and procedure-related factors implicated in complications of EST have already been reported in several single- and multi-centre prospective large series of patients [3,13,15,18,22]. Pancreatic contrast injection was an independent risk factor for post ERCP-pancreatitis in many previous studies [14,18,19,21,23,25]. Our study is the first report to reveal, using multivariate analysis, that the extent of pancreatic duct opacification is crucial regarding the potential risk of pancreatitis. Singular opacification of the duct up to the pancreatic tail was associated with a significantly increased risk of pancreatitis, whereas singular opacification of the duct limited to the pancreatic head had no elevated risk.

It is already known that repeated opacification of the pancreatic duct is associated with pancreatitis. We found that repeated opacification of the pancreatic duct within the head of more than two times raised the risk of pancreatitis significantly in univariate analysis. The same was true for opacification of the pancreatic body. However, two opacifications were already enough to increase the risk of pancreatitis significantly. Freeman et al. [19] found that one or more injections of contrast into the pancreatic duct were a multivariate risk factor with an adjusted odds ratio of 2.7. Andriulli et al. [22] reported that more than three pancreatic injections were predictive for post ERCP-pancreatitis in multivariate analysis. In the multi-centre study by Wang et al. [15], this factor was significant only in univariate analysis. A possible explanation for these findings is that the frequent use of guidewire cannulation in their procedures minimized unintentional injections into the wrong duct, but we did not look at the possible influence of single or multiple guidewire cannulations of the pancreatic duct. In the future the number of guide-wire cannulations of the pancreatic duct should be recorded because it is possible that this factor could also lead to a pancreatitis.

Previous randomized, controlled trials [26-28] and a meta-analysis [29] demonstrated that pancreatic stents were beneficial in reducing the incidence of pancreatitis in patients who are at high risk for this complication. However only one study [27] of the meta-analysis [29] used multivariate analysis. In the other studies, multivariate analyses of data were not reported. The sample size of included studies varied from 74 to 130 patients (38–46 patients in the stent groups). In our single centre study with a sample size of 471 ESTs (25.8% with pancreatic stents), the rate of post-interventional pancreatitis was not significantly decreased by the insertion of prophylactic stents (p=0.56). However, the number of pancreatic duct opacification was significantly higher in ESTs with inserted pancreatic stents than in ESTs without (p for trend 0.011). Also, pancreatic duct opacification (head vs. tail) was significantly more extensive in ESTs with inserted pancreatic stents than in ESTs without (p=0.009). Operators, aware that the risk of pancreatitis in these cases could be elevated, might have decided to insert a pancreatic stent due to deep or multiple pancreatic duct opacification. The comparison of the subgroup with duct opacification showed no significant difference of pancreatitis rate in those with versus without pancreatic stent (p=0.7). However, the total number of cases was too low to calculate whether the extent or number of duct opacification would have a significant influence. The method of prevention of post ERCP-pancreatitis by use of prophylactic pancreatic stents was not confirmed in our study. This aspect will need to be studied separately in the future.

Other important risk factors for post ERCP-pancreatitis, such as suspicion of SOD, female aged <60 years, and precut-technique, failed to show statistical significance in our study probably due to low case volume.

The incidence of post-interventional bleeding was 3-fold higher in cases with immediate bleeding following EST than without (6.1% versus 1.9%). This difference, though statistically insignificant (p=0.11), shows a tendency that intra-interventional bleeding seems to be a predictive factor of post-interventional bleeding, as stated by Freeman et al. [3]. However, some confusion exists in the literature about immediate bleeding following EST and true haemorrhage as defined in Cotton's [9] classification. In Barthet's [13] series, there was no correlation between immediate bleeding and haemorrhage as defined by Cotton's [9] classification.

Anatomic conditions contributed its part to post-interventional bleeding. The bleeding rates under normal and abnormal anatomic conditions (billroth II gastric resection, papilla hidden in a diverticula) were 1.6% and 3.9%, respectively. This difference was a trend and not statistically significant (p=0.185). If only a lateral view of the papilla could be managed, the bleeding rate was

high (28.6%; p=0.00002). In our record, a precut was not associated with the higher incidence of bleeding (p=0.586) that was mentioned by others [30]. Whether this finding was due to different instrumentation or current settings could not be answered.

Interestingly, bleeding was not more frequent under heparin, but only under a combination of heparin and antiplatelet therapy (p=0.007) - contrary to the results of Akashi et al. and Amelsberg et al. [31,32]. However it must be stated that the number of patients with antiplatelet and heparin therapy (five patients) was low. Thus the results - even if significant - should be confirmed in larger surveys. The protective effect of low-dose anticoagulation against post-interventional pancreatitis suggested by Rabenstein et al. [16] could not be confirmed, but there were only few data of patients who received heparin.

Post-interventional cholangitis was quite rare in our data (0.4%) compared to others' (0.9-4.4%, Table 5). Our patients received routine antibiotic prophylaxis (Ceftriaxone) – if not already under sufficient antibiotic coverage prior to the procedure. In contrast, Zinsser et al. [17] administered antibiotics only in cases of clinical signs of infection resulting in a higher rate of cholangitis. We believe that the small number of cholangitis with antibiotic coverage justifies its administration.

Despite the careful approach perforations had to be documented in 1.3% of ESTs. Precut revealed a 3-fold raised rate of perforation (2.7% vs. 0.8%), but was not statistically significant (p=0.159). Two out of 6 perforations were documented in ESTs that required precuts. We believe that significance failed to be shown due to the small number of perforations. The frequency of precuts in our trial (15.9%) was comparable to other trials.

There are several limitations to this study. Regarding the methods, one could argue that since the time period between intervention and follow-up was not strictly defined, post-interventional complications of EST may have been underestimated. In our study, a certain level of flexibility of follow-up assessment was necessary due to practical purposes reflecting a registry which should be easy to use on a daily basis. Many outpatients were discharged from day-clinic on the day of intervention. In particular, this group of patients was seen by their GP for follow-up. This compromise was accepted since in case of complications, GPs in the surroundings inevitably refer the patients to us. Taking the time period of follow-up with an interquartile range of 7 to 29 days (median 16 days) into account, it seems unlikely that the bleeding rate is underestimated. For pancreatitis, perforation, or sepsis/cholangitis, symptoms are generally rapidly evident. Classic late complications such as papillary stenosis and recurrent stones are not awaited within our post-interventional observation period. For the same reason, it was logistically reasonable that, at the cost of consistency, follow-up assessments were not performed by only one or few persons.

The duration of cannulation before using precut was not revealed but might have had an impact on outcome. It is known that a long attempt of cannulation and manipulation of the papilla increase the risk of complications, especially pancreatitis. This aspect could be integrated in future trials.

A methodological problem was the fact that it was not prospectively defined in which situations a prophylactic pancreatic stent should be inserted or not. This aspect is a bias since each operator could choose arbitrarily to put a stent in the pancreatic duct or not. We know that this therapeutic intervention was performed if the ERCP was thought to be troublesome. On this basis it is difficult to analyze the outcome in relation to pancreatic stents. Nevertheless, it reflects the daily clinical decision in many centres and at least this policy does not seem to bring a clear advantage. Surely prospective criteria would have been much better and more exact.

A further limitation is that the sample size was fairly small in comparison with several large-scale multi-centre studies (Table 5). A pre-study calculation of sample size was not performed simply because of the concept of the registry. However, it must be stated that the systematic meta-analysis of prospective studies published recently by Andriulli et al. [12] revealed that outcome results were not different after sub-grouping single-centre versus multi-centre studies. The sample size of selected single-centre studies varied between 210 and 1233 patients, of which four studies had a size of <300 patients and six had a size of <500 patients. By comparison, our prospective single-centre study had a representative sample size.

In the long run we think that the shared use of this sort of prospective sphincterotomy studies will improve the statistical significance of the observations.

In summary, the outcome of EST in our clinic matches with large international trials. It was found that the extent of pancreatic duct opacification (tail versus head of pancreas) seems to be a risk factor for post-interventional pancreatitis. The placement of prophylactic pancreatic stents remains controversial. The shared use of a prospective database registry as tool of quality assessment of EST may facilitate an objective comparison as basis for benchmarking.

Disclosure Statement

All authors, Dr Michael C Sulz, Dr Markus Sagmeister, Dr Martin Schelling, Dr Janek Binek, Dr Jan Borovicka, Professor Hanno Ulmer, and Professor Christa Meyenberger have no conflicts of interest or financial ties to disclose.

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References

[1] Mc Cune WS, Shorb PE, Moscovitz H. Endoscopic cannulation of the ampulla of vater: a preliminary report. Ann Surg 1968;167:752-756

[2] Carr-Locke DL. Overview of the role of ERCP in the management of biliary tract and pancreas. Gastrointest Endosc 2002;56:157-60

[3] Freeman M, Nelson D, Sherman S, et. al. Complications of endoscopic biliary sphincterotomy. N Engl J Med 1996;335:909-18

[4] Freeman ML, Guda NM. ERCP cannulation: a review of reported techniques. Gastrointest Endosc 2005;61:113-125

[5] Costamagna G, Familiari P, Marchese M, et al. Endoscopic biliopancreatic investigations and therapy. Best Pract Res Clin Gastroenterol 2008;22:865-881

[6] Kapral C, Duller C, Wewalka F, et al. Case volume and outcome of endoscopic retrograde cholangiography: results of a nationwide Austrian benchmarking project. Endoscopy 2008;40:625-30

[7] Baron TH, Petersen BT, Mergener K, et al. Quality indicators for endoscopic retrograde cholangiopancreatography. Gastrointest Endosc 2006;63:29-34

[8] Williams EJ, Taylor S, Fairclough P, et al.; BSG Audit of ERCP. Are we meeting the standards set for endoscopy? Results of a large-scale prospective survey of endoscopic retrograde cholangio-pancreatograph practice. Gut 2007;56:821-829

[9] Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc 1991;37:383-93

[10] Bjorkman DJ, Popp Jr. JW. Measuring the quality of endoscopy. Am J Gastroenterol 2006;101:864-865

[11] Faigel DO, Pike IM, Baron TH, et al. ASGE/ACG Taskforce on Quality in Endoscopy. Quality indicators for gastrointestinal endoscopic procedures: an introduction. Am J Gastroenterol 2006;101:866-72

[12] Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol 2007;102:1781-8

[13] Barthet M, Lesarvre N, Desjeux A, et al. Complications of endoscopic sphincterotomy: results from a single tertiary referral center. Endoscopy 2002;24:991-7

[14] Loperfido S, Angelini G, Benedetti G, et al. Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. Gastrointest Endosc 1998;48:1-10

[15] Wang P, Li Z-S, Liu F, et al. Risk factors for ERCP-related complications: a prospective multicenter study. Am J Gastroenterol 2009;104:31-40

[16] Rabenstein T, Schneider HT, Hahn EG, et al. 25 years of endoscopic sphincterotomy in Erlangen: Assessment of the experience in 3498 Patients. Endoscopy 1998; 30 Suppl 2:A194-A201

[17] Zinsser E, Hoffmann A, Will U, et al. Success and complication rates of diagnostic and therapeutic endoscopic retrograde cholangiopancreatography - a prospective study. Z Gastroenterol 1999;37:707-713

[18] Cheng CL, Sherman S, Watkins JL, et al. Risk factors for post-ERCP pancreatitis: A prospective multicenter study. Am J Gastroenterol 2006;101:1390-147

[19] Freeman ML, DiSario JA, Nelson DB, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. Gastrointest Endosc 2001;54:425-34

[20] Vandervoort J, Soetikno RM, Tham TCT, et al. Risk factors for complications after performance of ERCP. Gastrointest Endosc 2002;56:652-6

[21] Friedland S, Soetikno RM, Vandervoort J, et al. Bedside scoring system to predict the risk of developing pancreatitis following ERCP. Endoscopy 2002;34:483-8

[22] Andriulli A, Clemente R, Solmi L, et al. Gabexate or somatostatin administration before ERCP in patients at high risk for post-ERCP pancreatitis: a multicenter, placebo-controlled, randomized clinical trial. Gastrointest Endosc 2002;56:488-95.

[23] Masci E, Toti G, Mariani A, et al. Complications of diagnostic and therapeutic ERCP: a prospective multi center study. Am J Gastroenterol 2001;96:4417-4423

[24] Manes G, Di Giorgio P, Repici A, et al. An analysis

of the factors associated with the development of complications in patients undergoing precut sphincterotomy: a prospective, controlled, randomized, multicenter study. Am J Gastroenterol 2009;104:2412-2417

[25] Mehta SN, Pavone E, Barkun JS, et al. Predictors of post-ERCP complications in patients with suspected choledocholithiasis. Endoscopy1998;30:457-63

[26] Fazel A, Quadri A, Catalano MF, et al. Does a pancreatic duct stent prevent post-ERCP pancreatitis? A prospective randomized study. Gastrointest Endosc 2003;57:291-4

[27] Tarnasky PR, Palesch YY, Cunningham JT, et al. Pancreatic stenting prevents pancreatitis after biliary sphincterotomy in patients with sphincter of Oddi dysfunction. Gastroenterology 1998;115:1518-24

[28] Aizawa T, Ueno N. Stent placement in the pancreatic duct prevents pancreatitis after endoscopic sphincter dilation for removal of bile duct stones. Gastrointest Endosc 2001;54:209-13

[29] Singh P, Das A, Isenberg G, et al. Does prophylactic pancreatic stent placement reduce the risk of post-ERCP acute pancreatitis? A meta-analysis of controlled trials. Gastrointest Endosc 2004;60:544-50

[30] Ponchon T, Pilleul F. Diagnostic ERCP. Endoscopy 2002;34:29-42

[31] Akashi R, Kiyozumi T, Tanaka T, et al. Mechanism of pancreatitis caused by ERCP. Gastrointest Endosc 2002;55:50-54

[32] Amelsberg A, Fölsch UR. Complications in endoscopic papillotomy. Z Gastroenterol 1997;35:1111-1114