Part II, Section 3: Outcomes Of Treatment Using ERCP For Palliation of Pancreaticobiliary Malignancy – Comparison Of Strategies Using ERCP, Surgery, Or Interventional Radiology; A. Comparison of ERCP stent versus surgical bypass

Palliation of malignant biliary obstruction: ERCP endoprosthesis compared with surgical bypass
A. Prospective Randomized Controlled Trials

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Andersen, Sorensen, Kruse et al., 1989	50	50 pts with extrahepatic low biliary obstruction and jaundice Age>60y Pancreatic = 43 Biliary = 7 Both 7Fr and 10Fr stents were used in this study, predominantly 7Fr	**Survival (days),** median (range) Intent-to-treat ERCP (n=25): 84 (3-498) Surgery (n=25): 100 (10-642) Life-table analysis = n.s. Treatment received ERCP (n=30): 81 (3-564) Surgery (n=19): 108 (20-642) Life-table analysis = n.s. **Treatment failures** ERCP: 1 pt failed and treated with surgery Surgery: 3 patients failed at 13-53 days postop and treated successfully with ERCP (no statistical comparison reported) **Hospitalization (days),** median (range)[1] ERCP (n=25): 26 (3-210) Surgery (n=25): 27 (10-202) p=n.s. **Quality of life ratings, % survival time** mean (range): ERCP / Surgery Normal activity 21 (0-86) / 20 (0-91) Limited activity, No aid 36 (0-95) / 31 (0-80) Limited Activity, Aid needed 8 (0-100) / 14 (0-100) Bedridden 19 (0-100) / 18 (0-100) Massive aid needed 16 (0-100) / 17 (0-100) p = n.s.	**Perioperative death (≤ 30 days)** ERCP = 5 (20%) Surgery = 6 (24%) p=n.r. **Complications[2]** Cholangitis (%) ERCP = 28 Surgery = 16 p=n.r. Abscess (%) ERCP = 8 Surgery = 4 p=n.r. Total Severe Infection (%) ERCP = 36 Surgery = 20 p= n.s.	

[1] Comparison of hospital stay was not statistically significantly different when analyzed by treatment received.
[2] Comparison of infectious complication rates by treatment received was ERCP = 30% and surgery = 20%, which was not statistically significant

Palliation of malignant biliary obstruction: ERCP endoprosthesis compared with surgical bypass
A. Prospective Randomized Controlled Trials (cont'd)

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Shepherd, Royal, Ross et al., 1988	52	Pts w/ malignant distal CBD obstruction Randomized: ERCP stent (n=27) Surgical bypass (n=25) Results: ERCP stent (n=23) Surgical bypass (n=25) Baseline characteristics mostly comparable 10 Fr ERCP stents used	**Overall Survival (days),** median (range) ERCP 152 (39-411) Surgery 125 (52-354) Life table analysis=n.s. **Initial Hospitalization (days)**[3], median (range) ERCP (n=23) 5 (2-16) Surgery (n=25) 13 (8-49) p<0.002 **Readmission to Hospital** N (%) ERCP (n=23) 10 (43%) Surgery (n=25) 3 (12%) p=n.r. **Total Hospital stay (days),** median (range) ERCP 8 (2-30) Surgery 13 (8-49) p<0.01 **Relief of jaundice** ERCP (n=23) 21 (91%) Surgery (n=25) 23 (92%) p=n.r.	**Perioperative mortality** ERCP (n=23) 2 (9%) Surgery (n=25) 5 (20%) p=n.s. **Procedural complications, events** ERCP (n=23) 7 Surgery (n=25) 14 p=n.s. **Development of duodenal stenosis** ERCP 2 (9%) Surgery 1 (4%) p=n.r.	

[3] Calculated only in patients who were alive at 30 days postop

Palliation of malignant biliary obstruction: ERCP endoprosthesis compared with surgical bypass
A. Prospective Randomized Controlled Trials (cont'd)

Smith, Dowsett, Russell et al., 1994	204	Pts with probable malignant low bile duct obstruction ERCP[4] (n=101) Surgery (n=103) 10 Fr stents Baseline characteristics comparable	**Survival** (weeks), median ERCP (n=99) 21 Surgery (n=100) 26 p=n.s. **Technical Success** ERCP (n=100) 95 (95%) Surgery (n=101) 94 (94%) p=n.s. **Therapeutic success**[5] ERCP 92% Surgery 92% p=n.s. **Total Hospitalization** (days), median (range) ERCP (n=100) 19 (4-59) Surgery (n=101) 26 (8-85) p=n.s. **Recurrent obstructive jaundice** ERCP (n=100) 36 Surgery (n=101) 2 p=n.s.	**Perioperative Mortality** ERCP (n=100) 8% Surgery (n=101) 15% p=n.s. **Procedure-related Mortality** ERCP (n=100) 3 (3%) Surgery (n=101) 14 (14%) P=0.006 **Major Complications** ERCP (n=100) 11 (11%) Surgery (n=101) 29 (29%) p=0.02 **Minor Complications** ERCP (n=100) 18% Surgery (n=101) 29% p=n.s. **Late Gastric Bypass** ERCP (n=100) 10 Surgery (n=101) 5 p=n.s.	

[4] Stent placement was attempted first with ERCP approach. In 19 patients, a combined percutaneous transhepatic-endoscopic approach was required when initial ERCP failed.
[5] Defined as "a fall in serum bilirubin of at least 20% within 5 days in patients who had a successful procedure (in most patients confirmatory ultrasound evidence of biliary decompression was also obtained". Note data in study Table 3 does not agree with text.

Palliation of malignant biliary obstruction: ERCP endoprosthesis compared with surgical bypass

B. Retrospective studies

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Raikar, Melin, Ress et al., 1996	66	All pts had pancreatic carcinoma 34 ERCP stent 32 surgical bypass **Baseline Characteristics** No significant differences ERCP Surgery Age 72 (44-100) 69 (43-85) Mean PS 0.8 0.9 PS 0,1 79% 59% PS 2 9% 34% PS 3 12% 6% 10-12 Fr stents	**Survival (months),** mean (range) ERCP 9.7 (10d-35) Surgery 7.3 (7d-29) p=0.13 **Hospitalization (days), mean** ERCP 7 Surgery 14 p<0.001 **Rehospitalization (pts)** ERCP 12 Surgery 8 **Initial + Subsequent Costs** ERCP 17,738 Surgery 25,101 p<0.05	**Perioperative mortality** ERCP 1 (2.9%) Surgery 1 (3.5%) **Perioperative morbidity** ERCP 21% Surgery 33% p=n.s.	

Palliation of malignant biliary obstruction: ERCP endoprosthesis compared with surgical bypass

B. Retrospective studies

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Leung, Emergy, Cotton et al., 1983	98	Pts w/ malignant obstructive jaundice 64 ERCP stent 34 Surgical bypass **Baseline Characteristics** Statistical comparisons not reported ERCP Surgery Age 68 (35-91) 60 (25-73) Age>70y 44% 9% Location: Hilum/CHD 30% 3% CBD 14% 6% Pancreatic head 55% 85% Papilla 1.5% 6% 8-10 Fr stents	**Survival (months)** ERCP and Surgery both had median survival approximately 6 months. Not significantly different. **Technical Success** ERCP 89% Surgery 100% p=n.r. **Initial Hospitalization** (days), mean ERCP 14 (4-30) Surgery 30 (14-79) p=n.r.	**Perioperative Mortality** ERCP 10 (16%)[6] Surgery 3 (9%)[7] **Readmission for local complication**[8] ERCP 8 (13%) Surgery 3 (9%)	

[6] Causes of death include 4 metastases, 1 renal failure, 3 cholangitis, 1 pneumonia, 1 strangulated hernia

[7] Causes of death include 1 arterial thrombosis and 2 unknown.

[8] Local complications included cholangitis, recurrent jaundice, duodenal obstruction, or chest wall metastasis.

Part II, Section 3B. Studies comparing metal versus plastic stents to relieve biliary obstruction due to pancreaticobiliary malignancy

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Randomized Controlled Trials					
Davids, Groen, Rauws et al., 1992	105	Patients with irresectable distal bile-duct malignancy Pancreatic ca = 93 Papillary ca = 12 49 metal stent 56 straight polyethylene (poly) stent Baseline Characteristics Well-balanced	**Overall median survival (days)** Metal 175 Poly 147 p=0.45 **Median Patency of 1st stent (days)** Metal 273 Poly 126 p=0.006 **Occlusion rate for secondary poly stents** [9] Metal 0/14 (0%) Poly 11/23 (48%)[10] p=0.002 **Successful initial drainage** Metal 47/49 (96%)[11] Poly 53/56 (95%)[12] **Resource utilization** **Need for additional ERCP** Metal 64 Poly 102 p=n.r. Initial placement of a metal stent in 100 patients would prevent 50 ERCP procedures	**Perioperative mortality** Metal 7 (14%)[13] Poly 2 (4%)[14] p=0.047 **Early complications**[15] (7 days) Metal 6 (12%) Poly 6 (11%)	In the metal-stent group only, univariate analysis showed association between decreased stent patency and jaundice > 14 days before stent (p=0.01) as well as bilirubin > 300 μmol/L (p=0.03)

[9] All second stents implanted for occlusion were polyethylene stents
[10] Six patients required a 3rd stent after a median of 109 days. Three and two patients required and 4th or 5th stent, respectively.
[11] In 1 patient jaundice eventually subsided. The other patient died 11 days after stent placement, and autopsy revealed proximal kinking of the stent.
[12] Jaundice slowly subsided in all 3 patients.
[13] Causes of death were sepsis after recurrent cholangitis (1); cardiac failure (2); cachexia (4).
[14] Causes of death were cachexia (2).
[15] The incidence of mild cholangitis was similar between groups (6 metal; 5 poly). One poly stent patient developed cholecystitis.

Part II, Section 3B. Studies comparing metal versus plastic stents to relieve biliary obstruction due to pancreaticobiliary malignancy (cont'd)

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Randomized Controlled Trials					
Prat, Chapat, Ducot et al., 1998	101	Patients with malignant CBD strictures Not involving hilum Pancreatic ca = 65 Cholangioca = 21 Ampullary ca = 3 Metastatic = 12 Group 1 (n=33) 11.5Fr polyethylene stent, exchanged for dysfunction Group 2 (n=34) 11.5Fr polyethylene stent, exchanged every 3 months Group 3 (n=34) Self-expanding metal stent Baseline characteristics comparable	**Median survival (months)** Group 1 4.8 Group 2 5.6 Group 3 4.5 p=n.s. **Stent Patency or Median symptom-free survival[16] (months)** Group 1 3.2* Group 2 not reported* Group 3 4.8* * $p < 0.05$ comparing Group 1 with combined Groups 2 and 3. No significant difference between Group 2 and 3. **Bilirubin level reduction in 48 hours** Group 1 35.4% Group 2 34.3% Group 3 41% p=n.s. **Total Hospitalization (days)** Group 1 7.4 ± 1.5 Group 2 10.6 ± 1.7 $p_{2,3} = 0.01$ Group 3 5.5 ± 1.4 $p_{1,2}$ and $p_{1,3}$ = n.s. **Resource utilization** Total ERCP / ERCP per patient Group 1 57* / 1.7 ± 1.3 Group 2 85* / 2.5 ± 1.9 Group 3 40 / 1.2 ± 0.4 * $p_{1,2} = 0.05$ p=0.01, ANOVA	No significant difference in complications seen between groups. Overall procedure-related morbidity = 11.9% and mortality = 3.9%. **Proportion of mortality related to jaundice or sepsis** Group 1 11.5% Group 2 14.8% Group 3 7.4% p=n.s.	

[16] This was primary endpoint and defined as timespan between insertion of first stent and the first episode of stent dysfunction

Part II, Section 3B. Studies comparing metal versus plastic stents to relieve biliary obstruction due to pancreaticobiliary malignancy (cont'd)

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Randomized Controlled Trials					
Prat, Chapat, Ducot et al., 1998 (cont'd)	101		**Mean costs per patient (95% CI)** <u>Overall observed costs</u> Group 1 5547 (4082-7013) Group 2 6770 (5394-8146) Group 3 4643 (4207-5079) Overall cost advantage for group 3, p=n.r. <u>For pt surviving < 3months</u> Group 1 3715 Group 3 4246 (15% more than Group 1) <u>For pt surviving < 6 months</u> Group 1 4533 Group 2 4887 (8% more than Group 1 Group 3 4544 (same as group 1)		

Part II, Section 3B. Studies comparing metal versus plastic stents to relieve biliary obstruction due to pancreaticobiliary malignancy (cont'd)

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Retrospective Study					
Schmassmann, Von Gunten, Knuchel et al., 1996	165	Consec pts w/ irresect-able malignant biliary obstruction Initial stent placed: 95 metal stents ('92-93) 70 plastic stent ('90-91) Stent occlusion rx w/ plastic stent placement. Plastic stents were 14% 10 Fr and 86% 12 Fr Baseline characteristics were comparable for age, gender, bilirubin, type of tumor and stage, location of stricture, or associated procedures. 87% of metal stent and 100% of plastic stent patients had sphincterotomy.	**Median survival (months)**[17] Metal 6.5 Plastic 4 p<0.05 **Relief of jaundice after 3-5 weeks** Metal 95% Plastic 88% p = n.s. **Median patency of 1st stent (months)**[18] Metal 10 Plastic 4 p<0.001 **Median patency of 2nd stent, all plastic** (months) Metal initial 8 Plastic initial 3 p<0.05 **Resource utilization** Mean ERCP per patient Metal 1.2 Plastic 1.58 p<0.005 Thus, initial placement of metal stents in 100 patients would save 38 ERCP procedures.	**Perioperative Mortality** Metal 2% Plastic 3% p=n.s.	

[17] When 29 subjects (8 metal stent, 21 plastic stent) who died related to untreated stent dysfunction were excluded from the analysis, the remaining 136 subjects had similar survival between the two groups.

[18] Subgroup analysis did not show any significant difference between different locations (common bile duct vs. hilar or intrahepatic stricture) but numbers were small in the hilar and intrahepatic subgroups.

Part II, Section 4. Management of jaundice before surgical resection of pancreaticobiliary malignancy: Preoperative stent versus immediate surgery
A. Randomized Controlled Trials

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Lygidakis, van der Heyde, Lubbers et al., 1987	38	38 pts with resectable pancreatic head carcinoma Group A = 19 preop ERCP placed stent Group B = 19 w/o stent	**Laboratory values** Baseline: A / B; Preoperative: A / B WBC ** 9.3 / 8.2 / 14.6 / 9.1 Bilirubin * 18.4 / 19.2 / 11.5 / 20.1 Alk Phos* 895 / 689 / 498 / 697 AST/SGOT* 104 / 141 / 75 / 149 ALT/SGPT* 152 / 181 / 129 / 195 PT 3 / 3 / 3 / 3 Platelets 170 / 179 / 275 / 199 Clot time 75 / 76 / 65 / 71 * = significant reduction for Group A, p<0.002 ** = significant increase for Group A, p<0.001 Baseline / Postoperative Bile cult (+) 10 / 9 / 6 / 12 Blood cult (+) 4 / 5 / 1 / 6 Biliary pressure[19] -- / -- / 8 / 25 p<0.001 when all 3 correlated and combined No difference noted for hematocrit, creatinine, or albumin **Hospitalization (total days for group)** Preop / Postop / Combined Stent 135 / 304 / 439 No Stent 70 / 437 / 507 p=n.r.	**Perioperative Mortality** Stent = 0 No stent = 2 p=n.s. (1 sepsis, 1 aneurysm) **Perioperative morbidity** Stent = 3 No Stent = 14 p<0.005 **Peroperative Blood Loss** Stent = 800 ± 100 ml No Stent = 1800 ± 200 ml p = n.r. **Operative time** Stent = 5 ± 2 h No Stent = 7 ± 2 h p = n.r.	This study has been noted to have a high baseline rate of cholangitis in the no stent group. Leaving the Group B patients with clear signs of infection undrained preoperatively probably accounts for the higher rate of complications in this group.

[19] Mean cm H_20

Part II, Section 4. Management of jaundice before surgical resection of pancreaticobiliary malignancy: Preoperative stent versus immediate surgery
A. Randomized Controlled Trials (cont'd)

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Lai, Mok, Fan et al., 1994	87	Malignant obstructive jaundice Group A = preop stent, n=43 Group B = no preop stent, n=44	**Technical Success of preop stent =** 37 (86%) **Laboratory values** Baseline A B / Preoperative A B Bilirubin * 266 209 151 264 Alk Phos* 498 376 338 555 ALT/SGOT 122 132 77 114 AST/SGPT* 156 216 80 163 * = p<0.05 for preoperative comparison between groups No significant differences were noted between groups for Hb, Hct, BUN, creatinine, or albumin	**Hospital Mortality** (not specified to be 30-day) Stent (n=43) 6 (14%) No Stent (n=44) 6 (14%) p=n.s. **Postoperative Complications** Stent (n=41) 16 (39%) No Stent (n=44) 18 (41%) P<0.9 **Total Complications** Stent (n=41) 23 (56%) No Stent (n=44) 18 (41%) P<0.17 Level of obstruction had no statistically significant effect on morbidity and mortality	"Analysis of the available data [at the planned interim data analysis] showed that the estimated sample size was inadequate. As the hospital mortality of the two treatment groups were close, inclusion of the remaining patients as planned would have added no further information and the trial was therefore terminated."

Part II, Section 4. Management of jaundice before surgical resection of pancreaticobiliary malignancy: Preoperative stent versus immediate surgery
B. Retrospective Studies

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Sewnath, Birjmohun, Rauws et al., 2001 Same series as Karsten, Allema, Reinders et al., 1996 but subjects accrued June 1992 – Dec 2000	290	Patients with presumed resectable tumor in pancreatic head region 232 had preop drainage - 192 stent+papillotomy - 27 papillotomy alone - 13 required percutaneous combined drainage procedure 58 with no drainage were - 25 had dx ERCP only - 24 not jaundiced - 9 failed drainage and got immediate surgery Subgroups for analysis by preoperative bilirubin level Grp I (<40μmol/L) Grp II (40-100μmol/L) Grp III (>100 μmol/L)	**Degree of Preoperative Jaundice in Preop Drainage Patients** Preoperative bilirubin level (μmol/L) — Degree of Jaundice 177 (76%) <40 — none 32 (14%) 40-100 — moderate 23 (10%) >100 — severe **At least 50% reduction in bilirubin by bilirubin group** Grp I 87% Grp II 81% Grp III 78% **Postoperative Hospital Stay** median days(range) Grp I 13 (6-167) Grp II 15 (12-39) Grp III 15 (10-70) No drain 16 (8-222) p=0.09	**Drainage procedure-related complications** 14/232 (6%) had complication 4 duodenal perforation 4 pancreatitis 6 bleeding **Cholangitis** 27 (12%) patients and 21 (9%) needed stent replacement **Post-drainage morbidity** 77 (33%) developed recurrent jaundice from stent dysfunction **Postoperative Complication** Preop drain 50% No drainage 55% p=0.69 **Incidence of anastomotic leakage after surgery** Preop drain 14% No drainage 7% p=0.19 **Mortality** Preop drain 3/232 (1.3%) No drainage 0/58 p=n.r.	

Part II, Section 4. Management of jaundice before surgical resection of pancreaticobiliary malignancy: Preoperative stent versus immediate surgery
B. Retrospective Studies (cont'd)

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Karsten, Allema, Reinders et al., 1996	241	Patients with presumed resectable tumor in pancreatic head region 184 had preop drainage - 149 stent + papillotomy - 25 papillotomy alone - 10 external drainage when ERCP stent not possible 57 with no drainage were not jaundiced (n=33) or had immediate operation planned (n=24) 10 Fr Stents were placed only if papillotomy did not provide adequate drainage Baseline characteristics No significant differences between 4 groups in age, year of operation, tumor type, type of operation, *method of preoperative drainage* (??)	**Median reduction in bilirubin concentration** ERCP stent 82% ERCP papillotomy 74% External drainage 50% p=0.0036 **Bile Cultures (+)** (n=195) ERCP stent = 94% ERCP papillotomy = 59%, p=0.001 External drainage = 62%, p=0.01 No drainage = 34%, p=0.000001 Agreement between bile and other infection cultures in 48% (40/84)	**Cholangitis** ERCP stent = 51 episodes and 43 (29%) needed stent replacement Information on other groups not reported. **Postoperative Complication**[20] **Bilirubin vs. Use of preop drainage** Bili Conc μmol/L — Preop drainage — No Drain — p 0-40 61/118(52)* 20/34 (58) 0.6 40-100 21/38 (60) 1/1 (100) 1.0 > 100 20/28 (71)* 14/22 (63) 0.8 Total 102/184 (56) 35/57 (61) 0.4 * p=0.09 **Infective Complication** Stent 49/149 (33%) Papillotomy 11/25 (44%) External drain 6/10 (60%) No drainage 18/57 (32%) Total 84/241 (35%) p=n.r.	

[20] Authors conclude that preoperative biliary drainage did not reduce postoperative morbidity irrespective of the mode of biliary drainage applied.

An alternative conclusion, since the selection process favored preop drainage for jaundiced patients and no preop drainage for non-jaundiced patients, the observation that postoperative complication rates were similar regardless for those drained and not drained could suggest that the selective use of preoperative drainage reduces the complication rate to the level expected in those who do not require drainage.

Part II, Section 4. Management of jaundice before surgical resection of pancreaticobiliary malignancy: Preoperative stent versus immediate surgery
B. Retrospective Studies (cont'd)

Study	N	Population and Interventions	Outcomes	Adverse Events	Comments
Heslin, Brooks, Hochwald et al., 1998	74	Patients undergoing pancreaticoduodenectomy who were part of a separate RCT	**Postop Hospital Days** (median) Stent 11 No Stent 10 p=0.04 **Preop Laboratory Values** Serum bilirubin, AST/SGOT significantly lower than no stent group. Albumin and alkaline phosphatase trended lower but not statistically significant. BUN, creatinine, albumin, WBC no different.	**Perioperative Mortality** Stent 1 (2.6%) No Stent 0 (0%) p=0.34 **Perioperative Complications** Stent 23 (59%) No Stent 12 (34%) p=0.04	
ten Hoopen-Neumann, Gerhards, van Gulik et al., 1998	52	Patients with Klatskin tumor with planned resection 41 of 52 had preop stent Main reasons for no stent were technical failure or lack of proximal congestion of bile Baseline characteristics similar for gender and age, w/ slight differences in classification of hilar tumor between groups	**Total serum bilirubin**[21], mean (range) Stent 117 (12-511) No Stent 235 (14-412) p=0.008	**Occurrence of Implantation Metastasis, 1 yr** Stent = 8/41 (20%) No stent = 0 p = 0.18 4 of 8 patients with implantation metastases did not receive any postoperative radiation therapy. Overall, 37% of stented patients and 27% of non-stented patients did not receive radiotherapy (p=not reported)	

[21] Serum bilirubin levels reported in μmol/L (micromol/L)

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Quality					
Freeman, DiSario, Nelson, et al., 2001 Prospective, observational study	1,963 consecutive ERCPs in 11 U.S. centers during study periods ranging from 6 months to 3 years from December 1995 to December 1998. Simple endoscopic stent removals without attempted cannulation were excluded. Indication (%): Diagnostic=18.0 Manometry plus diagnostic=4.9 Therapeutic=77.1	Patient and procedure-related data were prospectively recorded by the endoscopist on a data collection sheet at the time of ERCP. 30-day follow-up was performed by a research assistant and was obtained by clinic or telephone interview with the patient, and by chart review. Risk factors were first evaluated by univariate analysis. Significant predictors on univariate analysis were then included in a forward stepwise multiple logistic regression model.	**Patient-related factors** Age Chronic pancreatitis Distal CBD diameter Gender History of acute pancreatitis of any etiology History of post-ERCP pancreatitis Pancreas divisum Presence of definite CBD stone Previous sphincterotomy Prior cholecystectomy Prior failed ERCP Recurrent abdominal pain Serum bilirubin Suspected SOD **Procedure factors:** >1 pancreatic contrast injection >1 pancreatic deep wire pass/cannulation Acinarization of pancreas Cholangiogram Pancreatogram Biliary sphincter balloon dilation for stone Biliary sphincterotomy Intramural contrast injection Minor papilla cannulation Moderate or difficult cannulation Pancreatic duct tissue sampling Pancreatic sphincterotomy Pancreatic stent placement Pancreatic stricture dilation Precut papillotomy SOD manometry **Provider factors:** Endoscopist performing >2 ERCP/week Training fellow involved	<u>Main Endpoint:</u> Pancreatitis (N=131)	No significant differences in the risk of pancreatitis between diagnostic and therapeutic ERCP. <u>Adjusted OR (95% CI) (Post-ERCP pancreatitis, n=131):</u> History of post-ERCP pancreatitis=5.35 (2.97-9.66) Biliary balloon sphincter dilation=4.51 (1.51-13.46) Moderate to difficult cannulation=3.41 (2.13-5.47) Pancreatic sphincterotomy=3.07 (1.64-5.75) <u>≥</u>1 pancreatic contrast injections=2.72 (1.43-5.17) Suspected SOD=2.60 (1.59-4.26) Female gender=2.51 (1.49-4.24) Normal serum bilirubin=1.89 (1.22-2.93) Absence of chronic pancreatitis=1.87 (1.00-3.48) <u>Cumulative adjusted OR associated with multiple risk factors:</u> Female=2.5 Female+normal bilirubin=4.8 Female+normal bilirubin+SOD=12.4 Female+normal bilirubin+difficult cannulation=16.2 Female+normal bilirubin+SOD+difficult cannulation=42.1

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Quality (cont'd)					
Masci, Toti, Mariani, et al., 2001 Prospective, observational study	2444 consecutive diagnostic or therapeutic ERCPs performed on 2103 patients from June 1997 to December 1998 in 9 endoscopic units in Italy. Mean age=64.6±15.7 years Gender=55.5% female Indication for ERCP/ES (%): Choledocholithiasis (including pancreatitis due to gallstones)=62.6 Placement of biliary stent for malignant obstruction=17.5 Treatment of SOD=7.3 Miscellaneous=2.5	Data was collected at the time of ERCP/ES and before hospital discharge. 150 variables including demographic details, referral pattern, clinical condition, medical history, results of blood tests, sedation, techinical procedures, and endoscopic and radiologic findings were collected. For each potential risk factor univariate analysis was conducted. Only factors significant in the univariate analysis were included in the Multivariable logistic regression analysis.	Patient factors: Age Characteristics of orifice of papilla Characteristics of papilla Clinical history Diameter of common bile duct Gender Indication for ERCP/ES Previous dilation of the papilla Stone size Stones in gallbladder Procedure factors: Biliary or pancreatic opacification Contrast medium Placement of nasobiliary drainage Placement of stent Sphincterotomy technique Stone removal	Main endpoint: Any complication[22] (n=121 pts) Including: Pancreatitis (n=44 proc) Hemorrhage (n=30 proc)	Adjusted OR (All complications, n=121) Age (≤ 60 years)=1.53 (95% CI=1.06-2.20) Sphincterotomy technique (precut vs. other)=1.70 (95% CI=1.10-2.68) Stone removal (no vs. yes)=2.52 (95% CI=1.44-4.53) Adjusted OR (Pancreatitis, n=44) Age (≤ 60 years)=2.11 (95% CI=1.16-3.80) Sphincterotomy technique (precut vs. other)=2.80 (95% CI=1.38-5.84) Stone removal (no vs. yes)=3.35 (95% CI=1.33-9.10) Adjusted OR (Hemorrhage, n=30) Sphincterotomy technique (precut vs. other)=2.45 (95% CI=1.60-5.39) Orifice of papilla of Vater (obstructed vs. other)=2.57 (95% CI=1.69-6.17)

[22] Complications of diagnostic or therapeutic ERCP defined as any adverse event requiring more than one night of hospitalization. Included Pancreatitis, Hemorrhage, Cholecystitis, Cholangitis, Perforation during ES, Perforaton during endoscope, Basket trapping, Cardiopulmonary events, Drug side effects, Deaths

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Quality (cont'd)					
Freeman, Nelson, Sherman, et al., 1996 Prospective, observational Study	2420 consecutive patients undergoing biliary sphincterotomy in 16 institutions in the U.S. and Canada from 1992 to 1994. 73 (3.0%) of patients were lost to follow-up and excluded from the analysis, leaving 2347 patients. Indication for sphincterotomy (%): Stone in CBD =68.2 Placement of biliary stent for malignant obstruction-13.2 Suspected SOD=11.6 Placement of a stent or dilation of benign strictures=4.2 Miscellaneous conditions=7.8 More than one indication for sphincterotomy was recorded for 5.0% of patients.	All sphincterotomies performed in an attempt to establish access to the bile duct were included. Patients in whom attempts at biliary cannulation without sphincterotomy failed and those who underwent pancreatic sphincterotomy were excluded. Data was collected at the time of the procedure, before discharge, and approximately 30 days after sphincterotomy. Patients were interviewed and charts were reviewed by means of a standardized questionnaire. Univariate analysis and simple logistic regression analysis were used to assess potentially relevant risk factors. Significant predictors were then included in a forward, stepwise logistic regression analysis to identify the most important risk factors for pancreatitis, hemorrhage, and overall complications. Patients for whom relevant data was missing were excluded from analysis.	<u>Patient factors:</u> Age Cholangitis Cirrhosis Coagulopathy before procedure Distal bile duct diameter Gender Indication other than BDS Number of coexisting illnesses Periampular diverticulum Sphincter of Oddi dysfunction Bilroth II gastrectomy <u>Procedure factors:</u> Acinarization of pancreas Bleeding during procedure Combined percutaneous-endoscopic procedure Dificulty of cannulation Emergency procedure Failed biliary access or drainage Number of pancreatic contrast injections Precut sphincterotomy <u>Provider factors:</u> Case volume University affiliated center Participation of a trainee	<u>Main Outcome:</u> All complications within 30 days <u>Including:</u> Pancreatitis Hemorrhage	<u>Adjusted OR (All complications, N=229 pts)</u> Difficulty of cannulation=3.05 (95% CI=1.83-5.08) Precut sphincterotomy=3.61(95% CI=1.78-7.34) Combined percutaneous-endoscopic procedure= 3.40 (95% CI=1.04-11.13) Suspected SOD=2.90 (95% CI=1.70-4.94) Cirrhosis=2.93 (95% CI=1.48-5.90) <u>Adjusted OR (Pancreatitis, N=127 pts)</u> Suspected Sphincter of Oddi dysfunction =5.01 (95% CI=2.73-9.22) Younger age=2.14 (95% CI=1.41-3.25) Precut sphincterotomy =4.34 (95% CI=1.73-10.88) Difficulty of cannulation =2.40 (95% CI=1.07-5.36) Number of pancreatic contrast injections =1.35 (95% CI=1.04-1.75) <u>Adjusted OR (Hemorrhage, N=48 pts)</u> Coagulopathy before procedure=3.32 (95% CI=1.54-7.18) Anticoagulation within 3 days of procedure=5.11 (95% CI=1.57-16.68) Cholangitis before procedure=2.59 (95% CI=1.38-4.86) Mean case volume of endoscopist - $\leq$1/week=2.17 (95% CI=1.12-4.17) Bleeding during procedure=1.74 (95% CI=1.15-2.65)

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Rabenstein, Schneider, Bulling, et al., 2000 Prospective, observational study	438 consecutive endoscopic sphincterotomies performed from September 1994 through December 1996. Mean age=61.3±16.4 years Gender=55.5% males Indication for sphincterotomy (%): CBD stones=37.7 Malignancies=23.3 Chronic pancreatitis= 21.9 Other=17.1	Patients were followed up using physical exams and blood samples at 4, 24, and 48 hours after ES. Clinical observations were recorded throughout the patient's hospital stay. After 30 days family physicians were contacted by phone or mail to monitor any later occurrence of complications. Inclusion criteria for the Multivariable logistic regression model were a univariate p-value of <0.1. Variables with a p-value >0.05 in the last step of the Multivariable model were excluded via variable selection. Only variables with a p-value <0.05 were included in the final model. Due to the low number of events, Multivariable analysis of hemorrhage was not conducted.	Patient factors: Age Anemia Coagulopathy Diabetes mellitus Gender NSAID treatment Intensive-care patient Pancreas divisum Pancreatic obstruction Previous gastrectomy Previous jaundice Previous post-ERCP pancreatitis Laparoscopic cholecystectomy Procedure factors: Anticoagulation Conventional cholecystectomy Emergency ES ES frequency Failed procedure Nasobiliary tube NKP involvement Pancreatic cannulation Pancreatic contrast Size of sphincterotomy Sphincterotomy procedures Operator factors: ES caseload Participation of trainee	Main Outcome: All complications Including: Acute pancreatitis Hemorrhage Cholangitis Technical	Adjusted OR (All complications, N=33) Age ≤60 years=2.9 (95% CI=1.33-6.21) Coagulopathy=9.7 (95% CI=1.95-48.10) Pancreas divisum=7.6 (95% CI=1.56-36.6) Pancreatic obstruction=0.07 (95% CI=0.01-0.59) AOR (Pancreatitis, N=19) Pancreas divisum=8.2 (95% CI=1.91-34.79) Endoscopist ES case load <40/year=3.8 (95% CI=1.44-10.00)

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Loperfido, Angelini, Benedetti, et al., 1998 Prospective, observational study	1827 Therapeutic ERCP drawn from 3,356 ERCPs carried out in 2,769 patients from 9 endoscopy centers in Italy during the period from February 1992 to January 1994. Every unit that participated included all patients who underwent ERCP, on an intention-to-treat basis. ERCP was performed by a single operator or team of no more than 3 endoscopists. Large centers performed more than 200 endoscopies/year (3 centers). Median age=66 years (range=7-93 years) Gender=45.5% male ERCP performed on an urgent basis in 9.5% of cases.	Data was collected at the time of ERCP, before discharge, and in cases of readmission, within 30 days. The attending physician's record and medical records were reviewed. Univariate and Multivariable analyses were conducted. A forward stepwise regression analysis was performed for the Multivariable analysis of complications.	<u>Patient factors:</u> Age Bile duct size Gender Jaundice Papillary diverticulum Billroth II gastrectomy <u>Procedure factors:</u> Emergency ERCP Intramural injection of contrast agents Pancreatic opacification Precut ES Pure vs. blended cut Repeat ERCP <u>Provider Factors:</u> Center size Small center, <150 ERCP/yr	<u>Main Outcome:</u> All complications <u>Including:</u> Pancreatitis Hemorrhage Cholangitis Retroperitoneal perforation	<u>Adjusted OR (Therapeutic ERCP, overall complications, N=98)</u> Small center=2.93 Precut=1.73 <u>Adjusted OR (Pancreatitis, N=29)</u> Age < 70 year=1.11 Pancreatic duct opacification=2.84 Nondilated duct=2.85 <u>Adjusted OR (Hemorrhage, n=21)</u> Small center=2.98 <u>Adjusted OR (Cholangitis, n=21)</u> Small center=4.22 Jaundice=4.14 <u>Adjusted OR (Retroperitoneal Perforation, n=12)</u> Billroth II procedure=11.70 Precut=7.19 Intramural injection=6.86

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Mehta, Pavone, Barkun, et al., 1998 Retrospective study (? Prospective database)	535 patients who underwent ERCP for suspected common bile duct stones over a five- year period in one university. 45 with complications and 490 randomly selected from 1194 uncomplicated cases. A single endoscopist carried out the majority of ERCPs. Mean age=56.6 ±18.5 years (range=17-91 years, median=59 years) Gender=38% male Sphincterotomy=47 %	Data were obtained by fellows and attending staff from an ongoing endoscopic database. Complementary information was collected from hospital charts, endoscopc reports, abdominal ultrasound, and ERCP films. Univariate and Multivariable analyses were conducted. The ability of a single clinical variable to predict the occurrence of a complication was assessed in this fashion. Multivariable logistic regression models were then constructed to evaluate the clinical and laboratory predictors. Predictors of complications were studied amongst all patients, as well as in subgroups of patients undergoing and not undergoing endoscopic sphincterotomy.	Patient factors: Age Amylase level CBD diameter CBD stones found at ERCP Gender History of pancreatitis Prelaparoscopic cholecystectomy Procedure factors: Pancreatic channel opacification Sphincterotomy	Main endpoint: Pancreatitis (n= 34)	*Subgroup undergoing endoscopic sphincterotomy:* Risk factors for pancreatitis: Age < 59 years (p=0.04) Absence of a CBD stone at ERCP (p=0.004) Subgroup NOT undergoing endoscopic sphincterotomy: Risk factors for pancreatitis: Pancreatic channel opacification (p=0.05)

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Neoptolemos, Shaw, and Carr-Locke, 1989 Retrospective study (part prospective)	190 patients who had ES were drawn from 439 consecutive patients who underwent operative exploration of the CBD and/or ES for CBD stones form 1981 to 1985. ES was the only intended procedure for 132 and in 58 cases it was followed by surgery as part of deliberate treatment.	Clinical and hematologic/ biochemical variables were captured at the time of admission. Medical risk factors were also recorded. Univariate analysis and Multivariable analysis was performed. Multivariable stepwise logistic regression analysis was used to identify independently significant factors for use in predicting complications.	<u>Patient factors:</u> Age Gender Jaundice Temperature Acute cholangitis Acute pancreatitis Medical risk factors Hemoglobin Hematocrit White blood cell count Urea Creatinine Total proteins Albumin Alkaline phosphatase Glutamyl transpeptidase Alanine transaminase Bilirubin Preoperative ES	<u>Main Outcome:</u> All complications <u>Including:</u> Acute pancreatitis (N=3) Hemorrhage (N=5) Acute cholangitis (N=15) Septicemia (N=4) empyema of gallbladder (N=2) Gastric erosions (N=2) Cardiac failure (N=2) Perforation (N=1) Death (N=11)	<u>Significant independent risk factors for post-ERCP complications (N=32):</u> Elevated bilirubin Elevated serum albumin.

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Tzovaras, Shukla, Kow, et al., 2000 Prospective, observational study	372 patients who had an ERCP performed between January 1, 1997 and December 31, 1997. Median age=66 years (range=13-95 years) Gender=42.2% male Indications (N): **Urgent (N=75)** Cholangitis=47 Acute biliary pancreatitis=21 Post-surgery complications=7 **Elective (N=297)** Choledocholithiasis =120 Malignant jaundice=52 Benign stricture/injury=51 Suspected SOD=40 Miscellaneous=34	Using a standardized form, data was collected during the procedure, and following discharge from the hospital at least once 4-6 weeks after the procedure at the outpatient clinic. Mortality and morbidity were defined as 30-day or in-hospital stay. Potential relevant risk factors were assessed separately with risk ratios and confidence intervals calculated for each variable. Significant predictors on univariate analysis were then included in a stepwise multiple regression analysis.	<u>Patient factors:</u> Age Previously failed ERCP Choledocholithiasis Gender Malignant jaundice <u>Procedure factors:</u> Sphincterotomy Stent manipulation Suspected SOD Therapeutic ERCP Urgent ERCP Balloon clearance Balloon dilation Basket clearance Manometry Need for PTC Needle-knife sphincterotomy	<u>Main Endpoint:</u> All Complications (N=21) <u>Including:</u> Death (N=5) Pancreatitis (N=5) Hemorrhage (N=1) Cholangitis (N=7) Perforation (N=2) Aspiration (N=1)	<u>Adjusted OR (95% CI) (All complications)</u> Need for PTC=10.27 (2.30-45.83) Suspected SOD=8.57 (2.59-28.43) Malignant jaundice=4.76 (1.46-15.58) Previously failed ERCP=4.66 (1-21.80)

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Motte, Deviere, Dumonceau, et al., 1991 Retrospective study (case-control)	105 total patients: 34 cases of septicemia (documented by positive blood culture) after ERCP stent placement and 71 selected controls (no documented bacteremia, infectious complication, or post-ERCP fever) drawn from 313 remaining patients who had ERCP stent placement. Mean age (+SD: Septicemia=69±11 No Septicemia=68±14 Gender (% male): Septicemia=56 No Septicemia=48	Patient charts reviewed for the following data: age, gender, underlying conditions, previous endoscopic procedures, cholangitis before endoscopic biliary therapy, antibiotic treatment administered before the procedure, type of biliary drainage, radiologic-endoscopic diagnosis, laboratory values, and microbiologic data Discriminant analysis performed with septicemia as the dependent variable and the clinical and biological data prior to the procedure as independent variables. A second analysis was performed including the clinical data following the endoscopic procedure. A discrimant analysis was also conducted of patients with *P. aeruginosa* (exogenous source) compared with patients with *E. coli* septicemia (endogenous source) to predict the microorganism involved .	Variables included in the primary analysis (variables preceding the procedure): Patient factors: Age Gender Associated Diseases Previous manipulations of the biliary tract Antibiotic therapy Prior Cholangitis Status as a preferred patient White blood cell counts Serum levels of bilirubin Alkaline phosphatase Level of stricture (CBD or hilum) Variables included in the second analysis (additional variables following the procedure): Procedure factors: Use of combined percutaneous and endoscopic drainage Quality of drainage (complete or incomplete)	Septicemia (n=34)	Prediction of septicemia including variables preceding the procedure: Prior Cholangitis (F=7.1)* White blood cell count (F=6.6)* * A linear combination of these variables failed to predict the outcome in 50% of cases. Prediction of septicemia including additional variables following the procedure: Quality of drainage incomplete (F=319.2)** **91% of cases identified. No other variable entered into this analysis. For the prediction of Pseudomonas aeruginosa septicemia including pre-procedure variables: Referral from another center (F=6.3)*** ***Age and antibiotic therapy were also selected resulting in the correct classification of 67% of cases. For the prediction of Pseudomonas aeruginosa septicemia including post-procedure variables: Referral (F=6.3) Combined percutaneous-endoscopic drainage (F=5.2) Diagnosis of hilum or CBD stricture (F=4.4)**** **** With the addition of age, these variables correctly classified 83% of cases.

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Lai, Lo, Choi, et al., 1989 Retrospective, cohort study	323 patients who underwent diagnostic ERCP at one institution from January 1984 to July 1987. All patients had biliary obstruction on endoscopic cholangiograms. The majority of patients (54%) had previous attacks of acute cholangitis.	Clinical records and cholangiograms were reviewed to identify risk factors for acute cholangitis. Univariate and stepwise logistic regression were used to identify significant risk factors for acute cholangitis.	<u>Patient factors:</u> Type of obstruction Type of lesion Total bilirubin Alkaline phosphatase Alanine transaminase (ALT) Asparatate transaminase (AST) Glutamyl transpeptidase White blood count Fever	<u>Main Outcome:</u> Acute cholangitis (n=21)	Acute Cholangitis, n=21: <u>Results of stepwise logistic regression:</u> Pathologic nature of the obstructive lesion, malignant vs. benign (discriminant coefficient=1.75, $p<0.002$) Fever (>37.5° C) within 72 hours prior to examination (discriminant coefficient=2.73, $p<0.0001$) ***<u>Subgroup analysis excluding the 43 febrile patients (n=280):</u>*** Nature of the biliary obstruction (discriminant coefficient=2.12, $p<0.01$) Serum AST $\leq$70 IU (discriminant coefficient=2.09, $p<0.04$)

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Boender, Nix, de Ridder, et al., 1994 Prospective, observational study	242 consecutive patients who underwent ERCP sphincterotomy for CBD stones. No previous gastric surgery, papillotomy, or other pancreatobiliary diseases such as cholangitis, pancreatitis, or parenchymal liver disease. Mean age=70 years (range=32-97 years) Gender=35.5% male Average duration of symptoms=9 months (8 days-10 years)	Endoscopic findings, therapeutic procedures, and acute complications of sphincterotomy were recorded during ERCP or within 5 days. In addition, 3 months after ERCP, a questionnaire was sent to the patient's general practitioner and referring specialist to ascertain the patient' clinical condition and remaining complaints and complications. Risk factors statistically analyzed using univariate and Multivariable logistic regression.	<u>Patient factors:</u> Age CBD size Location and presence of JPD Presence and position of diverticulum Presence of GB <u>Procedure factors:</u> Papillotomy procedure (Standard vs. precut ES) Drainage procedure Size of papillotomy Failed procedure	<u>Main Outcome:</u> All complications combined (N=34) <u>Including:</u> Pancreatitis Bleeding Cholangitis Retroperitoneal leakage	<u>Adjusted OR (All complications)</u> Precut vs,. standard papillotomy=4.9, p=0.001 Failed endoscopic biliary drainage vs. successful biliary drainage=34.8, p=0.007 Failed therapeutic precut vs. successful=5.9, p=0.098 Failed diagnostic precut vs successful=0.28, p=0.321 Location of papilla in relation to JPD -Outside vs. without=3.1, p=0.072 -Lower rim vs. without=4.3, p=0.015 -Inside vs. without=9.4, p=0.002.

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Nelson and Freeman, 1994 Retrospective study	189 patients (191 sphincterotomies) undergoing endoscopic biliary sphincterotomy form July 1987 to July 1991 at one institution. All sphincterotomies were performed by one of two gastroenterologists. Charts were unavailable for 4 patients and they were excluded from the analysis. Mean patient age=66±19 years Gender=57% male Indication for sphincterotomy (%): Choledocholithiasis = 38.2 Cholangitis=26.7 Tumor/stricture=13.6 Gallstone pancreatitis=8.4 SOD/papillary stenosis=8.9 Bile leak=2.1 Other=2.1	Data was recorded at the time of initial or follow-up endoscopy and charts were reviewed for laboratory. clinical parameters, medication use, type and outcome of interventions, and mortality. Relative risks with Fisher's Exact Test were used for univariate analysis of risk factors. Multiple logistic regression analysis with forward stepwise selection was then conducted.	<u>Patient factors:</u> Aspirin/NSAID use CBD diameter Hemodialysis Prothrombin time Sphincter of Oddi dysfunction <u>Procedure factors:</u> Bleeding at ES ES length	<u>Main Outcome:</u> Hemorrhage (n=10)	<u>Adjusted OR (Hemorrhage, n=10)</u> Hemodialysis=16.4 (95% CI=2.9-93.1) Prothrombin time 2s > control=12.1 (95% CI=1.8-90.9) Bleeding seen at ES=13.7 (95% CI=2.2-87.3)

Part V, Section 1: Multivariable Analyses

Article/Study Design	Study Population	Data Acquisition Methods/ Analysis	Risk Factors Assessed	Outcomes Assessed	Results
Fair Minus Quality					
Maldonado, Brady, Mamel, et al., 1999 Retrospective study	Records of 100 consecutive patients referred for suspected SOD and who underwent sphincter of Oddi manometry 1992–1996 at two university-affiliated hospitals reviewed. Group 1= patients who only had SOM (54%) Group II= patients who had SOM and ERCP with or without sphincterotomy (46%). Groups I and II further subdivided (A and B) into normal SOM and abnormal SOM (Group IA=79.6%, Group IB=20.4%, Group IIA=23.9%, Group IIB=76.1%). Mean age=47+14.2 years (range=23-83 years) Gender=9% male SOD biliary type II=37 patients SOD biliary type III=58 SOD pancreatic type II=1 patient SOD pancreatic type III=4 patients	Patient and procedure data recorded from the medical records. Univariate and Multivariable analyses were performed. Multiple regression analysis was used to determine the independent predictors of pancreatitis.	<u>Patient factors:</u> Age Clinical type of sphincter of Oddi dysfunction Gender <u>Procedure factors:</u> Doses of medication Duct cannulated ERCP with or without sphincterotomy performed during the same session Length of procedure Sphincter of Oddi pressures	<u>Main Outcome:</u> Pancreatitis	# pts w/ pancreatitis Grp I - SOM only (n=54) (A) 43 normal SOM 4 (B) 11 abnormal SOM 1 Grp II – SOM and ERCP (n=46) (A) 11 normal SOM 3 (B) 33 abnormal SOM got ES 9 2 abnormal SOM but no ES Multiple regression analysis, including all potential predictors revealed: Only ERCP had an independent association with the development of pancreatitis. Endoscopic sphincterotomy (ES) added no additional risk for pancreatitis beyond that associated with ERCP.