

Efficacy and safety assessment of ERCP in patients with malignant biliary obstruction

I. Shanmugarajah¹, M. Solhaug², O. Aslam², O. Reiertsen³

(1) Campus Ahus, Faculty of Medicine, University of Oslo, Nordbyhagen, Norway and Department of Gastrointestinal Surgery, Østfold Hospital Trust, Grålum, Norway ; (2) Campus Ahus, Faculty of Medicine, University of Oslo, Nordbyhagen, Norway ; (3) Campus Ahus, Institute of Clinical Medicine, University of Oslo, Nordbyhagen, Norway and Department of Gastrointestinal Surgery, Akershus University Hospital, Lørenskog, Norway.

Abstract

Background : To assess the efficacy and safety of Endoscopic retrograde cholangiopancreatography (ERCP) for malignant biliary obstruction (MBO).

Material and Methods : A review of all ERCP-procedures performed at Akershus University Hospital during the six year period between 2009-2014 was analysed. Data for the period 2009-2013 were obtained retrospectively and prospectively for 2014. Patients with jaundice due to MBO were selected for the present study.

Results : A total of 210 patients (51% females), median age of 70 years (range 33-96) were included. The total number of procedures were 314, whereof 218 (69%) were successful and 96 (31%) were failures. 292 procedures were palliative and 22 procedures were intended as 'bridge to surgery' whereof 15 patients underwent surgery. Pancreatic carcinoma occurred in 105 (50%) patients and was the most common reason for MBO. Straight plastic stents (I-stents) were applied in 145 (74%), double-pigtail stents (JJ-stents) in 29 (15%), self-expanding metal stent (SEMS) in 18 (9%) procedures and in 3 procedures (1.5%) an I-stent was inserted through an indwelling SEMS. Median duration of stent-patency in months was 2 (range 0-74) for I-stent, 1 (range 0-29) for JJ-stent and 4 (range 0-29) for SEMS. The rates of complication and mortality due to complication were 8.9% and 1.3% per procedure.

Conclusion : Adequate drainage of MBO by ERCP was obtained in 69%. The rates of complication and procedure related mortality were at acceptable levels. (*Acta gastroenterol. belg.* 2017, 80, 487-491).

Keywords : Endoscopic retrograde cholangiopancreatography, Malignant biliary obstruction; Stents, Complications; Mortality.

Introduction

Jaundice due to malignant biliary obstruction (MBO) is associated with poor prognosis (1). In other studies only 15-20% of patients presenting with MBO have operable disease (2). Different causes leads to MBO, both primary and secondary malignancies can be involved in the obstruction of the bile ducts. The single most common cause is pancreatic cancer, followed by liver-, bile duct - and gallbladder malignancy (1). The average annual number of new cases from hepatopancreatobiliary (HPB) malignancy reported to the Norwegian Cancer Registry has steadily increased from 386 in the five year period 1964-69 to 1128 in 2010-14, pancreatic cancer comprised 65% of all HPB cancers in 2014 (3). In 2014 995 deaths were caused by HPB malignancy (3). In 2014 the relative 5-year survival for hepatic and biliary malignancies were

less than 20% and for pancreatic malignancies just above 5% (3).

Palliative biliary drainage can be achieved endoscopically (ERCP), by percutaneous transhepatic biliary drainage (PTC) or surgically. Minimally invasive procedures are preferred, and ERCP is most frequently applied in the management of MBO (4-7). Endoscopic stenting is an effective method to drain both intrahepatic and extrahepatic obstructions (8).

The main role of ERCP in MBO is to achieve adequate biliary drainage. The purpose may be palliative in cases with inoperable disease, as a prerequisite for chemotherapy, or preoperatively as 'bridge to surgery' in cases with resectable disease and severe jaundice.

Achieving adequate biliary drainage prevents cholestasis and the complications of cholestasis, such as cholangitis, cholangitic abscess or secondary biliary cirrhosis (9). In addition to alleviate jaundice and pruritus, it also improves other symptoms of cancer and quality of life (10).

Drainage of MBO is achieved by insertion of a stent through the obstruction caused by the tumor. Self-expanding metal stents (SEMS), covered or partly covered, are expected to have longer patency than conventional plastic stents (PS), straight (I-stents) or double pigtail (JJ-stents), thus potentially reducing number of interventions per patient (2, 11). Selection of appropriate stent type for the individual patient is not always simple and recent studies have not given a final conclusion on how to decide based on clinical tools (12). Current guidelines for palliative drainage of malignant common bile duct obstruction recommend that if the patient has no established diagnosis of malignancy or expected survival is 4 months or less, should undergo ERCP with insertion of PS (13). Patients with established diagnosis of malignancy with expected survival of more than 4 months, should undergo ERCP with insertion of SEMS (13).

Correspondence to : Inthujan Shanmugarajah, M.D., Dept. of Gastrointestinal surgery, Østfold Hospital Trust, Kalnesveien 300, 1714 Grålum, Norway.
E-mail: Inthujan@live.no

Submission date : 04/01/2017
Acceptance date : 29/09/2017

The purpose of the present study was to assess the efficacy and safety of ERCP in the management of MBO.

Material and Methods

The present study is a review of patients undergoing ERCP for MBO at Akershus University Hospital in the six year period 2009-2014. The data were collected retrospectively in the period 2009-2013, and prospectively in 2014. The follow up was until the end of February 2016. The study was approved by the Data Protection Officer at Akershus University Hospital, with anonymization of data, but no request for individual informed consent. Thus, there was no need for further approval by the Regional Research Ethics Committee.

The procedures were performed by 11 endoscopists, seven of whom had more than 10 years' experience with ERCP and four started their ERCP-training during the study period and were closely supervised by the experienced endoscopists. Eighty-nine per cent of the procedures were performed by the experienced endoscopists and 11% by the trainees. Median number of ERCP procedures performed annually was 243 in the period 2009-2014, there was an increase in number of procedures from 158 in 2009 to 296 in 2014 due to 40 % increase of population in the hospitals' catchment area.

Data collection

All patients undergoing ERCP were identified by combining search in the electronic medical record system, DIPS, and the electronic endoscopy registry, Endobase, for the years 2009-2014. For the year 2014, data for the ERCP-procedures were collected prospectively, the endoscopists filled in a data-entry form for each procedure. Data regarding age, gender, pre-ERCP status, such as comorbidity and ASA-class, the ERCP procedure, and post ERCP-follow-up with regard to results, complications and mortality were recorded. Success rate, complication rate etc were calculated per procedure. In some patients, several ERCP-procedures were done to obtain adequate drainage.

Study population and selection

Patients undergoing ERCP because of jaundice due to MBO were included in the present study.

Endoscopic methods

The ERCP procedures were performed using Olympus duodenoscopes (TJF180-series), the patients were lying with the chest down on an X-ray transillumination table. Intravenous sedation were routinely administered, in selected cases deep sedation or general anesthesia were used. Cannulation was preferably attempted using a guide-wire through a sphincterotome before injection of

X-ray contrast. If the obstruction could be passed with a guidewire, a biliary stent was inserted, sphincterotomy was done if the endoscopist found it necessary.

ERCP was done with placement of either PS (I- or JJ-stents) or SEMS. PS of appropriate length and caliber were most commonly used, however, in selected cases SEMS, partly- or completely covered, were preferred.

Definitions

An ERCP-procedure with biliary cannulation and insertion of a biliary stent accomplishing adequate biliary drainage was classified as success. If introduction of the endoscope to duodenum, adequate biliary cannulation, passing of the obstruction with guidewire or stent was not obtained, the procedure was classified as failure. A complication was defined as an event or condition potentially unfavourable to the patient's health during the first 30 days after ERCP, which necessitated adjustment of medical or therapeutic intervention or causing irreversible damage (14). The severity of the complications were graded according to the Clavien-Dindo classification (15). Stent patency was defined as the time period until stent occlusion or the patient's death after stent insertion.

Statistical analyses

Data was analysed by using IBM SPSS statistics 22 software package. Most of the analysis was conducted using descriptive statistics. Continuous variables were presented as median with range. Categorical variables were summarized as frequency and percentage. Comparisons between groups were performed using the Mann-Whitney *U* test. Survival analysis was based on the Kaplan-Meier method with log rank test used to test for differences. Statistical significance was set as $P \leq 0.05$.

Results

A total of 210 patients (51% females) with a median age of 70 years (range 33-96) were included. There were no statistical significant differences in the distribution of age and ASA score between genders ($P = 0.70$, $P = 0.83$). The total number of ERCP procedures were 314, whereof 218 (69%) were successful and 96 (31%) were failures. In some patients with failure, new attempts were performed. The procedure had a success rate of 63% on the first attempt in the whole patient group (210 patients). 11 of 22 patients in a selected group went through the same procedure with success on the second attempt. One patient with two previous failure attempts had a third attempt, which was successful. Causes of failure were gastric retention, duodenal stenosis, tumor ingrowth, duodenal diverticulum, patient discomfort, and simply failure to achieve deep biliary cannulation of Papilla Vateri. 292 procedures were palliative and

Table 1. — **Diagnosis**

Origo of malignancy	N	(%)
Head of pancreas	105	(50)
Papilla Vateri	21	(10)
Extra- or intrahepatic bile ducts	24	(11.4)
Gallbladder	3	(1.4)
Liver	4	(1.9)
Metastasis from cancer of other origin	53	(25.2)
Total	210	(100)

22 procedures (22 patients) were intended as ‘bridge to surgery’ whereof 15 patients underwent surgery.

In this series the diagnosis were mainly based on CT- or MRI scans at the time of ERCP, only in few cases histopathological specimens of the primary lesion was obtained. The causes of MBO are listed in Table 1. HPB malignancy was detected in 75% whereof two thirds had pancreatic carcinoma.

Stents were inserted in 195 (62%) of the procedures, of which 61 (31%) where removal of an indwelling stent and insertion of new stent. In some of the procedures removal was accomplished, but not insertion of new stent, and thus classified as failure. I-stents were applied in 145 (74%), JJ-stents in 29 (15%), SEMS in 18 (9%) procedures and in 3 procedures (1.5%) an I-stent was inserted through an indwelling SEMS (Table 2). Median duration of stent-patency in months was 2 (range 0-74)

for I-stent, 1 (range 0-29) for JJ-stent and 4 (range 0-29) for SEMS.

Complications occurred in 28 of 314 procedures (8.9%), either during ERCP (peroperatively) and/or within 30 days (postoperatively). In some procedures, there were more than one complication. Complication occurred in 26 patients, whereof two patients had a complication related to two separate procedures. Further details of the complications are presented in Table 3. The distribution of ASA-group, age and gender in patients with and without complication showed no statistical differences (P = 0.65, P = 0.16, P = 0.34).

The overall 30-day mortality rate was 2.9% per procedure (9 patients). All these patients had advanced inoperable MBO. In five of these patients death was caused by advanced malignancy; two of whom had no complications, two other had a small retroperitoneal contrast leak, but no further problems related to this occurred, and one patient had a minor bleeding after biopsy of tumor in Papilla Vateri. In none of these cases adequate biliary drainage was obtained. Four patients (1.3%) developed fatal complications (Clavien-Dindo V): Two had cholangitis, one of whom also peptic ulcer with perforation, both developed MOF and died five, respectively 15 days after ERCP. One patient had post ERCP pancreatitis (PEP), developed MOF and died 6 days after ERCP. One patient died unexpectedly nine days after ERCP, autopsy revealed bilateral pneumonia. The Kaplan-Meier plot of survival after the first ERCP-procedure in relation to main diagnoses are shown in Figure 1, the differences between the groups were not

Table 2. — **Types of inserted stents**

	I-stents	JJ-stents	SEMS	SEMS+I	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
New stent	99 (50.8)	19 (9.7)	14 (7.18)	2 (1)	134 (68.7)
Change of stent	46 (23.6)	10 (5.2)	4 (2.05)	1 (0.5)	61 (31.3)
Total	145 (74.4)	29 (14.9)	18 (9.2)	3 (1.5)	195 (100)

I-stent : Straight plastic stents. JJ-stents : Double pigtail plastic stents. SEMS : Self-expanding metal stent.

Table 3. — **Complications of all ERCP-procedures in 210 patients with MBO**

Type of complication	Peroperatively N (%)	Postoperatively N (%)	Clavien-Dindo class			Procedure-related mortality N (%)
			I-II	III-IV	V	
Bleeding	4 (1.3)	5 (1.6)	7	2	-	-
Perforation	3 (1)	5 (1.6)	4	2	-	-
Pancreatitis	-	-	3	1	1	-
Cholangitis	-	9 (2.9)	1	6	2	1 (0.3)
Intraabdominal- infection	-	4 (1.3)	1	6	2	2 (0.6)
Other	2 (0.6)	6 (1.9)	3	1	-	-
Total	9 (2.9)	32 (10.2)	7	-	1	1 (0.3)
			25	12	4	4 (1.3)

In some procedures there were more than one complication.

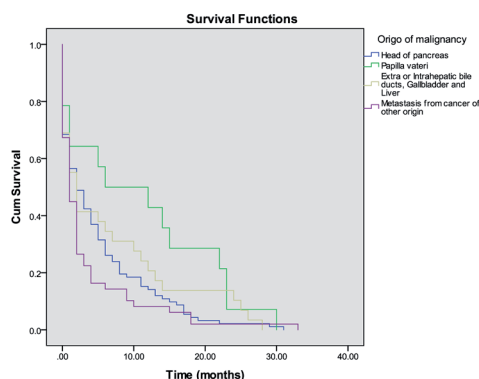


Figure 1. — Survival (months) from first ERCP-procedure in patients with MBO.

significant ($P = 0.08$). After two months 50% were alive, by the end of the observation period 16 patients were alive. Only 4 of 26 patients who had a complication were alive at the end of the study. The majority died of advanced malignant disease. The cause of death is unknown in two patients, who died in a nursing home, presumably due to disease progression.

Discussion

This study is a review of an established procedure, intending to assess the quality of the daily practice of ERCP in a Norwegian University Hospital.

Our findings suggest that the listed diagnoses in our data are similar to the common diagnoses as causes for MBO (1), pancreatic carcinoma is the most common cause for MBO, followed by other hepatobiliary malignancies. At the time when performing the ERCP the radiological imaging had not shown metastasis in all patients, but many of these patients had invasive cancer or metastasis detected later when referring to HPB surgery which in Norway is centralized to the regional hospitals. Some of these patients were detected early in the process and referred, reflecting those patients whom are still alive as per our data.

In the present study, PS was used in nearly 90% of the procedures and SEMS in 10%. Although the present study was not designed to compare SEMS and PS, the patency of SEMS was superior to that of PS. This is in accordance with other reports (11, 16), however, as SEMS were applied in only a small fraction of patients, selection bias may also have played a role. Other studies suggest SEMS to be preferred when expected survival is > 4 months, based on better patency, lower re-intervention, lower stent dysfunction, similar complication rate, cost-effectiveness, overall better outcome (2,13,16-18). The recommendation for choice of stent in patients with palliative treatment is based on the prognosis, but expected survival may be very difficult to assess reliably.

The overall complication rate per procedure of the present series (8.9%) is almost comparable to that

reported by Glomsaker et al (11.6%) in a survey from several Norwegian ERCP-centers (19). However, it must be taken into account that Glomsaker et al reported from a general population undergoing ERCP, including other indications such as common bile duct stones, biliary pancreatitis, postcholecystectomy biliary leak etc. The present report selected patients with MBO, who probably had a more compromised general health and a less favourable prognosis than the general ERCP population. This may also explain differences between our rates of cholangitis (2.9%), bleeding (2.9%), perforation (2%), PEP (1.6%), cardiopulmonary complications (0.95%), procedure related mortality (1.3%) compared to respectively $<1\%$, 1.3%, $<0.6\%$, 9.7%, 1% and $<0.5\%$, reported by others (20, 21). The survival plot in Figure 1 reflects the poor prognosis of patients with MBO due to inoperable disease.

Conclusion

The success rate of ERCP with insertion of stents in patients with MBO was 69%. The success rate probably dependent on the experience of the endoscopist performing the procedure. In the present series plastic stents were used in 89% of the procedures and SEMS in only 9%. The study was not designed to compare plastic stents with SEMS, and it seems that the recommendation of more frequent use of SEMS had a weak impact on our practice. Cancer in the head of pancreas was the cause of the biliary obstruction in 50% of the cases in this series. Complications occurred in almost 1 out of 10 procedures, with a procedure-related mortality of 1.3 % per procedure. It is likely that ERCP will continue to play an important role in the management of patients with MBO. However, there may be room for further improvements and development of stent technology as well as comparison of supplementary modalities like the percutaneous transhepatic route.

Acknowledgments

We want to thank the Research Department at Akershus University Hospital for valuable assistance making this project possible and for supervising the statistical analysis. Haldor Husby for his contribution for creating online registration form for data collection, patient data and for updating mortality data. We thank Sajitha Desingh, MD, for linguistic review.

Disclosure statement

The authors have no interest of conflict to report. The authors alone are responsible for the content and writing of the article.

References

1. SIEGEL R.L., MILLER K.D., JEMAL A. Cancer statistics, 2016. *CA Cancer J. Clin.*, 2016, **66** : 7-30.

2. PU L.Z., SINGH R., LOONG C.K., DE MOURA E.G. Malignant Biliary Obstruction: Evidence for Best Practice. *Gastroenterol. Res. Pract.*, 2016, **2016** : 1-7.
3. CANCER REGISTRY OF NORWAY IOPBCR. Cancer in Norway 2014. Cancer incidence, mortality, survival and prevalence in Norway. *CRN*. 2014, **2014** : 26-74.
4. ANDERSEN J.R., SORENSEN S.M., KRUSE A., ROKKJAER M., MATZEN P. Randomised trial of endoscopic endoprosthesis versus operative bypass in malignant obstructive jaundice. *Gut*, 1989, **30** : 1132-5.
5. SHEPHERD H.A., ROYLE G., ROSS A.P., DIBA A., ARTHUR M., COLIN-JONES D. Endoscopic biliary endoprosthesis in the palliation of malignant obstruction of the distal common bile duct: a randomized trial. *Br. J. Surg.*, 1988, **75** : 1166-8.
6. SPEER A.G., COTTON P.B., RUSSELL R.C., MASON R.R., HATFIELD A.R., LEUNG J.W., *et al.* Randomised trial of endoscopic versus percutaneous stent insertion in malignant obstructive jaundice. *Lancet*, 1987, **2** : 57-62.
7. SMITH A.C., DOWSETT J.F., RUSSELL R.C., HATFIELD A.R., COTTON P.B. Randomised trial of endoscopic stenting versus surgical bypass in malignant low bileduct obstruction. *Lancet*, 1994, **344** : 1655-60.
8. GLAZER E.S., HORN BROOK M.C., KROUSE R.S. A meta-analysis of randomized trials: immediate stent placement vs. surgical bypass in the palliative management of malignant biliary obstruction. *J. Pain Symptom Manage.*, 2014, **47** : 307-14.
9. LI M.K., CRAWFORD J.M. The pathology of cholestasis. *Semin. Liver Dis.*, 2004, **24** : 21-42.
10. BALLINGER A.B., MCHUGH M., CATNACH S.M., ALSTEAD E.M., CLARK M.L. Symptom relief and quality of life after stenting for malignant bile duct obstruction. *Gut*, 1994, **35** : 467-70.
11. SAWAS T., AL HALABI S., PARSI M.A., VARGO J.J. Self-expandable metal stents versus plastic stents for malignant biliary obstruction: a meta-analysis. *Gastrointest. Endosc.*, 2015, **82** : 256-67.e7.
12. WILCOX C.M., KIM H., SEAY T., VARADARAJULU S. Choice of plastic or metal stent for patients with jaundice with pancreaticobiliary malignancy using simple clinical tools: a prospective evaluation. *BMJ Open Gastroenterol.*, 2015, **2** : 1-6.
13. DUMONCEAU J.M., TRINGALI A., BLERO D., DEVIERE J., LAUGIERS R., HERESBACH D., *et al.* Biliary stenting: indications, choice of stents and results: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. *Endoscopy*, 2012, **44** : 277-98.
14. GOSLINGS J.C., GOUMA D.J. What is a surgical complication? *World J. Surg.*, 2008, **32** : 952.
15. DINDO D., DEMARTINES N., CLAVIEN P.A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann. Surg.*, 2004, **240** : 205-13.
16. ZORRON PU L., DE MOURA E.G., BERNARDO W.M., BARACAT F.I., MENDONCA E.Q., KONDO A., *et al.* Endoscopic stenting for inoperable malignant biliary obstruction: A systematic review and meta-analysis. *World J. Gastroenterol.*, 2015, **21** : 13374-85.
17. ALMADI M.A., BARKUN J.S., BARKUN A.N. Stenting in Malignant Biliary Obstruction. *Gastrointest. Endosc. Clin. N. Am.*, 2015, **25** : 691-711.
18. RUSTAGI T., JAMIDAR P.A. Endoscopic treatment of malignant biliary strictures. *Curr. Gastroenterol. Rep.*, 2015, **17** : 426.
19. GLOMSAKER T., HOFF G., KVALOY J.T., SOREIDE K., AABAKKEN L., SOREIDE J.A. Patterns and predictive factors of complications after endoscopic retrograde cholangiopancreatography. *Br. J. Surg.*, 2013, **100** : 373-80.
20. ANDERSON M.A., FISHER L., JAIN R., EVANS J.A., APPALANENI V., BEN-MENACHEM T., *et al.* Complications of ERCP. *Gastrointest. Endosc.*, 2012, **75** : 467-73.
21. KOCHAR B., AKSHINTALA V.S., AFGHANI E., ELMUNZER B.J., KIM K.J., LENNON A.M., *et al.* Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. *Gastrointest. Endosc.*, 2015, **81** : 143-9.