

Safety and Efficacy of ERCP Performed on Elderly and Very Elderly Patients in a Low Volume Provider Endoscopy Unit: Results from a Monocentric Retrospective Study with Control Group

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Abstract

ERCP is one of the most challenging and high-risk endoscopic procedures. The incidence of biliary tract pathologies is growing with an age-related trend and progresses as the population ages.

Both the age-related outcomes and the volume-related outcomes for ERCP are still debated and incompletely understood. Experts generally agree that the lower the volumes of ERCP provided, the higher procedure-related complication and failure rates are expected. Some studies showed that ERCP in elderly patients is comparable in terms of efficacy and safety to ERCP in younger patients. However, these data generally concern studies made in referral centers and high-volume providers of ERCP. This study analyzes the performance of ERCP when it is performed on elderly and very elderly patients in a low-volume center of biliary endoscopy.

Keywords: ERCP; Safety and Efficacy; Very Elderly Patients; Low-Volume Center; Biliary Endoscopy Complications

Abbreviations

ERCP: Endoscopic Retrograde Cholangiopancreatography; pt: Patients

Introduction

Over the past few decades, the ageing of the population has become a relevant process in almost all advanced developed countries. According to the World Health Organization (WHO 2020), in 2008 life-expectancy was estimated at 68, with a range of variability from 57 years for low-income countries (53 years in Africa), up to 80 years in high-income countries.

By 2050, the WHO estimates that around 1/6 of people will be over 65 years old (16%), while in 2019 the evaluation stands at around 1/9 (9%). In 2018, the number of subjects defined as elderly (over 65), for the first time, exceeded the number of children under 5 years of age [1].

In view of the overall, but uneven, average lengthening of life expectancy at birth, a proposal to increase the seniority threshold to 75 years, with local value depending on the individual nations, is under debate.

Together with the increase in the average age of the general population, an increase in the incidence of bilio-pancreatic pathologies in the elderly population was observed, in particular choledocholithiasis and malignant obstructive jaundice for whom, in case of surgery, the morbidity is high and post-operative mortality can reach 10%.

Endoscopic Retrograde Cholangiopancreatography (ERCP) is a complex procedure that allows the catheterization of the biliary or pancreatic system in order to carry out diagnostic and therapeutic manoeuvres. ERCP represents the gold standard treatment for several pathological conditions leading to obstruction of the extra-

hepatic biliary system such as choledocholithiasis and its complications, neoplasms of the bilio-pancreatic tract, complications of biliary tract surgery (Table 1). ERCP represents the treatment of choice in benign or malignant extra-hepatic obstructive pathologies, even in the elderly patient, despite a percentage of complications (acute post-ERCP pancreatitis, haemorrhage, perforation,

cardio-respiratory problems) between 5.1 and 8.4% and a mortality of 0.3 - 0.5%. In addition, the ERCP has a failure rate ranging from 3 to 15% [2,3], due to the operator’s inexperience or because of anatomical features (e.g. periampullary diverticula, biliary stenosis, previous upper GI surgery) which may preclude the catheterization of the biliary or pancreatic system [4].

Indications to the ERCP	Shortcomings
<ul style="list-style-type: none"> • Common bile duct stones (CBDS). • Iatrogenic or inflammatory stenosis (stenting drainage/endoscopic therapy/biliary sampling). • Malignant stenosis due to biliary, pancreatic or ampullary neoplasms (drainage with stent/biliary sampling). • Acute or recurrent cholangitis. • Acute biliary pancreatitis. • Suspected CBDS previous to laparoscopic cholecystectomy. • Biliary fistulas, biliary complications after liver transplantation. • Malformations (choledochal cysts, diverticula). • Intraductal parasitosis and echinococcus cysts. 	<ul style="list-style-type: none"> • Heart and/or acute respiratory failure. • Some neurological conditions. • Suspected intestinal perforation. • Coagulopathies that need to be treated as soon as possible (relative contraindication). • Esophageal substhenosis (depending on the extent).

Table 1

The overall rate of complications related to bilio-pancreatic disorders has been reduced over the last decade due to the improvement of the operative endoscopy and laparoscopic surgical techniques. Despite these improvements, in populations aged 90 and over, the surgical treatment of gallstone’s disease, particularly in the emergency setting of its complications (acute biliary pancreatitis and/or cholangitis), is still associated with a high mortality risk [4].

The age-related natural decline of the immune system, the so-called “immunosenescence”, seems to be the main predisposing factor that contributes to increased morbidity and mortality with age [5-7]. Specifically, elderly subjects are more susceptible to infections than young adults or middle-aged individuals [8]. In addition, major abdominal surgery induces a condition of immunosuppression, thus further contributing to the above complications in elderly patients [9]. Contrary to these epidemiologic findings, there is a growing body of evidence that diagnostic and therapeutic ERCP is a safe and effective procedure, especially in older patients over the age of 65 - 85 [10-14]. However, the literature on the practice of therapeutic ERCP in so-called “very elderly patients” (> 85 years) is still relatively limited.

The weight of the endoscopy unit’s volumes on ERCP’s outcomes is under debate, with studies suggesting discordant conclusions [15-17]. In 2017 a systematic review and meta-analysis on association between the endoscopist’s and centre’s ERCP volume

with the procedure success and adverse outcomes was published. The paper, including 59,437 patients underwent to ERCP for any diagnosis (13 studies) [18] showed that high volume endoscopists and high-volume centres had better procedure success rates (successful cannulation or success of all attempted therapies). No variation was found in mortality and adverse event rates.

Giving the fact that ERCP for malignant biliary obstruction is generally more challenging than ERCP for benign indications, a recent large study was conducted on a cohort of 39,702 patient underwent to ERCP for malignant obstruction to address the impact of provider volume in this setting [19]. This study reported higher mortality rates in low volume provider centres of both ERCP for all indications and ERCP for malignant biliary obstruction. As well as another study from North America in which is reported a significant relation between higher volume ERCP providers and reduced complications including unplanned hospital attendance [20].

Materials and Methods

Selection of the study population

In this study, a retrospective analysis was carried out on a cohort of patients with bilio-pancreatic pathologies in a single hospital center. 104 patients consecutively underwent to ERCP in a low volume biliary endoscopy unit (n. ERCP < 200 per year). Between January and December 2019, a total number of 124 ERCP were performed by two endoscopists.

For data analysis, the population of patients underwent to ERCP was divided into three age groups, consisting in a pool of “very elderly” patients, aged > 85 (group A: 25 pt.), a pool of “elderly” patients, aged 70 - 85 (group B: 48 pt.), and a “control” group, aged < 70 years (group C: 31 pt.).

Endpoint

This study focuses on the safety and efficacy of ERCP procedures performed in a low volume biliary endoscopy unit on elderly and very elderly patients.

The primary endpoints of the study are the comparison of the intra-procedural and post-procedural complications rates (< 72 hours), the ERCP-related mortality rates and the post-procedural hospital length of stay (n. of days) between the two older age groups (elderly and very-elderly) and the adult control group. Secondary endpoints were the analysis of the clinical features of the patients, the diagnoses and the endoscopic techniques used.

Data collection

The data were collected retrospectively using paper archive, di-

gital medical and discharge records, operative acts and endoscopic reports of patients consecutively underwent to ERCP procedure in the period between January and December 2019.

Statistical analysis

The categorical or ordinal variables (e.g. sex, success/failure, ASA, etc.) are shown in table 2. The Chi-square test was used to analyze any statistical association between the categorical variable in question and the stratification variable (age group A, B or C). On the other hand, the statistical analysis of quantitative variables with non-normal distribution (e.g. comorbidities, n. of days post-ERCP) was reported with Median [IR] (interquartile range) using the non-parametric Kruskal-Wallis test.

Results

Retrospective analysis of the cohort dataset of 104 patients resulted in a total of 124 ERCP procedures, of which 31 (24.9%; M 20, F 11) were performed in patients aged ≥ 85 years (Group A), 56 (45.8%; M 27, F 29) in patients with age range of 70 - 85 (Group B), 37 (29.7%; M 19, F 18) in patients aged ≤ 70 (Group C) (Table 2).

	Group A yrs > 85 (N = 25)	Group B yrs 70-85 (N = 48)	Group C yrs < 70 (N = 31)	N < 70	P value	Test
Patients N						
ERCP N	(N = 31)	(N = 56)	(N = 35)			
ERCP n.1	19 (76%)	42 (88%)	25 (81%)	31	0.2251	Fisher test
ERCP n.2	6 (24%)	4 (8%)	6 (19%)	31	0.2251	Fisher test
ERCP n.3	0 (0%)	2 (4%)	0 (0%)	31	0.2251	Fisher test
Sex F	8 (32%)	24 (50%)	14 (45%)	31	0.3371	Chi-square
Sex M	17 (68%)	24 (50%)	17 (55%)	31	0.3371	Chi-square
N co-morbidity	1 [1-2]	1 [0-1.5]	0 [0-1]	31	0.0176	Kruskal Wallis
ASA status						
(Grade 1)	0 (0%)	9 (19%)	3 (10%)	31	0.0027	Fisher test
(Grade 2)	7 (28%)	15 (31%)	15 (48%)	31	0.0027	Fisher test
(Grade 3)	8 (32%)	19 (40%)	12 (39%)	31	0.0027	Fisher test
(Grade 4)	10 (40%)	5 (10%)	1 (3%)	31	0.0027	Fisher test
Failed biliary cannulation	6 (24%)	13 (27%)	6 (19%)	31	0.7349	Chi-square
Sphincterotomy	12 (48%)	23 (48%)	22 (71%)	31	0.0975	Chi-square
Pre-cut	3 (100%)	6 (100%)	4 (100%)	4	1	Fisher test
Complications N	5 (20%)	5 (10,41%)	5 (16,12%)	5	0.7352	Chi-square
Mortality	2 (8%)	0	0	0	<0.005	Chi-square
Hospital length of stay post ERCP (N. of days)	4 [3-20]	5 [2-8]	5 [3-8]	26	0.748	Kruskal Wallis
IQ = Interquartile range; SD = Standard Deviation						

Table 2: Clinical and socio-demographic characteristics of the study cohort.

The median age was 88.2 years (range 85 - 99 years) in group A, 78.68 years in group B, 56.77 years in group C (range 43 - 58 years). Comorbidities were found to be present in the three groups with a prevalence that increases significantly as age increases (Figure 1): 1 [1 - 2] in group A; 1 [0 - 1.5] in Group B; 0 [0 - 1] in group C ($p = 0.0176$ with K-W test).

Figure 1: Comorbidity prevalence of age groups A-B-C.

As expected, there was also a significant increase in prevalence of grade 3 and 4 ASA classes as age grew ($p = 0.0027$ with F. test), as shown in the figure 2.

Figure 2: Prevalence of ASA grade in relation to age groups A-B-C.

The most frequent indication to ERCP in the three groups was choledocho-cholelithiasis, followed by acute biliary pancreatitis and choledocholithiasis (residual or isolated), although if in the

absence of a significant difference (Figure 3). On the other hand, a significant difference in the prevalence of malignant stenosis was founded: it resulted more frequent in group C of adult patients than expected for groups A and B (Figure 4).

Figure 3: Prevalence of indications to ERCP (first three per frequency) by age groups A-B-C.

Figure 4: Rate of indication to ERCP for K pancreas (Pk) and Colangio-K by age groups A-B-C.

This latter result is in contrast to epidemiology and literature data. The statistical difference could be the result of a bias in the study: as already reported, this data come from a cohort of patients treated at a low volume hospital. Thus, given the lack of some tools useful to make diagnosis in case of indeterminate biliary lesions (e.g. echoendoscopes to perform fine needle agobiopsy and/or slim fiberoptics endoscopes to carry out per oral cholangioscopy, with or without endobiliary forceps biopsies), it is likely to aspect same misdiagnosis of neoplastic lesions in a portion of patient-

ts who have received indication to ERCP, especially in older age groups.

No significant differences were recorded in the percentage of biliary cannulation (A = 76%; B = 73%; C = 81%; $p = 0.7349$), even if compared to a non-significant higher number of biliary sphincterotomy in the group C of adult patients than in the other two groups (A = 48%; B = 47.91%; C = 70.96%; $p = 0.0975$). To the extent expected, a significant difference in anatomical alterations (in particular for para-Vaterian diverticula) between the two advanced age groups and the adult patient's group has been observed (A = 32%; B = 25%; C = 6.45%; $p < 0.05$). The pre-cut of papilla with needle-knife was necessary in 12.5% of the biliary cannulations carried out, without evidence of any difference in the three groups of patients (A = 12%; B = 12.5%; C = 12.9%). No significant differences in complication rates were found (Figure 5). The most frequent complication was post-ERCP bleeding, without any significant difference of prevalence in the three age groups. Conversely, cardiopulmonary complications were found to be greater in groups A and B, even if without achieving statistical significance. Only one patient, belonging to the group A, has needed post-ERCP ICU stay.

Figure 5: Prevalence of complications by age groups A-B-C.

The total number of deaths - including those not related to the procedure - was 2, both belonging to the group of very elderly people (Figure 6). This latter finding has led to a statistically significant difference in mortality's incidence of the very elderly patients group compared to the other two groups (A = 8%; B = 0%; C = 0%; $p < 0.05$). However, it should be noted that of the two cases of death (89 and 90 years old patients, each with 3 major comorbidities), one is attributable to cardio-pulmonary complications of pre-procedural anesthesia, and the other regards a patient who underwent to urgent ERCP for acute cholangitis complicated by severe sepsis (a clinical condition in itself linked to a high mortality in fragile patients).

Figure 6: Overall mortality (peri-procedural and early) by age groups A-B-C.

A further or more ERCP per patient was repeated in 18 cases (17.30%), of whom 6 belonging to group A (A = 24%; B = 12.5%; C = 19.90%). The mainly reasons leading to a further procedure were the failure to cannulate the common bile duct (30% of the repeated exams), the occurrence of residual common bile duct stones after the first ERCP (41%) and the distal migration or occlusion of biliary plastic stents (25%). The cumulative risk of ERCP repetition need was not significant between the three groups (Fisher Test, $p = 0.2251$). Finally, no significant difference was found between the three age groups in the number of days of hospital stay after the endoscopic procedure (Figure 7).

Figure 7: In the diagram with box plot is shown the comparison between the number of days of post-ERCP hospital stay: the box represents the interquartile range, the row in the middle is the median, the red dot in the middle of the box is the average.

Discussion

As already reported, the incidence of bilio-pancreatic diseases is increasing due to the widespread ageing of the general popula-

tion, and this is particularly evident in the population group over 80 years of age [21]. In several countries around the world, the absolute number of older people who will specifically need ERCP procedures will increase in the next future [22].

However, the evidence on ERCP safety in this population group is still controversial [23-25].

Some studies on small cohorts of patients aged 65 to 80 have already evaluated this issue [10,11,26-28]. A recent systematic review by Day, *et al.* [29] has compared the efficacy and safety of ERCP in octogenarian to the “younger” elderly and adults. These works would lead to the conclusion that perforation, bleeding, cholangitis and other major complications of ERCP are not statistically different between the different age groups. However, the ERCP comparison data in this setting are still limited, so that patients over the age of 80 are still considered to be at higher risk of adverse events related to the procedure. It should also be pointed out that studies on this issue have examined patients treated in referral centers (often academic) for biliary tract endoscopy and high-volume providers of procedures.

According to available literature data, this is the first study to examine the efficacy and safety of ERCP performed on elderly and very elderly patients in a low-volume operative endoscopy center (< 200 ERCP per year). With regard to the relationship between the volume of ERCP provided and the success of the procedures, an interesting work was published in 2006 by Varadarajulu, *et al.* [16] The authors published data from a large retrospective study conducted in the US on a total number of 199,625 ERCP, carried out in 2629 hospitals which were classified in high (> 200 exams/year) and low volume provider of ERCP centers (these latter centres account for 75% of hospitals in the US, according to the records of the study) [16].

Varadarajulu’s study results, through multivariate logistic regression analysis, conclude that patients admitted for ERCP in high-volume hospitals have shorter hospital stay times and lower procedural failure rates than those undergoing ERCP in hospitals with low-volume endoscopy units. However, the same authors recognize among the limitations of their work the failure to analyze the rates of complications and re-intervention after ERCP and the absent distinction of outcomes by age group. In our work, the first statistical limitation is represented by the small sample size (no. 104 pt/124 ERCP), which is inevitable for a monocentric study

performed in a low volume unit of ERCP. The issue of sample size could explain the discordance with the results of literature related to the prevalence of bilio-pancreatic pathology types. 5: Moreover, this limitation could also provide a possible reason for the absence of significant associations between complications of ERCP and the age groups at the univariate and multivariate analyses.

In this work, it’s noteworthy that the similar global complication’s rate between the three age groups is not depending on the well-known protective effect of advanced age on post-ERCP pancreatitis [14,30-33] (one of the most common post ERCP complications).

In addition, due to monocentric and retrospective design of the study, these results cannot be generalized compared to other contexts of endoscopic treatment of bilio-pancreatic diseases in acute. Finally, having retrieved data from hospital records, it was not possible to obtain information on other important outcomes (mortality rates, complications and re-intervention) in the post-discharge phase of patients undergoing ERCP.

Conclusion

As reported by the literature data., this study shows that ERCP in elderly and very elderly patients is comparable in terms of efficacy and safety to ERCP in younger patients, even when it is carried out in centers providers of low volume of biliary endoscopy. In the study two deaths belonging to the age group of very elderly patients was observed, and that has led to a significant increase of mortality. However, neither of the two events occurred as consequence of any ERCP’s complication. Given the small sample size studied, further multicenter ERCP safety and efficacy studies on elderly patients in low volume endoscopy centers would be required to confirm these data, with longer follow-up of outcomes.

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Conflict of Interest

No conflict of interest to declare.

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