

ORIGINAL ARTICLE

Clinical relevance of gallbladder polyps; is cholecystectomy always necessary?

Madelon J.H. Metman^{1,*}, Pim B. Olthof^{1,2,3,*}, Johannes B.C. van der Wal¹, Thomas M. van Gulik², Daphne Roos¹ & Jan Willem T. Dekker¹

¹Department of Surgery, Reinier de Graaf Gasthuis, Delft, ²Department of Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam, and ³Department of Surgery, Erasmus Medical Center, Rotterdam, the Netherlands

Abstract

Background: Gallbladder polyps are common incidental findings during abdominal ultrasonography. Cholecystectomy is recommended for polyps equal or greater than 10 mm on ultrasound due to their malignant potential. However, the majority of lesions appear to be pseudopolyps with no malignant potential. Our aim was to determine the correlation between ultrasonographic findings and histopathological findings after cholecystectomy for gallbladder polyps in two institutions.

Method: A retrospective analysis was performed at two Dutch institutions of patients who underwent cholecystectomy. All cholecystectomies for suspected gallbladder polyps between January 2010 and August 2017 were included. Ultrasonographic and histopathological reports were analyzed.

Results: A total of 108 patients underwent cholecystectomy for gallbladder polyps. At abdominal ultrasound sixty-five patients (60.2%) were diagnosed with multiple gallbladder polyps. The mean diameter of the polyps was 11 mm. On pathological examination after cholecystectomy, only three specimens harbored true polyps. No anomalies were found in 48 (44%) patients and 51 (47%) had cholesterosis.

Conclusion: The prevalence of true gallbladder polyps was much lower in this study than reported in literature. After cholecystectomy for gallbladder polyps diagnosed by ultrasound, 97% of patients had non-neoplastic or not identifiable lesions in the gallbladder. These findings question the usefulness of current guidelines for management of suspected gallbladder polyps.

Received 7 May 2019; accepted 9 August 2019

Correspondence

M.J.H. Metman, Reinier de Graaf Gasthuis, Department of Surgery, Reinier de Graafweg 5, 2625 AD, Delft, the Netherlands. E-mail: mmetman@gmail.com

Introduction

Gallbladder polyps are elevated lesions of the gallbladder wall projecting into the lumen and are a common incidental finding during ultrasonography of the abdomen with a prevalence estimated between 0.3 and 9.5%.^{1–5} After cholecystectomy, polyps are found in 0.004–13.8% of the specimens.⁶

The majority of gallbladder polyps are benign pseudopolyps caused by cholesterol depositions, focal adenomyomatosis or hyperplastic lesions secondary to a local infection.⁷ Approximately 30% of suspected polyps are reported to be true adenomatous gallbladder polyps which have malignant potential.^{8,9} Due to its rapid and silent progression, gallbladder carcinoma is rarely resectable when diagnosed and prognosis is generally poor with a five-year survival rate less than 5%.⁹ Thus,

cholecystectomy performed for gallbladder polyps with a malignant potential is considered beneficial in preventing more invasive disease.

Current Dutch guidelines recommend cholecystectomy for gallbladder polyps equal to or larger than 10 mm based on abdominal ultrasound. In patients with primary sclerosing cholangitis (PSC) the risk of malignant transformation is increased and cholecystectomy is recommended for polyps equal or greater than 5 mm.¹⁰ Data from other studies suggest that age,¹¹ Indian ethnicity¹² and sessile gallbladder polyps¹³ are other risk factors for malignant potential. Up to now, these risk factors are not included in the Dutch guideline in contrast to the European guidelines.¹⁴

The yield of true gallbladder polyps at pathology examination in patients with suspected gallbladder polyps is however limited and not rarely, no lesions are found at all. The aim of this study was to determine the correlation between ultrasonographic

* Shared authorship.

findings and histopathological findings after cholecystectomy for suspected gallbladder polyps.

Methods

All consecutive patients who underwent cholecystectomy for gallbladder polyps at the University Medical Center Amsterdam, location AMC and the large community hospital the Reinier de Graaf Gasthuis between January 2010 and August 2017 were included. All cholecystectomies were reviewed from the hospitals' operation registration records to identify patients who underwent cholecystectomy for gallbladder polyps. The indications to perform cholecystectomy were gallbladder polyps of at least 10 mm or increasing in size during surveillance in accordance with the Dutch guidelines (Table 1). Patients with a history of primary sclerosing cholangitis were excluded from the analyses due to their increased risk of malignant transformation.¹⁵

Clinical parameters

Patient characteristics, radiology reports, and pathology reports were collected from the electronic medical records. Ultrasonography outcomes were scored according to the radiology report describing the size and number of the polyps. The number of abdominal ultrasounds per patient during surveillance was recorded. Furthermore, the indication for cholecystectomy after surveillance was obtained. If other imaging studies were performed, the presence of the gallbladder polyp was scored as reported in the radiology report.

During the study period, all gallbladder specimens underwent pathological examinations at the department of Pathology at the respective institution as part of standard clinical practice. Specimens were analysed according to the standard protocol. A representative part of the wall and a cross-section of the neck of the gallbladder were prepared for microscopy, as were sections through macroscopically abnormal lesions (e.g., polyps). The macro- and microscopic outcomes were obtained as reported by the pathologist in pathology reports.

All adverse events within 30 days after surgery were scored and graded according to Dindo *et al.*¹⁶

Results

During the study period, a total of 3547 patients underwent cholecystectomy in both centres. In 110 patients the primary

Table 1 Recommendations on the management of gallbladder polyps according to the Dutch guideline

Gallbladder polyp size	Recommendation
≤5 mm	No follow up
5–10 mm	Follow-up
>10 mm	Cholecystectomy

indication for cholecystectomy were suspected gallbladder polyps. Two of these patients were previously diagnosed with PSC and were excluded from the analyses. Baseline characteristics of the included patients are provided in Table 2.

The majority of patients (60%) were diagnosed with multiple polyps at ultrasonography, with a median diameter of 10^{7–11} mm. 54 patients initially underwent follow-up before proceeding to cholecystectomy. The reason to proceed to surgery was mostly growth of polyps during follow-up as suggested in the national guideline (Table 3).

In the majority of gallbladder specimens (65%) the pathologist did not observe any macroscopic abnormalities. Macroscopic polyp-like lesions were identified in 22 (20%) specimens, while the other specimens showed cholesterosis or irregular aspects of the gallbladder wall (Table 4). The microscopic findings are presented in Table 4. In total, three pyloric gland adenomas were found, whereas in all other specimens only benign findings without malignant potential were found. Two were diagnosed in the 19 patients from Amsterdam and the other one in a patient from Delft. None of these pyloric gland adenomas showed dysplasia or any signs of malignant transformation. Out of the 22 polyps observed at macroscopy, two were confirmed as pyloric gland adenomas, while the others were cholesterosis. The third pyloric gland adenoma was classified as an irregular aspect of the gallbladder wall at macroscopy.

Out of the 108 patients, three experienced adverse events of which three were graded Dindo IIIa or higher. One patient developed sepsis secondary to biliary leakage, one patient was operated for an incarcerated trocar hernia and the third patient was readmitted for percutaneous drainage of a biloma.

Table 2 Baseline characteristics

Baseline	N = 108
Hospital, n (%)	
- Amsterdam UMC	89 (82)
- Reinier de Graaf Gasthuis	19 (18)
Age, years, median (IQR)	
	56.0 (47–66)
Female gender, n (%)	
	63 (58)
ASA classification, n (%)	
- I	31 (29)
- II	63 (58)
- III	14 (13)
Polyps, n (%)	
- single	39 (36)
- multiple	65 (60)
Diameter, mm, median (IQR)	
	10 (7–11)
Diameter, n (%)	
- <5 mm	5 (6)
- 5–9 mm	38 (43)
- ≥10 mm	46 (52)

Table 3 Indication for surgery after surveillance

Follow-up	N = 54
Indication for surgery after surveillance, n (%)	
- Growth	35 (57)
- Symptomatic gallstones	11 (20)
- Multidisciplinary consultation team	2 (4)
- Patient request	2 (4)
- CA 19.9 increase	1 (2)
- NA*	3 (7)

Discussion

The present study demonstrated that in 108 patients who underwent cholecystectomy for suspected gallbladder polyps, only 3 patients had a pyloric gland adenoma without signs of malignant transformation. All other patients had no or benign anomalies at pathology without risk of malignant potential, primarily cholesterosis.

The reported prevalence of gallbladder polyps on ultrasound imaging ranges from 0.32 to 9.5, most likely due to differences in the method of patient selection in the individual studies, as well as regional differences.^{2-4,17,18} Most studies that examined the pathology results of gallbladder specimens resected for gallbladder polyps report that the majority represents pseudopolyps with no malignant potential such as cholesterosis or inflammatory polyps. Neoplastic polyps include adenoma and gallbladder carcinoma and represent 6–24% of findings in gallbladder specimens resected for suspected polyps.¹⁹

In the current study three neoplastic polyps were found among 108 specimens resected for suspected polyps, all of which were pyloric gland adenomas. The pyloric histological classification is the most common among gallbladder polyps. The exact risk of malignant transformation is unknown; in a series of 165 polyps of the pyloric subtype, 44 (27%) had high grade dysplasia or carcinoma in situ and only 2 (1%) harbored true adenocarcinoma.²⁰ Interestingly, in 48 specimens no anomalies were found at all and 51 specimens had cholesterosis as only anomaly. The 97% non-neoplastic and normal gallbladders question the current rationale for resection of these suspected gallbladder polyps. The three adenomas result in a number needed to resect of 36, in order to find one neoplastic lesion.

Ultrasound is the primary imaging modality for diagnosing gallbladder polyps, however, characterization is often difficult. Cholesterol polyps are usually multiple small echogenic non-shadowing smooth polyps adherent to the wall.²¹ True polyps tend to be single larger lesions, may show vascularity and are less echogenic. Other imaging techniques do not have a place in routine clinical practice, however, contrast-enhanced or endoscopic ultrasound might improve diagnostic accuracy, at the cost of their own distinct disadvantages, mostly invasiveness and costs.^{22,23} Also Magnetic Resonance Imaging (MRI) was shown to have some value in discriminating benign from malignant

polypoid gallbladder lesions.²⁴ However, the role of MRI in differentiating true polyps from pseudopolyps is less currently unknown.

Most guidelines recommend to consider cholecystectomy for polyps of 10 mm or larger, and for smaller but growing polyps. In the current cohort, 28 patients were scheduled for cholecystectomy for polyps <10 mm without initial follow-up, mostly at the patients' request. An additional 5 patients had initial follow-up and were later scheduled for cholecystectomy without growth of the polyp, symptoms, or any other clear reason other than the patients' request. Although the presence of a gallbladder polyp might put some patients under psychological stress and be perceived as a 'time bomb', none of the 33 had a true gallbladder polyp and adherence to the guideline might improve the polyp yield at pathology, or rather reduce unnecessary cholecystectomies.

A patient with a gallbladder polyp at ultrasound poses a difficult clinical problem. Imaging studies are not sufficiently accurate to differentiate between types of polyps and known risk factors for malignant potential are difficult to translate to an

Table 4 Post-surgical complications and histological findings

	N = 108
Morbidity, any, n (%)	4 (4)
Morbidity, Dindo IIIa or higher, n (%)	3 (3)
Gallstones, n (%)	43 (40)
Malignancy, n (%)	0 (0)
Chronic inflammation, n (%)	57 (53)
Macroscopic anomalies, n (%)	
- None	70 (65)
- Cholesterosis	8 (7)
- Irregular aspect gallbladderwall	8 (7)
- Polyp	22 (20)
Microscopic findings, n (%)	
- None	35 (32)
- Cholesterosis	51 (47)
- Aschoff-Rokitansky sinus	13 (12)
- Adenomyomatosis	3 (3)
- Pyloric gland adenoma	3 (3)
- Cholecystitis	1 (1)
- Lipoma	1 (1)
- Autolysis	1 (1)
Pathology conclusion, n (%)	
- Normal gallbladder	48 (44)
- Cholesterosis	51 (47)
- Adenomyomatosis	3 (3)
- Chronic cholecystitis	1 (1)
- Lipoma	1 (1)
- Pyloric gland adenoma	3 (3)
- Autolysis	1 (1)

individual patient. Adequate counseling is equally difficult without strong evidence. It seems warranted to discuss that the chances are high that no anomalies are found at histopathologic assessment of the gallbladder specimen. Therefore, gallbladder polyp is one of the diagnoses in which shared decision-making is essential in order to select the right treatment for each individual patient.

Although this study represents a relatively small series of cholecystectomies for gallbladder polyps, it likely represents real-life clinical practice in a Western hospital. Recently, a study was published collecting histopathological data from a Dutch nation-wide pathology registry and concluded based on pathological findings that however polyp size of 10 mm is the best available surgical threshold, it is still insufficient leading to overtreatment in with suspected gallbladder polyps.²⁵ Most larger clinical series are from Asian centres and since most biliary malignancies have a higher incidence in Far-Eastern territories, the polyp yield might be less in Western centres.²⁶ Therefore, adherence to the guideline is essential in order to avoid cholecystectomies with no or non-neoplastic polyps at pathology. A currently recruiting national prospective study (NTR7198) in the Netherlands might provide more insight in the criteria for cholecystectomy in case of suspected gallbladder polyps and may lead to alterations of the current Dutch guideline dating from 2003.

In 2017 an altered European guideline for the management of gallbladder polyps was published (Wiles 2017), recommending using patient's risk factors to establish the risk of gallbladder malignancy. These risk factors are age, PSC, Indian ethnicity and sessile polyp are the risk factor. Likewise, a single gallbladder polyp has a higher malignant potential.²⁷ The results of the above-mentioned national study combined with published literature will provide a strong foundation to update current Dutch guideline, regarding diagnostic tools and recommendations to perform cholecystectomy.

This study demonstrated that in a cohort of 108 cholecystectomies for suspected gallbladder polyps, only three neoplastic polyps were diagnosed at pathology. The weak correlation of ultrasound findings results in many unnecessary cholecystectomies using the current guidelines. Although the outcomes of elective cholecystectomies are favorable, novel diagnostic tools for detection of true polyps or identification of risk factors for polyps with malignant potential are essential in order to guide clinicians to proceed to surgery.

Conflicts of interest

None to declare.

References

1. Park JK, Yoon YB, Kim Y-T, Ryu JK, Yoon WJ, Lee SH *et al.* (2008 Sep) Management strategies for gallbladder polyps: is it possible to predict malignant gallbladder polyps? *Gut Liver* 2:88–94 [Internet] Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20485616>.
2. Pandey M, Khatri AK, Sood BP, Shukla RC, Shukla VK. (1996) Cholecystosonographic evaluation of the prevalence of gallbladder diseases: a university hospital experience. *Clin Imaging* 20: 269–272.
3. Okamoto M, Okamoto H, Kitahara F, Kobayashi K, Karikome K, Miura K *et al.* (1999) Ultrasonographic evidence of association of polyps and stones with gallbladder cancer. *Am J Gastroenterol* 94:446–450.
4. Lin WR, Lin DY, Tai DI, Hsieh SY, Lin CY, Sheen IS *et al.* (2008) Prevalence of and risk factors for gallbladder polyps detected by ultrasonography among healthy Chinese: analysis of 34 669 cases. *J Gastroenterol Hepatol* 23:965–969.
5. Kratzer W, Haenle MM, Voegtle A, Mason R a, Akinli AS, Hirschbuehl K *et al.* (2008) Ultrasonographically detected gallbladder polyps: a reason for concern? A seven-year follow-up study. *BMC Gastroenterol* 8:41 [Internet] Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2553794&tool=pmcentrez&rendertype=abstract>.
6. Yang HL, Sun YG, Wang Z. (1992 Mar) Polypoid lesions of the gallbladder: diagnosis and indications for surgery. *Br J Surg* 79:227–229 [Internet] Available from: <http://www.ncbi.nlm.nih.gov/pubmed/1555088>.
7. Elmasry M, Lindop D, Dunne DFJ, Malik H, Poston GJ, Fenwick SW. (2016) The risk of malignancy in ultrasound detected gallbladder polyps: a systematic review. *Int J Surg* 33:28–35 [Internet] Available from: <https://doi.org/10.1016/j.ijsu.2016.07.061>.
8. Mellnick VM, Menias CO, Sandrasegaran K, Hara AK, Kielar AZ, Brunt EM *et al.* (2015) Polypoid lesions of the gallbladder: disease spectrum with pathologic correlation. *Radiographics* 35:387–399 [Internet] Available from: <http://pubs.rsna.org/doi/full/10.1148/rg.352140095>.
9. Hundal R, Shaffer EA. (2014) Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol* 6:99–109.
10. Oncoline. (2013) Galweg- en galblaascarcinoom. *Land Werkgr Gastro Intest Tumoren* [Internet] Available from: <http://oncoline.nl/galweg-engalblaascarcinoom>.
11. Terzi C, Sökmen S, Seçkin S, Albayrak L, Uğurlu M. (2000) Polypoid lesions of the gallbladder: report of 100 cases with special reference to operative indications. *Surgery* 127:622–627.
12. Aldouri AQ, Malik HZ, Waytt J, Khan S, Ranganathan K, Kummaraganti S *et al.* (2009) The risk of gallbladder cancer from polyps in a large multiethnic series. *Eur J Surg Oncol* 35:45–51.
13. Bhatt NR, Gillis A, Smoothey CO, Awan FN, Ridgway PF. (2016) Evidence based management of polyps of the gall bladder: a systematic review of the risk factors of malignancy. *Surgeon* 14:278–286.
14. Wiles R, Thoeni RF, Barbu ST, Vashist YK, Rafaelsen SR, Dewhurst C *et al.* (2017) Management and follow-up of gallbladder polyps. *Eur Radiol* 27:3856–3866 [Internet] Available from: <http://link.springer.com/10.1007/s00330-017-4742-y>.
15. Buckles DC, Lindor KD, LaRusso NF, Petrovic LM, Gores GJ. (2002) In primary sclerosing cholangitis, gallbladder polyps are frequently malignant. *Am J Gastroenterol* 97:1138–1142.
16. Dindo D, Demartines N, Clavien PA. (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240:205–213.
17. Park JK, Yoon YB, Kim Y-T, Ryu JK, Yoon WJ, Lee SH *et al.* (2008) Management strategies for gallbladder polyps: is it possible to predict malignant gallbladder polyps? *Gut Liver* 2:88–94.
18. Babu BI, Dennison AR, Garcea G. (2015) Management and diagnosis of gallbladder polyps: a systematic review. *Langenbeck's Arch Surg* 400: 455–462.

19. Lee SR, Kim HO, Shin JH. (2018) Reasonable cholecystectomy of gallbladder polyp – 10 years of experience. *Asian J Surg* 42:332–337.
20. Albores-Saavedra J, Chablé-Montero F, González-Romo MA, Ramírez Jaramillo M, Henson DE. (2012) Adenomas of the gallbladder. Morphologic features, expression of gastric and intestinal mucins, and incidence of high-grade dysplasia/carcinoma in situ and invasive carcinoma. *Hum Pathol* 43:1506–1513.
21. Sugiyama M, Atomi Y, Kuroda A, Muto T, Wada N. (1995) Large cholesterol polyps of the gallbladder: diagnosis by means of US and endoscopic US. *Radiology* 196:493–497.
22. Park CH, Chung MJ, Oh TG, Park JY, Bang S, Park SW *et al.* (2013) Differential diagnosis between gallbladder adenomas and cholesterol polyps on contrast-enhanced harmonic endoscopic ultrasonography. *Surg Endosc Other Interv Tech* 27:1414–1421.
23. Fei X, Lu WP, Luo YK, Xu JH, Li YM, Shi HY *et al.* (2015) Contrast-enhanced ultrasound may distinguish gallbladder adenoma from cholesterol polyps: a prospective case–control study. *Abdom Imag* 40: 2355–2363.
24. Irie H, Kamochi N, Nojiri J, Egashira Y, Sasaguri K, Kudo S. (2011) High b-value diffusion-weighted MRI in differentiation between benign and malignant polypoid gallbladder lesions. *Acta Radiol* 52:236–240.
25. Wennmacker SZ, van Dijk AH, Raessens JHJ, van Laarhoven CJHM, Drenth JPH, de Reuver PR *et al.* (2019) Polyp size of 1 cm is insufficient to discriminate neoplastic and non-neoplastic gallbladder polyps. *Surg Endosc* 33:1564–1571 [Internet] Available from: <https://doi.org/10.1007/s00464-018-6444-1>.
26. Olthof PB, Miyasaka M, Koerkamp BG, Wiggers JK, Jarnagin WR, Noji T *et al.* (2018) A comparison of treatment and outcomes of perihilar cholangiocarcinoma between Eastern and Western centers. *HPB* 1–7 [Internet] Available from: <https://doi.org/10.1016/j.hpb.2018.07.014>.
27. Shinkai H, Kimura W, Muto T. (1998) Surgical indications for small polypoid lesions of the gallbladder. *Am J Surg* 175:114–117.