

Risk factors for asymptomatic choledocholithiasis; experience at the Hospital General de México

Factores de riesgo de la coledocolitiasis asintomática; experiencia en el Hospital General de México

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ABSTRACT

Introduction: Choledocholithiasis is the most common cause of obstruction of the bile ducts in patients with cholelithiasis. Without jaundice or biliary tract dilation, the diagnosis is very difficult to suspect, and patients may be diagnosed during surgery or at some point after the procedure. Magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography are reserved for cases in which choledocholithiasis is highly suspected; they are not routinely performed. **Objectives:** To determine the risk factors for asymptomatic choledocholithiasis in patients who underwent laparoscopic cholecystectomy. **Materials and methods:** A prospective, analytic, comparative study was conducted in patients undergoing laparoscopic cholecystectomy without clinical or radiological evidence suggesting choledocholithiasis. Based on intraoperative cholangiography, they were divided into two groups: with choledocholithiasis and without choledocholithiasis. A p value < 0.05 was considered statistically significant. **Results:** 53 women (77.9%) and 15 men (22.1%). Alkaline phosphatase (AP) was the only parameter significantly different between the groups ($p = 0.034$). An AP value > 90.5 U/L indicated a 12.4 higher risk for asymptomatic choledocholithiasis, with an 80% sensitivity and specificity. **Conclusions:** Prevalence of asymptomatic choledocholithiasis at the Hospital General de México is 13.2%. When a patient has cholelithiasis, with no jaundice or biliary tract dilation but an AP value above > 90.5 U/L, asymptomatic choledocholithiasis should be suspected.

RESUMEN

Introducción: La coledocolitiasis es la causa más común de obstrucción de las vías biliares en pacientes con coledocolitiasis. Sin ictericia o dilatación de la vía biliar, el diagnóstico es en extremo difícil de sospechar; es posible que sean diagnosticados durante la cirugía o tiempo después de la misma. La colangiografía por resonancia o colangiografía pancreatografía retrógrada endoscópica se reserva para los casos con alto índice de sospecha de coledocolitiasis. No se realizan de rutina. **Objetivos:** Conocer los factores de riesgo de la coledocolitiasis asintomática en pacientes operados de colecistectomía laparoscópica. **Material y métodos:** Se realizó un estudio prospectivo, analítico, comparativo en pacientes a quienes se realizó colecistectomía laparoscópica sin evidencia clínica o radiológica para sospechar coledocolitiasis. Con base en la colangiografía transoperatoria, se dividieron en dos grupos: sin coledocolitiasis y con coledocolitiasis. Se consideró $p < 0.05$ como estadísticamente significativo. **Resultados:** 53 mujeres (77.9%) y 15 hombres (22.1%). La fosfatasa alcalina (FA) fue el único parámetro con diferencia significativa entre los grupos ($p = 0.034$). Con FA > 90.5 U/L hubo un riesgo 12.4 veces mayor de presentar coledocolitiasis asintomática, con sensibilidad y especificidad de 80%. **Conclusiones:** La coledocolitiasis asintomática en el Hospital General de México es del 13.2%. Cuando un paciente con coledocolitiasis, sin ictericia y sin dilatación ultrasonográfica de la vía biliar tiene FA > 90.5 debemos sospechar la presencia de coledocolitiasis asintomática.

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INTRODUCTION

Cholelithiasis has a prevalence of 6% to 20% in white adults and up to 60-70% among the indigenous populations of America.¹ A study of 21,446 autopsies revealed an overall prevalence of gallstone disease of 14.3% (8.5% in males and 20.4% in females).²

The diagnosis of cholelithiasis is mainly based on clinical suspicion and corroborated by liver and biliary tract ultrasound (US). Laparoscopic cholecystectomy is the most recommended surgical technique.^{3,4}

Choledocholithiasis is defined as the presence of calculi in the common bile duct. When they originate within the biliary tract, it is known as "primary", whereas the term "secondary" refers to the displacement of calculi from the gallbladder to the biliary tract. The incidence of symptomatic choledocholithiasis is 10-20%. Obstruction of the biliary tract is incomplete in 90% of cases and complete in the rest.⁵ The most important complications of choledocholithiasis are pancreatitis, papillary stenosis, cholangitis, hepatic abscesses and secondary biliary cirrhosis. If there is no previous history of jaundice, acute pancreatitis or acute cholecystitis, if liver biochemistry is normal and if the common bile duct's diameter measures five millimeters or less by ultrasound, the presence of choledocholithiasis is highly unlikely.

Intraoperative cholangiography is the gold standard for the diagnosis of asymptomatic choledocholithiasis; it can be performed in 90% of cases,⁶ and it can detect unsuspected calculi. However, its routine or selective use remains controversial. A useful diagnostic alternative is intraoperative laparoscopic ultrasound, but it is rarely available in our country.

The treatment of common duct stones is controversial, particularly since the development of laparoscopy. In patients that have had acute pancreatitis, endoscopic retrograde cholangiopancreatography (ERCP) and sphincterotomy prior to laparoscopic cholecystectomy —preferably performing the surgery in the same hospitalization— is an accepted and safe practice with minimal mortality.⁷

Ever more often, ERCP and surgery are performed during the same anesthetic period,

with similar results to those obtained with two separate procedures, and reducing hospitalization costs.⁸⁻¹⁰

Echoendoscopy and magnetic resonance cholangiopancreatography have proven to be highly sensitive and specific in the diagnosis of choledocholithiasis, thus decreasing the number of unnecessary ECRPs. However, these resources are unavailable in a large number of hospitals.^{11,12}

The use of a choledoscope with a lateral working port is the best alternative to solve intraoperative choledocholithiasis, since it allows direct visualization of the bile ducts and calculi extraction, while preserving sphincter function.^{13,14}

The aim of this study is to identify risk factors for the development of asymptomatic choledocholithiasis (without jaundice, choloria or acholia) with no associated ultrasound findings (dilation, calculus, echoic shadow) in our hospital setting.

MATERIAL AND METHODS

We included patients presenting to the Department of General Surgery at the *Hospital General de México* with the diagnosis of gallstones from October 1st, 2012, through June 17th, 2014, scheduled to undergo laparoscopic cholecystectomy and who agreed to participate, this was a prospective, analytic, comparative study.

In order to obtain a sample from a finite population and create two independent groups, an alpha significance value of 0.05 and an 85% power were used for a two-tailed test and a data loss of 5%: a sample of 68 patients was calculated for this study (G*Power[®] 3.1.9).¹⁵

According to the radiological findings, patients were divided into two groups: group 1 (G1) included cases without choledocholithiasis in the intraoperative cholangiography and group 2 (G2) included patients with choledocholithiasis in the intraoperative cholangiography.

The comparative analysis was performed with the IBM[®] SPSS[®] Statistic V20 software. We obtained central tendency measures, chi-square or Fisher's exact test, odds ratios, ROC curve and Student's t test was applied to independent samples, with a significance value of $p < 0.05$.

Table 1: Study variables.

Variable	Group	Mean	SD ±	p
Age (years)	G1	37.85	14.22	0.289
	G2	43.44	17.42	
BMI	G1	26.93	4.60	0.237
	G2	28.93	5.30	
US Diameter Common bile duct (mm)	G1	4.30	1.28	0.279
	G2	4.82	1.64	
Diameter Portal vein (mm)	G1	6.40	3.79	0.265
	G2	7.90	4.36	
Laboratory AST (U/L)	G1	35.42	26.28	0.620
	G2	108.78	101.24	
ALT (U/L)	G1	41.10	36.72	0.630
	G2	205.33	227.87	
GGT (U/L)	G1	65.95	79.77	0.120
	G2	212.11	249.99	
AP (U/L)	G1	77.64	31.49	0.034**
	G2	155.22	90.85	
DB (mg/dL)	G1	0.24	0.19	0.164
	G2	0.67	0.85	
IB (mg/dL)	G1	0.53	0.32	0.153
	G2	0.71	0.46	
Amylase (U/L)	G1	61.39	34.84	0.700
	G2	56.78	18.06	
Lipase (U/L)	G1	39.64	17.63	0.460
	G2	34.89	18.94	

BMI = body mass index, AST = aspartate aminotransferase, ALT = alanine aminotransferase, GGT = gamma-glutamyl transferase, AP = alkaline phosphatase, DB = direct bilirubin, IB = indirect bilirubin.

RESULTS

We studied 68 patients with a diagnosis of gallstone disease and no previous history of jaundice, choloria or acholia that were admitted to the *Hospital General de México* for laparoscopic cholecystectomy: 53 were women (77.9%) and 15 were men (22.1%).

In all cases, laparoscopic cholecystectomy and intraoperative cholangiography were performed. According to the radiological findings, patients were divided into two

groups: group 1 (G1) included 59 cases without choledocholithiasis (86.8%), and group 2 (G2) had nine patients with choledocholithiasis (13.2%).

There were no significant differences between groups in terms of age and body mass index (BMI) (Table 1).

The only parameter with a significant difference was the level of alkaline phosphatase (AP), with a $p = 0.034$ and an effect of 0.5 (median difference). Therefore, a ROC curve was plotted for alkaline phosphatase, with FA value > 90.5 U/L to suspect choledocholithiasis in asymptomatic patient, a sensitivity of 0.8%, a specificity of 0.8%, and an area under the curve of 0.811 (Figure 1).

With this same variable, the odds ratio ($p = 0.002$) was 12.4 (95% CI, 2.3, 66.9), meaning that patients with an AP over 90.5 U/L had a probability 12.4 times higher of having choledocholithiasis.

There were no differences in the duration of surgery ($p = 0.52$) or in the amount of intraoperative bleeding ($p = 0.061$) between groups.

Choledocholithiasis was solved by postsurgical ERCP in all nine cases (100%) during the same hospitalization, since the calculi diameter was under 5 millimeters. There were no conversions of laparoscopic to open cholecystectomy.

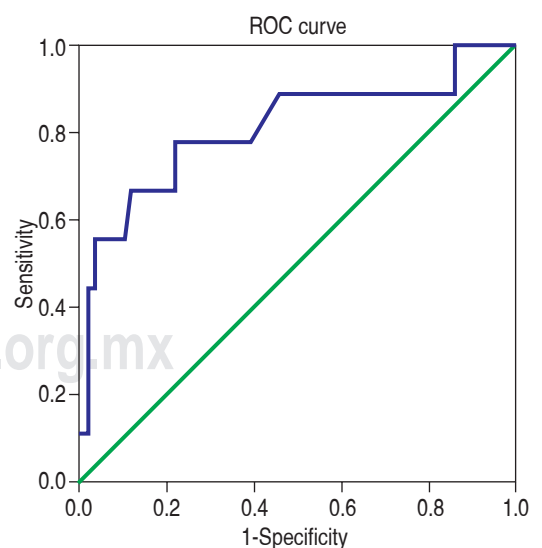


Figure 1: ROC curve for alkaline phosphatase.

The average duration of hospitalization in G1 was 1.3 days vs. 3.9 in G2 ($p = 0.01$) due to the time required for scheduling and performing the ERCP and its immediate follow-up. Only one case developed pancreatitis after ERCP.

No deaths occurred in the study.

DISCUSSION

The prevalence of asymptomatic choledocholithiasis ranges between 8% and 20% throughout the world;^{16,17} its prevalence was 13.2% at the *Hospital General de México*.

Multiple studies have attempted to detect biochemical values, algorithms or formulas that predict which patients may have calculi in the common bile duct. The American Society for Gastrointestinal Endoscopy (ASGE) proposed guidelines to classify the degree of suspicion of choledocholithiasis as high, medium or low. However, these criteria are only applicable if symptoms are present (increased bilirubin, cholangitis, biliary pancreatitis, findings on ultrasound). In asymptomatic cases, the diagnosis is a challenge for the surgeon, and prognostic scales for choledocholithiasis are of little use, since there is no jaundice or dilation of the biliary tract by ultrasound.^{18,19}

Intraoperative cholangiography is a safe method to use in minimally invasive surgery. In case small calculi are detected, ERCP is a good alternative to resolve choledocholithiasis.^{6,13,19,20}

CONCLUSION

In this study, alkaline phosphatase was the only abnormal variable suggesting choledocholithiasis in asymptomatic patients. A value over 90.5 U/L involves a risk 12.5 times higher for this condition, with a diagnostic sensitivity and specificity of 80%.

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