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Research Article

Do Biliary Leaks Alter the Risk of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis?

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Abstract

Objective: Gallstone disease is a common health problem in the general population. Cholecystectomy is the only option in cases requiring treatment. The procedure carries a risk of postoperative biliary leak. Endoscopic retrograde cholangiopancreatography is a safe and effective treatment method for biliary leaks. Post-endoscopic retrograde cholangiopancreatography pancreatitis is the most common complication of endoscopic retrograde cholangiopancreatography and although many cases are mild, serious clinical pictures and fatal cases may occur. In this article, we aimed to investigate if the biliary leak is an independent factor in the development of post-endoscopic retrograde cholangiopancreatography pancreatitis.

Methods: This retrospective study was carried out in Antalya Training and Research Hospital, University of Health Sciences, Department of Gastroenterology. Patients who underwent endoscopic retrograde cholangiopancreatography were investigated retrospectively through digital data in the hospital registry and procedure recordings. Between the years 2013 and 2023, 71 patients who underwent endoscopic retrograde cholangiopancreatography for post-cholecystectomy biliary leaks were included in the study. Patients who underwent endoscopic retrograde cholangiopancreatography for other causes were defined as the control group, consisting of 100 patients.

Results: Compared to the control group, which included patients without biliary leak who underwent endoscopic retrograde cholangiopancreatography, no significant difference was found in the development of post-endoscopic retrograde cholangiopancreatography in the biliary leak group. Post-endoscopic retrograde cholangiopancreatography development was related to longer post-procedural hospitalization times for both the biliary leakage and control groups and this difference was statistically significant.

Conclusion: Biliary leaks and their management is an important part of gastroenterology practice. Being mindful of factors that may increase procedure-related risks like post-endoscopic retrograde cholangiopancreatography is vital for both the patient and the healthcare team.

Keywords: Biliary leak, ERCP, post-ERCP pancreatitis, cholecystectomy

INTRODUCTION

Gallstone disease is a common and important health problem, especially in the developed world. More than 10% of the adult population is estimated to have gallstones and this rate is on an increasing trend due to the rise in incidence of obesity and metabolic syndrome.[1] While physical activity and diet modification may affect the disease course in some individuals, there are no documented medical treatment options for gallstone disease, and cholecystectomy is the only option when treatment is indicated.[2] Despite the relatively lower complication rate of laparoscopic cholecystectomy, postoperative complications are a major problem. Biliary leakage is a major and serious complication of cholecystectomy, with a rate between 0.2% and 2.2% among all cholecystectomies.[3] Endoscopic retrograde cholangiopancreatography (ERCP) is a safe and effective method and treatment of choice in the management of both minor and major postoperative bile leaks.[4]

Post-ERCP pancreatitis (PEP) is the most common complication of ERCP. Both patient and procedure-related factors play a role in the development of PEP and disease severity can vary from a mild inflammatory state to multi-organ failure and death.[5] Several mechanisms are assumed to influence PEP development. Cannulation trauma to the papilla, contrast media used during ERCP, the injection pressure of the contrast media, bacteria, and genetic factors are some of the prominent risk factors for PEP.[6]

In this study, we hypothesized biliary leaks may play a role both in favor of and against PEP development. Due to bile leakage, bile content and pressure of the choledochal duct would be decreased. This decrease would lead to less bile reflux to the pancreatic duct during cannulation,

lowering the risk of PEP in return. On the other hand, a decrease in choledochal duct bile content and pressure may lead to a relatively small choledochal diameter, leading to difficulties in cannulation and therefore increased PEP risk. We aimed to compare the PEP rates of patients with post-cholecystectomy biliary leaks to post-ERCP patients of other causes to determine a possible meaningful difference in PEP development between these 2 groups.

METHODS

This retrospective study was carried out in Antalya Training and Research Hospital, University of Health Sciences, Department of Gastroenterology. Patients who underwent ERCP were investigated retrospectively through digital data in the hospital registry and procedure records. Between the years 2013 and 2023, a near total of 10 000 ERCP patients were scanned. About 71 patients who underwent ERCP with the indication of post-cholecystectomy biliary leak were defined as the patient group. Patients who underwent ERCP for other causes were defined as the control group, consisting of 100 patients. Patients with malignant strictures and patients who underwent a prior ERCP and had a sphincterotomy were not included in the control group, as these 2 conditions would alter PEP outcomes. Procedural notes were recorded. Development of PEP was documented through patient follow-up notes in the wards. Post-ERCP amylase and lipase levels of patients were also noted, as well as post-ERCP imaging studies. Due to the retrospective nature of the study, the classification of biliary tract injuries could not be carried out; hence, all biliary leaks were investigated as a uniform group. All ERCP procedures were performed by 3 different gastroenterologists, each with at least 5 years of experience in the field. Each gastroenterologist performed at least a hundred ERCP procedures per year.

Baseline characteristics between the patients with biliary leak and control groups were compared using Fisher's exact test for binary variables. For continuous variables, we used the unpaired Student *t*-test for normally distributed data and the Mann–Whitney *U* test for non-normally distributed data. For comparing the presence or absence of PEP in both groups, Fisher's exact test was performed. For the subgroup analysis, either Fisher's exact test or Student's *t*-test was used appropriately. For the continuous and categorical variables, data were reported as means or range for continuous data or as percentages for categorical data. Two-tailed *P* values less than .05 were considered significant. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 26.0 for Windows (IBM Corp.; Armonk, NY, USA).

MAIN POINTS

- Biliary leaks was not found to be an independent factor in the development of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP).
- The development of PEP was related to a longer hospitalization time for both the biliary leak and control groups.
- Females were dominant in the patients who developed PEP in the control group, while males were dominant in the patients who developed PEP in the biliary leak group but these findings were not statistically significant.

Ethics committee approval was obtained from Antalya Training and Research Hospital, University of Health Sciences Ethics Committee (Date: March 17, 2022, Number: 109). No informed consent was needed for this study since the data was gathered retrospectively from the hospital database and procedure records.

RESULTS

A total of 171 patients were enrolled in the study. About 71 patients were in the biliary leakage group and 100 patients were in the control group. The baseline characteristics of the study population are given in Table 1.

There were 30 female patients in the biliary leakage group (42.3%) and 53 patients in the control group (53%). The mean age of patients was 52.2 (17-88) in the biliary leakage group and 57.1 (22-88) in the control group. Both the gender distribution and mean age between the patient and control groups did not differ statistically significantly. Post-ERCP pancreatitis rates were 15.5% (n=11) for the biliary leakage group and 14% (14) for the control group and there was no statistically significant difference between the 2 groups in terms of PEP development. Post-ERCP hospitalization meantime was 7.30 ± 5.3 for the biliary leakage group and 3.25 ± 2.5 for the control group and the difference was statistically significant.

We analyzed the post-ERCP mean hospitalization time in subgroups for both the biliary leakage and control groups split in terms of PEP development. Post-ERCP pancreatitis development was related to longer post-procedural hospitalization times for both the biliary leakage and control groups and this difference was statistically significant (Table 2).

Twenty-five patients developed PEP in the study group. Eleven of these patients were in the biliary leakage group and 14 were in the control group. Post-ERCP pancreatitis development rate was found to not differ between the 2 groups. We subdivided the patients who developed PEP according to their gender to determine a potential difference between female and male patients. Females were dominant in the patients who developed PEP in the control group (n=10, 71.4%), while males were dominant in the patients who developed PEP in the biliary leak group (n=8, 72.7%) but these findings were not statistically significant (*P*=.16) (Figure 1).

Table 1. Baseline Characteristics of the Study Population

	Biliary Leakage Group (n=71)	Control Group (n=100)	*P*
Female gender	30 (42.3%)	53 (53%)	.24
Age (mean years range)	52.2 (17-88)	57.1 (22-88)	.07
Patients with PEP	11 (15.5%)	14 (14%)	.78
Post-ERCP mean hospitalization time (days)	7.30 ± 5.3	3.25 ± 2.5	<.001

ERCP, endoscopic retrograde cholangiopancreatography; PEP, post-ERCP pancreatitis.

Table 2. Post-ERCP Mean Hospitalization Time (Days)

	Biliary Leakage Group (n=71)	Control Group (n=100)	*P*
PEP (−)	6.9 ± 5.3 (n=60)	2.9 ± 2.3 (n=86)	.005
PEP (+)	9.0 ± 5.6 (n=11)	5.0 ± 2.8 (n=14)	

ERCP, endoscopic retrograde cholangiopancreatography; PEP, post-ERCP pancreatitis.

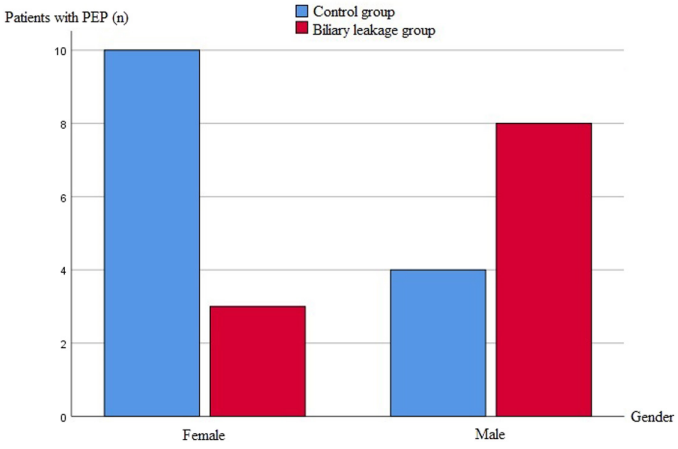

Figure 1. Subgroup analysis of post-endoscopic retrograde cholangiopancre atography pancreatitis patients in terms of gender between 2 study groups.

DISCUSSION

Bile leakage is a common and serious complication of cholecystectomies. With an increased number of procedures worldwide, post-cholecystectomy leaks are encountered more commonly in daily practice. The primary management of biliary leaks is ERCP, which in itself carries potential procedure-related complications such as PEP. In this study, we aimed to investigate the PEP development in a tertiary center in the fifth biggest city of Turkey among patients with biliary leakage.

We had 2 hypotheses that were contrary to each other in the planning stage of the study, as mentioned in the introduction section. Rooting from our hypothesis, we investigated whether biliary leakage was a factor in increasing or decreasing PEP development rates.

There were no significant differences in PEP development rates between the biliary leakage and control group, which were 15.5% and 14%, respectively. Post-ERCP pancreatitis rates are reported as 2%-10% in unselected patient groups, whereas there are reports as high as 40% in high-risk patients.[7] Being a tertiary referral center of the region, we owed the relatively high PEP rates in our study to the select and potentially high-risk patient group.

Post-ERCP hospitalization time was statistically significantly higher in patients who developed PEP for both the biliary leakage and control groups. This is an expected yet very important finding of the study, as the prolonged hospitalization time carries both additional health-related risks for the patients as well as an increased burden on the healthcare system both time and cost.

Stemming from the knowledge that pancreatitis rates can differ between genders according to underlying etiology, we investigated the PEP development to identify a possible difference between female and male patients.[8] Although female patients who developed PEP were higher in number in the control group and conversely male patients that developed PEP were higher in number in the biliary leakage group, the difference between the 2 was not statistically significant.

There are a few shortcomings of our study. First of all, the retrospective nature of the study was a limiting factor. Biliary leak subtypes were not recorded in a majority of the patients hence we could not classify the patients according to the type of biliary leakage. Second, as a tertiary gastroenterology unit, we accept patients from all over the region. Thus we encounter patients operated by various surgeons and some patients might have suffered a delay in the referral or been treated medically for a prolonged period of time, affecting the outcome of ERCP and PEP development.

Nevertheless, we believe this 10 years of experience with a large number of PEP patient groups in a tertiary gastroenterology unit reflects the importance of biliary leakage management. Prospectively planned studies with more detailed documentation of biliary leakage subtypes as well as procedure-related data will shed more light on the relationship between biliary leaks, their management, and post-ERCP complications.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Antalya Training and Research Hospital, University of Health Sciences (Date: March 17, 2022, Number: 109).

Informed Consent: No informed consent was needed for this study since the data was gathered retrospectively from the hospital database and procedure records.

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