Original Article

Malignant Potential of Gallbladder Polyps: Do they all have Surgical Indication?

Potencial Maligno de Pólipos Vesiculares: Todos têm Indicação Cirúrgica?

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ABSTRACT

Introduction: Gallbladder polyps (PV) are mucosal lesions that protrude into the lumen of the gallbladder. Most patients are diagnosed incidentally because they are asymptomatic. The presence of PV is a known risk factor for gallbladder cancer. According to the guidelines, cholecystectomy is recommended, which leads to unnecessary resection in one-third of patients, as the PV subsequently proves to be benign.

This study evaluates the malignant potential of vesicular polyps to determine whether they are all indications for laparoscopic cholecystectomy.

Methods: Retrospective observational study of 151 patients with an ultrasound diagnosis of vesicular polyps who underwent cholecystectomy performed at our centre from 2018 to 2022 inclusive. The prevalence of gallbladder polyps and gallbladder cancer in this population was assessed and predictive factors for malignancy were characterized using statistical analysis in SPSS (Statistical Package for Social Sciences) version 27.

Results: A total of 151 patients with an ultrasound diagnosis of vesicular polyps who had undergone cholecystectomy over five years were evaluated. Participants were divided into 84 (55.6%) asymptomatic and 67 (44.4%) symptomatic. Pathological anatomy confirmed the presence of PV in 96 (63.6%) surgical specimens and its absence in 55 (36.4%). Five (3.3%) cases of gallbladder

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cancer (GBC) were detected in the total. Among the cases with GBC, all participants were 60 or older; one (20%) was female and 4 (80%) were male. All patients had a history of gastrointestinal tract neoplasms and all cancer-related PVs measured between 6 and 9 mm in the longest axis.
Conclusion: Patients aged 60 years or older, with a PV with a larger axis dimension between 6 and 9 mm and with a history of gastrointestinal tract neoplasms have a higher risk of developing true bladder polyps and consequently a higher likelihood of GBC.

Keywords: Cholecystectomy, Laparoscopic; Gallbladder Neoplasms/diagnosis; Gallbladder Neoplasms/surgery; Polyps/diagnosis; Polyps/surgery

RESUMO

Introdução: Os pólipos da vesícula biliar (PV) são lesões da mucosa que se projetam para o lúmen da mesma. Na maioria dos pacientes, o seu diagnóstico é acidental, pois são assintomáticos. A presença de PV é um fator de risco conhecido para cancro da vesícula biliar (CVB). A colecistectomia é recomendada segundo *guidelines*, o que resulta na ressecção desnecessária num terço dos pacientes, pois, posteriormente, o PV revela benignidade.
Este estudo avalia o potencial maligno de pólipos vesiculares, com a finalidade de verificar se todos têm indicação para colecistectomia laparoscópica.
Métodos: Estudo observacional retrospetivo de 151 doentes com diagnóstico ecográfico de pólipos vesiculares submetidos a colecistectomia de 2018 a 2022, inclusive, seguidos no nosso centro. Avaliou-se a prevalência de PV e cancro da vesícula biliar nesta população e caracterizaram-se os fatores preditivos para malignidade tendo por base a análise estatística realizada no SPSS (Statistical Package for the Social Sciences) versão 27.
Resultados: Avaliaram-se 151 pacientes com diagnóstico ecográfico de pólipos vesiculares submetidos a colecistectomia num período de cinco anos. Os participantes dividiram-se em 84 (55,6%) assintomáticos e em 67 (44,4%) sintomáticos. Foi confirmada, por anatomia patológica, a presença de PV em 96 (63,6%) peças cirúrgicas e a ausência dos mesmos em 55 (36,4%). Identificaram-se 5 (3,3%) casos de CVB no total. Dentro dos casos com CVB, constatou-se que todos os participantes tinham 60 anos ou mais; um (20%) era do sexo feminino e 4 (80%) do sexo masculino. Todos os doentes tinham antecedentes de neoplasias do trato gastrointestinal e todos os PV associados a cancro mediam entre 6 e 9 mm de dimensão de maior eixo.
Conclusão: Pacientes com idade igual ou superior a 60 anos, com PV de dimensão de maior eixo entre 6 e 9 mm e com antecedentes de neoplasias do trato gastrointestinal têm um maior risco de formar pólipos vesiculares verdadeiros e, consequentemente, uma maior probabilidade de ter CVB.

Palavras-chave: Colecistectomia Laparoscópica; Neoplasias da Vesícula Biliar/cirurgia; Neoplasias da Vesícula Biliar/diagnóstico; Pólipos/cirurgia; Pólipos/diagnóstico

INTRODUCTION

Gallbladder polyps (GP) are mucosal lesions that project into the lumen of the gallbladder. Their diagnosis has been increasing due to technological advances, growing awareness of regular medical evaluations, and the evolution of imaging examinations, such as endoscopic or contrast ultrasound, abdominal computed tomography,[1] and magnetic resonance imaging.[2]

The prevalence of GP ranges from 0.3% to 12.3% in the general population.[3-5] Known risk factors include male sex, obesity, hepatitis B virus infection, metabolic syndrome, and dyslipidemia.[1]

GPs are grouped into pseudopolyps and true polyps.[4] Recent literature has shown that more than 70% are pseudopolyps,[3] mainly composed of cholesterol (60%), inflammatory components, and adenomyomatous hyperplasia.[4] Cholesterol polyps are incidentally detected in approximately 2% to 12% of pathology samples from cholecystectomies. These arise in the context of cholesterolosis and are the most common, especially those smaller than 10 mm in maximum dimension.[6,7]

The remaining percentage corresponds to true polyps (benign and malignant neoplasms). In the 2019 WHO classification, benign neoplasms were grouped into "intracholecystic papillary neoplasms" and "pyloric gland adenomas" (for tubular

ones with pyloric glands). Given the overlap between these two groups, the unifying term "intracholecystic papillary tubular neoplasm" was proposed for these lesions. Regarding malignant neoplasms, there are several types: adenocarcinomas (80%), mucinous cystadenomas, squamous cell carcinomas, adenoacanthomas, and other types.[8,9]

A recent systematic review revealed that about 3% of intracholecystic papillary tubular neoplasms are considered pre-malignant lesions (now called intracholecystic neoplasms) since they have atypical hyperplasia[4] with the potential to become adenocarcinoma,[1,5] therefore justifying early intervention.

It is believed that only 6% of all gallbladder carcinomas arise in association with an intracholecystic neoplasm, with favorable survival rates for gallbladder carcinomas associated with this neoplasm (60% to 90% 3-year survival) compared to carcinomas without a GP precursor (27% 3-year survival).[8]

Abdominal ultrasound is used for the initial study of gallbladder pathology.[10] GPs are incidentally detected in approximately 4% to 7% of patients,[2,11] and given this premise, biopsy proves unfeasible.[3] However, some studies show that it is possible to perform a biopsy using more invasive endoscopic techniques, such as fine-needle aspiration guided by ultrasound or cytology of transpapillary drainage of the gallbladder.[10,12,13]

In 2020, the European Society of Gastrointestinal and Abdominal Radiology (ESGAR), the European Association for Endoscopic Surgery and other Interventional Techniques (EAES), the International Society of Digestive Surgery–European Federation (EFISDS), and the European Society of Gastrointestinal Endoscopy (ESGE) updated the guidelines for evaluation and follow-up of GPs published in 2017. The review process followed the recommendations of ESGAR and the principles of the Appraisal of Guidelines, Research and Evaluation II (AGREE) instrument. Each article was classified according to its level of evidence using the Grading of Recommendations Assessment, Development, and Evaluation system (GRADE).[2,14]

The guidelines recommend abdominal ultrasound for the primary evaluation of GPs. This evaluation should take into account the size of the GPs, as the risk of malignancy is proportional to size.[2]

The main surgical indications include a single polyp, no pedunculated or broad-based lesions, and imaging exams that suggest malignant characteristics.[15] The incidence of malignancy is 8% to 10% for GPs larger than 10 mm, 1% to 3% for GPs of 6 to 9 mm, and 0% to 0.5% for GPs smaller than 5 mm, concerning the value of the maximum dimension.[2]

Cholecystectomy is recommended when the GP is 10 mm or more in maximum dimension.[2] This guideline results in unnecessary surgical risks and expenses,[4] as one-third of cholecystectomy specimens reveal benignity.[5,6]

Despite the low risk of malignancy, guidelines recommend cholecystectomy for patients with GPs of 6 to 9 mm in maximum dimension with one or more risk factors for malignancy (i.e., age over 60 years, Asian ethnicity, history of primary sclerosing cholangitis, or sessile polypoid lesion/wall thickening of 4 mm or more).[2,16] In contrast, patients with GPs of 6 to 9 mm without risk factors and those with polyps of maximum dimension equal to or less than 5 mm do not need surgical intervention and can be followed by abdominal ultrasound at 6 months and 1 and 2 years.

Within the 2-year follow-up period, if the lesion reaches 10 mm in maximum dimension, cholecystectomy is recommended. If the GP grows by 2 mm or more, the current size should be considered, along with the patient's risk factors. The risks and benefits of cholecystectomy should be explained, and if the patient does not wish to undergo or does not meet the essential conditions (due to associated comorbidities) for surgery, follow-up may not be performed. After 2 years and in the absence of GP growth or if the GP disappears, follow-up can be discontinued. Additionally, patients with GPs of maximum dimension equal to or less than 5 mm, without associated risk factors, may not require ultrasound follow-up.[2]

The presence of GPs is a well-known risk factor for gallbladder cancer (GBC).[1] Annually, worldwide, more than 200 000 patients are diagnosed [17]. This is the most common cancer of the biliary tract[9,18-20] despite being considered rare, as its incidence is only 1.5 to 12.8/100 000.[21] Risk factors for it include female sex, age over 60 years, genetic predisposition, geographic distribution, congenital abnormalities of the gallbladder, and the presence of chronic inflammatory disease.[19,20]

GBC in the early stage is commonly detected incidentally by the pathologist after cholecystectomy, given a presumed benign disease, namely gallstones. Most patients remain asymptomatic for a long time, which leads to a late diagnosis with a worse prognosis.[11,19] The first symptoms to appear are

nonspecific: abdominal pain, constitutional symptoms (weight loss, anorexia, fatigue, among others), and gastrointestinal tract disorders.[10]

For resectable GBC, a radical cholecystectomy is recommended that involves en bloc resection of the liver (anatomic resection of segments IVb and V) and portal lymphadenectomy, with or without resection of the cystic duct. There is evidence supporting the importance of adjuvant therapy, especially in patients with positive lymph nodes or the presence of tumor cells in the surgical margins (R1). In recent decades, post-operative results have improved, and considering that only a minority of patients are indicated for curative surgery, disease-free survival is 33.4 months,[10,22] and 5-year survival is approximately 10% to 50%, varying according to the stage of the disease at the time of surgery.[2]

Although previous studies have persisted in differentiating between neoplastic and non-neoplastic polyps, it may be more relevant to try to assess the risk of potential malignancy of the polyp, distinguishing between pseudopolyps and benign neoplastic from malignant. The main contribution of this study is based on the evaluation of the malignant potential of GPs detected by ultrasound, tomography, or magnetic resonance imaging, whether incidental findings or not, with the ultimate purpose of verifying if all had indication for laparoscopic cholecystectomy.

MATERIAL AND METHODS

1. STUDY DESIGN AND PARTICIPANTS

In this retrospective longitudinal observational study conducted over 6 months, 151 patients with an ultrasound diagnosis of gallbladder polyps who underwent cholecystectomy in the last 5 years (2018 to 2022, inclusive), followed at Centro Hospitalar Universitário de São João, EPE – Hospital de São João, were included. All patients who underwent cholecystectomies more than 5 years ago and all those who underwent cholecystectomy for reasons other than the presence of GPs were excluded. All participant data were collected in December 2022 through consultation of outpatient and inpatient clinical records.

This study was approved and consented to by the Ethics Committee for Health of Centro Hospitalar e Universitário São João (CHUSJ) in November 2022. According to national legislation and institutional requirements, no informed consent is necessary for participation in this study. The privacy, preservation, and confidentiality of data of all participants were guaranteed.

2. CLINICAL CHARACTERISTICS AND STUDY RESULTS

The following parameters were collected from each patient's clinical file: age, sex, pathological history, symptomatology, diagnostic method, complementary diagnostic exams (ultrasound), type of treatment performed, and pathological reports of the surgical specimen.

3. STATISTICAL ANALYSIS

Statistical analysis was performed in SPSS (Statistical Package for the Social Sciences), version 27. A statistically significant value was considered if $p<0.05$. A descriptive analysis of all variables was performed.

To assess the distribution of continuous variables, a histogram analysis was used, and the mean ± standard deviation was used to describe normal variables. To compare categorical variables, the chi-square test was used. To compare continuous variables, the Student's t-test was used for normally distributed variables.

RESULTS

This retrospective observational study integrated 151 patients with the preoperative diagnosis of GP, with 87 (57.6%) being female and 64 (42.4%) male.

Table 1 shows the frequency, percentage, and cumulative percentage of all variables studied, such as age, sex, pathological history, clinical presentation (type of symptoms), diagnostic method, and pathological characteristics of all participants. Ages ranged from 25 to 83 years; 93 (61.6%) patients were under 60 years of age, and 58 (38.4%) were 60 years or older. Regarding pathological history: 45 (29.8%) patients had dyslipidemia, 107 (70.9%) specific gallbladder alterations, 30 (19.9%) non-specific gallbladder alterations, 81 (53.6%) gallstones, 1 (0.7%) cholelithiasis, 61 (40.4%) cholesterolosis, 75 (49.7%) chronic cholecystitis, 27 (17.9%) hepatic steatosis, 1 (0.7%) non-alcoholic steatohepatitis, 14 (9.3%) obesity, 11 (7.3%) benign neoplasm of extrahepatic bile ducts, 24 (15.9%) gastrointestinal tract neoplasm, 28 (18.5%) other type of neoplasm. Regarding clinical presentation, participants were divided into 84 (55.6%) asymptomatic and 67 (44.4%) symptomatic. Among the symptomatic, 4 (2.6%) presented with heartburn, 8 (5.3%) general malaise, 24 (15.9%) cramping pain in the right hypochondrium, 7 (4.6%) nausea, 5 (3.3%) general malaise and cramping pain in the right hypochondrium, 15 (9.9%) general malaise, cramping pain in the right hypochondrium and nausea, 4 (2.6%) other types of symptoms. Regarding the diagnostic method of GPs, 116 (76.8%) patients were

Table 1. Frequency of demographic, pathologic antecedents, clinic, type of symptoms, diagnostic methods and anatomopathological variables of the total number of participants (Total participants= 151).

				Frequency	Percentage (%)
Age, years	<60			93	61.6
	≥60			58	38.4
Sex	Feminine			87	57.6
	Masculine			64	42.4
Pathologic antecedents	Dyslipidemia			45	29.8
	Specific gallbladder disorders			107	70.9
	Non-specific gallbladder disorders			30	19.9
	Lithiasis			81	53.6
	Cholelithiasis			1	0.7
	Cholesterolosis			61	40.4
	Chronic cholecystitis			75	49.7
	Hepatic steatosis			27	17.9
	Nonalcoholic steatohepatitis			1	0.7
	Obesity			14	9.3
	Benign neoplasm of extrahepatic bile ducts			11	7.3
	Neoplasm of the gastrointestinal tract			24	15.9
	Other type of neoplasm			28	18.5
Asymptomatic				84	55.6
Symptomatic				67	44.4
Type of symptoms	Heartburn			4	2.6
	General malaise			8	5.3
	Cramping pain in the right hypochondrium			24	15.9
	Nausea			7	4.6
	General malaise and cramping pain in the right upper quadrant			5	3.3
	General malaise and crampy right upper quadrant pain and nausea			15	9.9
	Others			4	2.6
Diagnostic methods	Findings on abdominal ultrasound			116	76.8
	Abdominal CT Findings			13	8.6
	Abdominal MRI findings			1	0.7
	Abdominal ultrasound with clinical suspicion			21	13.9
Pathologic anatomy	Chronic cholecystitis			113	74.8
	Cholesterolosis			65	43
	Lithiasis			19	12.6
	Adenomyomatous hyperplasia			14	9.3
	Polyps	Presence (n=96)	Chronic cholecystitis	64	42.38
			Cholesterolosis	42	27.82
			Lithiasis	2	1.32
			Adenomyomatous hyperplasia	8	5.3
			Gallbladder cancer	3	1.99
		Absence (n=55)	Chronic cholecystitis	49	32.45
			Cholesterolosis	23	15.23
			Lithiasis	17	11.26
			Adenomyomatous hyperplasia	6	3.97
			Gallbladder cancer	2	1.32
		Number	<3	41	27.2
			≥3	55	36.4
		Size	≥10 mm	11	11.5
			6-9 mm	32	33.3
			≤5 mm	53	55.2
	Gallbladder cancer			5	3.3

diagnosed by abdominal ultrasound, 13 (8.6%) by abdominal computed tomography, and 1 (0.7%) by abdominal magnetic resonance imaging, incidentally. Twenty-one (13.9%) were diagnosed with clinical suspicion through abdominal ultrasound. Regarding the pathological characteristics post-laparoscopic cholecystectomy, it was observed that 14 (9.3%) surgical specimens presented adenomyomatous hyperplasia, 65 (43%) cholesterolosis, 113 (74.8%) signs of chronic cholecystitis, 19 (12.6%) gallstones. It is added that the presence of GPs was confirmed in 96 (63.6%) surgical specimens and their absence in 55 (36.4%). Within the surgical specimens with detected GPs, there were 64 (42.38%) signs of chronic cholecystitis, 42 (27.82%) cholesterolosis, 2 (1.32%) gallstones, 8 (5.3%) adenomyomatous hyperplasia, and 3 (1.99%) GBC. Within the surgical specimens without detected GPs, there were 49 (32.45%) signs of chronic cholecystitis, 23 (15.23%) cholesterolosis, 17 (11.26%) gallstones, 6 (3.97%) adenomyomatous hyperplasia, and 2 (1.32%) GBC. Additionally, 41 (27.2%) specimens had fewer than 3 GPs, and 55 (36.4%) had 3 GPs or more. Among the identified GPs, 11 (11.5%) measured 10 mm or more, 32 (33.3%) between 6 and 9 mm, 53 (55.2%) 5 mm or less to the maximum dimension. Five (3.3%) cases of GBC were identified in a total of 151 surgical specimens evaluated.

Next, an evaluation and comparison were made between the number of GPs present in the surgical specimen and each of the parameters (age, sex, pathological history, clinical and pathological characteristics) – Table 2. Within the surgical specimens with fewer than 3 GPs (n=41), it

Table 2. Assessment and comparison between the number of PV present in the surgical specimen and each of the parameters (age, sex, pathological history, clinical and pathological-anatomical features).

		Multiple polyps		
		<3	≥3	*P* value
Age, years	<60	29	34	0.272
	≥60	12	21	
Sex	Feminine	26	30	0.666
	Masculine	15	25	
Pathologic antecedents	Dyslipidemia	12	12	0.171
	Specific gallbladder disorders	29	36	0.453
	Non-specific gallbladder disorders	6	14	0.390
	Lithiasis	21	28	0.698
	Cholelithiasis	0	0	0.415
	Cholesterolosis	17	30	0.008
	Chronic Cholecystitis	18	20	0.004
	Hepatic steatosis	13	8	0.023
	Non-alcoholic steatohepatitis	0	0	0.415
	Obesity	6	2	0.161
	Benign neoplasm of extrahepatic bile ducts	8	1	0.002
	Neoplasm of the Gastrointestinal Tract	10	5	0.127
	Other type of neoplasm	5	13	0.360
Clinic	Asymptomatic	28	31	0.083
	Symptomatic	13	24	
Pathologic anatomy	Adenomyomatous hyperplasia	7	1	0.034
	Cholesterolosis	19	23	0.883
	Chronic Cholecystitis	31	33	0.002
	Lithiasis	0	2	<0.001
	Size ≥ 10 mm	6	5	
	Size 6-9 mm	12	20	0.608
	Size ≤ 5 mm	23	30	
	Gallbladder cancer	1	2	0.935

N=Number; p= statistical significance

was observed that 29 belonged to patients under 60 years of age and 12 to patients 60 years or older; 26 were female and 15 were male. Regarding pathological history, 12 cases had dyslipidemia, 29 specific gallbladder disorders, 6 non-specific gallbladder disorders, 21 gallstones, 17 cholesterolosis, 18 chronic cholecystitis, 13 hepatic steatosis, 6 obesity, 8 benign neoplasm of extrahepatic bile ducts, 10 gastrointestinal tract neoplasm, and 5 other types of neoplasm. It was found that 28 were asymptomatic and 13 symptomatic. Pathological anatomy revealed that 7 of the surgical specimens had adenomyomatous hyperplasia, 19 cholesterolosis, 31 signs of chronic cholecystitis. Additionally, it revealed that 6 specimens had GPs with 10 mm or more, 12 had GPs between 6 and 9 mm, and 23 had GPs with 5 mm or less, in relation to the maximum dimension. Within the surgical specimens with fewer than 3 GPs, 1 case with GBC was identified.

Within the surgical specimens with 3 GPs or more (n=55), it was observed that 34 belonged to patients under 60 years of age and 21 to patients 60 years or older; 30 were female and 25 were male. Regarding pathological history, 12 cases had dyslipidemia, 36 specific gallbladder disorders, 14 non-specific gallbladder disorders, 28 gallstones, 30 cholesterolosis, 20 chronic cholecystitis, 8 hepatic steatosis, 2 obesity, 1 benign neoplasm of extrahepatic bile ducts, 5 gastrointestinal tract neoplasm, and 13 other types of neoplasm. It was found that 31 cases were asymptomatic and 24 symptomatic. Pathological anatomy showed that 1 surgical specimen presented adenomyomatous hyperplasia, 23 cholesterolosis, 33 signs of chronic cholecystitis, 2 gallstones. Additionally, it revealed that 5 specimens had GPs with 10 mm or more, 20 had GPs between 6 and 9 mm, and 30 GPs with 5 mm or less, to the maximum dimension. Within the surgical specimens with 3 GPs or more, 2 cases with GBC were identified.

A statistically significant difference was found, within the pathological history, in cholesterolosis (p=0.008), chronic cholecystitis (p=0.004), hepatic steatosis (p=0.023), and benign neoplasm of extrahepatic bile ducts (p=0.002). Of the pathological anatomy characteristics, the presence of adenomyomatous hyperplasia (p=0.034), signs of chronic cholecystitis (p=0.002), and gallstones (p=<0.001) were statistically significant, in the comparison between the two groups (fewer than 3 GPs and 3 GPs or more).

Next, the presence or absence of gallbladder cancer was compared within each of the parameters evaluated in the participants of this study, such as age, sex, pathological history, clinical presentation, and characteristics of pathological anatomy (Table 3). Within the cases without GBC (n=146), it was found that 93 (63.7%) participants were under 60 years of age and 53 (36.3%) were 60 years or older; 86 (58.9%) were female and 60 (41.1%) were male. Regarding pathological history, 43 (29.5%) patients had dyslipidemia, 104 (71.2%) specific gallbladder disorders, 28 (19.2%) non-specific gallbladder disorders, 79 (54.1%) gallstones, 1 (0.7%) cholelithiasis, 61 (41.8%) cholesterolosis, 72 (49.3%) chronic cholecystitis, 26 (17.8%) hepatic steatosis, 1 (0.7%) non-alcoholic steatohepatitis, 14 (9.6%) obesity, 11 (7.5%) benign neoplasm of extrahepatic bile ducts, 19 (13%) gastrointestinal tract neoplasm, and 27 (18.5%) other types of neoplasm. It was found that 82 (56.2%) were asymptomatic and 64 (43.8%) symptomatic. Pathological anatomy showed that 14 (9.6%) surgical specimens presented adenomyomatous hyperplasia, 65 (44.5%) cholesterolosis, 109 (74.7%) signs of chronic cholecystitis, 18 (12.3%) gallstones. It is added that 93 (63.7%) were surgical specimens with GPs, 53 (36.3%) without GPs, 40 (27.4%) had fewer than 3 GPs, 53 (36.3%) had 3 GPs or more, 11 (11.8%) had GPs with 10 mm or more, 29 (31.2%) had GPs between 6 and 9 mm, 53 (57%) had GPs with 5 mm or less, relative to the maximum dimension.

Within the cases with GBC (n=5), it was found that all participants were 60 years or older; 1 (20%) was female and 4 (80%) were male. Regarding pathological history, 2 (40%) patients had dyslipidemia, 3 (60%) specific gallbladder disorders, 2 (40%) non-specific gallbladder disorders, 2 (40%) gallstones, 3 (60%) chronic cholecystitis, 1 (20%) hepatic steatosis, 5 (100%) gastrointestinal tract neoplasm, 1 (20%) another type of neoplasm. It was found that 2 (40%) of the cases were asymptomatic and 3 (60%) symptomatic. Pathological anatomy revealed 4 (80%) signs of chronic cholecystitis, 1 (20%) gallstones. It is added that 3 (60%) were surgical specimens with GPs, 2 (40%) without GPs, 1 (20%) had fewer than 3 GPs, 2 (40%) had 3 GPs or more, 3 (100%) had GPs between 6 and 9 mm, relative to the maximum dimension.

Statistically significant differences were observed in age (p=0.007), in pathological history, in the presence of gastrointestinal tract neoplasm (p=<0.001), and in pathological anatomy characteristics, in the maximum dimension of GPs (p=0.045), and the comparison between the two groups (presence or absence of GBC).

Table 3. Assessment of the presence or absence of GC within each of the parameters (age, sex, pathological history, clinical and pathological-anatomical features).

				Gallbladder Cancer		
				A, N (%)	P, N (%)	*P* value
Age, years	<60			93 (63,7)	0 (0)	0.007
	≥60			53 (36,3)	5 (100)	
Sex	Feminine			86 (58,9)	1 (20)	0.083
	Masculine			60 (41,1)	4 (80)	
Pathological antecedents	Dyslipidemia			43 (29,5)	2 (40)	0.612
	Specific gallbladder disorders			104 (71,2)	3 (60)	0.587
	Non-specific gallbladder disorders			28 (19,2)	2 (40)	0.251
	Lithiasis			79 (54,1)	2 (40)	0.534
	Cholelithiasis			1 (0,7)	0 (0)	0.853
	Cholesterolosis			61 (41,8)	0 (0)	0.061
	Chronic Cholecystitis			72 (49,3)	3 (60)	0.638
	Hepatic steatosis			26 (17,8)	1 (20)	0.900
	Non-alcoholic steatohepatitis			1 (0,7)	0 (0)	0.853
	Obesity			14 (9,6)	0 (0)	0.467
	Benign neoplasm of extrahepatic bile ducts			11 (7,5)	0 (0)	0.524
	Neoplasm of the Gastrointestinal Tract			19 (13)	5 (100)	<0.001
	Other type of neoplasm			27 (18,5)	1 (20)	0.932
Clinic	Asymptomatic			82 (56,2)	2 (40)	0.474
	Symptomatic			64 (43,8)	3 (60)	
Pathologic anatomy	Chronic Cholecystitis			109 (74,7)	4 (80)	0.787
	Cholesterolosis			65 (44,5)	0 (0)	0.070
	Lithiasis			18 (12,3)	1 (20)	0.611
	Adenomyomatous hyperplasia			14 (9,6)	0 (0)	0.467
	Polyps	Presence	Chronic Cholecystitis	109 (74,7)	2 (40)	0.742
			Cholesterolosis	65 (44,5)	0 (0)	0.128
			Lithiasis	18 (12,3)	0 (0)	0.507
			Adenomyomatous hyperplasia	14 (9,6)	0 (0)	0.576
		Absence		53 (36,3)	2 (40)	
		Number	<3	40 (27,4)	1 (20)	0.935
			≥3	53 (36,3)	2 (40)	
		Size	≥10 mm	11 (11,8)	0 (0)	
			6-9 mm	29 (31,2)	3 (100)	0.045
			≤5 mm	53 (57)	0 (0)	

P=Presence; A=Absence; N=Number; p= statistical significance.

DISCUSSION

From a careful analysis of Tables 1, 2, and 3, interesting results emerge, such as the percentage of patients who indicated laparoscopic cholecystectomy due to the presence of GPs being higher in the group under 60 years than in the group with 60 years or more, which would not be expected.[2,16] A possible explanation for this result could be based on the fact that the surgical risk is higher in the group with 60 years or more (due to associated comorbidities and age itself), serving as a surgical contraindication and, for this reason, a more conservative approach is preferred.

In most cholecystectomized patients, it was expected that dyslipidemia, specific and non-specific gallbladder disorders, gallstones, cholesterolosis, chronic cholecystitis, obesity, benign neoplasm of extrahepatic bile ducts, and other types of neoplasm would be present as pathological history,[1] which was confirmed. It revealed that more than 50% of patients had a diagnosis of specific gallbladder disorders and had gallstones.

Most cases were asymptomatic and clinically not relevant, as expected.[3] Among the symptomatic, the most common

symptom was cramping pain in the right hypochondrium, which is to the literature.[10,23]

Most cases of GPs were diagnosed incidentally by abdominal ultrasound, either incidentally or by clinical suspicion, which was expected.[2,10] The accessibility and diagnostic accuracy of abdominal ultrasound explain its important role in current European guidelines.[2,10] Other diagnostic tests, such as computed tomography and magnetic resonance, were less used as they are less practical and more expensive.

The presence of signs of chronic cholecystitis is a crucial factor in assessing the risk of developing GPs and GBC because it was present in more than 50% of all surgical specimens analyzed, as well as in 4 of the five patients with GBC. It should be noted that GPs were absent in 55 surgical specimens from laparoscopic cholecystectomies sent for pathological anatomy. This information could be explained by the fact that abdominal ultrasound is operator-dependent, by the uniqueness of each patient's biotype, and/or by the fact that it was a pseudopolyp and it disappeared, leading to the impossibility of isolating GPs. It was concluded that, assuming that the indication for cholecystectomy was only the presence of GPs, 55 out of 151 patients were unnecessarily cholecystectomized, which is predicted in the literature, as it happens in at least one-third of patients.[5,6]

Moreover, in 151 patients with indications for laparoscopic cholecystectomy due to the presence of GPs, only 5 had gallbladder cancer, of which 3 cases had associated GPs, which validates the aforementioned.[5,6]

Most patients with GPs had 3 or more polyps. In the comparison between the group with fewer than 3 GPs and the one with 3 GPs or more, it was concluded that there were more patients with a history of cholesterolosis, chronic cholecystitis, and detection of adenomyomatous hyperplasia in the surgical specimen in the group of 3 GPs or more; and there were more patients with hepatic steatosis, benign neoplasm of extrahepatic bile ducts, and signs of chronic cholecystitis and gallstones in the surgical specimen in the group with fewer than 3 GPs. Therefore, a history of cholesterolosis, chronic cholecystitis, and the presence of adenomyomatous hyperplasia is associated with a higher number of polyps, while a history of hepatic steatosis, benign neoplasm of extrahepatic bile ducts, signs of chronic cholecystitis, and gallstones is associated with a lower number of polyps.

In this study, it was concluded that most GPs found in the surgical specimens measured 5 mm or less in maximum dimension. This result conflicts with current evidence, as GPs that are 10 mm or more that present formal indication for cholecystectomy.[2] It was not possible to find information that would justify the surgical decision. Thus, it is assumed that these cases of cholecystectomies for GPs with 5 mm or less should have associated risk factors.

Of the 5 patients diagnosed with GBC, all were 60 years or older, which is in line with recent studies that consider age over 60 years as a risk factor for malignancy of GPs [2, 16]. Most cases of GBC were male, which is not expected, as female sex is considered a risk factor for GBC.[19,20] All patients had a history of gastrointestinal tract neoplasms and all GPs associated with cancer measured between 6 and 9 mm in maximum dimension.

The clinical relevance of this study is based on reflection about the formal indication for laparoscopic cholecystectomy when GPs are present. It is questioned whether, in fact, all detected GPs have surgical indications and what factors influence this decision. Equally relevant are the characteristics inherent to the patient, risk factors, and characteristics of the polyp/polyps, which validate surgical indication vs. surveillance.

The main limitations of this study arise from its retrospective, passing through the limitation in the collection of participant data, the dependence on what is or is not computerized about the patient, the lack of standardization of pathological reports of surgical specimens, and the lack of follow-up of the inherent cases. It is concluded that a standardization of the recording method would be crucial, from the diary of outpatient consultations to the pathological reports. Other limitations are based on the fact that this study was conducted in a single hospital center and with a small sample of participants, which decreases the representativeness of the results in the general population. A larger population sample would undoubtedly be crucial in order to draw more universal and statistically significant conclusions because statistical significance was removed from many results, such as a relationship between sex, presence of dyslipidemia, specific gallbladder disorders, cholesterolosis, chronic cholecystitis, obesity,[2,16,19,20] and the presence of GPs.

Despite the small sample of cases included in this study (n=151), it was conducted in a Central, reference Hospital in Portugal (CHUSJ) and covered a period of 5 years (2018 to 2022, inclusive), which increases the significance and validity of the sample, being a strong point of this study. We analyzed the data of all cholecystectomized patients with a previous

diagnosis of GP. The large set of potential predictors analyzed is also a strength of our study.

In future studies, a pertinent question to be clarified is whether, among people who were unnecessarily operated on, quality and survival suffered changes. In a future study, it would be pertinent to evaluate patients undergoing cholecystectomy for a diagnosis other than GP, in how many patients polyps were found and what their histology was.

CONCLUSION

In conclusion, patients aged 60 years or older, with GPs of maximum dimension between 6 and 9 mm, and with a history of gastrointestinal tract neoplasms have a higher risk of forming true gallbladder polyps and, consequently, a higher probability of having GBC. These conclusions are in line with current and most recent studies, except for the part of the maximum dimension in which the dimension greater than or equal to 10 mm is considered the highest risk of malignancy.[2] In this study, the results obtained support the importance

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

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FA and EB: Contributed to the design, analysis, and writing of the manuscript and contributed to the final manuscript.
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FA e EB: Contribuíram para a conceção, análise, redação do manuscrito e contribuíram para o manuscrito final.
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