

GALLBLADDER POLYPS: HOW SHOULD THEY BE TREATED AND WHEN?

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ABSTRACT

OBJECTIVE. The objective of this study was to determine the correct therapeutic management for patients with gallbladder polyps (GPs), what type of surveillance should be employed and how to differentiate between benign and malignant polyps in addition to also providing reassurance in cases of “cancerophobia”. Study design: This was a 5-years retrospective study. Location: The study was conducted at a Surgery Department at the *Hospitais da Universidade de Coimbra*. Population: We analyzed all patients operated on at the Surgery Service II from January 2003 to December 2007 who had had a preoperative diagnosis of GP.

METHODS. Clinicopathological correlations were traced for all patients. The following were analyzed: demographic data, clinical presentation, principal symptoms, associated pathologies, supplementary tests and diagnoses.

RESULTS. We studied 93 patients, 91 of whom had benign polyps and two of whom had malignant polyps. Of the 91 benign polyps, 73 (78.5%) were cholesterol polyps, 14 (15%) were hyperplastic and two (2.2%) were adenomas. Two (2.2%) patients had malignant polyps, both adenogallbladder carcinomas. The mean diameter of benign polyps was 6 mm and 40 (43%) patients had multiple lesions. The mean diameter of malignant and premalignant polyps taken together was 18.8 mm, all were single polyps and the mean age of this patient subset was 57.7 years.

CONCLUSION. It was concluded that the surgical option for GPs is cholecystectomy and that this should only be undertaken in cases where there are clinical signs of GP; polyps with diameters greater than 10 mm; fast-growing polyps; sessile polyps or wide-based polyps; polyps with long pedicles; patient aged over 50; concurrent gallstones; polyps of the gallbladder infundibulum or abnormal gallbladder wall ultrasound.

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INTRODUCTION

Lesions that project from the gallbladder wall into the gallbladder interior are called gallbladder polyps (GPs).¹ Diagnosis of GP has increased greatly due to widespread use of abdominal ultrasound,¹ and is now a common motive for surgery consultations. In the majority of patients, diagnosis is an incidental finding of a routine abdominal ultrasound, or of one performed because of another pathology. Gallbladder polyps are diagnosed in around 5% of patients in the general population.³

Gallbladder polyps are classified as benign or malignant.¹⁻⁴

Benign GPs are subdivided into: pseudotumors (cholesterol polyps, inflammatory polyps; cholesterosis and hyperplasia); epithelial tumors (adenomas) and mesenchymatous tumors (fibroma, lipoma, hemangioma).^{2,3,5}

Malignant GPs are gallbladder carcinomas.²

Recent studies have shown that the majority of GPs are benign and that 90% of them are cholesterol polyps. These emerge because of cholesterol decompensation,¹ with accumulation of

cholesterol in histiocytes covered with columnar epithelium.⁵ They are normally attached to the vesicular mucosa by a delicate pedicle, are characteristically found in multiples (>3) and are small and the gallbladder mucosa is intact.³ They are often associated with vesicular cholesterosis and have no malignant potential whatsoever.

Vesicular cholesterosis is characterized by diffuse deposition of cholesterol and lipid esters in macrophages of the lamina propria, creating a surface of yellow papules, with a diameter of around 1 mm.²

Inflammatory polyps are uncommon. They are local epithelial proliferation inflammatory reactions with infiltration of inflammatory cells and are often associated with chronic cholecystitis.²

Although adenomas are benign polyps they can exhibit premalignant behavior.^{2,3} These lesions are habitually pedunculated single lesions and may be associated with gallstones or chronic cholecystitis. Some authors claim that many gallbladder carcinomas emerge from dysplastic epithelium, in a

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progression from adenoma to adenocarcinoma that is already known.^{4,5}

The poor prognosis of gallbladder carcinoma patients means it is important to differentiate between benign polyps and malignant or premalignant polyps, in order to choose the appropriate treatment.

The objective of this review was to determine the correct therapeutic approach for these patients and what type of surveillance is needed and also to provide reassurance in cases of "cancerophobia".

METHODS

This paper describes the results of a review of the international literature on the subject and a retrospective study of patients operated at the Surgery Service II at the *Hospitais da Universidade de Coimbra* (H.U.C).

A retrospective study was undertaken on all patients operated at the Surgery Service II from January 2003 to December 2007 and clinicopathological correlations with preoperative GP diagnoses were analyzed. Patients with GP who were not referred for surgical treatment were excluded. These patients' clinical files were reviewed and data was collated on demographics, clinical presentation, principle symptoms, associated pathologies, supplementary tests and diagnoses. Surgery, postoperative complications and 1-year postoperative follow-up were all analyzed.

The imaging exam chosen to investigate these patients was abdominal ultrasound, which has sensitivity and specificity greater than 90% for diagnosis of GPs, even where lesions have small dimensions.

RESULTS

During the study period, 95 patients with a preoperative diagnosis of GP were treated, but two patients were excluded from the study because clinical files were missing.

The patients studied had a mean age of 48.3 years (ages ranging from 21 to 69 years) and there were 31 men and 62 women at a ratio of 1:2.

The symptoms presented were as follows: 46 patients had dyspepsia, nine patients had epigastralgia, five patients had recurrent pain in the right hypochondrium, one had acute cholecystitis and 32 patients had not presented symptoms and GP had been diagnosed as a result of ultrasound findings. Thirty-three patients had an associated pathology.

All patients had abdominal ultrasound, 11 patients had serial ultrasound and three had abdominal CT (Computerized Axial Tomography). Patients who underwent abdominal CT did so for suspected gallbladder carcinoma. All patients had gallbladder polyps confirmed by anatomopathological study. Abdominal ultrasound achieved 100% sensitivity for diagnosis of gallbladder polyps in our patients. Twelve patients also had concomitant gallstones, which were only diagnosed with preoperative ultrasound in 10 cases.

Laparoscopic cholecystectomy was performed on 86 patients and classical cholecystectomy on six patients, while one patient underwent classical cholecystectomy with segmentectomy IV and Va with lymphadenectomy of the hepatic hilum.

All surgical specimens were sent for anatomopathological study and it was found that 91 patients had benign polyps and two patients had malignant polyps. Of the 91 benign polyps, 73 (78.5%) were cholesterol polyps, 14 (15%) were hyperplasia and two (2.2%) were adenomas. Two (2.2%) patients had malignant polyps, which were gallbladder adenocarcinomas. The mean diameter of the benign polyps was 6 mm, the mean age of these patients was 48.2 years and 40 (43%) patients had multiple lesions. The mean diameter of the malignant polyps was 21.5 mm, all were single lesions and the mean age of these patients was 58.5 years.

Analyzing the malignant and premalignant (adenomas) polyps together, the mean diameter was 18.8 mm, all were single lesions and mean age was 57.7 years, (Tables I and II).

In this study none of the malignant or premalignant lesions were smaller than 10 mm and the only patient who was not over 50 was 49 years old.

	<10 mm	>10 mm
Benign polyps	79	10
Malignant and premalignant polyps	0	4
	<50 Years	>50 Years
Benign polyps	48	40
Malignant and premalignant polyps	1	3

Postoperative morbidity was 4.3%; two patients (2.2%) had superficial infections of the surgical wound and two patients (2.2%) had diarrhea. Mortality was zero.

When the patients' preoperative clinical status was compared with their postoperative status, during 1-year follow-up, it was found that 78 patients (83.9%) still had the same complaints and had obtained no clinical benefit from surgery.

DISCUSSION

Gallbladder polyps are nowadays the most common surgical vesicular pathology and are found during routine abdominal ultrasound with ever-growing frequency. Many studies have been conducted into the prevalence in the general population, with figures ranging from 4.6% to 6.9%.^{5,6}

In this study, prevalence was greater among women than among men, in contrast with the majority of publications in which the ratio is the inverse, being more prevalent in men.⁵

The majority of patients are asymptomatic; in our series 34.4% did not present any clinical sign and 49.5% of the patients only presented dyspepsia. Clinically, GPs may cause some patients to suffer nausea, vomiting and occasional pain in the right hypochondrium, due to intermittent obstructions caused by small fragments of cholesterol that become detached from the gallbladder mucosa. There are descriptions of polyps that protrude greatly obstructing the cystic canal or the primary biliary ducts, causing acute cholecystitis or obstructive jaundice, but these are very rare complications.⁵

Abdominal ultrasound is the ideal exam for diagnosing GPs, not only because of its accessibility and low cost, but also because of its elevated sensitivity and specificity, respectively 93% and 95.8%.^{1,3,4,5} The polyps can be located, counted and measured with ultrasound, and the three layers of the gallbladder wall and any abnormalities can be viewed. The sensitivity of abdominal ultrasound for diagnosis of GP is superior to both oral cholecystography and CT. Experienced imaging specialists can use ultrasound to distinguish a cholesterol polyp from an adenoma or an adenocarcinoma. A cholesterol polyp shows as a mass with similar echogenicity to the gallbladder wall and with no shadow cone.^{4,5,7,8,9} However, the distinction is difficult to make, and the status of polyps as benign or malignant cannot be determined with abdominal ultrasound alone. Intravenous cholecystography is a safe technique, but gallbladder polyps do not become sufficiently opaque.⁷ Abdominal CT is incapable of detecting low density lesions and its sensitivity for diagnosis of GPs is between 44% and 77%. It is useful for studying gallbladder carcinoma, anatomic correlations and for investigating metastases of the ganglia.^{1,7} Retrograde endoscopic cholangiography and percutaneous transhepatic cholangiography allow the biliary anatomy to be observed and its pathologies identified, but they are both invasive procedures associated with complications.

All of the studies published in the international literature are designed to identify discriminatory factors that allow benign polyps to be differentiated from malignant ones; namely the size of the polyp, growth rate and pedicle, in addition to gallbladder wall abnormalities.²

The relationship between adenoma and adenocarcinoma, which has already been described and confirmed by several authors, is proportional to the size and growth of the lesion in question; adenomas are smaller than 12 mm, *in situ* adenocarcinomas are from 12 mm to 30 mm and invasive adenocarcinomas are larger than 30 mm.⁵

The majority of polyps are benign, are composed of cholesterol and have no potential for malignancy whatsoever.¹ Comparative studies have concluded that 94% of benign lesions are smaller than 10 mm and 88% of malignant lesions are larger than 10 mm.^{5,6}

The treatment for gallbladder polyps is planned cholecystectomy, which, despite its low morbidity and mortality at specialized centers, is always an invasive approach and should only be performed when there is a demonstrable benefit for the patient.

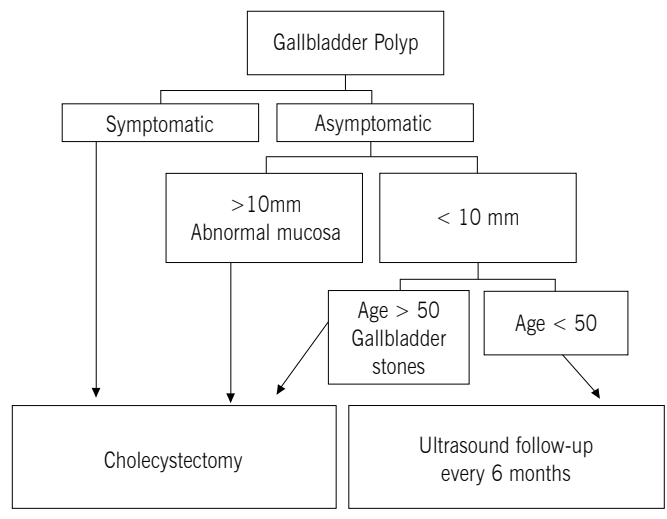
The poor prognosis of patients with gallbladder carcinomas, with mean life expectancy of less than 6 months for those whose lesions cannot be completely excised, means that a GP with a diameter greater than 10 mm, gallbladder wall abnormalities or a rapidly growing GP are indications for cholecystectomy.¹⁻⁵

Longitudinal follow-up studies show that small lesions (<10 mm) that are monitored with imaging technology have a low incidence of carcinoma³ and over a 5-year follow-up period no morphological abnormalities, in terms of the size of polyps, were observed in around 88% of patients.^{5,8,10,11}

Malignant GPs are significantly more common in patients aged over 50 and are single lesions of a sessile nature with a diameter of more than 10 mm.^{1,2,3,6} This is borne-out by the results from our patient series, where the odds ratio was 3.6. The small size of our patient sample meant that Fisher's exact test did not detect significant differences.

It can be concluded that the surgical treatment option for GPs is cholecystectomy and that this should only be undertaken when the following conditions are true: clinical signs of GP; polyps with diameters greater than 10 mm; fast-growing polyps; sessile polyps or wide-based polyps; polyps with long pedicles; patient aged over 50; concurrent gallstones; polyps of the gallbladder infundibulum or abnormal gallbladder wall ultrasound findings. (Figure 1).

Figure 1 - Summary of gallbladder polyp management³



Young patients with polyps smaller than 10 mm, who are asymptomatic or have dyspeptic complaints only, do not need any treatment other than clinical follow-up with ultrasound every six months.

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