

ORIGINAL ARTICLE

Treatment and surveillance of polypoid lesions of the gallbladder in the United Kingdom

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Abstract

Objectives: The increase in the routine use of abdominal imaging has led to a parallel surge in the identification of polypoid lesions in the gallbladder. True gallbladder polyps (GBP) have malignant potential and surgery can prevent or treat early gallbladder cancer. In an era of constraint on health care resources, it is important to ensure that surgery is offered only to patients who have appropriate indications. The aim of this study was to assess treatment and surveillance policies for GBP among hepatobiliary and upper gastrointestinal tract surgeons in the UK in the light of published evidence.

Methods: A questionnaire on the management of GBP was devised and sent to consultant surgeon members of the Association of Upper Gastrointestinal Surgeons (AUGIS) of Great Britain and Ireland with the approval of the AUGIS Committee. It included eight questions on indications for laparoscopic cholecystectomy and surveillance based on GBP (size, number, growth rate) and patient (age, comorbidities, ethnicity) characteristics.

Results: A total of 79 completed questionnaires were returned. The vast majority of surgeons (>75%) stated that they would perform surgery when a single GBP reached 10 mm in size. However, there was a lack of uniformity in the management of multiple polyps and polyp growth rate, with different surveillance protocols for patients treated conservatively.

Conclusions: Gallbladder polyps are a relatively common finding on abdominal ultrasound scans. The survey showed considerable heterogeneity among surgeons regarding treatment and surveillance protocols. Although no randomized controlled trials exist, national guidelines would facilitate standardization, the formulation of an appropriate algorithm and appropriate use of resources.

Keywords

gallbladder polyps, laparoscopic cholecystectomy, gallbladder cancer, polypoid lesions of the gallbladder, polyp growth rate, adenomatous polyp

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Introduction

Polypoid lesions of the gallbladder (PLG) are reported increasingly as a result of the wider use of abdominal ultrasound (US) and do not represent a rare finding in general and subspecialty clinics. Estimated prevalences of PLG vary, but they are generally considered to occur in around 5% of the population in the

Western world.¹ The majority of PLG are benign, and cholesterol polyps, adenomyomatosis and inflammatory polyps are the most common aetiologies. A small minority (5%) of PLG are 'true' adenomatous gallbladder polyps (GBP) with malignant potential.² It is estimated that 3–8% of GBP are malignant³ and that of adenomatous polyps measuring > 10 mm, about 50% will harbour cancerous cells.^{4,5} In the UK, approximately 50 000 laparoscopic cholecystectomies (LCs) are performed each year, of which 800–4000 are estimated to be for GBP.^{6–8} Currently, cholecystectomy is usually considered appropriate for large polyps (>10 mm), based on the assumption that the risk for malignant

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transformation rises steeply in polyps measuring >10 mm. However, some studies have shown that, although uncommon, malignant polyps can be smaller in size, especially in the Asian population.⁹ Age, number of polyps and growth rate are less clear indications for surgery. Gallbladder polyps that arise in a context of primary sclerosing cholangitis (PSC) are considered to carry a higher risk for malignancy and thus cholecystectomy is advocated even for GBP of <10 mm.¹⁰ No conclusive data are available regarding surveillance protocols for GBP that are not removed because the natural history of incidentally found GBP is still uncertain and the lack of randomized controlled trials (RCTs) does not help the surgeon's decision-making process. In January 2010, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) updated its guidelines on the clinical application of laparoscopic biliary tract surgery and concluded that: 'the management of gallbladder polyps remains controversial. A reasonable approach would include laparoscopic cholecystectomy for larger, especially single, polyps or those with associated symptoms with watchful waiting for small (<5 mm) asymptomatic polyps (Level II grade B evidence).'¹¹

The aim of this study was to evaluate current treatment and surveillance strategies for GBP among hepatobiliary and upper gastrointestinal (GI) tract surgeons in the UK and Ireland and to discuss these in the light of the published literature.

Materials and methods

A questionnaire containing multiple-choice items on the management of GBP was devised and sent by e-mail to consultant surgeon members of the Association of Upper Gastrointestinal Surgeons (AUGIS) of Great Britain and Ireland with the approval of the AUGIS Committee. The e-mail included a link to a survey website (<http://www.surveymonkey.com>). Responses to the questionnaire were collected anonymously. The survey required only one answer to each question and included no open questions. The survey focused on: (i) indications for treatment; (ii) surveillance protocols for patients who fall outside criteria for surgery, and (iii) patient selection.

Items related to the following questions:

- 1 When would LC be considered for a single GBP according to size?
- 2 When would LC be considered for multiple GBP according to the size of the larger polyps?
- 3 What growth rate of polyps between surveillance US scans would prompt the surgeon to consider LC?
- 4 When would LC be considered in relation to an increase in the number of polyps on surveillance US?
- 5 What is the protocol for the follow-up of patients who do not match criteria for surgery?
- 6 Which patients would be considered for surgery according to ASA (American Society of Anesthesiologists) grade?

Table 1 When would laparoscopic cholecystectomy be considered for a single gallbladder polyp according to size?

Answer options	Responses, n (%)
One polyp measuring ≥ 12 mm on ultrasound	0
One polyp measuring ≥ 10 mm on ultrasound	60 (75.9%)
One polyp measuring ≥ 8 mm on ultrasound	4 (5.1%)
One polyp measuring ≥ 5 mm on ultrasound	8 (10.1%)
One polyp of any dimension	4 (5.1%)
Only when associated with gallstones (asymptomatic)	0
Only when associated with biliary symptoms	3 (3.8%)
Never recommend cholecystectomy	0

7 Which patients according to age would be considered for surgery (assuming there are no medical or anaesthetic contraindications)?

8 Is the threshold for surgery for asymptomatic solitary or multiple polyps influenced by ethnicity?

Results and discussion

A total of 402 e-mails were sent to consultant surgeon members of AUGIS and 79 completed questionnaires were returned (19.7% response rate).

Gallbladder polyps are generally thought to be asymptomatic and indeed are commonly described as incidental findings on radiological imaging. A smaller proportion of patients may be symptomatic with typical biliary symptoms, but GBP are often associated with gallstones, which makes it difficult to establish whether they are responsible for the reported symptomatology.^{12,13} There is general agreement that small (<10 mm) symptomatic polyps should be removed.¹⁴ Gallbladder cancer (GBC) is a relatively rare neoplasm in the UK, but cumulative 5-year survival rates are only 5–10% and the removal of premalignant lesions in a relatively minor surgical operation is appealing.¹⁵ However, although LC is well established and is considered a 'safe' surgical procedure that can be performed in a day case context in the majority of patients, complications can still arise and the appropriateness of surgical indications is paramount when resources are limited.

Question 1: when would LC be considered in single GBP?

A total of 75.9% of surgeons agreed that 10 mm is regarded as the size threshold for surgery for a single polyp, although 20.2% of responders said they would consider surgery for smaller polyps (Table 1). There is a general consensus that solitary polyps of >10 mm are an indication for LC as a result of the increased risk for malignancy. It is considered that 45–67% of GBP of >10 mm are malignant.^{5,7,8,13,16} Koga *et al.* reviewed 411 patients who underwent cholecystectomy and found that of 40 GBP, eight were adenocarcinomas.⁴ Seven of eight (87.5%) cancers and two of

32 (6.3%) GBP measured >10 mm, and seven of nine (77.8%) polypoid lesions measuring >10 mm were malignant.⁴ Other studies recommend LC for polyps of <10 mm in size when there are symptoms or concomitant presumed risk factors for cancer such as age >50 years or gallstones.^{13,17,18} Ito *et al.* studied a cohort of 417 patients with PLG detected on US and concluded that small PLG (<10 mm) can safely be observed and that PLG of <6 mm in size on US rarely represent true adenomas.¹² Although a plethora of data suggest that 10 mm should be considered as a cut-off size for LC, other studies recommend caution. A recent retrospective study of 130 patients in the Mayo Clinic reported an incidence of 7.4% of neoplasia in polyps of <10 mm.¹⁹ Polyp size of >6 mm, local invasion and vascularity on US and history of PSC were considered significant risk factors for malignancy.¹⁹ Shinkai *et al.* observed in a cohort of 74 patients that 6% of adenomas/carcinomas occurred in polyps of <5 mm.²⁰ Roa *et al.* analysed pathological features of 219 GBP post-LC in a Chilean population and found 15% to be adenomas and >67% of adenomatous polyps to measure <10 mm; adenomas with malignant degeneration were <5 mm in two of eight patients with underlying carcinoma.²¹ Thus, it is clear that larger polyps are likely to harbour neoplastic tissue, but neoplasia cannot be confidently excluded in smaller polyps. Similarly, Park *et al.*³ studied a cohort of 1558 patients and found that in 45.5% of cancerous polyps (15/33), the size of the GBP at diagnosis was <10 mm; these authors suggested that the size-related threshold should be lowered to 8 mm, although this would improve US sensitivity by only 9% and decrease specificity by 8%. Park and colleagues concluded that even small polyps carry a risk for malignancy and longterm follow-up of GBP would help to detect and treat early GBC.³ Although endoscopic US has been shown to improve diagnostic accuracy (benign vs. malignant) by up to 97% in the diagnosis of smaller PLG, this approach is logistically and economically impractical.²² On the basis of the reported literature, although the risk for malignant transformation appears to be very low for polyps of <10 mm, it is the present authors' opinion that it would not seem unreasonable to consider lowering the size threshold for LC to <10 mm, although no clear cut-off can be recommended.

Question 2: when would LC be considered in multiple GBP?

In multiple GBP, 50.6% of responding surgeons would consider LC when at least one of the polyps reaches 10 mm, and 34.1% of surgeons would recommend LC even when the largest lesion measures <10 mm (Table 2). There is less clarity regarding the treatment of multiple GBP.²⁰ The number of lesions is unreliable in determining the likelihood of gallbladder neoplasm. Cholesterol polyps and adenomyomatosis tend to be multiple, whereas adenomatous polyps are often solitary.²⁰ Yang and colleagues analysed 172 histologically proven PLG after cholecystectomy; malignant lesions were seen in 7.6% ($n = 13$) of post-cholecystectomy specimens, and all of them were >10 mm in

Table 2 When would laparoscopic cholecystectomy be considered for multiple gallbladder polyps?

Answer options	Responses, n (%)
Multiple polyps, the largest measuring ≥ 12 mm on ultrasound	1 (1.3%)
Multiple polyps, the largest measuring ≥ 10 mm on ultrasound	40 (50.6%)
Multiple polyps, the largest measuring ≥ 8 mm on ultrasound	5 (6.3%)
Multiple polyps, the largest measuring ≥ 5 mm on ultrasound	11 (13.9%)
Multiple polyps of any dimension	11 (13.9%)
Only when associated with gallstones (asymptomatic)	0
Only when associated with biliary symptoms	10 (12.7%)
Never	1 (1.3%)

Table 3 What growth rate of polyps between surveillance ultrasounds would prompt the surgeon to consider a laparoscopic cholecystectomy?

Answer options	Responses, n (%)
≥ 1 mm	5 (6.3%)
≥ 2 mm	11 (13.9%)
≥ 5 mm	22 (28%)
None unless the polyp reaches the 'critical size'	41 (51.8%)

size and were solitary.¹⁷ Shinkai *et al.* found that neoplastic polyps tended to be single (adenoma, mean number of polyps 1.40 ± 0.89 ; cancer, mean number of polyps 1.16 ± 0.40), whereas half of cholesterol-related polyps were multiple (mean number of polyps 3.09 ± 3.31).²⁰ However, when there were fewer than three lesions, neoplasm was found in 37% of polyps measuring 5–10 mm in diameter, prompting these authors to recommend an aggressive surgical approach for small GBP numbering fewer than three, regardless of size.²⁰

Question 3: what growth rate of polyps prompts consideration of LC?

A total of 48.2% of responding surgeons said they would perform LC for any growth, whereas 51.8% would consider surgery only when the polyp reaches the threshold for single polyp size (more commonly 10 mm) (Table 3). Many studies have attempted to clarify the natural history of GBP and reported growth rates are extremely variable. Ito and colleagues¹² retrospectively analysed 417 patients with GBP detected on abdominal US. In patients who were monitored with serial abdominal US, 86% of polyps did not change in size and 6% grew in size. Shin and colleagues²³ retrospectively reviewed 145 patients who eventually underwent cholecystectomy. They found that a growth rate of <6 mm/month had

Table 4 When would laparoscopic cholecystectomy be considered in relation to an increase in the number of polyps on surveillance ultrasound?

Answer options	Responses, n (%)
For any increase	18 (22.8%)
Only for an increase of three or more	8 (10.1%)
Only for an increase of five or more	10 (12.6%)
Never	43 (54.4%)

a negative predictive value of >90%. However, on multivariate analysis the growth rate was not associated with malignancy, regardless of polyp size. Thus, the investigators concluded that GBP of <10 mm do not need to be removed simply because they grow.²³ Colecchia and colleagues²⁴ prospectively followed 56 patients with small GBP (<10 mm) over 5 years with annual abdominal US. No patients developed any clinical symptoms, and no changes in polyp morphology were observed, suggesting that the natural history of small GBP is benign. Csendes *et al.*²⁵ studied 111 patients with PLG measuring <10 mm, of whom 80% had PLG of <5 mm in size and 74% had single polyps. Thirteen patients underwent cholecystectomy at their own request, and 14 patients in whom an increase in the number or size of PLG was found on follow-up also underwent cholecystectomy.²⁵ The remaining patients who did not undergo surgery were followed for a mean of 71 months. In the non-operative patients, PLG remained static in size in 50.0% of patients, increased in size or number in 26.5%, and shrank or disappeared in 23.5%. In the patients who underwent surgery, no GBC was found. The authors concluded that PLG of <10 mm did not progress to malignancy.²⁵ However, Park *et al.*³ analysed over 1500 patients with a median follow-up of 37 months and demonstrated invasive cancer in GBP that grew from an original size of <10 mm ($n = 15/33$). It is not possible to find in the literature any specific growth rate suggestive of increased risk for malignancy.

Question 4: what increase in polyp numbers prompts consideration of LC?

Answers to this item reflected a lack of consensus: 45.6% of respondents recommended LC when an increase in the number of polyps is detected (22.8% for any increase; 22.7% when three to five more polyps were identified), whereas 54.5% stated they would never recommend cholecystectomy (Table 4). The number of polyps may increase or decrease between interval scans, but no specific data on the likelihood of neoplasm have been reported in this setting.

Question 5: what is the protocol for patients outwith criteria for surgery?

Overall, 57.9% of surgeons said they would suggest US surveillance at intervals of 6 months to 1 year for a maximum of 5 years if there were no change in GBP features, whereas 15.7% would continue surveillance for life (Table 5). A total of 10.5% would not

Table 5 What is the protocol for the follow-up of patients who do not match the criteria for surgery? (total answers to question 5 – $n = 76$)

Answer options	Responses, n (%)
US every 6 months for life or until the polyp/polyps reaches a critical size	3 (3.9%)
US every year for life or until the polyp/polyps reaches a critical size	9 (11.8%)
US every 6 months for 2–5 years and then stop; there should not be any significant variation in size (± 1 mm) or number	13 (17.1%)
US every year for 2–5 years then stop; there should not be any significant variation in size (± 1 mm) or number	31 (40.8%)
Never follow up	8 (10.5%)
Other	12 (15.8%)

US, ultrasound.

suggest any follow-up and another 15.8% suggested variable protocols, mostly including surveillance for up to 1 year if there were no change in findings. This item probably represents the most controversial issue as there is no agreement in the literature on what might constitute an appropriate surveillance programme. The majority of studies recommend 6-monthly US studies in the first instance and suggest that, if there is no change after 1 year, the frequency of examination should be determined on a case-by-case basis in relation to risk factors.^{3,24,26,27} Other studies suggest initial 3-monthly scans with the purpose of identifying rapidly growing polyps,^{28,29} and a recent retrospective series did not recommend further surveillance for polyps of <6 mm and reported inconclusive data for polyps of >7 mm.³⁰ Several studies have followed low-risk lesions for ≤ 15 years without reporting any marked change in the size of lesions or the development of GBC.^{31,32} Rapid growth can, however, be missed in intervals as short as 4 months.⁵ The length of follow-up is also unclear and some authors have suggested that ongoing surveillance should be continued for as long as 10 years.²⁷

Question 6: which patients should be considered for surgery based on ASA grade?

There is little in the literature about patient selection once an LC is recommended, but it is interesting to note that when contemplating surgery, the majority of responding surgeons would recommend LC to all patients unless there were an absolute anaesthetic contraindication, but 13.0% would consider LC only in patients with ASA grades of 1 or 2 (Table 6).

Question 7: which patients should be considered for surgery based on age?

A total of 54.5% of responding surgeons said they would consider all patients for LC regardless of age if they met the criteria for LC (assuming there were no absolute contraindications), but 29.9% would exclude patients aged >80 years and 14.3% would exclude patients aged >70 years (Table 7). Polyps in elderly patients (aged

Table 6 Which patients would be considered for surgery according to ASA (American Society of Anesthesiologists) grade? (total answers to question 6 – $n = 77$)

Answer options	Responses, n (%)
All patients unless an absolute anaesthetic contraindication	49 (63.6%)
Only patients with ASA grades of 1–3	18 (23.4%)
Only patients with ASA grades of 1 or 2	10 (13.0%)

Table 7 Which patients according to age would be considered for surgery (assuming there are no medical or anaesthetic contraindications)? (total answers to question 7 – $n = 77$)

Answer options	Responses, n (%)
All patients regardless of age	42 (54.5%)
Only patients aged <80 years	23 (29.9%)
Only patients aged <70 years	11 (14.3%)
Only patients aged <65 years	1 (1.3%)
Only patients aged >50 years	0

Table 8 Is the threshold for surgery for asymptomatic solitary or multiple polyps influenced by ethnicity?

Answer options	Responses, n (%)
Yes	8 (10.1%)
No	71 (89.9%)

>50 years or >60 years, depending on the study considered) are more likely to be neoplastic in nature, perhaps as a result of the protracted presence of GBP or increased mutagenesis.^{4,13,17}

Question 8: is consideration for surgery influenced by ethnicity?

Overall, 89.9% of surgeons said they would not change their approach to GBP treatment according to the patient's ethnicity (Table 8). It is, however, well established that some non-White populations, most notably Indian and Chilean groups, are at increased risk for GBC.³³ A study among UK Indian patients who underwent abdominal US ($n = 1169$) showed that the incidence of cancer in GBP in such a population could potentially be higher than in the White population.⁹ Findings showed two cases of GBC in 36 (5.6%) Indian patients with GBP, compared with two cases of GBC in 2228 (0.09%) White GBP patients ($P < 0.001$). Of subjects with a single GBP, regardless of its size, Indian patients seem to have a risk for developing GBC of one in 13 (7.7%), whereas White patients have an equivalent risk of one in 670 (0.15%). Although the study included a very small number of cancers, the results might suggest that the size threshold for LC should be lowered for single GBP in this patient subgroup.⁹

Conclusions

The treatment and surveillance of GBP are still controversial as a result of the lack of specific guidelines and RCTs. Gurusamy

and colleagues³⁴ emphasized the difficulties inherent in organizing such a study that arise from the need to blind operators, the long follow-up period required, the high likelihood of drop-out, and the need to manage growing polyps and new-onset biliary pain in the control cohort. The present survey, although it targeted only surgeon members of a specific association, who certainly represent only a small sample of those engaged in this area of practice in the UK, indicates that the majority of surgeons would recommend LC for a single polyp that reaches 10 mm in size. Generally, the presence of multiple polyps *per se* is not considered an indication for surgery; 51.8% of respondents did not consider that growth rate necessarily mandates LC unless the polyp achieves the appropriate size (usually 10 mm), and 54.5% would not recommend LC when the number of polyps increased between scans. Surveillance protocols differ, but 73.6% of surgeons would agree to ongoing surveillance for ≥ 5 years. The majority of surgeons would consider surgery in all patients regardless of age, assuming there were no anaesthetic contraindications, but only a minority are influenced by the patient's ethnicity.

In the absence of RCTs, the provision of national guidelines might help to reduce heterogeneity and standardize treatment and surveillance of patients with GBP.

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Conflicts of interest

None declared.

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