

PREVALENCE OF GALLSTONES IN 1,229 PATIENTS SUBMITTED TO SURGICAL LAPAROSCOPIC TREATMENT OF GERD AND ESOPHAGEAL ACHALASIA: ASSOCIATED CHOLECYSTECTOMY WAS A SAFE PROCEDURE

Prevalência de colelitíase em 1.229 pacientes submetidos ao tratamento cirúrgico laparoscópico de DRGE e megaesôfago: a colecistectomia associada mostra-se segura

Rubens Antonio Aissar **SALLUM**, Eduardo Messias Hirano **PADRÃO**, Sergio **SZACHNOWICZ**, Francisco C. B. C. **SEGURO**, Edno Tales **BIANCHI**, Ivan **CECCONELLO**

From the Divisão de Cirurgia do Esôfago, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (Esophageal Surgical Division, Hospital das Clínicas, University of São Paulo Medical School), São Paulo, SP, Brazil.

ABSTRACT - Background: Association between esophageal achalasia/ gastroesophageal reflux disease (GERD) and cholelithiasis is not clear. Epidemiological data are controversial due to different methodologies applied, the regional differences and the number of patients involved. Results of concomitant cholecystectomy associated to surgical treatment of both diseases regarding safety is poorly understood. **Aim:** To analyze the prevalence of cholelithiasis in patients with esophageal achalasia and gastroesophageal reflux submitted to cardiomyotomy or fundoplication. Also, to evaluate the safety of concomitant cholecystectomy. **Methods:** Retrospective analysis of 1410 patients operated from 2000 to 2013. They were divided into two groups: patients with GERD submitted to laparoscopic hiatoplasty plus Nissen fundoplication and patients with esophageal achalasia to laparoscopic cardiomyotomy plus partial fundoplication. It was collected epidemiological data, specific diagnosis and subgroups, the presence or absence of gallstones, surgical procedure, operative and clinical complications and mortality. All groups/subgroups were compared. **Results:** From 1,229 patients with GERD or esophageal achalasia, submitted to laparoscopic cardiomyotomy or fundoplication, 138 (11.43%) had cholelithiasis, occurring more in females (2.38:1) with mean age of 50,27 years old. In 604 patients with GERD, 79 (13,08%) had cholelithiasis. Lower prevalence occurred in Barrett's esophagus patients 7/105 (6.67%) (p=0.037). In 625 with esophageal achalasia, 59 (9.44%) had cholelithiasis, with no difference between chagasic and idiopathic forms (p=0.677). Complications of patients with or without cholecystectomy were similar in fundoplication and cardiomyotomy (p=0.78 and p=1.00). There was no mortality or complications related to cholecystectomy in this series. **Conclusions:** Prevalence of cholelithiasis was higher in patients submitted to fundoplication (GERD). Patients with chagasic or idiopathic forms of achalasia had the same prevalence of cholelithiasis. Gallstones occurred more in GERD patients without Barrett's esophagus. Simultaneous laparoscopic cholecystectomy was proved safe.

HEADINGS - Esophageal achalasia, idiopathic. Chagas disease. Gastroesophageal reflux. Cholelithiasis. Cholecystectomy. Fundoplication. Cardiomyotomy.

Correspondence:

Rubens Antonio Aissar Sallum
 E-mail: rubenssallum@globo.com

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RESUMO - Racional: São controversas as relações entre megaesôfago e doença do refluxo gastroesofágico (DRGE) com colelitíase, especialmente a forma mais adequada de conduzir pacientes com ambas. Dados epidemiológicos são díspares devido às diversas metodologias aplicadas, às diferenças regionais e à quantidade de pacientes envolvidos. **Objetivo:** Estudar a prevalência de colelitíase em pacientes submetidos às operações de refluxo gastroesofágico e megaesôfago (chagásicos ou não) e a segurança da colecistectomia estar associada. **Método:** Análise retrospectiva de 1410 pacientes operados entre 2000 e 2013. Eles foram divididos em dois grupos: os com DRGE e operados por hiato-plastia/fundoplicatura a Nissen laparoscópicas e os com acalásia por cardiomiectomia e fundoplicatura parcial laparoscópicas. Foram coletados dados epidemiológicos, diagnóstico, a presença ou não de litíase biliar, tratamento cirúrgico efetuado, complicações clínicas ou cirúrgicas e mortalidade. Todos os grupos e subgrupos foram comparados. **Resultados:** Foram estudados 1229 pacientes portadores de megaesôfago e/ou DRGE, operados por fundoplicatura com hiato-plastia, nos casos de DRGE, e cardiomiectomia com fundoplicatura, nos casos de megaesôfago, no período de 2000 a 2013, verificando-se presença de colelitíase ou colecistectomia prévia. A colelitíase ocorreu mais no sexo feminino (2,38:1) e na faixa etária entre os 50 e 70 anos. A prevalência global foi de 11,43%; 13,08% na DRGE, menor nos portadores de esôfago de Barrett (6,67%) sendo a diferença significativa (p=0,037); e 9,44% no megaesôfago, não havendo diferença significativa entre os chagásicos e os idiopáticos (p=0,677). Não houve mortalidade ou complicações relacionadas à colecistectomia nesta série. **Conclusões:** A prevalência de colelitíase é maior nos pacientes com DRGE do que nos com megaesôfago. Não há diferenças na prevalência de colelitíase nos pacientes com megaesôfago chagásico e não chagásico. É mais frequente litíase biliar nos pacientes sem esôfago de Barrett em relação portadores. A colecistectomia videolaparoscópica simultânea se mostrou-se segura.

INTRODUCTION

Cholelithiasis is one of the most common disorder of the digestive tract. Halldestam E et al.¹⁰, in England, obtained prevalences from 15-25% in women and 13-18% in men. In the United States, Friedman et al.⁹ obtained 10% in men and 20% in women, in a population between 55 and 65 years old. In Brazil there are few studies about the subject. Coelho JC et al.⁴ achieved rates of 12.9% in females and 5.4% in males when evaluating 1,000 persons with abdominal ultrasonography. Rocha A. et al.²³ in 750 autopsies showed 6.9% prevailing in females (4:1). Nakaie M et al.²⁰ found 186 (18.9%) cases of gallbladder stones when evaluating 984 autopsies.

Cholelithiasis risk factors are advanced age, diabetes mellitus, history of cardiovascular disease, stroke, previous abdominal operations³, pancreatitis¹² and hepatic cirrhosis¹⁵. However, the occurrence of gallstones in Chagas disease and gastroesophageal reflux disease (GERD) is still controversial.

Chagas disease is endemic in Brazil, affecting around eight million people. It is estimated that it can cause esophageal achalasia in about 5% of cases²¹. The protozoan *Trypanosoma cruzi*, transmitted by the bug *Triatoma panstrongylus*, is the etiologic agent and the first symptoms appear several years after infection. In the esophagus motor disorders start with reduction around 50% of neural plexus, and esophageal dilatation with 80-90%¹⁴. Late autoimmune reaction is the most accepted ethiopathogenic mechanism^{13,24}.

Theoretically, Chagas disease can also affect the gallbladder. By the same pathophysiological mechanisms of esophageal achalasia, the organ has their nervous plexus affected and consequently the motility⁶. It is thought that the gallbladder hypomotility is one of the pathophysiological reasons for developing cholelithiasis^{5,6}.

In the current literature there are few and controversial studies that compare the prevalence of cholelithiasis in chagasic and non-chagasic individuals. Rocha A, et al.²², analyzing 2517 consecutive autopsies concluded that the chagasic population showed the frequency of gallstones similar to the non-chagasic and that a relative reduction in prevalence into the chagasic women group was found (6:1 to 2:1). However, when analyzing only the group with gastrointestinal disease (esophageal and colonic forms), the occurrence of gallstones was significantly higher. Pinotti HW, et al.²¹, studying the occurrence of cholelithiasis in patients with esophageal achalasia, observed 8.45% cases of gallstones in 201 patients; more frequent in females (1.43:1). These rates were not different when compared to the control group.

Recently, Crema et al.⁷ in 152 cases of esophageal achalasia, 90% due to Chagas, obtained 28.4% of cholelithiasis, against 7% only in idiopathic cases demonstrating a significant higher presence of gallstones in cases of chagasic megaesophagus.

As well as Chagas disease, gastroesophageal reflux disease (GERD)^{2,16,19} has a high prevalence in adult population and can also be related directly to cholelithiasis.

In Brazil, evaluating 3,934 individuals, Oliveira SS et al.⁸ obtained prevalence of 31.3% for GERD, more common in women. The association between cholelithiasis and GERD remains uncertain. In two studies, the relationship between them was not found, Avidan B et al.¹ evaluated on a case-control study, while Martinez Pancorbo C et al.¹⁷ a transversal cohort study.

The prevalence of gallstones in Chagas disease and gastroesophageal reflux disease patients compared to people without such illnesses is uncertain, in part resulting from different methodologies and locations of the published epidemiologic studies. Nowadays, especially with the advent of videolaparoscopic treatment of esophageal diseases, the

diagnosis of cholelithiasis is especially important due to the possibility of simultaneous surgical treatment of esophageal and biliary disorders in a minimally invasive procedure.

The primary objective of this study is to evaluate retrospectively the prevalence of gallstones in patients referred to laparoscopic surgery for gastroesophageal reflux disease and esophageal achalasia. Secondly, was to assess the demographic factors that influenced those prevalences and morbidity associated to the concomitant cholecystectomy.

METHODS

It was retrospectively studied 1410 patients in the Esophageal Surgical Division of Hospital das Clínicas, Department of Gastroenterology, School of Medicine, University of São Paulo, São Paulo, Brazil, operated from 2000 to 2013. They were divided into two groups: patients with GERD submitted to laparoscopic hiatoplasty plus Nissen fundoplication, and patients with esophageal achalasia submitted to laparoscopic cardiomyotomy plus partial fundoplication.

Esophageal achalasia patients were subdivided into two groups: one with Chagas' disease (positive serology and/or epidemiology), and another with idiopathic cause. Patients with GERD were differentiated in those with or without Barrett's esophagus. Abdominal ultrasonography was routinely done in all patients for the diagnosis of cholelithiasis.

Patients with recurrent forms of GERD and achalasia, or advanced dolicoesophagus who underwent esophagectomy, submitted to other treatment were excluded.

It was collected in the database: name/hospital register, age, gender, specific diagnosis and subgroups, the presence or absence of gallstones, surgical procedure, operative and clinical complications and mortality.

It was also analyzed and compared the prevalence of global cholelithiasis, according to sex, age, in patients with GERD, achalasia and subgroups.

In GERD, the prevalence of cholelithiasis was compared between patients with and without Barrett's esophagus, and those with achalasia, comparison was achieved as chagasic or idiopathic.

Postoperative complications and lethality was also compared in all groups.

The results were analyzed by Fischer's test, with significance level at 5%.

RESULTS

Of 1410 cases, 181 were excluded, 78 in the GERD and 103 in the achalasia group. Thus, there were analyzed in this series 1229 patients.

Females were 680 (55.3%) and 549 (44.6%) males; mean age was 50.27 years with the distribution illustrated by Figure 1. The overall prevalence of cholelithiasis was 11.23% with higher prevalence in females (2.38:1). Considering only the group of GERD, females had prevalence in a rate of 3.3:1 ($p=0.00$), and the achalasia group no significant difference between sex and cholelithiasis was found ($p=0.056$).

Of the 601 patients with GERD, 79 (13.08%) had cholelithiasis. Barrett's esophagus was found in 105 (17.38%). The average age was 51.44 ± 13.45 years with 353 (58.44%) female and 251 (41.56%) male. There was a significant difference in the prevalence of cholelithiasis among the subgroups without Barrett, 72 (14.43%), and with Barrett, seven (6.67%, $p=0.037$).

In patients with achalasia, 59 (9.44%) had cholelithiasis. The average age was 49.16 ± 15.27 years. Females were 327 (52.32%) and 298 (47.68%) male. Comparing patients with

Chagasic and idiopathic cause, 26 (10.12%) versus 33 (8.97%) had cholelithiasis, resulting in a non-significant difference (p=0.677).

Comparing GERD group and achalasia, cholelithiasis occurred more in patients with GERD (p=0.047), but also the prevalence of women was higher in the group (p=0.034, Table 1)

TABLE 1 - Global prevalence of cholelithiasis and in esophageal achalasia and GERD groups according to gender and age

	n	Females/males n(%)	Mean age years	Cholelithiasis n(%)
Global	1229	680 (55.43%)/549 (44.67%)	50.27±14,45	138 (11.23%)
Esophageal achalasia	625	327 (52.32%)/298 (47,68%)	49.16±15,27	59 (9.44%)
Chagasic	257	120(46.69%)/137 (53.33%)		26 (10.14%)
Idiopathic	368	207 (56.25%)/161 (43.75%)		33 (8.97%)
GERD	604	353 (58.44%)/ 251 (41.56%)	51.44±13.45	79 (13.08%)
Barrett	105	39 (37.14%)/66 (62.86%)		7 (6.67%)
No Barrett	499	314 (62.93%)/185 (37.07%)		72 (14.43%)

In achalasia group, 30 complications occurred. Of these, only one (3.12%) occurred in 32 simultaneous cholecystectomy (p=1.00). None of the complications were related to the cholecystectomy. In the GERD group 42 complications occurred. Of these, three (5.00%) were in 60 simultaneous cholecystectomy (p=0.78), and similarly than achalasia group; none was associated with complications from the cholecystectomy. No mortality was found in all cases (Table 2).

TABLE 2 - Complications and mortality in GERD and esophageal achalasia groups with and without association with cholecistectomy

Disease/surgery	GERD (Hiatoplasty + fundoplication)	Achalasia (cardiomyotomy + fundoplication)
No cholecistectomy	544	593
Complications/ mortality	39(7.10%) 0	29 (4.89%) 0
Colecistectomy	60	32
Complications/ mortality	3 (5.00%) 0	1 (3.12%) 0
	p=0,78	p=1

DISCUSSION

This study analyzed the largest published series evaluating the prevalence of gallstones in patients with GERD and esophageal achalasia, who underwent to surgical treatment, as well as the concomitant cholecystectomy relationship not previously described in the literature.

The overall prevalence of gallstones in GERD and achalasia was similar to other smaller series and to the epidemiological prevalence in the population. A higher prevalence of cholelithiasis in females was still detected^{4,9,10,12,15,20,21,23}.

In patients with GERD, the prevalence of gallstones detected was higher in the subgroup without Barrett. Higher frequency of men in patients with Barrett's associated with a possible bias of more liberal indication for surgery in patients with cholelithiasis and simple GERD may probably explain this difference. Such data is different from the few series found,

which usually associates Barrett's esophagus with greater prevalence of gallstones^{11,18}.

In patients with achalasia, the prevalence of cholelithiasis was close to the gallstones in the adult population. There was no difference detected of gallstones between Chagasic and idiopathic patients, which is consistent with some previous studies^{20,21}, but different from some others^{7,23}. The theory that in Chagas disease the involvement of gastrointestinal tract denervation of the gallbladder leads to cholestasis and consequent higher incidence of cholelithiasis, cannot be confirm on these data. The higher frequency of men in the achalasia group may be a possible factor affecting the statistics.

The laparoscopic associated cholecystectomy was demonstrated as safe as procedure in both groups studied in this series. Minor complications were similar in GERD and achalasia groups and not different with or without cholecistectomy associated. No mortality or biliary complications related to the removal of the gallbladder was observed. All operations were done into a high-volume hospital with a trained staff for complex videolaparoscopic procedures. Perhaps, this can be a bias on data. Although all these procedures have been performed by residents of the 4th year in digestive surgery program and assisted by the esophageal surgical staff, these results are consistent with others, associating laparoscopic cholecystectomy with antireflux surgery²⁵. In the other hand, no studies were found associating laparoscopic cholecystectomy with surgery for esophageal achalasia.

CONCLUSION

The prevalence of cholelithiasis on GERD (13.08%) was higher than in patients with esophageal achalasia (9.44%). No difference was detected in the prevalence of gallstones between chagasic (10.14%) and idiopathic achalasia (8.97%). In GERD, there was a higher prevalence of gallstones in those without Barrett's esophagus (14.43%) compared with Barrett (6.67%). The laparoscopic associated cholecystectomy in achalasia and GERD was safe with no mortality or complications related to the procedure in this series.

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