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Endoscopic Retrograde Cholangiopancreatography – Utilization and outcomes in a 10-year population based cohort

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SUMMARY

Article Focus:

- Due to increasing use of quality metrics, accurate measures of utilization and procedural adverse event risks are necessary to establish benchmarks for quality, and are best determined from community-based studies.
- There are no reports of community-based utilization of ERCP in the US.
- The aims of this population-based study were to determine the utilization of ERCP including changes over time, the incidence of inpatient admissions for adverse events within 30 days of ERCP, and risk factors for procedural related adverse events.

Key Messages:

- Population utilization of ERCP in Olmsted County MN rose over the ten year period from 1997 to 2006, driven specifically by increases in therapeutic procedures. The most common indications for ERCP were therapy of choledocholithiasis and to determine etiology of acute pancreatitis.
- Admissions within 30 days after ERCP are common, but are usually unrelated. Complications of ERCP remain rare at 5.3% and no deaths were directly related.
- Risk factors associated with adverse events from ERCP include younger age, BMI ≥35, pancreatic duct cannulation, outpatient procedures, intraprocedure sphincterotomy bleeding, difficulty grade, and patient's first ERCP.

Strengths and Limitations:

Strengths:

- Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community.
- The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and adverse events of ERCP with full details of procedures and subsequent hospitalizations can be assessed.

Limitations:

- The study is a retrospective review with inherent potential biases.
- The skills of the endoscopists are likely at a higher level than endoscopists in smaller community hospitals. Therefore, the adverse event rate in this community setting could be lower than one would expect in other community settings.

ABSTRACT

Objective: To determine utilization of ERCP; incidence of inpatient admissions for complications occurring within 30 days of ERCP; and risk factors for procedural related complications, in a population based study.

Design: Retrospective cohort study

Setting: Olmsted County, MN

Participants: All adult residents of Olmsted County, MN, who underwent ERCP from 1997 to 2006.

Interventions: Diagnostic and therapeutic ERCPs were assessed.

Primary and Secondary outcome measures: Patient and procedural characteristics and complications within 30 days; and rates of ERCP utilization and unplanned admissions and risk factors for admissions.

Results: In ten years, 1072 ERCPs were performed on 827 individual patients. Average utilization of ERCP was 83.1 ERCPs/100,000 persons/year, with an increase from 58.0 to 104.8 ERCPs/100,000 persons/year over time, driven by increases in therapeutic procedures. Within 30 days after 236 procedures, 62 admissions were definitely related to the index ERCP. The complication rate was 5.3%, including pancreatitis(26, 2.4%), infection/cholangitis(16, 1.5%),

bleeding(15, 1.4%), and perforation(4, 0.37%). 30-day mortality was 2.4%; none of which were directly related to the ERCP or complications thereof. Risk factors identified through multivariate analysis to be associated with adverse events included: age <45 years(p=0.0498); BMI ≥35(p=0.0024); pancreatic duct cannulation(p=0.0026); outpatient procedure(p<0.0001); intraprocedure sphincterotomy bleeding(*P*<0.0001); difficulty grade(*P*=0.115); and patient's first ERCP(*P*=0.0394).

Limitations: Retrospective study.

Conclusions: Population utilization of ERCP rose during the study period, specifically in therapeutic procedures. Admissions within 30 days of ERCP are common, but often unrelated. Complications of ERCP remain rare and deaths quite unusual.

Abbreviations:

AE – adverse event

EGD – esophagogastroduodenoscopy

ERCP - endoscopic retrograde cholangiopancreatography

EUS – endoscopic ultrasound

MRCP - magnetic resonance cholangiopancreatography

BACKGROUND

Since its first description in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has become an established modality for the diagnosis and treatment of pancreaticobiliary disorders[1, 2]. Over the years, ERCP has evolved from a purely diagnostic, to a mainly therapeutic procedure. Around 500,000 ERCPs are performed annually in the United States (US) with adverse event (AE) rates between 4% and 10%,[3] and mortality between 0.05% and 1%[4-7]. The most common AEs following ERCP include pancreatitis, hemorrhage, and infection, which occured in 4% to7% of procedures[3, 6, 8]. There is an increased risk of AEs after therapeutic procedures and in patients with suspected Sphincter of Oddi dysfunction[6]. Since ERCP is the endoscopic procedure with the highest cost and AE rates, diagnostic ERCP is now avoided in favor of other diagnostic modalities such as less-invasive endoscopic ultrasound (EUS) and non-invasive magnetic resonance cholangiopancreatography (MRCP)[2, 3, 9]. In an era of increasing utilization of quality metrics, accurate measures of utilization rates and procedural adverse event risks are necessary to establish meaningful benchmarks for quality, and are best determined from community-based studies.

There are no reports of community-based utilization of ERCP in the US, but there are several from Europe[8, 10]. Published reports of ERCP related AEs have all been single-centered or multi-centered studies from tertiary care centers and affected by referral bias, leading to high estimates of risk that may not apply to the general population. All adverse events of procedures done at tertiary care centers may not be captured since the patients may seek care for AEs closer to their homes and thus, lost to follow-up.

The aims of this population-based study were to determine (1) the utilization of ERCP, including changes over time; (2) the incidence of inpatient admissions for AEs within 30 days of

ERCP; and (3) risk factors for procedural related AEs among residents of Olmsted County, MN over a ten-year period from 1997-2006. The findings of this study are unique, as they represent population based estimates of utilization and risks associated with ERCP and may serve as more accurate and clinically meaningful data for clinical decision making and development of quality benchmarks.

METHODS

Study Design: A retrospective cohort study was conducted with approval of the Institutional Review Board of Mayo Clinic in compliance with federal regulations of the U.S. Department of Health and Human Services for protection of human subjects and the Health Information Protection and Portability Act. Billing records from Mayo Clinic and associated hospitals were queried for Olmsted County residents who had undergone an ERCP during a ten-year period from January 1, 1997 to December 31, 2006. ERCPs were identified using CPT codes for ERCP, including 43260, 43261, 43262, 43263, 43264, 43265, 43267, 43268, 43269, 43271, 43272, and 47999. Utilization characteristics for EUS were determined in the same population using codes 43232, 43238, and 43242 and for MRCP using codes 74181, 74182, and 74183. Subjects also had to be age ≥ 18 years, live in Olmsted County, and have valid authorization to review medical records for research purposes in accordance with Minnesota State statutes.

Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community. Olmsted County comprises over 100,000 persons, of whom 85% are Caucasian and 50% are women; socio-demographically, the community is similar to the US population. Over half of the county's population is seen at one of the Mayo Clinic facilities; 95% of local residents will have had at least one medical contact with

a local care provider (*e.g.*, for dental X-rays, sports physical examinations, pre-employment examinations, minor illness, and routine medical care) during any 4-year period[11]. Mayo Clinic has a common medical record system with its two affiliated hospitals (Saint Mary's and Rochester Methodist) for 90 years. Mayo Clinic's single record system contains both inpatient and outpatient data. Diagnoses and surgical procedures recorded in these records are indexed. It includes diagnoses made for outpatients seen in office or clinic consultations, emergency room visits, and diagnoses recorded for hospital inpatients, autopsy examinations, or on death certificates. The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and AEs of ERCP with full details of the hospitalization can be assessed.

Medical records were reviewed retrospectively by the primary author. Patient and procedural characteristics, as well as AEs within 30 days were recorded. As many as 170 variables were collected for each procedure and recorded into a database.

Primary outcomes measured were (1) utilization rates of unique ERCP procedures in the adult population (age 18 years and older) of Olmsted County from 1997-2006, and (2) the rate of unplanned admissions within 30 days following ERCP for ERCP-related AEs. Secondary outcomes included patient and procedural characteristics, predictive of having an unplanned admission within 30 days after ERCP for an ERCP-related AE.

Utilization metrics included the patients' age, sex, race, Charlson score at the time of ERCP[12], body mass index (BMI), cholecystectomy within 30 days prior to ERCP, altered anatomy (including gastrojejunostomy, Whipple anatomy, hepatico- and choledocho-jejunostomy), presence of cirrhosis, and previous history of ERCP. Indications for ERCP were then examined as biliary versus pancreatic, diagnostic versus therapeutic, and graded for

complexity using the previously published Morriston Hospital ERCP grading scale (Table IA)[13]. Diagnostic procedures had a CPT code of 43260 where no intervention was performed, other than a cholangiogram or pancreatogram; all other procedures were therapeutic. Multiple intra-procedural details, including presence of a trainee, type and amount of sedation used, and biliary and pancreatic ductal interventions were noted. Success of the procedure was recorded as the ability to cannulate the intended duct and achieve the intended therapy.

AEs recorded included unplanned admissions; sedation-related events, including pulmonary and cardiovascular events; infection; pancreatitis; bleeding; perforation; need for repeat endoscopic procedure; or mortality within 30 days. These outcomes were determined as being related to the index ERCP by author review. AEs were deemed to be definitely related, probably related, possibly related, or definitely unrelated to the index ERCP. Possibly related AEs included patients admitted with abdominal pain, but without evidence of definite pancreatitis by laboratory studies or documented cholangitis. Probably related AEs included biliary or pancreatic stent dysfunction leading to repeat the procedure within 30 days of the index procedure, but without any of the defined AEs of pancreatitis, infection, perforation, and gastrointestinal bleeding. The latter AEs were categorized as mild, moderate, and severe, according to established consensus criteria (Table IB)[6] Patients undergoing elective surgery including cholecystectomy within 30 days of ERCP were also identified.

Table IA: Morriston Hospital ERCP grading scale

Procedure	Grade
Diagnostic ERCP	I
Biliary sphincterotomy, balloon sphincteroplasty, removal of extrahepatic stones ≤1 cm using basket and/or balloon	II
Precut sphincterotomy, large stones removal (>1cm), intrahepatic stone removal, mechanical lithotripsy, stricture dilatation,	III

cytology, stent insertion, and naso-biliary drain	
Sphincter of Oddi manometry, diagnostic and therapeutic ERCP after Billroth II surgery, minor papilla sphincterotomy, endoscopic ampullectomy, and all pancreatic duct therapeutic procedures. Cholangioscopy, laser lithotripsy, electrohydraulic lithotripsy, combined procedures (PTC and ERCP), and other advanced bile duct therapeutic procedures	IV

Ragunath et al, Post Grad Med J, 2003

ERCP - endoscopic retrograde cholangiopancreatography

PTC – percutaneous transhepatic cholangiography

Table IB: Consensus criteria for ERCP complications

	Mild	Moderate	Severe
Bleeding	Clinical evidence of bleeding (ie not just endoscopic) Hemoglobin drop <3g No need for transfusion	Transfusion: 4 units or less No angiographic intervention or surgery	Transfusion: 5 units or more or intervention (angiographic or surgical)
Perforation	Possible, or only very slight leak of fluid or contrast dye Treatable by fluids and suction for 3 days or less	Any definite perforation treated medically for 4-10 days	Medical treatment for more than 10 days or intervention (percutaneous or surgical)
Pancreatitis	Clinical pancreatitis: amylase at least thrice the upper limit of normal at more than 24 hours after the procedure requiring admission or prolongation of planned admission to 2-3 days	Pancreatitis requiring hospitalization for 4-10 days	Pancreatitis requiring hospitalization for more than 10 days, or hemorrhagic pancreatitis, phlegmon, or intervention (percutaneous drainage or surgery)
Infection (cholangitis)	>38 degrees Celsius at 24-48 hours	Febrile or septic illness requiring>3 days of hospital treatment or endoscopic or percutaneous intervention	Septic shock or surgery

Cotton et al, GIE, 1991

Statistical Analysis

Univariate analyses were performed to obtain descriptive statistics for patient and procedural characteristics. Annual incidence was determined by dividing the number of ERCPs performed on the study subjects during a calendar year by the adult population of Olmsted County during that period, according to County records and normalized to 100,000 persons. To test for associations between patient and procedural characteristics and ERCP related AEs, values of these characteristics were compared between subjects who experienced ERCP-related AEs and subjects who did not by two sample t-tests for continuous variables, and chi square test for discrete variables. Multivariable logistic regression analyses were used to determine patient and procedural characteristics predictive of ERCP-related AEs. *P*-values less than 0.05 were considered statistically significant. All analyses for this study were done using SAS statistical software (SAS version 9.1 for Windows; SAS Institute Inc., Cary, North Carolina).

RESULTS

Demographic characteristics

In the 10-year period from January, 1, 1997 to December, 31, 2006, 1072 ERCPs were performed on 827 individual adult patients in Olmsted County. Patient demographic characteristics can be seen in Table II. Prior to the index cholecystectomy, 232 (28%) patients had a previous cholecystectomy; 21 (2%) patients had altered anatomy, and 20 (1.9%) were taking clopidogrel or warfarin at the time of the ERCP. There were 153 patients who had more than one ERCP during the 10-year period, and the mean number of ERCPs in these patients was 1.3.

Table II: Patient Characteristics

Age at time of ERCP (years)	
mean (sd)	57.6 (19.8)
18-44 years	283 (26.4%)
45-64 years	357 (33.3%)
> 65+ years	432 (40.3%)
Gender	
Female, n (%)	522 (63.1)
Race	
Caucasian	688 (83.2%)
African American	15 (1.8%)
Other/unknown	124 (15.0%)
Charlson index at time of ERCP	
mean (sd)	3.2 (3.2)
BMI at time of ERCP	
mean (sd)	28.5 (7.2)
< 25	341 (32.4%)
25-34	517 (49.1%)
35+	194 (18.4%)

ERCP – endoscopic retrograde cholangiopancreatography
BMI – body mass index

Utilization characteristics

Average utilization of ERCP was 83.1 ERCPs per 100,000 persons/year, with an increasing trend in utilization from 58.0 to 104.8 ERCPs per 100,000 persons/year over the 10-year period. Therapeutic ERCPs increased over the same timeframe from 42.9 to 93.9 ERCPs per 100,000 persons/year (average 68.7). However, diagnostic ERCPs decreased slightly from 15.1 to 10.9 and averaged 14.4 ERCPs per 100,000 persons/year. EUS and MRCP utilization in the same population also steadily increased over this time period (Figure I).

Procedural characteristics

Procedural characteristics can be seen in Table III. Of the 1072 ERCPs performed over the 10-year period, 606(56.5%) were performed as an inpatient procedure, while 889 (82.9%) were therapeutic. The proportion of therapeutic procedures from 2002-2006 was higher than from 1997-2001 (86.6% vs 77.5%, *P*=0.0001). The difficulty grades, as defined by Morriston Hospital ERCP grading scale, were mostly Grade II(494, 46.1%) and Grade III(297, 27.7%) procedures overall; however, there was a two-fold increase in Grade IV procedures in the second five-year period, compared to the first (15.3% vs 7.2%, P<0.0001). ERCP was performed primarily for a biliary indication in 853 (79.6%) and a pancreatic indication in 95 (8.9%) with 122 (11.4%) for both a biliary and pancreatic indication. The commonest biliary indications included choledocholithiasis (500, 46.6%), biliary colic in the absence of documented choledocholithiasis (307, 28.6%), and relief of malignant biliary obstruction (116, 10.8%). The commonest pancreatic indications for ERCP were to determine etiology of acute pancreatitis (135, 12.6%), or recurrent acute pancreatitis (34, 3.2%), and chronic pancreatic fluid collection (18, 1.7%). Suspected sphincter of Oddi dysfunction was the indication in only (19, 1.7%) of ERCPs. A trainee was involved in 667 (62.2%) cases.

Biliary sphincterotomy was performed in 620 (57.8%) procedures; the pancreatic duct was injected in 404 (37.7%) cases and was cannulated in 255 (23.8%) procedures. Biliary stents were placed in 185 (17.3%) cases; prophylactic pancreatic stents were placed in 59 (5.5%) patients. Placement of pancreatic stents increased in the second 5-year period, compared to the first (8.1% vs 1.6%, *P*<0.0001). Ampullectomy was performed in 7 (0.7%) cases and 16 (1.5%) cases were transgastric or transduodenal débridements of pancreatic necrosis (15 of which

occurred in the second 5-year period, *P*=0.0053). Only 31 (2.9%) of ERCPs were deemed as failures as the goal of the procedure was not achieved, resulting in a 97.1% success rate. None of the patients received any prophylaxis to prevent post-ERCP pancreatitis.

Table III: Procedural Characteristics

	(%)
Cholecystectomy within 30 days prior to ERCP	113 (10.5)
Altered anatomy	21 (2.0)
Anticoagulation	20 (1.9)
Prior ERCP	277 (25.8)
Biliary indications	975 (91.0)
Cholangitis	56 (5.2)
Cholecystitis	41 (3.8)
Bleeding	4 (0.4)
Choledocholithiasis	500 (46.6)
Malignant stricture	116 (10.8)
Hilar stricture	5 (0.5)
Benign stricture	46 (4.3)
Ca pancreas	21 (2)
Papillary stenosis	8 (0.7)
Ca ampulla	14 (1.3)
Anastomotic stricture	29 (2.7)
Post cholecystectomy	69 (6.4)
Suspected SOD	19 (1.8)
PSC	21 (2)
Bile leaks	23 (2.1)
Biliary colic	307 (28.6)
Biliary dilation	27 (2.5)
Stent removal	52 (4.9)
Elevated AST and ALT	76 (7.1)
Pancreatic indications	217 (20.2)
Acute pancreatitis	135 (12.6)
Recurrent acute pancreatitis	34 (3.2)
Chronic pancreatitis	17 (1.6)
Cyst	8 (0.7)
Duct leak	9 (0.8)
Duct stricture	7 (0.7)

Acute fluid collection	7 (0.7)
Chronic fluid collection	18 (1.7)
Necrosectomy	14 (1.3)
Inpatient	606 (56.5)
Therapeutic	889 (82.9)
Difficulty grade	
I	152 (14.2)
II	494 (46.1)
III	297 (27.7)
IV	129 (12.0)
Trainee present	667 (62.2)
Anesthesia	
Conscious sedation	1030 (96.1)
Fentanyl	51 (4.8)
Versed	1028 (95.8)
Benadryl	6 (0.6)
Demerol	979 (91.2)
Phenergan	90 (8.4)
Droperidol	25 (2.3)
General (or propofol)	42 (3.9)
Peri-ampullary diverticulum	117 (10.9)
Biliary sphincterotomy	620 (57.8)
Precut biliary sphincterotomy	125 (11.7)
Biliary stent placed	185 (17.3)
Pancreatic sphincterotomy	13 (1.2)
Pancreatic duct stent placed	59 (5.5)
Ampullectomy	7 (0.7)
Transgastric/transduodenal drainage	16 (1.5)
Sphincterotomy bleeding noted during procedure	45 (4.2)

ERCP – endoscopic retrograde cholangiopancreatography
AST – aspartate aminotransferase
ALT – alanine aminotransferase

Sedation

Only 42(3.9%) of procedures were done with anesthesia support. Of the remaining ERCPs done under moderate sedation, the mean dose of fentanyl was 159 ± 86mcg (in 51 ERCPs), midazolam 6.1 ± 2.6mg (1028 ERCPs), meperidine 97 ± 46mg (979 ERCPs), and promethazine 21 ± 8mg (90 ERCPs).

Outcomes

Following 1072 ERCPs in Olmsted County, over ten years, there were 273 admissions to the hospital within 30 days after 236 procedures (22% of all procedures). Table IV lists the outcomes in the study cohort. Of the 273 admissions, only 62 (22.7%) were definitely related to the index ERCP procedure, with another 2 (0.7%) probably related, and 4 (1.4%) possibly related to the procedure. Of the remaining 205 admissions unrelated to procedural AEs of the index ERCP, 79 were planned for elective surgeries, including cholecystectomy. Intraprocedural AEs were rare, with 20 (1.9%) necessitating a change in intra-procedural anesthesia; no deaths occurred during the procedure. There were 47 sphincterotomy-induced intra-procedural bleeding episodes treated with various modalities, including epinephrine injection, cautery and tamponade.

The AE rate was 5.3% including pancreatitis (26, 2.4%), infection/cholangitis (16, 1.5%), bleeding (15, 1.4%), and perforation (4, 0.37%). 53 cases were determined to be mild to moderate; however, 3 infections, all 4 perforations, and 1 bleed were considered severe. The 30-day mortality rate was 2.4%. None of the deaths were directly related to the ERCP or AEs thereof. Repeat ERCP procedures were required in 93 (8.7%) patients and 45 (4.2%) had an esophagogastroduodenoscopy (EGD) within 30 days of the index ERCP.

Table IV: Procedure Outcomes

	(%)
Success	041 (97.1)
Death	
During procedure	0 (0.0)
Within 30 days	26 (2.4)
Need for repeat procedure within 30 days	
ERCP	93 (8.7)
EGD	45 1 (4.2)
Number of readmissions within 30 days	273
Definitely related to procedure	62 (22.7)
Possibly related to procedure	6 (2.2)
Definitely not related to procedure	205 (75.1)
Surgery within 30 days	
Elective cholecystectomy	52 (4.9)
Elective Whipple	16 (5.9)
Other elective	11 (4.0)
Emergent cholecystectomy	6 (2.2)
ERCP complications requiring readmit	53 (4.9)
Pancreatitis	26 (2.4)
Mild	18
Moderate	8
Severe	0
Infection/cholangitis	16 (1.5)
Mild	6
Moderate	7
Severe	3
Bleeding	15 (1.4)
Mild	6
Moderate	8
Severe	1
Perforation	4 (0.37)
Mild	0
Moderate	0
Severe	4

Risk factors for AEs

In order to determine if there were identifiable risk factors for AEs arising from ERCP in our cohort, the relative frequency and distribution of patient and procedural characteristics were compared between patients who had a procedural AE and those who did not (Table V). Patient characteristics identified through multivariate analysis to be associated with AEs included: age less than 45 years (OR 2.23 (95% CI 1.03 – 4.84) for age <45 years vs ≥65 years, *P*=0.0498); and BMI ≥35 (OR 0.31 (95% CI 0.14 – 0.72) for BMI 25-34 vs ≥35, *P*=0.0024). Procedural characteristics identified to be associated with increased risk of AEs included: patient's first ERCP (OR 2.22 (95% CI 1.04 – 4.75), *P*=0.0394); pancreatic duct cannulation (OR 2.7 (95%CI 1.4 - 5.1), *P*=0.0026); outpatient procedure (OR 5.4 (95% CI 2.6 – 11.4), *P*<0.0001); intraprocedure sphincterotomy bleeding (OR 10.0 (95% CI 3.8 – 26.1), *P*<0.0001); difficulty grade (OR 8.9 (95% CI 1.9 – 43.1) for grade 4 vs 1, *P*=0.0204).

Table V. Multivariate analysis of risk factors for post-ERCP complications

Risk factor	Odds ratio (95% CI)	*P*-value
Age <45 vs ≥65	2.23 (1.03 – 4.84)	0.0498 *
Age 45-64 vs ≥65	1.3 (0.62 – 2.72)	0.6697
Female gender	1.2 (0.61 – 2.21)	0.6412
BMI <25 vs ≥35	0.84 (0.40 – 1.74)	0.1972
BMI 25-34 vs ≥35	0.31 (0.14 – 0.72)	0.0024 *
No previous ERCP	2.22 (1.04 – 4.75)	0.0394 *
Outpatient ERCP	5.4 (2.6 – 11.4)	<0.0001 *
Pancreatic duct cannulation	2.7 (1.4 – 5.1)	0.0026 *

Absence of trainee	1.36	(0.72 – 2.59)	0.3487
Intraprocedure sphincterotomy bleeding	10.0	(3.8 – 26.1)	<0.0001 *
Difficulty grade 1 vs 4	0.11	(0.02 – 0.54)	0.0204 *
Difficulty grade 2 vs 4	0.45	(0.18 – 1.14)	0.9199
Difficulty grade 3 vs 4	0.94	(0.42 – 2.13)	0.0129 *

DISCUSSION

In the adult Olmsted County study population, which is considered representative of the US population, ERCP utilization rates nearly doubled over the ten-year period from January 1, 1997 to December 31, 2006 from 58.0 to 104.8 cases per 100,000 persons/year. This trend was influenced by a substantial increase in the rate of therapeutic procedures and a slight decrease in diagnostic procedures. Importantly, ERCP was performed predominantly for common 'bread and butter' indications including cholangitis, biliary colic, and pancreatitis. This information underscores the fact that ERCP is currently mainly a therapeutic modality, and should be available at a community-based level. Training in ERCP should be focussed on gaining expertise mainly for removal of common duct stones and relief of distal biliary obstruction. For a community based gastroenterologist, the need for more complex procedures is rare, and these procedures should be carried out at tertiary care centres.

ERCP utilization rates in Olmsted County in this study are in some ways divergent with national data. For instance, Mazen Jamal et al queried the Nationwide Inpatient Sample (NIS) data for ERCP utilization rates from 1996 to 2002[14]. They found that the rate of inpatient ERCPs dropped from 74.95/100,000 persons in 1996 to 59.70/100,000 in 2002, driven mostly by

a decrease in diagnostic procedures, while there was a slight concomitant increase in therapeutic procedures. However, because they were using NIS sample, data are not available on outpatient utilization of ERCP. In contrast, outpatient procedures comprised 43.5% of procedures in our study.

Over the study period, overall utilization of EUS and MRCP have also increased in Olmsted County. ERCP is likely now utilized almost exclusively for therapeutic purposes because of the diagnostic abilities of EUS and MRCP, and the improvements in contrast-enhanced CT scans. Also, increased use of EUS and MRCP might actually result in more therapeutic ERCP as seen in our study, which contradicts popular belief that utilization of ERCP has decreased over time with increased use of other diagnostic modalities.

Unplanned admissions commonly occur after ERCP (22% within 30 days), but are most often not related to procedural AEs, which occur in 5.3% of all patients undergoing ERCP. Unplanned admissions within 30 days after a procedure are increasingly being counted as negative indicators of healthcare quality[15]. However, our data suggest that in the case of ERCP, this outcome measure may not be a valid indicator of the quality of the procedure itself and is likely related to either underlying disease, a finding of the procedure itself that leads to elective surgery, or possibly to other comorbidities. Identification and complete capture of 30-day admissions is a strength of our study, in comparison to past studies, where capturing remote AEs were incomplete [6]. Because this is a population-based study, and Mayo Clinic is the only provider for ERCP in the population, all AEs were identified.

Severe procedural AEs, including pancreatitis (2.4%), bleeding (1.5%), infection (1.4%), and mortality related to the procedure (0%), were uncommon. Most AEs were mild to moderate, and at rates similar to previously published reports[3, 6]. In a systematic review of 21 surveys of

ERCP, AE rates in a population of 16,855 patients were 6.85%, with pancreatitis, infection and bleeding occurring in 3.5%, 1.4% and 1.3% of cases[3]; mortality rate was 0.33%. Cotton et al. reported on 11,497 procedures at multiple centers and found a 4.0% AE rate, with rates of 2.6% for pancreatitis and 0.3% for bleeding. Mortality rate in this cohort was 0.06%[6]. Although 2.4% of patients in our study died within 30 days of the ERCP, none of these deaths were ERCP-related, and there were no intra- or peri-procedural deaths in our study. Because the AE rates in our study are not appreciably different than the rates reported in the literature, it is likely that ERCP procedures carried out at tertiary care centres are associated with low adverse event rates.

Numerous studies have enumerated various risk factors for AEs following ERCP[6, 8, 10, 16, 17]. Commonly accepted risk factors for any AE after ERCP include suspected sphincter of Oddi dysfunction, cirrhosis, difficult cannulation, performance of precut sphincterotomy, percutaneous biliary access, and lower ERCP case volumes, with young age, pancreatic duct contrast injection and failed biliary drainage identified in some studies. In our study, younger patient age, higher BMI, first ERCP, pancreatic duct cannulation, intra-procedural post sphincterotomy bleeding, therapeutic procedures, and outpatient procedures were identified as risk factors for any AE through a multivariate analysis.

Consistent with our findings, younger age has been previously shown to be a risk factor for AEs, especially post-ERCP pancreatitis (PEP)[5, 8, 10]. Pancreatic duct cannulation is known to be a risk-factor for development of PEP[6]. Toward the end of this study period, data emerged supporting the use of prophylactic pancreatic duct stents to decrease the incidence of PEP and were published. In our study period, in only 59 (5.5%) procedures, we placed a pancreatic duct stent. Hence, our study is not able to adequately define the rate of PEP with routine placement of prophylactic pancreatic stents.

One limitation of our study is that it is a retrospective review of data with its inherent biases. However, the data were manually abstracted by a single gastroenterologist from an electronic medical record, and significant adverse events and hospitalizations are not likely to have been missed. Another limitation is that even though the population studied is a county-based population, the skills of the endoscopists are at a higher level than endoscopists in smaller community hospitals. Therefore, the AE rate in this community setting could be lower than one would expect in community settings at large.

In conclusion, our study shows that utilization of ERCP at a population level continues to rise; specifically utilization of therapeutic procedures. The most common indications for ERCP remain relief of biliary colic or cholangitis, and this procedure may be carried out with moderate sedation. Adverse events of ERCP remain uncommon and deaths are rare. The study adds important epidemiologic data on trends in the utilization of ERCP, as well as population-based estimates of the risk of adverse events from ERCP that will be useful in clinical decision making and determination of resource allocation. The findings of the study may also impact ERCP training criteria.

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Figure Legends

Table IA. Morriston Hospital ERCP grading scale (Ragunath et al, Post Grad Med J, 2003)

Table IB. Consensus criteria for ERCP complications (Cotton et al, GIE, 1991)

Table II. Patient Characteristics

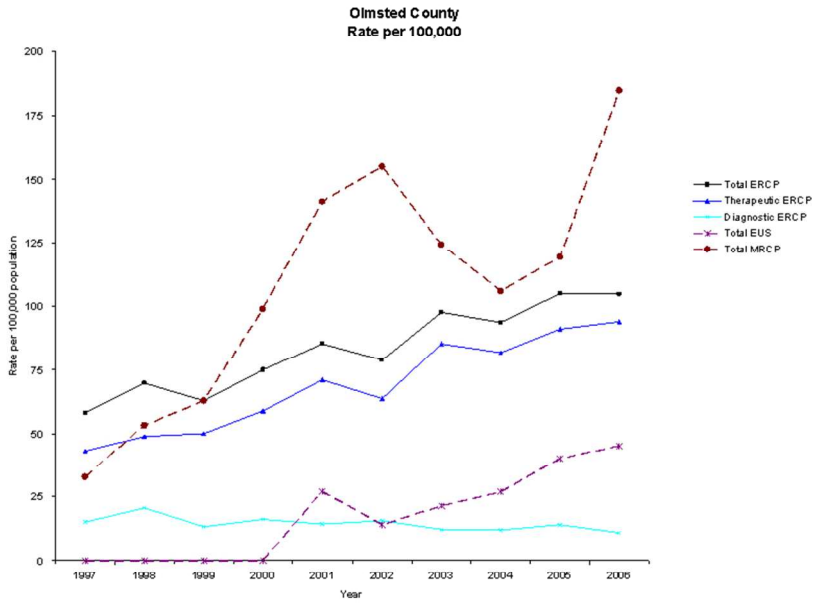
Table III. Procedural Characteristics

Table IV. Procedure Outcomes

Table V. Multivariate analysis of risk factors for post-ERCP complications

Figure I. Utilization characteristics of ERCP, EUS, and MRCP in Olmsted County over 10-year period.

Figure 1.



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STROBE STATEMENT checklist of items that should be included in reports of Observational Studies

SECTION/TOPIC	Item No.	Checklist Item	Reported on page No.
TITLE AND ABSTRACT	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2, 3
INTRODUCTION			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4, 5
METHODS			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6
Participants	6	(a) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5,6
		(b) *Cohort study*—For match studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6,7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7,8
		(b) Describe any methods used to examine subgoups and interactions	
		(c) Explain how missing data were addressed	
		(d) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
RESULTS			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	8,9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarize follow-up time (e.g., average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time *Case-control study*—Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study*—Report numbers of outcome events or summary measures	10
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make	10

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		clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	(d) Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	
DISCUSSION			
Key results	18	Summarize key results with reference to study objectives	12,13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalizability	21	Discuss the generalizability (external validity) of the study results	15
OTHER INFORMATION			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Endoscopic Retrograde Cholangiopancreatography – Utilization and outcomes in a 10-year population based cohort

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Endoscopic Retrograde Cholangiopancreatography – Utilization and outcomes in a 10-year population based cohort

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Extra data is available by contacting the corresponding author.

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Tables – 5

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Keywords: ERCP, utilization, complications, hospitalization

SUMMARY

Article Focus:

- Due to increasing use of quality metrics, accurate measures of utilization and procedural adverse event risks are necessary to establish benchmarks for quality, and are best determined from community-based studies.
- There are no reports of community-based utilization of ERCP in the US.
- The aims of this population-based study were to determine the utilization of ERCP including changes over time, the incidence of inpatient admissions for adverse events within 30 days of ERCP, and risk factors for procedural related adverse events.

Key Messages:

- Population utilization of ERCP in Olmsted County MN rose over the ten year period from 1997 to 2006, driven specifically by increases in therapeutic procedures. The most common indications for ERCP were therapy of choledocholithiasis and to determine etiology of acute pancreatitis.
- Admissions within 30 days after ERCP are common, but are usually unrelated. Complications of ERCP remain infrequent at 5.3% and no deaths were directly related.
- Risk factors associated with adverse events from ERCP include younger age, BMI ≥35, pancreatic duct cannulation, outpatient procedures, intraprocedure sphincterotomy bleeding, difficulty grade, and patient's first ERCP.

Strengths and Limitations:

Strengths:

- Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community.
- The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and adverse events of ERCP with full details of procedures and subsequent hospitalizations can be assessed.

Limitations:

- The study is a retrospective review with inherent potential biases.
- The skills of the endoscopists are likely at a higher level than endoscopists in smaller community hospitals. Therefore, the adverse event rate in this community setting could be lower than one would expect in other community settings.

ABSTRACT

Objective: To determine utilization of ERCP; incidence of inpatient admissions for complications occurring within 30 days of ERCP; and risk factors for procedural related complications, in a population based study.

Design: Retrospective cohort study

Setting: Olmsted County, MN

Participants: All adult residents of Olmsted County, MN, who underwent ERCP from 1997 to 2006.

Interventions: Diagnostic and therapeutic ERCPs were assessed.

Primary and Secondary outcome measures: Patient and procedural characteristics and complications within 30 days; and rates of ERCP utilization and unplanned admissions and risk factors for admissions.

Results: In ten years, 1072 ERCPs were performed on 827 individual patients. Average utilization of ERCP was 83.1 ERCPs/100,000 persons/year, with an increase from 58.0 to 104.8 ERCPs/100,000 persons/year over time, driven by increases in therapeutic procedures. Within 30 days after 236 procedures, 62 admissions were definitely related to the index ERCP. The complication rate was 5.3%, including pancreatitis(26, 2.4%), infection/cholangitis(16, 1.5%),

bleeding(15, 1.4%), and perforation(4, 0.37%). 30-day mortality was 2.4%; none of which were directly related to the ERCP or complications thereof. Risk factors identified through multivariate analysis to be associated with adverse events included: age <45 years(p=0.0498); BMI ≥35(p=0.0024); pancreatic duct cannulation(p=0.0026); outpatient procedure(p<0.0001); intraprocedure sphincterotomy bleeding(*P*<0.0001); difficulty grade(*P*=0.115); and patient's first ERCP(*P*=0.0394).

Limitations: Retrospective study.

Conclusions: Population utilization of ERCP rose during the study period, specifically in therapeutic procedures. Admissions within 30 days of ERCP are common, but often unrelated. Complications of ERCP remain infrequent and deaths quite unusual.

Abbreviations:

AE – adverse event

EGD – esophagogastroduodenoscopy

ERCP - endoscopic retrograde cholangiopancreatography

EUS – endoscopic ultrasound

MRCP - magnetic resonance cholangiopancreatography

BACKGROUND

Since its first description in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has become an established modality for the diagnosis and treatment of pancreaticobiliary disorders[1 2]. Over the years, ERCP has evolved from a purely diagnostic, to a mainly therapeutic procedure. Around 500,000 ERCPs are performed annually in the United States (US) with adverse event (AE) rates between 4% and 10%,[3] and mortality between 0.05% and 1%[4-7]. The most common AEs following ERCP include pancreatitis, hemorrhage, and infection, which occured in 4% to7% of procedures[3 6 8]. There is an increased risk of AEs after therapeutic procedures and in patients with suspected Sphincter of Oddi dysfunction[6]. Since ERCP is the endoscopic procedure with the highest cost and AE rates, diagnostic ERCP is now avoided in favor of other diagnostic modalities such as less-invasive endoscopic ultrasound (EUS) and non-invasive magnetic resonance cholangiopancreatography (MRCP)[2 3 9]. In an era of increasing utilization of quality metrics, accurate measures of utilization rates and procedural adverse event risks are necessary to establish meaningful benchmarks for quality, and are best determined from community-based studies.

There are no reports of community-based utilization of ERCP in the US, but there are several from Europe[8 10]. Published reports of ERCP related AEs have all been single-centered or multi-centered studies from tertiary care centers and affected by referral bias, leading to high estimates of risk that may not apply to the general population. All adverse events of procedures done at tertiary care centers may not be captured since the patients may seek care for AEs closer to their homes and thus, lost to follow-up.

The aims of this population-based study were to determine (1) the utilization of ERCP, including changes over time; (2) the incidence of inpatient admissions for AEs within 30 days of

ERCP; and (3) risk factors for procedural related AEs among residents of Olmsted County, MN over a ten-year period from 1997-2006. The findings of this study are unique, as they represent population based estimates of utilization and risks associated with ERCP and may serve as more accurate and clinically meaningful data for clinical decision making and development of quality benchmarks.

METHODS

Study Design: A retrospective cohort study was conducted with approval of the Institutional Review Board of Mayo Clinic in compliance with federal regulations of the U.S. Department of Health and Human Services for protection of human subjects and the Health Information Protection and Portability Act. All patients provided consent for medical record review. Billing records from Mayo Clinic and associated hospitals were queried for Olmsted County residents who had undergone an ERCP during a ten-year period from January 1, 1997 to December 31, 2006. ERCPs were identified using CPT codes for ERCP, including 43260, 43261, 43262, 43263, 43264, 43265, 43267, 43268, 43269, 43271, 43272, and 47999. Utilization characteristics for EUS were determined in the same population using codes 43232, 43238, and 43242 and for MRCP using codes 74181, 74182, and 74183. Subjects also had to be age ≥ 18 years, live in Olmsted County, and have valid authorization to review medical records for research purposes in accordance with Minnesota State statutes.

Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community. Olmsted County comprises over 100,000 persons, of whom 85% are Caucasian and 50% are women; socio-demographically, the community is similar to the US population. Over half of the county's population is seen at one of

the Mayo Clinic facilities; 95% of local residents will have had at least one medical contact with a local care provider (*e.g.*, for dental X-rays, sports physical examinations, pre-employment examinations, minor illness, and routine medical care) during any 4-year period[11]. Mayo Clinic has a common medical record system with its two affiliated hospitals (Saint Mary's and Rochester Methodist) for 90 years. Mayo Clinic's single record system contains both inpatient and outpatient data. Diagnoses and surgical procedures recorded in these records are indexed. It includes diagnoses made for outpatients seen in office or clinic consultations, emergency room visits, and diagnoses recorded for hospital inpatients, autopsy examinations, or on death certificates. The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and AEs of ERCP with full details of the hospitalization can be assessed.

Medical records were reviewed retrospectively by the primary author. Patient and procedural characteristics, as well as AEs within 30 days were recorded. As many as 170 variables were collected for each procedure and recorded into a database.

Primary outcomes measured were (1) utilization rates of unique ERCP procedures in the adult population (age 18 years and older) of Olmsted County from 1997-2006, and (2) the rate of unplanned admissions within 30 days following ERCP for ERCP-related AEs. Secondary outcomes included patient and procedural characteristics, predictive of having an unplanned admission within 30 days after ERCP for an ERCP-related AE.

Utilization metrics included the patients' age, sex, race, Charlson score at the time of ERCP[12], body mass index (BMI), cholecystectomy within 30 days prior to ERCP, altered anatomy (including gastrojejunostomy, Whipple anatomy, hepatico- and choledocho-jejunostomy), presence of cirrhosis, and previous history of ERCP. Indications for ERCP were

then examined as biliary versus pancreatic, diagnostic versus therapeutic, and graded for complexity using the previously published Morriston Hospital ERCP grading scale (Table IA)[13]. Diagnostic procedures had a CPT code of 43260 where no intervention was performed, other than a cholangiogram or pancreatogram; all other procedures were therapeutic. Multiple intra-procedural details, including presence of a trainee, type and amount of sedation used, and biliary and pancreatic ductal interventions were noted. Success of the procedure was recorded as the ability to cannulate the intended duct and achieve the intended therapy.

AEs recorded included unplanned admissions; sedation-related events, including pulmonary and cardiovascular events; infection; pancreatitis; bleeding; perforation; need for repeat endoscopic procedure; or mortality within 30 days. These outcomes were determined as being related to the index ERCP by author review. AEs were deemed to be definitely related, probably related, possibly related, or definitely unrelated to the index ERCP. Possibly related AEs included patients admitted with abdominal pain, but without evidence of definite pancreatitis by laboratory studies or documented cholangitis. Probably related AEs included biliary or pancreatic stent dysfunction leading to repeat the procedure within 30 days of the index procedure, but without any of the defined AEs of pancreatitis, infection, perforation, and gastrointestinal bleeding. The latter AEs were categorized as mild, moderate, and severe, according to established consensus criteria (Table IB)[6 14] Patients undergoing elective surgery including cholecystectomy within 30 days of ERCP were also identified.

Statistical Analysis

Univariate analyses were performed to obtain descriptive statistics for patient and procedural characteristics. Annual incidence was determined by dividing the number of ERCPs performed

on the study subjects during a calendar year by the adult population of Olmsted County during that period, according to County records and normalized to 100,000 persons. To test for associations between patient and procedural characteristics and ERCP related AEs, values of these characteristics were compared between subjects who experienced ERCP-related AEs and subjects who did not by two sample t-tests for continuous variables, and chi square test for discrete variables. Multivariable logistic regression analyses were used to determine patient and procedural characteristics predictive of ERCP-related AEs. *P*-values less than 0.05 were considered statistically significant. All analyses for this study were done using SAS statistical software (SAS version 9.1 for Windows; SAS Institute Inc., Cary, North Carolina).

RESULTS

Demographic characteristics

In the 10-year period from January, 1, 1997 to December, 31, 2006, 1072 ERCPs were performed on 827 individual adult patients in Olmsted County. Patient demographic characteristics can be seen in Table II. Prior to the index cholecystectomy, 232 (28%) patients had a previous cholecystectomy; 21 (2%) patients had altered anatomy, and 20 (1.9%) were taking clopidogrel or warfarin at the time of the ERCP. There were 153 patients who had more than one ERCP during the 10-year period, and the mean number of ERCPs in these patients was 1.3.

Utilization characteristics

Average utilization of ERCP was 83.1 ERCPs per 100,000 persons/year, with an increasing trend in utilization from 58.0 to 104.8 ERCPs per 100,000 persons/year over the 10-year period.

Therapeutic ERCPs increased over the same timeframe from 42.9 to 93.9 ERCPs per 100,000 persons/year (average 68.7). However, diagnostic ERCPs decreased slightly from 15.1 to 10.9 and averaged 14.4 ERCPs per 100,000 persons/year. EUS and MRCP utilization in the same population also steadily increased over this time period (Figure I).

Procedural characteristics

Procedural characteristics can be seen in Table III. Of the 1072 ERCPs performed over the 10-year period, 606(56.5%) were performed on inpatients, while 889 (82.9%) were therapeutic. The proportion of therapeutic procedures from 2002-2006 was higher than from 1997-2001 (86.6% vs 77.5%, *P*=0.0001). The difficulty grades, as defined by Morriston Hospital ERCP grading scale, were mostly Grade II(494, 46.1%) and Grade III(297, 27.7%) procedures overall; however, there was a two-fold increase in Grade IV procedures in the second five-year period, compared to the first (15.3% vs 7.2%, P<0.0001). ERCP was performed primarily for a biliary indication in 853 (79.6%) and a pancreatic indication in 95 (8.9%) with 122 (11.4%) for both a biliary and pancreatic indication. The commonest biliary indications included choledocholithiasis (500, 46.6%), biliary colic in the absence of documented choledocholithiasis (307, 28.6%), and relief of malignant biliary obstruction (116, 10.8%). The commonest pancreatic indications for ERCP were to determine etiology of acute pancreatitis (135, 12.6%), or recurrent acute pancreatitis (34, 3.2%), and chronic pancreatic fluid collection (18, 1.7%). Suspected sphincter of Oddi dysfunction was the indication in only (19, 1.7%) of ERCPs. A trainee was involved in 667 (62.2%) cases.

Biliary sphincterotomy was performed in 620 (57.8%) procedures; the pancreatic duct was injected in 404 (37.7%) cases and was cannulated in 255 (23.8%) procedures. Biliary stents

were placed in 185 (17.3%) cases; prophylactic pancreatic stents were placed in 59 (5.5%) patients. Placement of pancreatic stents increased in the second 5-year period, compared to the first (8.1% vs 1.6%, $P<0.0001$). Ampullectomy was performed in 7 (0.7%) cases and 16 (1.5%) cases were transgastric or transduodenal débridements of pancreatic necrosis (15 of which occurred in the second 5-year period, $P=0.0053$). Only 31 (2.9%) of ERCPs were deemed as failures as the goal of the procedure was not achieved, resulting in a 97.1% success rate. None of the patients received any prophylaxis to prevent post-ERCP pancreatitis.

Sedation

Only 42(3.9%) of procedures were done with anesthesia support. Of the remaining ERCPs done under moderate sedation, the mean dose of fentanyl was 159 ± 86mcg (in 51 ERCPs), midazolam 6.1 ± 2.6mg (1028 ERCPs), meperidine 97 ± 46mg (979 ERCPs), and promethazine 21 ± 8mg (90 ERCPs).

Outcomes

Following 1072 ERCPs in Olmsted County, over ten years, there were 273 admissions to the hospital within 30 days after 236 procedures (22% of all procedures). Table IV lists the outcomes in the study cohort. Of the 273 admissions, only 62 (22.7%) were definitely related to the index ERCP procedure, with another 2 (0.7%) probably related, and 4 (1.4%) possibly related to the procedure. Of the remaining 205 admissions unrelated to procedural AEs of the index ERCP, 79 were planned for elective surgeries, including cholecystectomy. Intraprocedural AEs were infrequent, with 20 (1.9%) necessitating a change in intra-procedural anesthesia; no deaths occurred during the procedure. There were 47 sphincterotomy-induced intra-procedural bleeding

episodes treated with various modalities, including epinephrine injection, cautery and tamponade.

The AE rate was 5.3% including pancreatitis (26, 2.4%), infection/cholangitis (16, 1.5%), bleeding (15, 1.4%), and perforation (4, 0.37%). 53 cases were determined to be mild to moderate; however, 3 infections, all 4 perforations, and 1 bleed were considered severe. The 30-day mortality rate was 2.4%. None of the deaths were directly related to the ERCP or AEs thereof. Repeat ERCP procedures were required in 93 (8.7%) patients and 45 (4.2%) had an esophagogastroduodenoscopy (EGD) within 30 days of the index ERCP.

Risk factors for AEs

In order to determine if there were identifiable risk factors for AEs arising from ERCP in our cohort, the relative frequency and distribution of patient and procedural characteristics were compared between patients who had a procedural AE and those who did not (Table V). Patient characteristics identified through multivariate analysis to be associated with AEs included: age less than 45 years (OR 2.23 (95% CI 1.03 – 4.84) for age <45 years vs ≥65 years, *P*=0.0498); and BMI ≥35 (OR 0.31 (95% CI 0.14 – 0.72) for BMI 25-34 vs ≥35, *P*=0.0024). Procedural characteristics identified to be associated with increased risk of AEs included: patient's first ERCP (OR 2.22 (95% CI 1.04 – 4.75), *P*=0.0394); pancreatic duct cannulation (OR 2.7 (95%CI 1.4 - 5.1), *P*=0.0026); outpatient procedure (OR 5.4 (95% CI 2.6 – 11.4), *P*<0.0001); intraprocedure sphincterotomy bleeding (OR 10.0 (95% CI 3.8 – 26.1), *P*<0.0001); difficulty grade (OR 8.9 (95% CI 1.9 – 43.1) for grade 4 vs 1, *P*=0.0204).

DISCUSSION

In the adult Olmsted County study population, which is considered representative of the US population, ERCP utilization rates nearly doubled over the ten-year period from January 1, 1997 to December 31, 2006 from 58.0 to 104.8 cases per 100,000 persons/year[15]. This trend was influenced by a substantial increase in the rate of therapeutic procedures and a slight decrease in diagnostic procedures. Importantly, ERCP was performed predominantly for common 'bread and butter' indications including cholangitis, biliary colic, and pancreatitis. This information underscores the fact that ERCP is currently mainly a therapeutic modality, and should be available at a community-based level. Training in ERCP should be focussed on gaining expertise mainly for removal of common duct stones and relief of distal biliary obstruction. For a community based gastroenterologist, the need for more complex procedures is rare, and these procedures should be carried out at tertiary care centres.

ERCP utilization rates in Olmsted County in this study are in some ways divergent with national data. For instance, Mazen Jamal et al queried the Nationwide Inpatient Sample (NIS) data for ERCP utilization rates from 1996 to 2002[16]. They found that the rate of inpatient ERCPs dropped from 74.95/100,000 persons in 1996 to 59.70/100,000 in 2002, driven mostly by a decrease in diagnostic procedures, while there was a slight concomitant increase in therapeutic procedures. However, because they were using NIS sample, data are not available on outpatient utilization of ERCP. In contrast, outpatient procedures comprised 43.5% of procedures in our study.

Over the study period, overall utilization of EUS and MRCP have also increased in Olmsted County. ERCP is likely now utilized almost exclusively for therapeutic purposes because of the diagnostic abilities of EUS and MRCP, and the improvements in contrast-

enhanced CT scans. Also, increased use of EUS and MRCP might actually result in more therapeutic ERCP as seen in our study, which contradicts popular belief that utilization of ERCP has decreased over time with increased use of other diagnostic modalities.

Unplanned admissions commonly occur after ERCP (22% within 30 days), but are most often not related to procedural AEs, which occur in 5.3% of all patients undergoing ERCP. Unplanned admissions within 30 days after a procedure are increasingly being counted as negative indicators of healthcare quality[17]. However, our data suggest that in the case of ERCP, this outcome measure may not be a valid indicator of the quality of the procedure itself and is likely related to either underlying disease, a finding of the procedure itself that leads to elective surgery, or possibly to other comorbidities. Identification and complete capture of 30-day admissions is a strength of our study, in comparison to past studies, where capturing remote AEs were incomplete [6]. Because this is a population-based study, and Mayo Clinic is the only provider for ERCP in the population, all AEs were identified.

Severe procedural AEs, including pancreatitis (2.4%), bleeding (1.5%), infection (1.4%), and mortality related to the procedure (0%), were uncommon. Most AEs were mild to moderate, and at rates similar to previously published reports[3 6]. In a systematic review of 21 surveys of ERCP, AE rates in a population of 16,855 patients were 6.85%, with pancreatitis, infection and bleeding occurring in 3.5%, 1.4% and 1.3% of cases[3]; mortality rate was 0.33%. Cotton et al. reported on 11,497 procedures at multiple centers and found a 4.0% AE rate, with rates of 2.6% for pancreatitis and 0.3% for bleeding. Mortality rate in this cohort was 0.06%[6]. Although 2.4% of patients in our study died within 30 days of the ERCP, none of these deaths were ERCP-related, and there were no intra- or peri-procedural deaths in our study. Because the AE rates in

our study are similar to the rates reported in the literature, it is likely that ERCP procedures carried out at other tertiary care centres are also associated with low adverse event rates.

Numerous studies have enumerated various risk factors for AEs following ERCP[6 8 10 18 19]. Commonly accepted risk factors for any AE after ERCP include suspected sphincter of Oddi dysfunction, cirrhosis, difficult cannulation, performance of precut sphincterotomy, percutaneous biliary access, and lower ERCP case volumes, with young age, pancreatic duct contrast injection and failed biliary drainage identified in some studies. In our study, younger patient age, higher BMI, first ERCP, pancreatic duct cannulation, intra-procedural post sphincterotomy bleeding, therapeutic procedures, and outpatient procedures were identified as risk factors for any AE through a multivariate analysis.

Consistent with our findings, younger age has been previously shown to be a risk factor for AEs, especially post-ERCP pancreatitis (PEP)[5 8 10]. Pancreatic duct cannulation is known to be a risk-factor for development of PEP[6]. Toward the end of this study period, data emerged supporting the use of prophylactic pancreatic duct stents to decrease the incidence of PEP and were published. In our study period, in only 59 (5.5%) procedures, we placed a pancreatic duct stent. Hence, our study is not able to adequately define the rate of PEP with routine placement of prophylactic pancreatic stents.

One limitation of our study is that it is a retrospective review of data with its inherent biases. However, the data were manually abstracted by a single gastroenterologist from an electronic medical record, and significant adverse events and hospitalizations are not likely to have been missed. Another limitation is that even though the population studied is a county-based population, the skills of the endoscopists are at a higher level than endoscopists in smaller community hospitals. Therefore, the AE rate in this community setting could be lower than one

would expect in community settings at large. Another notable limitation is that Sphincter of Oddi dysfunction and complications of pancreatitis, diagnoses often referred to a tertiary center, were underrepresented in our study.

In conclusion, our study shows that utilization of ERCP at a population level continues to rise; specifically utilization of therapeutic procedures. The most common indications for ERCP remain relief of biliary colic or cholangitis, and this procedure may be carried out with moderate sedation. Adverse events of ERCP remain uncommon and deaths are infrequent. The study adds important epidemiologic data on trends in the utilization of ERCP, as well as population-based estimates of the risk of adverse events from ERCP that will be useful in clinical decision making and determination of resource allocation. The findings of the study may also impact ERCP training criteria.

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Figure Legends

Table IA. Morriston Hospital ERCP grading scale (Ragunath et al, Post Grad Med J, 2003)

Table IB. Consensus criteria for ERCP complications (Cotton et al, GIE, 1991)

Table II. Patient Characteristics

Table III. Procedural Characteristics

Table IV. Procedure Outcomes

Table V. Multivariate analysis of risk factors for post-ERCP complications

Figure I. Utilization characteristics of ERCP, EUS, and MRCP in Olmsted County over 10-year period.

Table IA: Morriston Hospital ERCP grading scale [13]

Procedure	Grade
Diagnostic ERCP	I
Biliary sphincterotomy, balloon sphincteroplasty, removal of extrahepatic stones ≤1 cm using basket and/or balloon	II
Precut sphincterotomy, large stones removal (>1cm), intrahepatic stone removal, mechanical lithotripsy, stricture dilatation, cytology, stent insertion, and naso-biliary drain	III
Sphincter of Oddi manometry, diagnostic and therapeutic ERCP after Billroth II surgery, minor papilla sphincterotomy, endoscopic ampullectomy, and all pancreatic duct therapeutic procedures. Cholangioscopy, laser lithotripsy, electrohydraulic lithotripsy, combined procedures (PTC and ERCP), and other advanced bile duct therapeutic procedures	IV

ERCP - endoscopic retrograde cholangiopancreatography
PTC – percutaneous transhepatic cholangiography

Table IB: Consensus criteria for ERCP complications [14]

	Mild	Moderate	Severe
Bleeding	Clinical evidence of bleeding (ie not just endoscopic) Hemoglobin drop <3g No need for transfusion	Transfusion: 4 units or less No angiographic intervention or surgery	Transfusion: 5 units or more or intervention (angiographic or surgical)
Perforation	Possible, or only very slight leak of fluid or contrast dye Treatable by fluids and suction for 3 days or less	Any definite perforation treated medically for 4-10 days	Medical treatment for more than 10 days or intervention (percutaneous or surgical)
Pancreatitis	Clinical pancreatitis: amylase at least thrice the upper limit of normal at more than 24 hours after the procedure requiring admission or prolongation of planned admission to 2-3 days	Pancreatitis requiring hospitalization for 4-10 days	Pancreatitis requiring hospitalization for more than 10 days, or hemorrhagic pancreatitis, phlegmon, or intervention (percutaneous drainage or surgery)
Infection (cholangitis)	>38 degrees Celsius at 24-48 hours	Febrile or septic illness requiring>3 days of hospital treatment or endoscopic or percutaneous intervention	Septic shock or surgery

Table II: Patient Characteristics

Age at time of ERCP (years)	
mean (sd)	57.6 (19.8)
18-44 years	283 (26.4%)
45-64 years	357 (33.3%)
> 65+ years	432 (40.3%)
Gender	
Female, n (%)	522 (63.1)
Race	
Caucasian	688 (83.2%)
African American	15 (1.8%)
Other/unknown	124 (15.0%)
Charlson index at time of ERCP[12]	
mean (sd)	3.2 (3.2)
BMI at time of ERCP	
mean (sd)	28.5 (7.2)
< 25	341 (32.4%)
25-34	517 (49.1%)
35+	194 (18.4%)

ERCP – endoscopic retrograde cholangiopancreatography
BMI – body mass index

Table III: Procedural Characteristics

	(%)
Cholecystectomy within 30 days prior to ERCP	113 (10.5)
Altered anatomy	21 (2.0)
Anticoagulation	20 (1.9)
Prior ERCP	277 (25.8)
Biliary indications	975 (91.0)
Cholangitis	56 (5.2)
Cholecystitis	41 (3.8)
Bleeding	4 (0.4)
Choledocholithiasis	500 (46.6)
Malignant stricture	116 (10.8)
Hilar stricture	5 (0.5)
Benign stricture	46 (4.3)
Ca pancreas	21 (2)
Papillary stenosis	8 (0.7)
Ca ampulla	14 (1.3)
Anastomotic stricture	29 (2.7)
Post cholecystectomy	69 (6.4)
Suspected SOD	19 (1.8)
PSC	21 (2)
Bile leaks	23 (2.1)
Biliary colic	307 (28.6)
Biliary dilation	27 (2.5)
Stent removal	52 (4.9)
Elevated AST and ALT	76 (7.1)
Pancreatic indications	217 (20.2)
Acute pancreatitis	135 (12.6)
Recurrent acute pancreatitis	34 (3.2)
Chronic pancreatitis	17 (1.6)
Cyst	8 (0.7)
Duct leak	9 (0.8)
Duct stricture	7 (0.7)
Acute fluid collection	7 (0.7)
Chronic fluid collection	18 (1.7)
Necrosectomy	14 (1.3)
Inpatient	606 (56.5)

Therapeutic	889 (82.9)
Difficulty grade	
I	152 (14.2)
II	494 (46.1)
III	297 (27.7)
IV	129 (12.0)
Trainee present	667 (62.2)
Anesthesia	
Conscious sedation	1030 (96.1)
Fentanyl	51 (4.8)
Versed	1028 (95.8)
Benadryl	6 (0.6)
Demerol	979 (91.2)
Phenergan	90 (8.4)
Droperidol	25 (2.3)
General (or propofol)	42 (3.9)
Peri-ampullary diverticulum	117 (10.9)
Biliary sphincterotomy	620 (57.8)
Precut biliary sphincterotomy	125 (11.7)
Biliary stent placed	185 (17.3)
Pancreatic sphincterotomy	13 (1.2)
Pancreatic duct stent placed	59 (5.5)
Ampullectomy	7 (0.7)
Transgastric/transduodenal drainage	16 (1.5)
Sphincterotomy bleeding noted during procedure	45 (4.2)

ERCP – endoscopic retrograde cholangiopancreatography
AST – aspartate aminotransferase
ALT – alanine aminotransferase

Table IV: Procedure Outcomes

	(%)
Success	041 (97.1)
Death	
During procedure	0 (0.0)
Within 30 days	26 (2.4)
Need for repeat procedure within 30 days	
ERCP	93 (8.7)
EGD	45 1 (4.2)
Number of readmissions within 30 days	273
Definitely related to procedure	62 (22.7)
Possibly related to procedure	6 (2.2)
Definitely not related to procedure	205 (75.1)
Surgery within 30 days	
Elective cholecystectomy	52 (4.9)
Elective Whipple	16 (5.9)
Other elective	11 (4.0)
Emergent cholecystectomy	6 (2.2)
ERCP complications requiring readmit	53 (4.9)
Pancreatitis	26 (2.4)
Mild	18
Moderate	8
Severe	0
Infection/cholangitis	16 (1.5)
Mild	6
Moderate	7
Severe	3
Bleeding	15 (1.4)
Mild	6
Moderate	8
Severe	1
Perforation	4 (0.37)
Mild	0
Moderate	0

Severe	4

Table V. Multivariate analysis of risk factors for post-ERCP complications

Risk factor	Odds ratio (95% CI)	*P*-value
Age <45 vs ≥65	2.23 (1.03 – 4.84)	0.0498 *
Age 45-64 vs ≥65	1.3 (0.62 – 2.72)	0.6697
Female gender	1.2 (0.61 – 2.21)	0.6412
BMI <25 vs ≥35	0.84 (0.40 – 1.74)	0.1972
BMI 25-34 vs ≥35	0.31 (0.14 – 0.72)	0.0024 *
No previous ERCP	2.22 (1.04 – 4.75)	0.0394 *
Outpatient ERCP	5.4 (2.6 – 11.4)	<0.0001 *
Pancreatic duct cannulation	2.7 (1.4 – 5.1)	0.0026 *
Absence of trainee	1.36 (0.72 – 2.59)	0.3487
Intraprocedure sphincterotomy bleeding	10.0 (3.8 – 26.1)	<0.0001 *
Difficulty grade 1 vs 4	0.11 (0.02 – 0.54)	0.0204 *
Difficulty grade 2 vs 4	0.45 (0.18 – 1.14)	0.9199
Difficulty grade 3 vs 4	0.94 (0.42 – 2.13)	0.0129 *

Endoscopic Retrograde Cholangiopancreatography – Utilization and outcomes in a 10-year population based cohort

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SUMMARY

Article Focus:

- Due to increasing use of quality metrics, accurate measures of utilization and procedural adverse event risks are necessary to establish benchmarks for quality, and are best determined from community-based studies.
- There are no reports of community-based utilization of ERCP in the US.
- The aims of this population-based study were to determine the utilization of ERCP including changes over time, the incidence of inpatient admissions for adverse events within 30 days of ERCP, and risk factors for procedural related adverse events.

Key Messages:

- Population utilization of ERCP in Olmsted County MN rose over the ten year period from 1997 to 2006, driven specifically by increases in therapeutic procedures. The most common indications for ERCP were therapy of choledocholithiasis and to determine etiology of acute pancreatitis.
- Admissions within 30 days after ERCP are common, but are usually unrelated. Complications of ERCP remain infrequent at 5.3% and no deaths were directly related.
- Risk factors associated with adverse events from ERCP include younger age, BMI ≥35, pancreatic duct cannulation, outpatient procedures, intraprocedure sphincterotomy bleeding, difficulty grade, and patient's first ERCP.

Strengths and Limitations:

Strengths:

- Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community.
- The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and adverse events of ERCP with full details of procedures and subsequent hospitalizations can be assessed.

Limitations:

- The study is a retrospective review with inherent potential biases.
- The skills of the endoscopists are likely at a higher level than endoscopists in smaller community hospitals. Therefore, the adverse event rate in this community setting could be lower than one would expect in other community settings.

ABSTRACT

Objective: To determine utilization of ERCP; incidence of inpatient admissions for complications occurring within 30 days of ERCP; and risk factors for procedural related complications, in a population based study.

Design: Retrospective cohort study

Setting: Olmsted County, MN

Participants: All adult residents of Olmsted County, MN, who underwent ERCP from 1997 to 2006.

Interventions: Diagnostic and therapeutic ERCPs were assessed.

Primary and Secondary outcome measures: Patient and procedural characteristics and complications within 30 days; and rates of ERCP utilization and unplanned admissions and risk factors for admissions.

Results: In ten years, 1072 ERCPs were performed on 827 individual patients. Average utilization of ERCP was 83.1 ERCPs/100,000 persons/year, with an increase from 58.0 to 104.8 ERCPs/100,000 persons/year over time, driven by increases in therapeutic procedures. Within 30 days after 236 procedures, 62 admissions were definitely related to the index ERCP. The complication rate was 5.3%, including pancreatitis(26, 2.4%), infection/cholangitis(16, 1.5%),

bleeding(15, 1.4%), and perforation(4, 0.37%). 30-day mortality was 2.4%; none of which were directly related to the ERCP or complications thereof. Risk factors identified through multivariate analysis to be associated with adverse events included: age <45 years(p=0.0498); BMI ≥35(p=0.0024); pancreatic duct cannulation(p=0.0026); outpatient procedure(p<0.0001); intraprocedure sphincterotomy bleeding(*P*<0.0001); difficulty grade(*P*=0.115); and patient's first ERCP(*P*=0.0394).

Limitations: Retrospective study.

Conclusions: Population utilization of ERCP rose during the study period, specifically in therapeutic procedures. Admissions within 30 days of ERCP are common, but often unrelated. Complications of ERCP remain infrequent and deaths quite unusual.

Abbreviations:

AE – adverse event

EGD – esophagogastroduodenoscopy

ERCP - endoscopic retrograde cholangiopancreatography

EUS – endoscopic ultrasound

MRCP - magnetic resonance cholangiopancreatography

BACKGROUND

Since its first description in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has become an established modality for the diagnosis and treatment of pancreaticobiliary disorders[1 2]. Over the years, ERCP has evolved from a purely diagnostic, to a mainly therapeutic procedure. Around 500,000 ERCPs are performed annually in the United States (US) with adverse event (AE) rates between 4% and 10%,[3] and mortality between 0.05% and 1%[4-7]. The most common AEs following ERCP include pancreatitis, hemorrhage, and infection, which occured in 4% to7% of procedures[3 6 8]. There is an increased risk of AEs after therapeutic procedures and in patients with suspected Sphincter of Oddi dysfunction[6]. Since ERCP is the endoscopic procedure with the highest cost and AE rates, diagnostic ERCP is now avoided in favor of other diagnostic modalities such as less-invasive endoscopic ultrasound (EUS) and non-invasive magnetic resonance cholangiopancreatography (MRCP)[2 3 9]. In an era of increasing utilization of quality metrics, accurate measures of utilization rates and procedural adverse event risks are necessary to establish meaningful benchmarks for quality, and are best determined from community-based studies.

There are no reports of community-based utilization of ERCP in the US, but there are several from Europe[8 10]. Published reports of ERCP related AEs have all been single-centered or multi-centered studies from tertiary care centers and affected by referral bias, leading to high estimates of risk that may not apply to the general population. All adverse events of procedures done at tertiary care centers may not be captured since the patients may seek care for AEs closer to their homes and thus, lost to follow-up.

The aims of this population-based study were to determine (1) the utilization of ERCP, including changes over time; (2) the incidence of inpatient admissions for AEs within 30 days of

ERCP; and (3) risk factors for procedural related AEs among residents of Olmsted County, MN over a ten-year period from 1997-2006. The findings of this study are unique, as they represent population based estimates of utilization and risks associated with ERCP and may serve as more accurate and clinically meaningful data for clinical decision making and development of quality benchmarks.

METHODS

Study Design: A retrospective cohort study was conducted with approval of the Institutional Review Board of Mayo Clinic in compliance with federal regulations of the U.S. Department of Health and Human Services for protection of human subjects and the Health Information Protection and Portability Act. All patients provided consent for medical record review. Billing records from Mayo Clinic and associated hospitals were queried for Olmsted County residents who had undergone an ERCP during a ten-year period from January 1, 1997 to December 31, 2006. ERCPs were identified using CPT codes for ERCP, including 43260, 43261, 43262, 43263, 43264, 43265, 43267, 43268, 43269, 43271, 43272, and 47999. Utilization characteristics for EUS were determined in the same population using codes 43232, 43238, and 43242 and for MRCP using codes 74181, 74182, and 74183. Subjects also had to be age ≥ 18 years, live in Olmsted County, and have valid authorization to review medical records for research purposes in accordance with Minnesota State statutes.

Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community. Olmsted County comprises over 100,000 persons, of whom 85% are Caucasian and 50% are women; socio-demographically, the community is similar to the US population. Over half of the county's population is seen at one of

the Mayo Clinic facilities; 95% of local residents will have had at least one medical contact with a local care provider (*e.g.*, for dental X-rays, sports physical examinations, pre-employment examinations, minor illness, and routine medical care) during any 4-year period[11]. Mayo Clinic has a common medical record system with its two affiliated hospitals (Saint Mary's and Rochester Methodist) for 90 years. Mayo Clinic's single record system contains both inpatient and outpatient data. Diagnoses and surgical procedures recorded in these records are indexed. It includes diagnoses made for outpatients seen in office or clinic consultations, emergency room visits, and diagnoses recorded for hospital inpatients, autopsy examinations, or on death certificates. The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and AEs of ERCP with full details of the hospitalization can be assessed.

Medical records were reviewed retrospectively by the primary author. Patient and procedural characteristics, as well as AEs within 30 days were recorded. As many as 170 variables were collected for each procedure and recorded into a database.

Primary outcomes measured were (1) utilization rates of unique ERCP procedures in the adult population (age 18 years and older) of Olmsted County from 1997-2006, and (2) the rate of unplanned admissions within 30 days following ERCP for ERCP-related AEs. Secondary outcomes included patient and procedural characteristics, predictive of having an unplanned admission within 30 days after ERCP for an ERCP-related AE.

Utilization metrics included the patients' age, sex, race, Charlson score at the time of ERCP[12], body mass index (BMI), cholecystectomy within 30 days prior to ERCP, altered anatomy (including gastrojejunostomy, Whipple anatomy, hepatico- and choledocho-jejunostomy), presence of cirrhosis, and previous history of ERCP. Indications for ERCP were

then examined as biliary versus pancreatic, diagnostic versus therapeutic, and graded for complexity using the previously published Morriston Hospital ERCP grading scale (Table IA)[13]. Diagnostic procedures had a CPT code of 43260 where no intervention was performed, other than a cholangiogram or pancreatogram; all other procedures were therapeutic. Multiple intra-procedural details, including presence of a trainee, type and amount of sedation used, and biliary and pancreatic ductal interventions were noted. Success of the procedure was recorded as the ability to cannulate the intended duct and achieve the intended therapy.

AEs recorded included unplanned admissions; sedation-related events, including pulmonary and cardiovascular events; infection; pancreatitis; bleeding; perforation; need for repeat endoscopic procedure; or mortality within 30 days. These outcomes were determined as being related to the index ERCP by author review. AEs were deemed to be definitely related, probably related, possibly related, or definitely unrelated to the index ERCP. Possibly related AEs included patients admitted with abdominal pain, but without evidence of definite pancreatitis by laboratory studies or documented cholangitis. Probably related AEs included biliary or pancreatic stent dysfunction leading to repeat the procedure within 30 days of the index procedure, but without any of the defined AEs of pancreatitis, infection, perforation, and gastrointestinal bleeding. The latter AEs were categorized as mild, moderate, and severe, according to established consensus criteria (Table IB)[6 14] Patients undergoing elective surgery including cholecystectomy within 30 days of ERCP were also identified.

Statistical Analysis

Univariate analyses were performed to obtain descriptive statistics for patient and procedural characteristics. Annual incidence was determined by dividing the number of ERCPs performed

on the study subjects during a calendar year by the adult population of Olmsted County during that period, according to County records and normalized to 100,000 persons. To test for associations between patient and procedural characteristics and ERCP related AEs, values of these characteristics were compared between subjects who experienced ERCP-related AEs and subjects who did not by two sample t-tests for continuous variables, and chi square test for discrete variables. Multivariable logistic regression analyses were used to determine patient and procedural characteristics predictive of ERCP-related AEs. *P*-values less than 0.05 were considered statistically significant. All analyses for this study were done using SAS statistical software (SAS version 9.1 for Windows; SAS Institute Inc., Cary, North Carolina).

RESULTS

Demographic characteristics

In the 10-year period from January, 1, 1997 to December, 31, 2006, 1072 ERCPs were performed on 827 individual adult patients in Olmsted County. Patient demographic characteristics can be seen in Table II. Prior to the index cholecystectomy, 232 (28%) patients had a previous cholecystectomy; 21 (2%) patients had altered anatomy, and 20 (1.9%) were taking clopidogrel or warfarin at the time of the ERCP. There were 153 patients who had more than one ERCP during the 10-year period, and the mean number of ERCPs in these patients was 1.3.

Utilization characteristics

Average utilization of ERCP was 83.1 ERCPs per 100,000 persons/year, with an increasing trend in utilization from 58.0 to 104.8 ERCPs per 100,000 persons/year over the 10-year period.

Therapeutic ERCPs increased over the same timeframe from 42.9 to 93.9 ERCPs per 100,000 persons/year (average 68.7). However, diagnostic ERCPs decreased slightly from 15.1 to 10.9 and averaged 14.4 ERCPs per 100,000 persons/year. EUS and MRCP utilization in the same population also steadily increased over this time period (Figure I).

Procedural characteristics

Procedural characteristics can be seen in Table III. Of the 1072 ERCPs performed over the 10-year period, 606(56.5%) were performed on inpatients, while 889 (82.9%) were therapeutic. The proportion of therapeutic procedures from 2002-2006 was higher than from 1997-2001 (86.6% vs 77.5%, *P*=0.0001). The difficulty grades, as defined by Morriston Hospital ERCP grading scale, were mostly Grade II(494, 46.1%) and Grade III(297, 27.7%) procedures overall; however, there was a two-fold increase in Grade IV procedures in the second five-year period, compared to the first (15.3% vs 7.2%, P<0.0001). ERCP was performed primarily for a biliary indication in 853 (79.6%) and a pancreatic indication in 95 (8.9%) with 122 (11.4%) for both a biliary and pancreatic indication. The commonest biliary indications included choledocholithiasis (500, 46.6%), biliary colic in the absence of documented choledocholithiasis (307, 28.6%), and relief of malignant biliary obstruction (116, 10.8%). The commonest pancreatic indications for ERCP were to determine etiology of acute pancreatitis (135, 12.6%), or recurrent acute pancreatitis (34, 3.2%), and chronic pancreatic fluid collection (18, 1.7%). Suspected sphincter of Oddi dysfunction was the indication in only (19, 1.7%) of ERCPs. A trainee was involved in 667 (62.2%) cases.

Biliary sphincterotomy was performed in 620 (57.8%) procedures; the pancreatic duct was injected in 404 (37.7%) cases and was cannulated in 255 (23.8%) procedures. Biliary stents

were placed in 185 (17.3%) cases; prophylactic pancreatic stents were placed in 59 (5.5%) patients. Placement of pancreatic stents increased in the second 5-year period, compared to the first (8.1% vs 1.6%, $P<0.0001$). Ampullectomy was performed in 7 (0.7%) cases and 16 (1.5%) cases were transgastric or transduodenal débridements of pancreatic necrosis (15 of which occurred in the second 5-year period, $P=0.0053$). Only 31 (2.9%) of ERCPs were deemed as failures as the goal of the procedure was not achieved, resulting in a 97.1% success rate. None of the patients received any prophylaxis to prevent post-ERCP pancreatitis.

Sedation

Only 42(3.9%) of procedures were done with anesthesia support. Of the remaining ERCPs done under moderate sedation, the mean dose of fentanyl was 159 ± 86mcg (in 51 ERCPs), midazolam 6.1 ± 2.6mg (1028 ERCPs), meperidine 97 ± 46mg (979 ERCPs), and promethazine 21 ± 8mg (90 ERCPs).

Outcomes

Following 1072 ERCPs in Olmsted County, over ten years, there were 273 admissions to the hospital within 30 days after 236 procedures (22% of all procedures). Table IV lists the outcomes in the study cohort. Of the 273 admissions, only 62 (22.7%) were definitely related to the index ERCP procedure, with another 2 (0.7%) probably related, and 4 (1.4%) possibly related to the procedure. Of the remaining 205 admissions unrelated to procedural AEs of the index ERCP, 79 were planned for elective surgeries, including cholecystectomy. Intraprocedural AEs were infrequent, with 20 (1.9%) necessitating a change in intra-procedural anesthesia; no deaths occurred during the procedure. There were 47 sphincterotomy-induced intra-procedural bleeding

episodes treated with various modalities, including epinephrine injection, cautery and tamponade.

The AE rate was 5.3% including pancreatitis (26, 2.4%), infection/cholangitis (16, 1.5%), bleeding (15, 1.4%), and perforation (4, 0.37%). 53 cases were determined to be mild to moderate; however, 3 infections, all 4 perforations, and 1 bleed were considered severe. The 30-day mortality rate was 2.4%. None of the deaths were directly related to the ERCP or AEs thereof. Repeat ERCP procedures were required in 93 (8.7%) patients and 45 (4.2%) had an esophagogastroduodenoscopy (EGD) within 30 days of the index ERCP.

Risk factors for AEs

In order to determine if there were identifiable risk factors for AEs arising from ERCP in our cohort, the relative frequency and distribution of patient and procedural characteristics were compared between patients who had a procedural AE and those who did not (Table V). Patient characteristics identified through multivariate analysis to be associated with AEs included: age less than 45 years (OR 2.23 (95% CI 1.03 – 4.84) for age <45 years vs ≥65 years, *P*=0.0498); and BMI ≥35 (OR 0.31 (95% CI 0.14 – 0.72) for BMI 25-34 vs ≥35, *P*=0.0024). Procedural characteristics identified to be associated with increased risk of AEs included: patient's first ERCP (OR 2.22 (95% CI 1.04 – 4.75), *P*=0.0394); pancreatic duct cannulation (OR 2.7 (95%CI 1.4 - 5.1), *P*=0.0026); outpatient procedure (OR 5.4 (95% CI 2.6 – 11.4), *P*<0.0001); intraprocedure sphincterotomy bleeding (OR 10.0 (95% CI 3.8 – 26.1), *P*<0.0001); difficulty grade (OR 8.9 (95% CI 1.9 – 43.1) for grade 4 vs 1, *P*=0.0204).

DISCUSSION

In the adult Olmsted County study population, which is considered representative of the US population, ERCP utilization rates nearly doubled over the ten-year period from January 1, 1997 to December 31, 2006 from 58.0 to 104.8 cases per 100,000 persons/year[15]. This trend was influenced by a substantial increase in the rate of therapeutic procedures and a slight decrease in diagnostic procedures. Importantly, ERCP was performed predominantly for common 'bread and butter' indications including cholangitis, biliary colic, and pancreatitis. This information underscores the fact that ERCP is currently mainly a therapeutic modality, and should be available at a community-based level. Training in ERCP should be focussed on gaining expertise mainly for removal of common duct stones and relief of distal biliary obstruction. For a community based gastroenterologist, the need for more complex procedures is rare, and these procedures should be carried out at tertiary care centres.

ERCP utilization rates in Olmsted County in this study are in some ways divergent with national data. For instance, Mazen Jamal et al queried the Nationwide Inpatient Sample (NIS) data for ERCP utilization rates from 1996 to 2002[16]. They found that the rate of inpatient ERCPs dropped from 74.95/100,000 persons in 1996 to 59.70/100,000 in 2002, driven mostly by a decrease in diagnostic procedures, while there was a slight concomitant increase in therapeutic procedures. However, because they were using NIS sample, data are not available on outpatient utilization of ERCP. In contrast, outpatient procedures comprised 43.5% of procedures in our study.

Over the study period, overall utilization of EUS and MRCP have also increased in Olmsted County. ERCP is likely now utilized almost exclusively for therapeutic purposes because of the diagnostic abilities of EUS and MRCP, and the improvements in contrast-

enhanced CT scans. Also, increased use of EUS and MRCP might actually result in more therapeutic ERCP as seen in our study, which contradicts popular belief that utilization of ERCP has decreased over time with increased use of other diagnostic modalities.

Unplanned admissions commonly occur after ERCP (22% within 30 days), but are most often not related to procedural AEs, which occur in 5.3% of all patients undergoing ERCP. Unplanned admissions within 30 days after a procedure are increasingly being counted as negative indicators of healthcare quality[17]. However, our data suggest that in the case of ERCP, this outcome measure may not be a valid indicator of the quality of the procedure itself and is likely related to either underlying disease, a finding of the procedure itself that leads to elective surgery, or possibly to other comorbidities. Identification and complete capture of 30-day admissions is a strength of our study, in comparison to past studies, where capturing remote AEs were incomplete [6]. Because this is a population-based study, and Mayo Clinic is the only provider for ERCP in the population, all AEs were identified.

Severe procedural AEs, including pancreatitis (2.4%), bleeding (1.5%), infection (1.4%), and mortality related to the procedure (0%), were uncommon. Most AEs were mild to moderate, and at rates similar to previously published reports[3 6]. In a systematic review of 21 surveys of ERCP, AE rates in a population of 16,855 patients were 6.85%, with pancreatitis, infection and bleeding occurring in 3.5%, 1.4% and 1.3% of cases[3]; mortality rate was 0.33%. Cotton et al. reported on 11,497 procedures at multiple centers and found a 4.0% AE rate, with rates of 2.6% for pancreatitis and 0.3% for bleeding. Mortality rate in this cohort was 0.06%[6]. Although 2.4% of patients in our study died within 30 days of the ERCP, none of these deaths were ERCP-related, and there were no intra- or peri-procedural deaths in our study. Because the AE rates in

our study are similar to the rates reported in the literature, it is likely that ERCP procedures carried out at other tertiary care centres are also associated with low adverse event rates.

Numerous studies have enumerated various risk factors for AEs following ERCP[6 8 10 18 19]. Commonly accepted risk factors for any AE after ERCP include suspected sphincter of Oddi dysfunction, cirrhosis, difficult cannulation, performance of precut sphincterotomy, percutaneous biliary access, and lower ERCP case volumes, with young age, pancreatic duct contrast injection and failed biliary drainage identified in some studies. In our study, younger patient age, higher BMI, first ERCP, pancreatic duct cannulation, intra-procedural post sphincterotomy bleeding, therapeutic procedures, and outpatient procedures were identified as risk factors for any AE through a multivariate analysis.

Consistent with our findings, younger age has been previously shown to be a risk factor for AEs, especially post-ERCP pancreatitis (PEP)[5 8 10]. Pancreatic duct cannulation is known to be a risk-factor for development of PEP[6]. Toward the end of this study period, data emerged supporting the use of prophylactic pancreatic duct stents to decrease the incidence of PEP and were published. In our study period, in only 59 (5.5%) procedures, we placed a pancreatic duct stent. Hence, our study is not able to adequately define the rate of PEP with routine placement of prophylactic pancreatic stents.

One limitation of our study is that it is a retrospective review of data with its inherent biases. However, the data were manually abstracted by a single gastroenterologist from an electronic medical record, and significant adverse events and hospitalizations are not likely to have been missed. Another limitation is that even though the population studied is a county-based population, the skills of the endoscopists are at a higher level than endoscopists in smaller community hospitals. Therefore, the AE rate in this community setting could be lower than one

would expect in community settings at large. Another notable limitation is that Sphincter of Oddi dysfunction and complications of pancreatitis, diagnoses often referred to a tertiary center, were underrepresented in our study.

In conclusion, our study shows that utilization of ERCP at a population level continues to rise; specifically utilization of therapeutic procedures. The most common indications for ERCP remain relief of biliary colic or cholangitis, and this procedure may be carried out with moderate sedation. Adverse events of ERCP remain uncommon and deaths are infrequent. The study adds important epidemiologic data on trends in the utilization of ERCP, as well as population-based estimates of the risk of adverse events from ERCP that will be useful in clinical decision making and determination of resource allocation. The findings of the study may also impact ERCP training criteria.

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Figure Legends

Table IA. Morriston Hospital ERCP grading scale (Ragunath et al, Post Grad Med J, 2003)

Table IB. Consensus criteria for ERCP complications (Cotton et al, GIE, 1991)

Table II. Patient Characteristics

Table III. Procedural Characteristics

Table IV. Procedure Outcomes

Table V. Multivariate analysis of risk factors for post-ERCP complications

Figure I. Utilization characteristics of ERCP, EUS, and MRCP in Olmsted County over 10-year period.

Table IA: Morriston Hospital ERCP grading scale [13]

Procedure	Grade
Diagnostic ERCP	I
Biliary sphincterotomy, balloon sphincteroplasty, removal of extrahepatic stones ≤1 cm using basket and/or balloon	II
Precut sphincterotomy, large stones removal (>1cm), intrahepatic stone removal, mechanical lithotripsy, stricture dilatation, cytology, stent insertion, and naso-biliary drain	III
Sphincter of Oddi manometry, diagnostic and therapeutic ERCP after Billroth II surgery, minor papilla sphincterotomy, endoscopic ampullectomy, and all pancreatic duct therapeutic procedures. Cholangioscopy, laser lithotripsy, electrohydraulic lithotripsy, combined procedures (PTC and ERCP), and other advanced bile duct therapeutic procedures	IV

ERCP - endoscopic retrograde cholangiopancreatography
PTC – percutaneous transhepatic cholangiography

Table IB: Consensus criteria for ERCP complications [14]

	Mild	Moderate	Severe
Bleeding	Clinical evidence of bleeding (ie not just endoscopic) Hemoglobin drop <3g No need for transfusion	Transfusion: 4 units or less No angiographic intervention or surgery	Transfusion: 5 units or more or intervention (angiographic or surgical)
Perforation	Possible, or only very slight leak of fluid or contrast dye Treatable by fluids and suction for 3 days or less	Any definite perforation treated medically for 4-10 days	Medical treatment for more than 10 days or intervention (percutaneous or surgical)
Pancreatitis	Clinical pancreatitis: amylase at least thrice the upper limit of normal at more than 24 hours after the procedure requiring admission or prolongation of planned admission to 2-3 days	Pancreatitis requiring hospitalization for 4-10 days	Pancreatitis requiring hospitalization for more than 10 days, or hemorrhagic pancreatitis, phlegmon, or intervention (percutaneous drainage or surgery)
Infection (cholangitis)	>38 degrees Celsius at 24-48 hours	Febrile or septic illness requiring>3 days of hospital treatment or endoscopic or percutaneous intervention	Septic shock or surgery

Table II: Patient Characteristics

Age at time of ERCP (years)	
mean (sd)	57.6 (19.8)
18-44 years	283 (26.4%)
45-64 years	357 (33.3%)
> 65+ years	432 (40.3%)
Gender	
Female, n (%)	522 (63.1)
Race	
Caucasian	688 (83.2%)
African American	15 (1.8%)
Other/unknown	124 (15.0%)
Charlson index at time of ERCP[12]	
mean (sd)	3.2 (3.2)
BMI at time of ERCP	
mean (sd)	28.5 (7.2)
< 25	341 (32.4%)
25-34	517 (49.1%)
35+	194 (18.4%)

ERCP – endoscopic retrograde cholangiopancreatography
BMI – body mass index

Table III: Procedural Characteristics

	(%)
Cholecystectomy within 30 days prior to ERCP	113 (10.5)
Altered anatomy	21 (2.0)
Anticoagulation	20 (1.9)
Prior ERCP	277 (25.8)
Biliary indications	975 (91.0)
Cholangitis	56 (5.2)
Cholecystitis	41 (3.8)
Bleeding	4 (0.4)
Choledocholithiasis	500 (46.6)
Malignant stricture	116 (10.8)
Hilar stricture	5 (0.5)
Benign stricture	46 (4.3)
Ca pancreas	21 (2)
Papillary stenosis	8 (0.7)
Ca ampulla	14 (1.3)
Anastomotic stricture	29 (2.7)
Post cholecystectomy	69 (6.4)
Suspected SOD	19 (1.8)
PSC	21 (2)
Bile leaks	23 (2.1)
Biliary colic	307 (28.6)
Biliary dilation	27 (2.5)
Stent removal	52 (4.9)
Elevated AST and ALT	76 (7.1)
Pancreatic indications	217 (20.2)
Acute pancreatitis	135 (12.6)
Recurrent acute pancreatitis	34 (3.2)
Chronic pancreatitis	17 (1.6)
Cyst	8 (0.7)
Duct leak	9 (0.8)
Duct stricture	7 (0.7)
Acute fluid collection	7 (0.7)
Chronic fluid collection	18 (1.7)
Necrosectomy	14 (1.3)
Inpatient	606 (56.5)

Therapeutic	889 (82.9)
Difficulty grade	
I	152 (14.2)
II	494 (46.1)
III	297 (27.7)
IV	129 (12.0)
Trainee present	667 (62.2)
Anesthesia	
Conscious sedation	1030 (96.1)
Fentanyl	51 (4.8)
Versed	1028 (95.8)
Benadryl	6 (0.6)
Demerol	979 (91.2)
Phenergan	90 (8.4)
Droperidol	25 (2.3)
General (or propofol)	42 (3.9)
Peri-ampullary diverticulum	117 (10.9)
Biliary sphincterotomy	620 (57.8)
Precut biliary sphincterotomy	125 (11.7)
Biliary stent placed	185 (17.3)
Pancreatic sphincterotomy	13 (1.2)
Pancreatic duct stent placed	59 (5.5)
Ampullectomy	7 (0.7)
Transgastric/transduodenal drainage	16 (1.5)
Sphincterotomy bleeding noted during procedure	45 (4.2)

ERCP – endoscopic retrograde cholangiopancreatography
AST – aspartate aminotransferase
ALT – alanine aminotransferase

Table IV: Procedure Outcomes

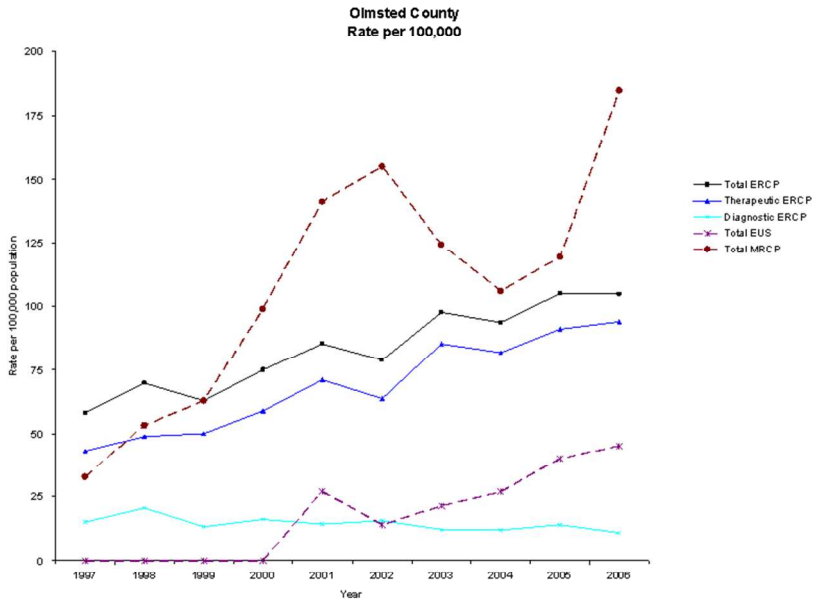
	(%)
Success	041 (97.1)
Death	
During procedure	0 (0.0)
Within 30 days	26 (2.4)
Need for repeat procedure within 30 days	
ERCP	93 (8.7)
EGD	45 1 (4.2)
Number of readmissions within 30 days	273
Definitely related to procedure	62 (22.7)
Possibly related to procedure	6 (2.2)
Definitely not related to procedure	205 (75.1)
Surgery within 30 days	
Elective cholecystectomy	52 (4.9)
Elective Whipple	16 (5.9)
Other elective	11 (4.0)
Emergent cholecystectomy	6 (2.2)
ERCP complications requiring readmit	53 (4.9)
Pancreatitis	26 (2.4)
Mild	18
Moderate	8
Severe	0
Infection/cholangitis	16 (1.5)
Mild	6
Moderate	7
Severe	3
Bleeding	15 (1.4)
Mild	6
Moderate	8
Severe	1
Perforation	4 (0.37)
Mild	0
Moderate	0

Severe	4

Table V. Multivariate analysis of risk factors for post-ERCP complications

Risk factor	Odds ratio (95% CI)	*P*-value
Age <45 vs ≥65	2.23 (1.03 – 4.84)	0.0498 *
Age 45-64 vs ≥65	1.3 (0.62 – 2.72)	0.6697
Female gender	1.2 (0.61 – 2.21)	0.6412
BMI <25 vs ≥35	0.84 (0.40 – 1.74)	0.1972
BMI 25-34 vs ≥35	0.31 (0.14 – 0.72)	0.0024 *
No previous ERCP	2.22 (1.04 – 4.75)	0.0394 *
Outpatient ERCP	5.4 (2.6 – 11.4)	<0.0001 *
Pancreatic duct cannulation	2.7 (1.4 – 5.1)	0.0026 *
Absence of trainee	1.36 (0.72 – 2.59)	0.3487
Intraprocedure sphincterotomy bleeding	10.0 (3.8 – 26.1)	<0.0001 *
Difficulty grade 1 vs 4	0.11 (0.02 – 0.54)	0.0204 *
Difficulty grade 2 vs 4	0.45 (0.18 – 1.14)	0.9199
Difficulty grade 3 vs 4	0.94 (0.42 – 2.13)	0.0129 *

Figure 1.



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STROBE STATEMENT checklist of items that should be included in reports of Observational Studies

SECTION/TOPIC	Item No.	Checklist Item	Reported on page No.
TITLE AND ABSTRACT	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2, 3
INTRODUCTION			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4, 5
METHODS			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6
Participants	6	(a) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5,6
		(b) *Cohort study*—For match studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6,7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7,8
		(b) Describe any methods used to examine subgoups and interactions	
		(c) Explain how missing data were addressed	
		(d) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
RESULTS			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	8,9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarize follow-up time (e.g., average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time *Case-control study*—Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study*—Report numbers of outcome events or summary measures	10
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make	10

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		clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	(d) Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	
DISCUSSION			
Key results	18	Summarize key results with reference to study objectives	12,13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalizability	21	Discuss the generalizability (external validity) of the study results	15
OTHER INFORMATION			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Endoscopic Retrograde Cholangiopancreatography – Utilization and outcomes in a 10-year population based cohort

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Endoscopic Retrograde Cholangiopancreatography – Utilization and outcomes in a 10-year population based cohort

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SUMMARY

Article Focus:

- Due to increasing use of quality metrics, accurate measures of utilization and procedural adverse event risks are necessary to establish benchmarks for quality, and are best determined from community-based studies.
- There are no reports of community-based utilization of ERCP in the US.
- The aims of this population-based study were to determine the utilization of ERCP including changes over time, the incidence of inpatient admissions for adverse events within 30 days of ERCP, and risk factors for procedural related adverse events.

Key Messages:

- Population utilization of ERCP in Olmsted County MN rose over the ten year period from 1997 to 2006, driven specifically by increases in therapeutic procedures. The most common indications for ERCP were therapy of choledocholithiasis and to determine etiology of acute pancreatitis.
- Admissions within 30 days after ERCP are common, but are usually unrelated. Complications of ERCP remain infrequent at 5.3% and no deaths were directly related.
- Risk factors associated with adverse events from ERCP include younger age, BMI ≥35, pancreatic duct cannulation, outpatient procedures, intraprocedure sphincterotomy bleeding, difficulty grade, and patient's first ERCP.

Strengths and Limitations:

Strengths:

- Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community.
- The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and adverse events of ERCP with full details of procedures and subsequent hospitalizations can be assessed.

Limitations:

- The study is a retrospective review with inherent potential biases.
- The skills of the endoscopists are likely at a higher level than endoscopists in smaller community hospitals. Therefore, the adverse event rate in this community setting could be lower than one would expect in other community settings.

ABSTRACT

Objective: To determine utilization of ERCP; incidence of inpatient admissions for complications occurring within 30 days of ERCP; and risk factors for procedural related complications, in a population based study.

Design: Retrospective cohort study

Setting: Olmsted County, MN

Participants: All adult residents of Olmsted County, MN, who underwent ERCP from 1997 to 2006.

Interventions: Diagnostic and therapeutic ERCPs were assessed.

Primary and Secondary outcome measures: Patient and procedural characteristics and complications within 30 days; and rates of ERCP utilization and unplanned admissions and risk factors for admissions.

Results: In ten years, 1072 ERCPs were performed on 827 individual patients. Average utilization of ERCP was 83.1 ERCPs/100,000 persons/year, with an increase from 58.0 to 104.8 ERCPs/100,000 persons/year over time, driven by increases in therapeutic procedures. Within 30 days after 236 procedures, 62 admissions were definitely related to the index ERCP. The complication rate was 5.3%, including pancreatitis(26, 2.4%), infection/cholangitis(16, 1.5%),

bleeding(15, 1.4%), and perforation(4, 0.37%). 30-day mortality was 2.4%; none of which were directly related to the ERCP or complications thereof. Risk factors identified through multivariate analysis to be associated with adverse events included: age <45 years(p=0.0498); BMI ≥35(p=0.0024); pancreatic duct cannulation(p=0.0026); outpatient procedure(p<0.0001); intraprocedure sphincterotomy bleeding(*P*<0.0001); difficulty grade(*P*=0.115); and patient's first ERCP(*P*=0.0394).

Limitations: Retrospective study.

Conclusions: Population utilization of ERCP rose during the study period, specifically in therapeutic procedures. Admissions within 30 days of ERCP are common, but often unrelated. Complications of ERCP remain infrequent and deaths quite unusual.

Abbreviations:

AE – adverse event

EGD – esophagogastroduodenoscopy

ERCP - endoscopic retrograde cholangiopancreatography

EUS – endoscopic ultrasound

MRCP - magnetic resonance cholangiopancreatography

BACKGROUND

Since its first description in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has become an established modality for the diagnosis and treatment of pancreaticobiliary disorders[1 2]. Over the years, ERCP has evolved from a purely diagnostic, to a mainly therapeutic procedure. Around 500,000 ERCPs are performed annually in the United States (US) with adverse event (AE) rates between 4% and 10%,[3] and mortality between 0.05% and 1%[4-7]. The most common AEs following ERCP include pancreatitis, hemorrhage, and infection, which occured in 4% to7% of procedures[3 6 8]. There is an increased risk of AEs after therapeutic procedures and in patients with suspected Sphincter of Oddi dysfunction[6]. Since ERCP is the endoscopic procedure with the highest cost and AE rates, diagnostic ERCP is now avoided in favor of other diagnostic modalities such as less-invasive endoscopic ultrasound (EUS) and non-invasive magnetic resonance cholangiopancreatography (MRCP)[2 3 9]. In an era of increasing utilization of quality metrics, accurate measures of utilization rates and procedural adverse event risks are necessary to establish meaningful benchmarks for quality, and are best determined from community-based studies.

There are no reports of community-based utilization of ERCP in the US, but there are several from Europe[8 10]. Published reports of ERCP related AEs have all been single-centered or multi-centered studies from tertiary care centers and affected by referral bias, leading to high estimates of risk that may not apply to the general population. All adverse events of procedures done at tertiary care centers may not be captured since the patients may seek care for AEs closer to their homes and thus, lost to follow-up.

The aims of this population-based study were to determine (1) the utilization of ERCP, including changes over time; (2) the incidence of inpatient admissions for AEs within 30 days of

ERCP; and (3) risk factors for procedural related AEs among residents of Olmsted County, MN over a ten-year period from 1997-2006. The findings of this study are unique, as they represent population based estimates of utilization and risks associated with ERCP and may serve as more accurate and clinically meaningful data for clinical decision making and development of quality benchmarks.

METHODS

Study Design: A retrospective cohort study was conducted with approval of the Institutional Review Board of Mayo Clinic in compliance with federal regulations of the U.S. Department of Health and Human Services for protection of human subjects and the Health Information Protection and Portability Act. All patients provided consent for medical record review. Billing records from Mayo Clinic and associated hospitals were queried for Olmsted County residents who had undergone an ERCP during a ten-year period from January 1, 1997 to December 31, 2006. ERCPs were identified using CPT codes for ERCP, including 43260, 43261, 43262, 43263, 43264, 43265, 43267, 43268, 43269, 43271, 43272, and 47999. Utilization characteristics for EUS were determined in the same population using codes 43232, 43238, and 43242 and for MRCP using codes 74181, 74182, and 74183. Subjects also had to be age ≥ 18 years, live in Olmsted County, and have valid authorization to review medical records for research purposes in accordance with Minnesota State statutes.

Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community. Olmsted County comprises over 100,000 persons, of whom 85% are Caucasian and 50% are women; socio-demographically, the community is similar to the US population. Over half of the county's population is seen at one of

the Mayo Clinic facilities; 95% of local residents will have had at least one medical contact with a local care provider (*e.g.*, for dental X-rays, sports physical examinations, pre-employment examinations, minor illness, and routine medical care) during any 4-year period[11]. Mayo Clinic has a common medical record system with its two affiliated hospitals (Saint Mary's and Rochester Methodist) for 90 years. Mayo Clinic's single record system contains both inpatient and outpatient data. Diagnoses and surgical procedures recorded in these records are indexed. It includes diagnoses made for outpatients seen in office or clinic consultations, emergency room visits, and diagnoses recorded for hospital inpatients, autopsy examinations, or on death certificates. The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and AEs of ERCP with full details of the hospitalization can be assessed.

Medical records were reviewed retrospectively by the primary author. Patient and procedural characteristics, as well as AEs within 30 days were recorded. As many as 170 variables were collected for each procedure and recorded into a database.

Primary outcomes measured were (1) utilization rates of unique ERCP procedures in the adult population (age 18 years and older) of Olmsted County from 1997-2006, and (2) the rate of unplanned admissions within 30 days following ERCP for ERCP-related AEs. Secondary outcomes included patient and procedural characteristics, predictive of having an unplanned admission within 30 days after ERCP for an ERCP-related AE.

Utilization metrics included the patients' age, sex, race, Charlson score at the time of ERCP[12], body mass index (BMI), cholecystectomy within 30 days prior to ERCP, altered anatomy (including gastrojejunostomy, Whipple anatomy, hepatico- and choledocho-jejunostomy), presence of cirrhosis, and previous history of ERCP. Indications for ERCP were

then examined as biliary versus pancreatic, diagnostic versus therapeutic, and graded for complexity using the previously published Morriston Hospital ERCP grading scale (Table IA)[13]. Diagnostic procedures had a CPT code of 43260 where no intervention was performed, other than a cholangiogram or pancreatogram; all other procedures were therapeutic. Multiple intra-procedural details, including presence of a trainee, type and amount of sedation used, and biliary and pancreatic ductal interventions were noted. Success of the procedure was recorded as the ability to cannulate the intended duct and achieve the intended therapy.

AEs recorded included unplanned admissions; sedation-related events, including pulmonary and cardiovascular events; infection; pancreatitis; bleeding; perforation; need for repeat endoscopic procedure; or mortality within 30 days. These outcomes were determined as being related to the index ERCP by author review. AEs were deemed to be definitely related, probably related, possibly related, or definitely unrelated to the index ERCP. Possibly related AEs included patients admitted with abdominal pain, but without evidence of definite pancreatitis by laboratory studies or documented cholangitis. Probably related AEs included biliary or pancreatic stent dysfunction leading to repeat the procedure within 30 days of the index procedure, but without any of the defined AEs of pancreatitis, infection, perforation, and gastrointestinal bleeding. The latter AEs were categorized as mild, moderate, and severe, according to established consensus criteria (Table IB)[6 14] Patients undergoing elective surgery including cholecystectomy within 30 days of ERCP were also identified.

Statistical Analysis

Univariate analyses were performed to obtain descriptive statistics for patient and procedural characteristics. Annual incidence was determined by dividing the number of ERCPs performed

on the study subjects during a calendar year by the adult population of Olmsted County during that period, according to County records and normalized to 100,000 persons. To test for associations between patient and procedural characteristics and ERCP related AEs, values of these characteristics were compared between subjects who experienced ERCP-related AEs and subjects who did not by two sample t-tests for continuous variables, and chi square test for discrete variables. Multivariable logistic regression analyses were used to determine patient and procedural characteristics predictive of ERCP-related AEs. *P*-values less than 0.05 were considered statistically significant. All analyses for this study were done using SAS statistical software (SAS version 9.1 for Windows; SAS Institute Inc., Cary, North Carolina).

RESULTS

Demographic characteristics

In the 10-year period from January, 1, 1997 to December, 31, 2006, 1072 ERCPs were performed on 827 individual adult residents of Olmsted County. The total number of ERCPs done during this time period was 13056 including the non-residents of Olmsted County. Patient demographic characteristics can be seen in Table II. Prior to the index cholecystectomy, 232 (28%) patients had a previous cholecystectomy; 21 (2%) patients had altered anatomy, and 20 (1.9%) were taking clopidogrel or warfarin at the time of the ERCP. There were 153 patients who had more than one ERCP during the 10-year period, and the mean number of ERCPs in these patients was 1.3.

Utilization characteristics

Average utilization of ERCP was 83.1 ERCPs per 100,000 persons/year, with an increasing trend in utilization from 58.0 to 104.8 ERCPs per 100,000 persons/year over the 10-year period. Therapeutic ERCPs increased over the same timeframe from 42.9 to 93.9 ERCPs per 100,000 persons/year (average 68.7). However, diagnostic ERCPs decreased slightly from 15.1 to 10.9 and averaged 14.4 ERCPs per 100,000 persons/year. EUS and MRCP utilization in the same population also steadily increased over this time period (Figure I).

Procedural characteristics

Procedural characteristics can be seen in Table III. Of the 1072 ERCPs performed over the 10-year period, 606(56.5%) were performed on inpatients, while 889 (82.9%) were therapeutic. The proportion of therapeutic procedures from 2002-2006 was higher than from 1997-2001 (86.6% vs 77.5%, P=0.0001). The difficulty grades, as defined by Morriston Hospital ERCP grading scale, were mostly Grade II(494, 46.1%) and Grade III(297, 27.7%) procedures overall; however, there was a two-fold increase in Grade IV procedures in the second five-year period, compared to the first (15.3% vs 7.2%, P<0.0001). ERCP was performed primarily for a biliary indication in 853 (79.6%) and a pancreatic indication in 95 (8.9%) with 122 (11.4%) for both a biliary and pancreatic indication. The commonest biliary indications included choledocholithiasis (500, 46.6%), biliary colic in the absence of documented choledocholithiasis (307, 28.6%), and relief of malignant biliary obstruction (116, 10.8%). The commonest pancreatic indications for ERCP were to determine etiology of acute pancreatitis (135, 12.6%), or recurrent acute pancreatitis (34, 3.2%), and chronic pancreatic fluid collection (18, 1.7%). Suspected sphincter of Oddi dysfunction was the indication in only (19, 1.7%) of ERCPs. A trainee was involved in 667 (62.2%) cases.

Biliary sphincterotomy was performed in 620 (57.8%) procedures; the pancreatic duct was injected in 404 (37.7%) cases and was cannulated in 255 (23.8%) procedures. In some cases, the intent was to cannulate the bile duct, but pancreatic duct injection occurred during the process. Biliary stents were placed in 185 (17.3%) cases; prophylactic pancreatic stents were placed in 59 (5.5%) patients. Placement of pancreatic stents increased in the second 5-year period, compared to the first (8.1% vs 1.6%, $P<0.0001$). Ampullectomy was performed in 7 (0.7%) cases and 16 (1.5%) cases were transgastric or transduodenal débridements of pancreatic necrosis (15 of which occurred in the second 5-year period, $P=0.0053$). Only 31 (2.9%) of ERCPs were deemed as failures as the goal of the procedure was not achieved, resulting in a 97.1% success rate. None of the patients received any prophylaxis to prevent post-ERCP pancreatitis.

Sedation

Only 42(3.9%) of procedures were done with anesthesia support. Of the remaining ERCPs done under moderate sedation, the mean dose of fentanyl was 159 ± 86mcg (in 51 ERCPs), midazolam 6.1 ± 2.6mg (1028 ERCPs), meperidine 97 ± 46mg (979 ERCPs), and promethazine 21 ± 8mg (90 ERCPs).

Outcomes

Following 1072 ERCPs in Olmsted County, over ten years, there were 273 admissions to the hospital within 30 days after 236 procedures (22% of all procedures). Table IV lists the outcomes in the study cohort. Of the 273 admissions, only 62 (22.7%) were definitely related to the index ERCP procedure, with another 2 (0.7%) probably related, and 4 (1.4%) possibly related to the

procedure. Of the remaining 205 admissions unrelated to procedural AEs of the index ERCP, 79 were planned for elective surgeries, including cholecystectomy. Intraprocedural AEs were infrequent, with 20 (1.9%) necessitating a change in intra-procedural anesthesia; no deaths occurred during the procedure. There were 47 sphincterotomy-induced intra-procedural bleeding episodes treated with various modalities, including epinephrine injection, cautery and tamponade.

The AE rate was 5.3% including pancreatitis (26, 2.4%), infection/cholangitis (16, 1.5%), bleeding (15, 1.4%), and perforation (4, 0.37%). 53 cases were determined to be mild to moderate; however, 3 infections, all 4 perforations, and 1 bleed were considered severe. The 30-day mortality rate was 2.4%; 69% of deaths were due to underlying malignancy, 12% were due to infections unrelated to the ERCP, and 19% were due to other causes including stroke, respiratory failure, and dementia. None of the deaths were directly related to the ERCP or AEs thereof. Repeat ERCP procedures were required in 93 (8.7%) patients and 45 (4.2%) had an esophagogastroduodenoscopy (EGD) within 30 days of the index ERCP.

Risk factors for AEs

In order to determine if there were identifiable risk factors for AEs arising from ERCP in our cohort, the relative frequency and distribution of patient and procedural characteristics were compared between patients who had a procedural AE and those who did not (Table V). Patient characteristics identified through multivariate analysis to be associated with AEs included: age less than 45 years (OR 2.23 (95% CI 1.03 – 4.84) for age <45 years vs ≥65 years, *P*=0.0498); and BMI ≥35 (OR 0.31 (95% CI 0.14 – 0.72) for BMI 25-34 vs ≥35, *P*=0.0024). Procedural characteristics identified to be associated with increased risk of AEs included: patient's first

ERCP (OR 2.22 (95% CI 1.04 – 4.75), *P*=0.0394); pancreatic duct cannulation (OR 2.7 (95%CI 1.4 - 5.1), *P*=0.0026); outpatient procedure (OR 5.4 (95% CI 2.6 – 11.4), *P*<0.0001); intraprocedure sphincterotomy bleeding (OR 10.0 (95% CI 3.8 – 26.1), *P*<0.0001); difficulty grade (OR 8.9 (95% CI 1.9 – 43.1) for grade 4 vs 1, *P*=0.0204).

DISCUSSION

In the adult Olmsted County study population, which is considered representative of the US population, ERCP utilization rates nearly doubled over the ten-year period from January 1, 1997 to December 31, 2006 from 58.0 to 104.8 cases per 100,000 persons/year[15]. This trend was influenced by a substantial increase in the rate of therapeutic procedures and a slight decrease in diagnostic procedures. Importantly, ERCP was performed predominantly for common 'bread and butter' indications including cholangitis, biliary colic, and pancreatitis. This information underscores the fact that ERCP is currently mainly a therapeutic modality, and should be available at a community-based level. Training in ERCP should be focussed on gaining expertise mainly for removal of common duct stones and relief of distal biliary obstruction. For a community based gastroenterologist, the need for more complex procedures is rare, and these procedures should be carried out at tertiary care centres.

ERCP utilization rates in Olmsted County in this study are in some ways divergent with national data. For instance, Mazen Jamal et al queried the Nationwide Inpatient Sample (NIS) data for ERCP utilization rates from 1996 to 2002[16]. They found that the rate of inpatient ERCPs dropped from 74.95/100,000 persons in 1996 to 59.70/100,000 in 2002, driven mostly by a decrease in diagnostic procedures, while there was a slight concomitant increase in therapeutic

procedures. However, because they were using NIS sample, data are not available on outpatient utilization of ERCP. In contrast, outpatient procedures comprised 43.5% of procedures in our study.

Over the study period, overall utilization of EUS and MRCP have also increased in Olmsted County. ERCP is likely now utilized almost exclusively for therapeutic purposes because of the diagnostic abilities of EUS and MRCP, and the improvements in contrast-enhanced CT scans. Also, increased use of EUS and MRCP might actually result in more therapeutic ERCP as seen in our study, which contradicts popular belief that utilization of ERCP has decreased over time with increased use of other diagnostic modalities.

Unplanned admissions commonly occur after ERCP (22% within 30 days), but are most often not related to procedural AEs, which occur in 5.3% of all patients undergoing ERCP. Unplanned admissions within 30 days after a procedure are increasingly being counted as negative indicators of healthcare quality[17]. However, our data suggest that in the case of ERCP, this outcome measure may not be a valid indicator of the quality of the procedure itself and is likely related to either underlying disease, a finding of the procedure itself that leads to elective surgery, or possibly to other comorbidities. Identification and complete capture of 30-day admissions is a strength of our study, in comparison to past studies, where capturing remote AEs were incomplete [6]. Because this is a population-based study, and Mayo Clinic is the only provider for ERCP in the population, all AEs were identified.

Severe procedural AEs, including pancreatitis (2.4%), bleeding (1.5%), infection (1.4%), and mortality related to the procedure (0%), were uncommon. Most AEs were mild to moderate, and at rates similar to previously published reports[3 6]. In a systematic review of 21 surveys of ERCP, AE rates in a population of 16,855 patients were 6.85%, with pancreatitis, infection and

bleeding occurring in 3.5%, 1.4% and 1.3% of cases[3]; mortality rate was 0.33%. Cotton et al. reported on 11,497 procedures at multiple centers and found a 4.0% AE rate, with rates of 2.6% for pancreatitis and 0.3% for bleeding. Mortality rate in this cohort was 0.06%[6]. Although 2.4% of patients in our study died within 30 days of the ERCP, none of these deaths were ERCP-related, and there were no intra- or peri-procedural deaths in our study. Because the AE rates in our study are similar to the rates reported in the literature, it is likely that ERCP procedures carried out at other tertiary care centres are also associated with low adverse event rates.

Numerous studies have enumerated various risk factors for AEs following ERCP[6 8 10 18 19]. Commonly accepted risk factors for any AE after ERCP include suspected sphincter of Oddi dysfunction, cirrhosis, difficult cannulation, performance of precut sphincterotomy, percutaneous biliary access, and lower ERCP case volumes, with young age, pancreatic duct contrast injection and failed biliary drainage identified in some studies. In our study, younger patient age, higher BMI, first ERCP, pancreatic duct cannulation, intra-procedural post sphincterotomy bleeding, therapeutic procedures, and outpatient procedures were identified as risk factors for any AE through a multivariate analysis.

Consistent with our findings, younger age has been previously shown to be a risk factor for AEs, especially post-ERCP pancreatitis (PEP)[5 8 10]. Pancreatic duct cannulation is known to be a risk-factor for development of PEP[6]. Toward the end of this study period, data emerged supporting the use of prophylactic pancreatic duct stents to decrease the incidence of PEP and were published. In our study period, in only 59 (5.5%) procedures, we placed a pancreatic duct stent. Hence, our study is not able to adequately define the rate of PEP with routine placement of prophylactic pancreatic stents.

One limitation of our study is that it is a retrospective review of data with its inherent biases. However, the data were manually abstracted by a single gastroenterologist from an electronic medical record, and significant adverse events and hospitalizations are not likely to have been missed. Another limitation is that even though the population studied is a county-based population, the skills of the endoscopists are at a higher level than endoscopists in smaller community hospitals. Therefore, the AE rate in this community setting could be lower than one would expect in community settings at large. While MRCP is widely available, wherever MRI is available, EUS availability is limited to those centres with trained endosonographers; it is possible that the latter may affect regional utilization of ERCP for diagnostic purposes. Another notable limitation is that Sphincter of Oddi dysfunction and complications of pancreatitis, diagnoses often referred to a tertiary center, were underrepresented in our study.

In conclusion, our study shows that utilization of ERCP at a population level continues to rise; specifically utilization of therapeutic procedures. The most common indications for ERCP remain relief of biliary colic or cholangitis, and this procedure may be carried out with moderate sedation. Adverse events of ERCP remain uncommon and deaths are infrequent. The study adds important epidemiologic data on trends in the utilization of ERCP, as well as population-based estimates of the risk of adverse events from ERCP that will be useful in clinical decision making and determination of resource allocation. The findings of the study may also impact ERCP training criteria.

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None

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Nayantara Coelho-Prabhu, MD - conception and design; analysis and interpretation of the data; drafting of the article; final approval of the article.

Nilay D. Shah, PhD - conception and design; analysis and interpretation of the data; critical revision of the article for important intellectual content.

Holly Van Houten - analysis and interpretation of the data.

Patrick S Kamath, MD - conception and design; critical revision of the article for important intellectual content.

Todd H Baron, MD, FASGE - conception and design; critical revision of the article for important intellectual content; final approval of the article.

Data sharing

Any additonal data can be obtained from the corresponding author. This includes procedural details on all ERCPs including patient characteristics, indication, sedation, trainee involvement, therapies utilised during the ERCP, complications, billing codes.

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Figure Legends

Table IA. Morriston Hospital ERCP grading scale (Ragunath et al, Post Grad Med J, 2003)

Table IB. Consensus criteria for ERCP complications (Cotton et al, GIE, 1991)

Table II. Patient Characteristics

Table III. Procedural Characteristics

Table IV. Procedure Outcomes

Table V. Multivariate analysis of risk factors for post-ERCP complications

Figure I. Utilization characteristics of ERCP, EUS, and MRCP in Olmsted County over 10-year period.

Table IA: Morriston Hospital ERCP grading scale [13]

Procedure	Grade
Diagnostic ERCP	I
Biliary sphincterotomy, balloon sphincteroplasty, removal of extrahepatic stones ≤1 cm using basket and/or balloon	II
Precut sphincterotomy, large stones removal (>1cm), intrahepatic stone removal, mechanical lithotripsy, stricture dilatation, cytology, stent insertion, and naso-biliary drain	III
Sphincter of Oddi manometry, diagnostic and therapeutic ERCP after Billroth II surgery, minor papilla sphincterotomy, endoscopic ampullectomy, and all pancreatic duct therapeutic procedures. Cholangioscopy, laser lithotripsy, electrohydraulic lithotripsy, combined procedures (PTC and ERCP), and other advanced bile duct therapeutic procedures	IV

ERCP - endoscopic retrograde cholangiopancreatography
PTC – percutaneous transhepatic cholangiography

Table IB: Consensus criteria for ERCP complications [14]

	Mild	Moderate	Severe
Bleeding	Clinical evidence of bleeding (ie not just endoscopic) Hemoglobin drop <3g No need for transfusion	Transfusion: 4 units or less No angiographic intervention or surgery	Transfusion: 5 units or more or intervention (angiographic or surgical)
Perforation	Possible, or only very slight leak of fluid or contrast dye Treatable by fluids and suction for 3 days or less	Any definite perforation treated medically for 4-10 days	Medical treatment for more than 10 days or intervention (percutaneous or surgical)
Pancreatitis	Clinical pancreatitis: amylase at least thrice the upper limit of normal at more than 24 hours after the procedure requiring admission or prolongation of planned admission to 2-3 days	Pancreatitis requiring hospitalization for 4-10 days	Pancreatitis requiring hospitalization for more than 10 days, or hemorrhagic pancreatitis, phlegmon, or intervention (percutaneous drainage or surgery)
Infection (cholangitis)	>38 degrees Celsius at 24-48 hours	Febrile or septic illness requiring>3 days of hospital treatment or endoscopic or percutaneous intervention	Septic shock or surgery

Table II: Patient Characteristics

Age at time of ERCP (years)	
mean (sd)	57.6 (19.8)
18-44 years	283 (26.4%)
45-64 years	357 (33.3%)
> 65+ years	432 (40.3%)
Gender	
Female, n (%)	522 (63.1)
Race	
Caucasian	688 (83.2%)
African American	15 (1.8%)
Other/unknown	124 (15.0%)
Charlson index at time of ERCP[12]	
mean (sd)	3.2 (3.2)
BMI at time of ERCP	
mean (sd)	28.5 (7.2)
< 25	341 (32.4%)
25-34	517 (49.1%)
35+	194 (18.4%)

ERCP – endoscopic retrograde cholangiopancreatography
BMI – body mass index

Table III: Procedural Characteristics

	(%)
Cholecystectomy within 30 days prior to ERCP	113 (10.5)
Altered anatomy	21 (2.0)
Anticoagulation	20 (1.9)
Prior ERCP	277 (25.8)
Biliary indications	975 (91.0)
Cholangitis	56 (5.2)
Cholecystitis	41 (3.8)
Bleeding	4 (0.4)
Choledocholithiasis	500 (46.6)
Malignant stricture	116 (10.8)
Hilar stricture	5 (0.5)
Benign stricture	46 (4.3)
Ca pancreas	21 (2)
Papillary stenosis	8 (0.7)
Ca ampulla	14 (1.3)
Anastomotic stricture	29 (2.7)
Post cholecystectomy	69 (6.4)
Suspected SOD	19 (1.8)
PSC	21 (2)
Bile leaks	23 (2.1)
Biliary colic	307 (28.6)
Biliary dilation	27 (2.5)
Stent removal	52 (4.9)
Elevated AST and ALT	76 (7.1)
Pancreatic indications	217 (20.2)
Acute pancreatitis	135 (12.6)
Recurrent acute pancreatitis	34 (3.2)
Chronic pancreatitis	17 (1.6)
Cyst	8 (0.7)
Duct leak	9 (0.8)
Duct stricture	7 (0.7)
Acute fluid collection	7 (0.7)
Chronic fluid collection	18 (1.7)
Necrosectomy	14 (1.3)
Inpatient	606 (56.5)

Therapeutic	889 (82.9)
Difficulty grade	
I	152 (14.2)
II	494 (46.1)
III	297 (27.7)
IV	129 (12.0)
Trainee present	667 (62.2)
Anesthesia	
Conscious sedation	1030 (96.1)
Fentanyl	51 (4.8)
Versed	1028 (95.8)
Benadryl	6 (0.6)
Demerol	979 (91.2)
Phenergan	90 (8.4)
Droperidol	25 (2.3)
General (or propofol)	42 (3.9)
Peri-ampullary diverticulum	117 (10.9)
Biliary sphincterotomy	620 (57.8)
Precut biliary sphincterotomy	125 (11.7)
Biliary stent placed	185 (17.3)
Pancreatic sphincterotomy	13 (1.2)
Pancreatic duct stent placed	59 (5.5)
Ampullectomy	7 (0.7)
Transgastric/transduodenal drainage	16 (1.5)
Sphincterotomy bleeding noted during procedure	45 (4.2)

ERCP – endoscopic retrograde cholangiopancreatography
AST – aspartate aminotransferase
ALT – alanine aminotransferase

Table IV: Procedure Outcomes

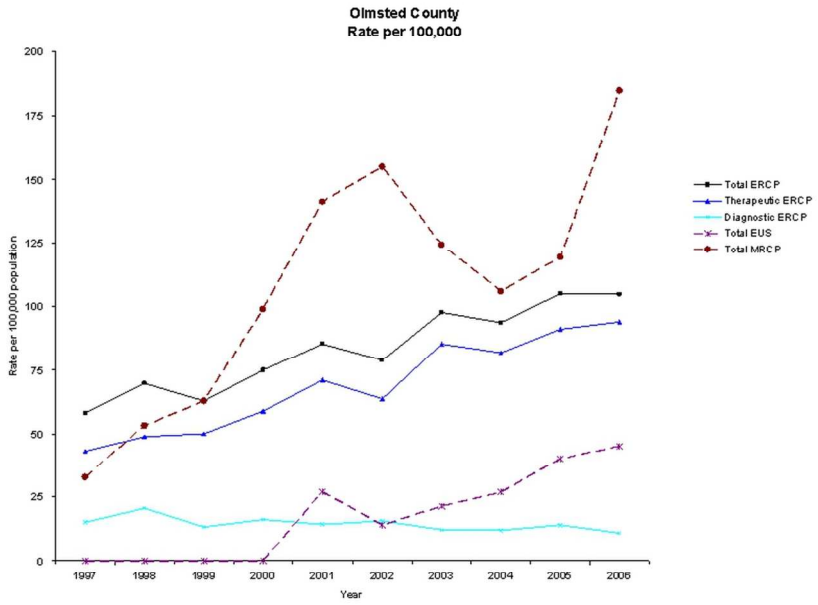
	(%)
Success	041 (97.1)
Death	
During procedure	0 (0.0)
Within 30 days	26 (2.4)
Need for repeat procedure within 30 days	
ERCP	93 (8.7)
EGD	45 1 (4.2)
Number of readmissions within 30 days	273
Definitely related to procedure	62 (22.7)
Possibly related to procedure	6 (2.2)
Definitely not related to procedure	205 (75.1)
Surgery within 30 days	
Elective cholecystectomy	52 (4.9)
Elective Whipple	16 (5.9)
Other elective	11 (4.0)
Emergent cholecystectomy	6 (2.2)
ERCP complications requiring readmit	53 (4.9)
Pancreatitis	26 (2.4)
Mild	18
Moderate	8
Severe	0
Infection/cholangitis	16 (1.5)
Mild	6
Moderate	7
Severe	3
Bleeding	15 (1.4)
Mild	6
Moderate	8
Severe	1
Perforation	4 (0.37)
Mild	0
Moderate	0

Severe	4

Table V. Multivariate analysis of risk factors for post-ERCP complications

Risk factor	Odds ratio (95% CI)	*P*-value
Age <45 vs ≥65	2.23 (1.03 – 4.84)	0.0498 *
Age 45-64 vs ≥65	1.3 (0.62 – 2.72)	0.6697
Female gender	1.2 (0.61 – 2.21)	0.6412
BMI <25 vs ≥35	0.84 (0.40 – 1.74)	0.1972
BMI 25-34 vs ≥35	0.31 (0.14 – 0.72)	0.0024 *
No previous ERCP	2.22 (1.04 – 4.75)	0.0394 *
Outpatient ERCP	5.4 (2.6 – 11.4)	<0.0001 *
Pancreatic duct cannulation	2.7 (1.4 – 5.1)	0.0026 *
Absence of trainee	1.36 (0.72 – 2.59)	0.3487
Intraprocedure sphincterotomy bleeding	10.0 (3.8 – 26.1)	<0.0001 *
Difficulty grade 1 vs 4	0.11 (0.02 – 0.54)	0.0204 *
Difficulty grade 2 vs 4	0.45 (0.18 – 1.14)	0.9199
Difficulty grade 3 vs 4	0.94 (0.42 – 2.13)	0.0129 *

Figure 1.



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STROBE STATEMENT checklist of items that should be included in reports of Observational Studies

SECTION/TOPIC	Item No.	Checklist Item	Reported on page No.
TITLE AND ABSTRACT	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2, 3
INTRODUCTION			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4, 5
METHODS			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6
Participants	6	(a) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5,6
		(b) *Cohort study*—For match studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6,7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7,8
		(b) Describe any methods used to examine subgoups and interactions	
		(c) Explain how missing data were addressed	
		(d) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
RESULTS			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	8,9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarize follow-up time (e.g., average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time *Case-control study*—Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study*—Report numbers of outcome events or summary measures	10
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make	10

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		clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	(d) Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	
DISCUSSION			
Key results	18	Summarize key results with reference to study objectives	12,13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalizability	21	Discuss the generalizability (external validity) of the study results	15
OTHER INFORMATION			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Endoscopic Retrograde Cholangiopancreatography – Utilization and outcomes in a 10-year population based cohort

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Extra data is available by contacting the corresponding author.

Word count – Text – 3197

Tables – 5

Figures – 1

Keywords: ERCP, utilization, complications, hospitalization

SUMMARY

Article Focus:

- Due to increasing use of quality metrics, accurate measures of utilization and procedural adverse event risks are necessary to establish benchmarks for quality, and are best determined from community-based studies.
- There are no reports of community-based utilization of ERCP in the US.
- The aims of this population-based study were to determine the utilization of ERCP including changes over time, the incidence of inpatient admissions for adverse events within 30 days of ERCP, and risk factors for procedural related adverse events.

Key Messages:

- Population utilization of ERCP in Olmsted County MN rose over the ten year period from 1997 to 2006, driven specifically by increases in therapeutic procedures. The most common indications for ERCP were therapy of choledocholithiasis and to determine etiology of acute pancreatitis.
- Admissions within 30 days after ERCP are common, but are usually unrelated. Complications of ERCP remain infrequent at 5.3% and no deaths were directly related.
- Risk factors associated with adverse events from ERCP include younger age, BMI ≥35, pancreatic duct cannulation, outpatient procedures, intraprocedure sphincterotomy bleeding, difficulty grade, and patient's first ERCP.

Strengths and Limitations:

Strengths:

- Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community.
- The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and adverse events of ERCP with full details of procedures and subsequent hospitalizations can be assessed.

Limitations:

- The study is a retrospective review with inherent potential biases.
- The skills of the endoscopists are likely at a higher level than endoscopists in smaller community hospitals. Therefore, the adverse event rate in this community setting could be lower than one would expect in other community settings.

ABSTRACT

Objective: To determine utilization of ERCP; incidence of inpatient admissions for complications occurring within 30 days of ERCP; and risk factors for procedural related complications, in a population based study.

Design: Retrospective cohort study

Setting: Olmsted County, MN

Participants: All adult residents of Olmsted County, MN, who underwent ERCP from 1997 to 2006.

Interventions: Diagnostic and therapeutic ERCPs were assessed.

Primary and Secondary outcome measures: Patient and procedural characteristics and complications within 30 days; and rates of ERCP utilization and unplanned admissions and risk factors for admissions.

Results: In ten years, 1072 ERCPs were performed on 827 individual patients. Average utilization of ERCP was 83.1 ERCPs/100,000 persons/year, with an increase from 58.0 to 104.8 ERCPs/100,000 persons/year over time, driven by increases in therapeutic procedures. Within 30 days after 236 procedures, 62 admissions were definitely related to the index ERCP. The complication rate was 5.3%, including pancreatitis(26, 2.4%), infection/cholangitis(16, 1.5%),

bleeding(15, 1.4%), and perforation(4, 0.37%). 30-day mortality was 2.4%; none of which were directly related to the ERCP or complications thereof. Risk factors identified through multivariate analysis to be associated with adverse events included: age <45 years(p=0.0498); BMI ≥35(p=0.0024); pancreatic duct cannulation(p=0.0026); outpatient procedure(p<0.0001); intraprocedure sphincterotomy bleeding(*P*<0.0001); difficulty grade(*P*=0.115); and patient's first ERCP(*P*=0.0394).

Limitations: Retrospective study.

Conclusions: Population utilization of ERCP rose during the study period, specifically in therapeutic procedures. Admissions within 30 days of ERCP are common, but often unrelated. Complications of ERCP remain infrequent and deaths quite unusual.

Abbreviations:

AE – adverse event

EGD – esophagogastroduodenoscopy

ERCP - endoscopic retrograde cholangiopancreatography

EUS – endoscopic ultrasound

MRCP - magnetic resonance cholangiopancreatography

BACKGROUND

Since its first description in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has become an established modality for the diagnosis and treatment of pancreaticobiliary disorders[1 2]. Over the years, ERCP has evolved from a purely diagnostic, to a mainly therapeutic procedure. Around 500,000 ERCPs are performed annually in the United States (US) with adverse event (AE) rates between 4% and 10%,[3] and mortality between 0.05% and 1%[4-7]. The most common AEs following ERCP include pancreatitis, hemorrhage, and infection, which occured in 4% to7% of procedures[3 6 8]. There is an increased risk of AEs after therapeutic procedures and in patients with suspected Sphincter of Oddi dysfunction[6]. Since ERCP is the endoscopic procedure with the highest cost and AE rates, diagnostic ERCP is now avoided in favor of other diagnostic modalities such as less-invasive endoscopic ultrasound (EUS) and non-invasive magnetic resonance cholangiopancreatography (MRCP)[2 3 9]. In an era of increasing utilization of quality metrics, accurate measures of utilization rates and procedural adverse event risks are necessary to establish meaningful benchmarks for quality, and are best determined from community-based studies.

There are no reports of community-based utilization of ERCP in the US, but there are several from Europe[8 10]. Published reports of ERCP related AEs have all been single-centered or multi-centered studies from tertiary care centers and affected by referral bias, leading to high estimates of risk that may not apply to the general population. All adverse events of procedures done at tertiary care centers may not be captured since the patients may seek care for AEs closer to their homes and thus, lost to follow-up.

The aims of this population-based study were to determine (1) the utilization of ERCP, including changes over time; (2) the incidence of inpatient admissions for AEs within 30 days of

ERCP; and (3) risk factors for procedural related AEs among residents of Olmsted County, MN over a ten-year period from 1997-2006. The findings of this study are unique, as they represent population based estimates of utilization and risks associated with ERCP and may serve as more accurate and clinically meaningful data for clinical decision making and development of quality benchmarks.

METHODS

Study Design: A retrospective cohort study was conducted with approval of the Institutional Review Board of Mayo Clinic in compliance with federal regulations of the U.S. Department of Health and Human Services for protection of human subjects and the Health Information Protection and Portability Act. All patients provided consent for medical record review. Billing records from Mayo Clinic and associated hospitals were queried for Olmsted County residents who had undergone an ERCP during a ten-year period from January 1, 1997 to December 31, 2006. ERCPs were identified using CPT codes for ERCP, including 43260, 43261, 43262, 43263, 43264, 43265, 43267, 43268, 43269, 43271, 43272, and 47999. Utilization characteristics for EUS were determined in the same population using codes 43232, 43238, and 43242 and for MRCP using codes 74181, 74182, and 74183. Subjects also had to be age ≥ 18 years, live in Olmsted County, and have valid authorization to review medical records for research purposes in accordance with Minnesota State statutes.

Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community. Olmsted County comprises over 100,000 persons, of whom 85% are Caucasian and 50% are women; socio-demographically, the community is similar to the US population. Over half of the county's population is seen at one of

the Mayo Clinic facilities; 95% of local residents will have had at least one medical contact with a local care provider (*e.g.*, for dental X-rays, sports physical examinations, pre-employment examinations, minor illness, and routine medical care) during any 4-year period[11]. Mayo Clinic has a common medical record system with its two affiliated hospitals (Saint Mary's and Rochester Methodist) for 90 years. Mayo Clinic's single record system contains both inpatient and outpatient data. Diagnoses and surgical procedures recorded in these records are indexed. It includes diagnoses made for outpatients seen in office or clinic consultations, emergency room visits, and diagnoses recorded for hospital inpatients, autopsy examinations, or on death certificates. The unique advantage of our data is that Mayo Clinic is the only center performing ERCP in the entire county and, therefore, population based utilization and AEs of ERCP with full details of the hospitalization can be assessed.

Medical records were reviewed retrospectively by the primary author. Patient and procedural characteristics, as well as AEs within 30 days were recorded. As many as 170 variables were collected for each procedure and recorded into a database.

Primary outcomes measured were (1) utilization rates of unique ERCP procedures in the adult population (age 18 years and older) of Olmsted County from 1997-2006, and (2) the rate of unplanned admissions within 30 days following ERCP for ERCP-related AEs. Secondary outcomes included patient and procedural characteristics, predictive of having an unplanned admission within 30 days after ERCP for an ERCP-related AE.

Utilization metrics included the patients' age, sex, race, Charlson score at the time of ERCP[12], body mass index (BMI), cholecystectomy within 30 days prior to ERCP, altered anatomy (including gastrojejunostomy, Whipple anatomy, hepatico- and choledocho-jejunostomy), presence of cirrhosis, and previous history of ERCP. Indications for ERCP were

then examined as biliary versus pancreatic, diagnostic versus therapeutic, and graded for complexity using the previously published Morriston Hospital ERCP grading scale (Table IA)[13]. Diagnostic procedures had a CPT code of 43260 where no intervention was performed, other than a cholangiogram or pancreatogram; all other procedures were therapeutic. Multiple intra-procedural details, including presence of a trainee, type and amount of sedation used, and biliary and pancreatic ductal interventions were noted. Success of the procedure was recorded as the ability to cannulate the intended duct and achieve the intended therapy.

AEs recorded included unplanned admissions; sedation-related events, including pulmonary and cardiovascular events; infection; pancreatitis; bleeding; perforation; need for repeat endoscopic procedure; or mortality within 30 days. These outcomes were determined as being related to the index ERCP by author review. AEs were deemed to be definitely related, probably related, possibly related, or definitely unrelated to the index ERCP. Possibly related AEs included patients admitted with abdominal pain, but without evidence of definite pancreatitis by laboratory studies or documented cholangitis. Probably related AEs included biliary or pancreatic stent dysfunction leading to repeat the procedure within 30 days of the index procedure, but without any of the defined AEs of pancreatitis, infection, perforation, and gastrointestinal bleeding. The latter AEs were categorized as mild, moderate, and severe, according to established consensus criteria (Table IB)[6 14] Patients undergoing elective surgery including cholecystectomy within 30 days of ERCP were also identified.

Statistical Analysis

Univariate analyses were performed to obtain descriptive statistics for patient and procedural characteristics. Annual incidence was determined by dividing the number of ERCPs performed

on the study subjects during a calendar year by the adult population of Olmsted County during that period, according to County records and normalized to 100,000 persons. To test for associations between patient and procedural characteristics and ERCP related AEs, values of these characteristics were compared between subjects who experienced ERCP-related AEs and subjects who did not by two sample t-tests for continuous variables, and chi square test for discrete variables. Multivariable logistic regression analyses were used to determine patient and procedural characteristics predictive of ERCP-related AEs. *P*-values less than 0.05 were considered statistically significant. All analyses for this study were done using SAS statistical software (SAS version 9.1 for Windows; SAS Institute Inc., Cary, North Carolina).

RESULTS

Demographic characteristics

In the 10-year period from January, 1, 1997 to December, 31, 2006, 1072 ERCPs were performed on 827 individual adult residents of Olmsted County. The total number of ERCPs done during this time period was 13056 including the non-residents of Olmsted County. Patient demographic characteristics can be seen in Table II. Prior to the index cholecystectomy, 232 (28%) patients had a previous cholecystectomy; 21 (2%) patients had altered anatomy, and 20 (1.9%) were taking clopidogrel or warfarin at the time of the ERCP. There were 153 patients who had more than one ERCP during the 10-year period, and the mean number of ERCPs in these patients was 1.3.

Utilization characteristics

Average utilization of ERCP was 83.1 ERCPs per 100,000 persons/year, with an increasing trend in utilization from 58.0 to 104.8 ERCPs per 100,000 persons/year over the 10-year period. Therapeutic ERCPs increased over the same timeframe from 42.9 to 93.9 ERCPs per 100,000 persons/year (average 68.7). However, diagnostic ERCPs decreased slightly from 15.1 to 10.9 and averaged 14.4 ERCPs per 100,000 persons/year. EUS and MRCP utilization in the same population also steadily increased over this time period (Figure I).

Procedural characteristics

Procedural characteristics can be seen in Table III. Of the 1072 ERCPs performed over the 10-year period, 606(56.5%) were performed on inpatients, while 889 (82.9%) were therapeutic. The proportion of therapeutic procedures from 2002-2006 was higher than from 1997-2001 (86.6% vs 77.5%, *P*=0.0001). The difficulty grades, as defined by Morriston Hospital ERCP grading scale, were mostly Grade II(494, 46.1%) and Grade III(297, 27.7%) procedures overall; however, there was a two-fold increase in Grade IV procedures in the second five-year period, compared to the first (15.3% vs 7.2%, P<0.0001). ERCP was performed primarily for a biliary indication in 853 (79.6%) and a pancreatic indication in 95 (8.9%) with 122 (11.4%) for both a biliary and pancreatic indication. The commonest biliary indications included choledocholithiasis (500, 46.6%), biliary colic in the absence of documented choledocholithiasis (307, 28.6%), and relief of malignant biliary obstruction (116, 10.8%). The commonest pancreatic indications for ERCP were to determine etiology of acute pancreatitis (135, 12.6%), or recurrent acute pancreatitis (34, 3.2%), and chronic pancreatic fluid collection (18, 1.7%). Suspected sphincter of Oddi dysfunction was the indication in only (19, 1.7%) of ERCPs. A trainee was involved in 667 (62.2%) cases.

Biliary sphincterotomy was performed in 620 (57.8%) procedures; the pancreatic duct was injected in 404 (37.7%) cases and was cannulated in 255 (23.8%) procedures. In some cases, the intent was to cannulate the bile duct, but pancreatic duct injection occurred during the process. Biliary stents were placed in 185 (17.3%) cases; prophylactic pancreatic stents were placed in 59 (5.5%) patients. Placement of pancreatic stents increased in the second 5-year period, compared to the first (8.1% vs 1.6%, $P<0.0001$). Ampullectomy was performed in 7 (0.7%) cases and 16 (1.5%) cases were transgastric or transduodenal débridements of pancreatic necrosis (15 of which occurred in the second 5-year period, $P=0.0053$). Only 31 (2.9%) of ERCPs were deemed as failures as the goal of the procedure was not achieved, resulting in a 97.1% success rate. None of the patients received any prophylaxis to prevent post-ERCP pancreatitis.

Sedation

Only 42(3.9%) of procedures were done with anesthesia support. Of the remaining ERCPs done under moderate sedation, the mean dose of fentanyl was 159 ± 86mcg (in 51 ERCPs), midazolam 6.1 ± 2.6mg (1028 ERCPs), meperidine 97 ± 46mg (979 ERCPs), and promethazine 21 ± 8mg (90 ERCPs).

Outcomes

Following 1072 ERCPs in Olmsted County, over ten years, there were 273 admissions to the hospital within 30 days after 236 procedures (22% of all procedures). Table IV lists the outcomes in the study cohort. Of the 273 admissions, only 62 (22.7%) were definitely related to the index ERCP procedure, with another 2 (0.7%) probably related, and 4 (1.4%) possibly related to the

procedure. Of the remaining 205 admissions unrelated to procedural AEs of the index ERCP, 79 were planned for elective surgeries, including cholecystectomy. Intraprocedural AEs were infrequent, with 20 (1.9%) necessitating a change in intra-procedural anesthesia; no deaths occurred during the procedure. There were 47 sphincterotomy-induced intra-procedural bleeding episodes treated with various modalities, including epinephrine injection, cautery and tamponade.

The AE rate was 5.3% including pancreatitis (26, 2.4%), infection/cholangitis (16, 1.5%), bleeding (15, 1.4%), and perforation (4, 0.37%). 53 cases were determined to be mild to moderate; however, 3 infections, all 4 perforations, and 1 bleed were considered severe. The 30-day mortality rate was 2.4%; 69% of deaths were due to underlying malignancy, 12% were due to infections unrelated to the ERCP, and 19% were due to other causes including stroke, respiratory failure, and dementia. None of the deaths were directly related to the ERCP or AEs thereof. Repeat ERCP procedures were required in 93 (8.7%) patients and 45 (4.2%) had an esophagogastroduodenoscopy (EGD) within 30 days of the index ERCP.

Risk factors for AEs

In order to determine if there were identifiable risk factors for AEs arising from ERCP in our cohort, the relative frequency and distribution of patient and procedural characteristics were compared between patients who had a procedural AE and those who did not (Table V). Patient characteristics identified through multivariate analysis to be associated with AEs included: age less than 45 years (OR 2.23 (95% CI 1.03 – 4.84) for age <45 years vs ≥65 years, *P*=0.0498); and BMI ≥35 (OR 0.31 (95% CI 0.14 – 0.72) for BMI 25-34 vs ≥35, *P*=0.0024). Procedural characteristics identified to be associated with increased risk of AEs included: patient's first

ERCP (OR 2.22 (95% CI 1.04 – 4.75), *P*=0.0394); pancreatic duct cannulation (OR 2.7 (95%CI 1.4 - 5.1), *P*=0.0026); outpatient procedure (OR 5.4 (95% CI 2.6 – 11.4), *P*<0.0001); intraprocedure sphincterotomy bleeding (OR 10.0 (95% CI 3.8 – 26.1), *P*<0.0001); difficulty grade (OR 8.9 (95% CI 1.9 – 43.1) for grade 4 vs 1, *P*=0.0204).

DISCUSSION

In the adult Olmsted County study population, which is considered representative of the US population, ERCP utilization rates nearly doubled over the ten-year period from January 1, 1997 to December 31, 2006 from 58.0 to 104.8 cases per 100,000 persons/year[15]. This trend was influenced by a substantial increase in the rate of therapeutic procedures and a slight decrease in diagnostic procedures. Importantly, ERCP was performed predominantly for common 'bread and butter' indications including cholangitis, biliary colic, and pancreatitis. This information underscores the fact that ERCP is currently mainly a therapeutic modality, and should be available at a community-based level. Training in ERCP should be focussed on gaining expertise mainly for removal of common duct stones and relief of distal biliary obstruction. For a community based gastroenterologist, the need for more complex procedures is rare, and these procedures should be carried out at tertiary care centres.

ERCP utilization rates in Olmsted County in this study are in some ways divergent with national data. For instance, Mazen Jamal et al queried the Nationwide Inpatient Sample (NIS) data for ERCP utilization rates from 1996 to 2002[16]. They found that the rate of inpatient ERCPs dropped from 74.95/100,000 persons in 1996 to 59.70/100,000 in 2002, driven mostly by a decrease in diagnostic procedures, while there was a slight concomitant increase in therapeutic

procedures. However, because they were using NIS sample, data are not available on outpatient utilization of ERCP. In contrast, outpatient procedures comprised 43.5% of procedures in our study.

Over the study period, overall utilization of EUS and MRCP have also increased in Olmsted County. ERCP is likely now utilized almost exclusively for therapeutic purposes because of the diagnostic abilities of EUS and MRCP, and the improvements in contrast-enhanced CT scans. Also, increased use of EUS and MRCP might actually result in more therapeutic ERCP as seen in our study, which contradicts popular belief that utilization of ERCP has decreased over time with increased use of other diagnostic modalities.

Unplanned admissions commonly occur after ERCP (22% within 30 days), but are most often not related to procedural AEs, which occur in 5.3% of all patients undergoing ERCP. Unplanned admissions within 30 days after a procedure are increasingly being counted as negative indicators of healthcare quality[17]. However, our data suggest that in the case of ERCP, this outcome measure may not be a valid indicator of the quality of the procedure itself and is likely related to either underlying disease, a finding of the procedure itself that leads to elective surgery, or possibly to other comorbidities. Identification and complete capture of 30-day admissions is a strength of our study, in comparison to past studies, where capturing remote AEs were incomplete [6]. Because this is a population-based study, and Mayo Clinic is the only provider for ERCP in the population, all AEs were identified.

Severe procedural AEs, including pancreatitis (2.4%), bleeding (1.5%), infection (1.4%), and mortality related to the procedure (0%), were uncommon. Most AEs were mild to moderate, and at rates similar to previously published reports[3 6]. In a systematic review of 21 surveys of ERCP, AE rates in a population of 16,855 patients were 6.85%, with pancreatitis, infection and

bleeding occurring in 3.5%, 1.4% and 1.3% of cases[3]; mortality rate was 0.33%. Cotton et al. reported on 11,497 procedures at multiple centers and found a 4.0% AE rate, with rates of 2.6% for pancreatitis and 0.3% for bleeding. Mortality rate in this cohort was 0.06%[6]. Although 2.4% of patients in our study died within 30 days of the ERCP, none of these deaths were ERCP-related, and there were no intra- or peri-procedural deaths in our study. Because the AE rates in our study are similar to the rates reported in the literature, it is likely that ERCP procedures carried out at other tertiary care centres are also associated with low adverse event rates.

Numerous studies have enumerated various risk factors for AEs following ERCP[6 8 10 18 19]. Commonly accepted risk factors for any AE after ERCP include suspected sphincter of Oddi dysfunction, cirrhosis, difficult cannulation, performance of precut sphincterotomy, percutaneous biliary access, and lower ERCP case volumes, with young age, pancreatic duct contrast injection and failed biliary drainage identified in some studies. In our study, younger patient age, higher BMI, first ERCP, pancreatic duct cannulation, intra-procedural post sphincterotomy bleeding, therapeutic procedures, and outpatient procedures were identified as risk factors for any AE through a multivariate analysis.

Consistent with our findings, younger age has been previously shown to be a risk factor for AEs, especially post-ERCP pancreatitis (PEP)[5 8 10]. Pancreatic duct cannulation is known to be a risk-factor for development of PEP[6]. Toward the end of this study period, data emerged supporting the use of prophylactic pancreatic duct stents to decrease the incidence of PEP and were published. In our study period, in only 59 (5.5%) procedures, we placed a pancreatic duct stent. Hence, our study is not able to adequately define the rate of PEP with routine placement of prophylactic pancreatic stents.

One limitation of our study is that it is a retrospective review of data with its inherent biases. However, the data were manually abstracted by a single gastroenterologist from an electronic medical record, and significant adverse events and hospitalizations are not likely to have been missed. Another limitation is that even though the population studied is a county-based population, the skills of the endoscopists are at a higher level than endoscopists in smaller community hospitals. Therefore, the AE rate in this community setting could be lower than one would expect in community settings at large. While MRCP is widely available, wherever MRI is available, EUS availability is limited to those centres with trained endosonographers; it is possible that the latter may affect regional utilization of ERCP for diagnostic purposes. Another notable limitation is that Sphincter of Oddi dysfunction and complications of pancreatitis, diagnoses often referred to a tertiary center, were underrepresented in our study.

In conclusion, our study shows that utilization of ERCP at a population level continues to rise; specifically utilization of therapeutic procedures. The most common indications for ERCP remain relief of biliary colic or cholangitis, and this procedure may be carried out with moderate sedation. Adverse events of ERCP remain uncommon and deaths are infrequent. The study adds important epidemiologic data on trends in the utilization of ERCP, as well as population-based estimates of the risk of adverse events from ERCP that will be useful in clinical decision making and determination of resource allocation. The findings of the study may also impact ERCP training criteria.

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Figure Legends

Table IA. Morriston Hospital ERCP grading scale (Ragunath et al, Post Grad Med J, 2003)

Table IB. Consensus criteria for ERCP complications (Cotton et al, GIE, 1991)

Table II. Patient Characteristics

Table III. Procedural Characteristics

Table IV. Procedure Outcomes

Table V. Multivariate analysis of risk factors for post-ERCP complications

Figure I. Utilization characteristics of ERCP, EUS, and MRCP in Olmsted County over 10-year period.

Table IA: Morriston Hospital ERCP grading scale [13]

Procedure	Grade
Diagnostic ERCP	I
Biliary sphincterotomy, balloon sphincteroplasty, removal of extrahepatic stones ≤1 cm using basket and/or balloon	II
Precut sphincterotomy, large stones removal (>1cm), intrahepatic stone removal, mechanical lithotripsy, stricture dilatation, cytology, stent insertion, and naso-biliary drain	III
Sphincter of Oddi manometry, diagnostic and therapeutic ERCP after Billroth II surgery, minor papilla sphincterotomy, endoscopic ampullectomy, and all pancreatic duct therapeutic procedures. Cholangioscopy, laser lithotripsy, electrohydraulic lithotripsy, combined procedures (PTC and ERCP), and other advanced bile duct therapeutic procedures	IV

ERCP - endoscopic retrograde cholangiopancreatography
PTC – percutaneous transhepatic cholangiography

Table IB: Consensus criteria for ERCP complications [14]

	Mild	Moderate	Severe
Bleeding	Clinical evidence of bleeding (ie not just endoscopic) Hemoglobin drop <3g No need for transfusion	Transfusion: 4 units or less No angiographic intervention or surgery	Transfusion: 5 units or more or intervention (angiographic or surgical)
Perforation	Possible, or only very slight leak of fluid or contrast dye Treatable by fluids and suction for 3 days or less	Any definite perforation treated medically for 4-10 days	Medical treatment for more than 10 days or intervention (percutaneous or surgical)
Pancreatitis	Clinical pancreatitis: amylase at least thrice the upper limit of normal at more than 24 hours after the procedure requiring admission or prolongation of planned admission to 2-3 days	Pancreatitis requiring hospitalization for 4-10 days	Pancreatitis requiring hospitalization for more than 10 days, or hemorrhagic pancreatitis, phlegmon, or intervention (percutaneous drainage or surgery)
Infection (cholangitis)	>38 degrees Celsius at 24-48 hours	Febrile or septic illness requiring>3 days of hospital treatment or endoscopic or percutaneous intervention	Septic shock or surgery

Table II: Patient Characteristics

Age at time of ERCP (years)	
mean (sd)	57.6 (19.8)
18-44 years	283 (26.4%)
45-64 years	357 (33.3%)
> 65+ years	432 (40.3%)
Gender	
Female, n (%)	522 (63.1)
Race	
Caucasian	688 (83.2%)
African American	15 (1.8%)
Other/unknown	124 (15.0%)
Charlson index at time of ERCP[12]	
mean (sd)	3.2 (3.2)
BMI at time of ERCP	
mean (sd)	28.5 (7.2)
< 25	341 (32.4%)
25-34	517 (49.1%)
35+	194 (18.4%)

ERCP – endoscopic retrograde cholangiopancreatography
BMI – body mass index

Table III: Procedural Characteristics

	(%)
Cholecystectomy within 30 days prior to ERCP	113 (10.5)
Altered anatomy	21 (2.0)
Anticoagulation	20 (1.9)
Prior ERCP	277 (25.8)
Biliary indications	975 (91.0)
Cholangitis	56 (5.2)
Cholecystitis	41 (3.8)
Bleeding	4 (0.4)
Choledocholithiasis	500 (46.6)
Malignant stricture	116 (10.8)
Hilar stricture	5 (0.5)
Benign stricture	46 (4.3)
Ca pancreas	21 (2)
Papillary stenosis	8 (0.7)
Ca ampulla	14 (1.3)
Anastomotic stricture	29 (2.7)
Post cholecystectomy	69 (6.4)
Suspected SOD	19 (1.8)
PSC	21 (2)
Bile leaks	23 (2.1)
Biliary colic	307 (28.6)
Biliary dilation	27 (2.5)
Stent removal	52 (4.9)
Elevated AST and ALT	76 (7.1)
Pancreatic indications	217 (20.2)
Acute pancreatitis	135 (12.6)
Recurrent acute pancreatitis	34 (3.2)
Chronic pancreatitis	17 (1.6)
Cyst	8 (0.7)
Duct leak	9 (0.8)
Duct stricture	7 (0.7)
Acute fluid collection	7 (0.7)
Chronic fluid collection	18 (1.7)
Necrosectomy	14 (1.3)
Inpatient	606 (56.5)

Therapeutic	889 (82.9)
Difficulty grade	
I	152 (14.2)
II	494 (46.1)
III	297 (27.7)
IV	129 (12.0)
Trainee present	667 (62.2)
Anesthesia	
Conscious sedation	1030 (96.1)
Fentanyl	51 (4.8)
Versed	1028 (95.8)
Benadryl	6 (0.6)
Demerol	979 (91.2)
Phenergan	90 (8.4)
Droperidol	25 (2.3)
General (or propofol)	42 (3.9)
Peri-ampullary diverticulum	117 (10.9)
Biliary sphincterotomy	620 (57.8)
Precut biliary sphincterotomy	125 (11.7)
Biliary stent placed	185 (17.3)
Pancreatic sphincterotomy	13 (1.2)
Pancreatic duct stent placed	59 (5.5)
Ampullectomy	7 (0.7)
Transgastric/transduodenal drainage	16 (1.5)
Sphincterotomy bleeding noted during procedure	45 (4.2)

ERCP – endoscopic retrograde cholangiopancreatography
AST – aspartate aminotransferase
ALT – alanine aminotransferase

Table IV: Procedure Outcomes

	(%)
Success	041 (97.1)
Death	
During procedure	0 (0.0)
Within 30 days	26 (2.4)
Need for repeat procedure within 30 days	
ERCP	93 (8.7)
EGD	45 1 (4.2)
Number of readmissions within 30 days	273
Definitely related to procedure	62 (22.7)
Possibly related to procedure	6 (2.2)
Definitely not related to procedure	205 (75.1)
Surgery within 30 days	
Elective cholecystectomy	52 (4.9)
Elective Whipple	16 (5.9)
Other elective	11 (4.0)
Emergent cholecystectomy	6 (2.2)
ERCP complications requiring readmit	53 (4.9)
Pancreatitis	26 (2.4)
Mild	18
Moderate	8
Severe	0
Infection/cholangitis	16 (1.5)
Mild	6
Moderate	7
Severe	3
Bleeding	15 (1.4)
Mild	6
Moderate	8
Severe	1
Perforation	4 (0.37)
Mild	0
Moderate	0

Severe	4

Table V. Multivariate analysis of risk factors for post-ERCP complications

Risk factor	Odds ratio (95% CI)	*P*-value
Age <45 vs ≥65	2.23 (1.03 – 4.84)	0.0498 *
Age 45-64 vs ≥65	1.3 (0.62 – 2.72)	0.6697
Female gender	1.2 (0.61 – 2.21)	0.6412
BMI <25 vs ≥35	0.84 (0.40 – 1.74)	0.1972
BMI 25-34 vs ≥35	0.31 (0.14 – 0.72)	0.0024 *
No previous ERCP	2.22 (1.04 – 4.75)	0.0394 *
Outpatient ERCP	5.4 (2.6 – 11.4)	<0.0001 *
Pancreatic duct cannulation	2.7 (1.4 – 5.1)	0.0026 *
Absence of trainee	1.36 (0.72 – 2.59)	0.3487
Intraprocedure sphincterotomy bleeding	10.0 (3.8 – 26.1)	<0.0001 *
Difficulty grade 1 vs 4	0.11 (0.02 – 0.54)	0.0204 *
Difficulty grade 2 vs 4	0.45 (0.18 – 1.14)	0.9199
Difficulty grade 3 vs 4	0.94 (0.42 – 2.13)	0.0129 *