

Polypoid Lesions of the Gallbladder: A Five-Year Retrospective Study of Cholecystectomy Specimens

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Abstract

Introduction: Polypoid lesions of gallbladder (PLG) are a diverse group of disease ranging from inflammatory to malignant pathology. Their understanding and characterization clinically and pathologically would help in decision making regarding their management.

Methods: A retrospective analytic study was conducted at the Department of Pathology between April 15th 2019 to April 14th 2025. We studied the histopathology reports of all cholecystectomies done in that period to determine the frequency and types of PLGs. A comparison of clinicopathological characteristics such as age of patient, site of polyp, whether the lesions were single or multiple was done. ROC analysis was done to establish a size cut off to differentiate neoplastic from non-neoplastic polyps.

Results: We received 2134 cholecystectomy specimen of which 72 (3.4%) had polypoid lesions of gallbladder. There was a female preponderance (61%). Neoplastic polyps (n=44, 61%) were more common than non-neoplastic polyps. Among neoplastic polyps, 26 were benign and 18 were malignant. The ROC analysis recognized an ideal cutoff of 9mm at which the sensitivity and specificity of detection of malignancy is 68.2% and 89.3% respectively (AUC = 0.862).

Conclusion: Polypoid lesions of the gallbladder were encountered in 72 (3.4%) of all cholecystectomy specimens. Age of more than 50 years and size of 9mm are the most useful features to distinguish neoplastic from non-neoplastic lesion. Malignant polypoid lesion of gallbladder tends to present late in our population.

Keywords: Cholecystectomy; Gallbladder; Malignancy; Polyps; Polypoid lesion of Gallbladder (PLG).

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Disclosures:

Ethical Clearance: Taken

Conflict of interest: None

Financial aid: None

Copyright information:



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How to cite this article:

Shrivastav S, Shrestha SM, KC B, Pradhan S. Polypoid Lesions of the Gallbladder: A Five-Year Retrospective Study of Cholecystectomy Specimens. J Soc Surg Nep. 2025;28(2):43-49.

DOI:

<https://doi.org/10.3126/jssn.v28i2.91606>

Introduction

Cholecystectomy is one of the most frequently performed surgical procedures worldwide. Among the specimens examined postoperatively, polypoid lesions of the gallbladder (PLG), or gallbladder polyps, are occasionally seen. While these lesions are often discovered incidentally, their detection rates are higher in countries where routine ultrasound screening is widely practiced, such as Japan.¹

The reported incidence of gallbladder polyps varies across studies, ranging from 2% to 12% of cholecystectomy specimens.^{2,3} Gallbladder polyp comprises a heterogeneous group of lesions, which may be either reactive and non-neoplastic or neoplastic, including malignant transformations. Broadly, they are categorized into two groups, where non-neoplastic polyps include cholesterol polyps, inflammatory polyps, fibromyoglandular polyps, and hyperplastic polyps, while neoplastic polyps, include benign entities like pyloric gland adenoma and intracholecystic papillary neoplasm (ICPN), as well as malignant tumors, most commonly being adenocarcinomas.⁴⁻⁹

Accurate classification is essential for proper management. Understanding their clinicopathological features may allow for improved preoperative risk stratification, enabling surgeons to distinguish potentially malignant lesions and determine the need for surgical intervention.¹⁰ Important characteristics include polyp size, number, anatomical location, histological subtype, and presence of associated mucosal changes. For neoplastic lesions, additional factors such as grade of dysplasia, depth of invasion, and lymph node involvement are crucial. Comparing these characteristics may help establish predictive parameters for differentiating non-neoplastic from neoplastic lesions.^{11,12}

The primary aim of this study was to analyze the spectrum of gallbladder polypoid lesions in cholecystectomy specimens over a five-year period at our institution. Specific objectives include to determine the frequency and types of gallbladder polyps across different age groups and sexes, to compare clinicopathological characteristics—including size, number, and associated mucosal changes—between neoplastic and non-neoplastic polyps, to establish a size cut-off for differentiating neoplastic from non-neoplastic lesions and to describe the features of malignant gallbladder polyps, including site, size, histological type, and extent of tumor spread.

Methods

This was a retrospective descriptive and analytical study conducted at the Department of Pathology, Tribhuvan University Teaching Hospital. Histopathology records of all cholecystectomy specimens received between April 15, 2019, and April 14, 2025 were reviewed. The database was searched for the keywords “polyp” and “polypoid” to identify cases for inclusion.

For each case, the following information was extracted:

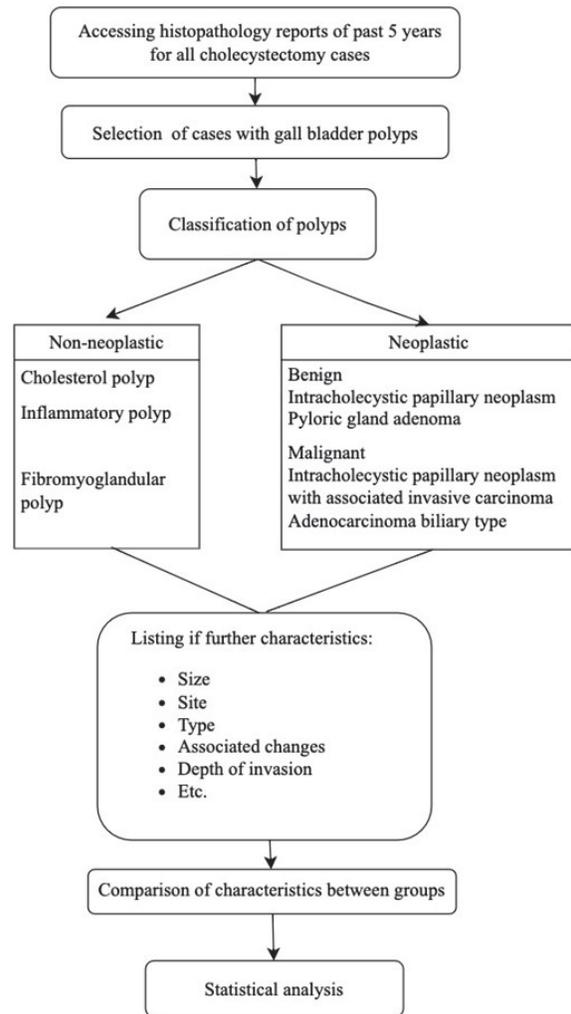


Figure 1. Workflow of the study.

Polyp characteristics: type, size, number, and anatomical location. Associated mucosal change such as metaplasia, adenomyosis, or cholesterosis was recorded. For malignant polyps: extent of invasion, T stage, and lymph node involvement was also added. **Figure 1** represents our workflow.

Results

We received 2134 cholecystectomy specimens over the past 5 years at our center. Polyps and polypoid lesions were found in 72 of these cases which is 3.4% of all cholecystectomies. Of the 72 polyps, 28 (38.9%) cases were in males while 44 (61.1%) cases were in females. This shows a female preponderance which was also seen in the number of cholecystectomies. The age range of the patients with polyps was from 11 years to 81 years. The mean±SD age was 48±15.7 years. The different types of polyps that we encountered were 28 non-neoplastic (NN) polyps and 44 neoplastic polyps as shown in **figure 2**.

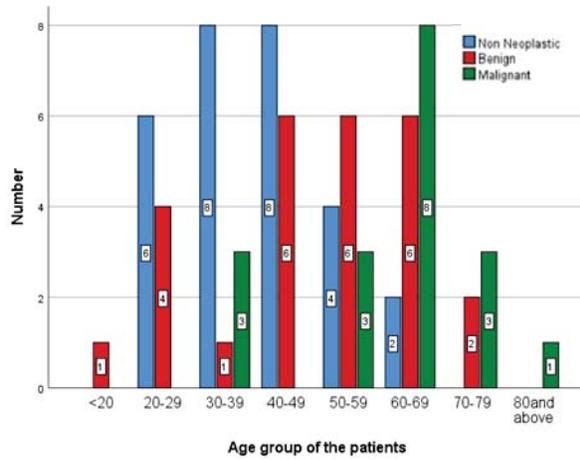


Figure 2. Types of gallbladder polyps in different age groups

There was a significant difference in the distribution of these polypoid lesions above the age of 50 years where the frequency of neoplastic polyps became more than the non-neoplastic polyps which is highlighted in the **table 1** below. **Figure 3** shows distribution according to sex.

Table 1. Distribution of different categories of polypoid lesions of gall bladder in age groups below 50 and 50 and above.

Age group	Non-Neoplastic n(%)	Neoplastic n(%)
<50	22(59.5)	15(40.5%)
≥50	6(17.1)	29(82.9%)
Total	28(38.9%)	44(81.5%)

Histological subtypes:

Amongst the non-neoplastic polyps, the most common lesion was the cholesterol polyp (n=21). Other non-neoplastic types included inflammatory and fibromyoglandular polyps, as shown in **Table 2** and **Figure 4** shows photomicrographs

Table 2. Types and subtypes of PLGs

Type	Subtype	Number
Non-neoplastic polyps	Cholesterol polyps	21
	Inflammatory	2
	Fibromyoglandular	2
	Polypoid pyloric gland metaplasia	2
	Hyperplastic polyp	1
Benign polyps	Intracholecystic papillary neoplasm	13
	Pyloric gland adenoma	12
	Polypoid BIN	1
Malignant polyps	ICPN with invasion	5
	Adenocarcinoma Biliary	7
	Adenocarcinoma Intestinal	2
	Adenocarcinoma Mucinous	1
	Adenocarcinoma NOS	3

Table 3. Comparison of characteristics of PLGs.

	Non-neoplastic n=28	Benign n=26	Malignant n= 18	p-value
Sex				
Male (n=28)	9 (32.1%)	9 (32.1%)	10 (35.7%)	0.242
Female (n=44)	19 (43.2%)	17 (38.6%)	8 (18.2%)	
Mean age	40 ±11.85	48 ±16.22	60 ±12.58	
Size				
Range	0.2-1.5	0.2-5	0.7-7cm	
Mean	0.65 ±0.895	1.26 ±1.17	3.232 ±1.75	
0-1cm	26 (63.4%)	14 (34.15%)	1 (2.4%)	<0.001
1.1-2cm	1 (7.1%)	9 (64.3%)	4 (28.6%)	
>2cm	1 (5.9%)	3 (17.6%)	13 (76.5%)	
Number				
Solitary	23 (35.9%)	24 (37.5%)	17 (26.6%)	0.34
Multiple	5 (62.5%)	2 (25%)	1 (12.5%)	
Site				
Neck	0	3 (100%)	0	
Neck + body	0	0	2 (100%)	
Body	20 (55.6%)	10 (27.8%)	6 (16.7%)	
Body + fundus	2 (20%)	2 (20%)	6 (60%)	
Fundus	5 (26.3%)	10 (52.6%)	4 (21.1%)	
Fundus, neck and body	1 (100%)	0	0	
Unknown	0	1 (100%)	0	

of some of these entities. In 20 cases, the polyps were located in the body and only in 8 cases they were located in the fundus. In 5 cases there were multiple polyps, in 1 case there were 2 polyps and in all other cases there were solitary polyps.

As shown in **table 3**, the size of the polyps ranged from 0.2-1.5cm. The mean size was 0.49cm. When polyps occurred as 2 two or more in number, they were non neoplastic in 62.5% cases. However, this was not a statistically significant finding. Additional finding of pyloric gland metaplasia, intestinal metaplasia and adenomyosis was seen in one case each.

Among the benign polyps, half of them, i.e. 13 cases were intracholecystic papillary neoplasm while 12 were reported

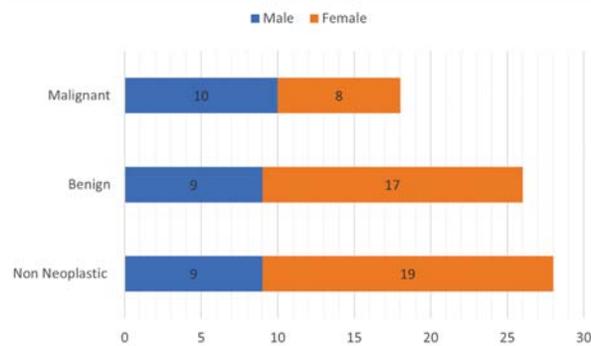


Figure 3. Sex distribution of different polypoid lesions of gallbladder.

as pyloric gland adenomas and 1 one was a polypoid Biliary intraepithelial neoplasm. In one case the polyp was sent detached and therefore the site could not be determined. Low grade dysplasia was identified in 8 of these lesions while high grade dysplasia was identified in 4 cases. BIN was described in 3 cases intracholecystic papillary neoplasm. A comparison of the above characteristics between different types of polyps is given in **table 3**. The p-values are derived by using t-test for quantitative variables and chi-squared test for categorical variables.

The neoplastic polyps were significantly larger than the non-neoplastic polyps with >90% polyps in the range of >1cm being neoplastic.

We went on to test the size cutoff of 1cm as a cutoff for neoplastic polyps and found that the sensitivity of size >1 cm for the neoplasia is 65.9% and specificity is 92.9%. In accordance with the literature, in our cohort, the ROC analysis has revealed a very close cut-off, namely 9 mm, with AUC = 0.862 [0.772–0.952, 95% CI] (**Figure 5**). At this threshold, the sensitivity was 68.2% and specificity was 89.3%. **Table 4** shows sensitivity and specificity of different cut-off points.

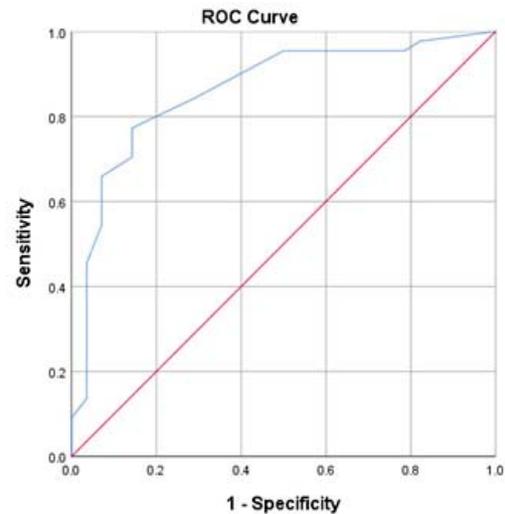


Figure 5. The ROC analysis has revealed a cut-off of 9 mm, with AUC = 0.862 [0.772–0.952, 95% CI]. At this threshold, the sensitivity was 68.2% and specificity was 89.3%.

Table 4. ROC analysis

Coordinates of the Curve		
Test Result Variable(s): sizemm		
Positive if Greater Than or Equal To	Sensitivity	1 - Specificity
2.50	.977	.821
5.50	.841	.286
9.00	.682	.107
11.00	.659	.071
13.50	.545	.071
16.00	.455	.036
19.00	.409	.036
23.00	.318	.036

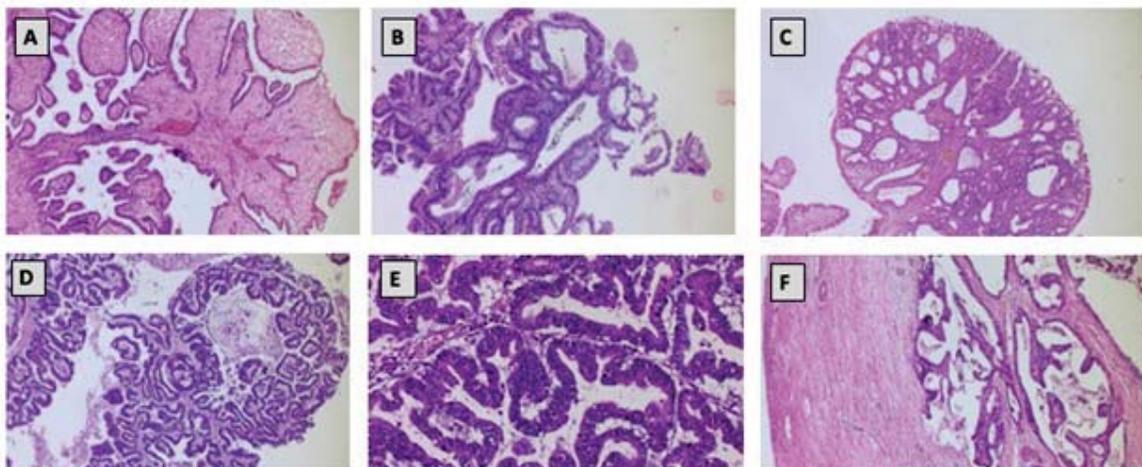


Figure 4. Photomicrographs of some of the polypoid lesions. (A)Cholesterol polyp, H&E,200x; (B) Pyloric gland adenoma, H&E, 50x; (C) ICPN Low Grade, H&E, 50 x; (D) ICPN High Grade , H&E, 50x; (E) ICPN High Graderdae , H&E, 200x; (F) Adenocarcinoma , H&E,200x

The different mucosal changes associated with these polyps in the surrounding mucosa is described in the **table 5**.

Table 5. Mucosal changes associated with different non-neoplastic and benign polyps.

Types of polyps	Associated changes	Number
Non-neoplastic polyps (n=28)	Cholesterolosis	14
	Pyloric metaplasia	1
	Intestinal metaplasia	1
Benign polyps (n=26)	Cholesterolosis	5
	Pyloric gland metaplasia	3
	Fundic gland metaplasia	1
	Adenomyosis	1
	Biliary intraepithelial neoplasia	3

There were 18 malignant polypoid lesions, which consisted of Intracholecystic papillary neoplasms associated with invasive carcinoma, adenocarcinoma of biliary subtype, adenocarcinoma intestinal subtype, adenocarcinoma of mucinous subtype and adenocarcinoma, NOS. Their frequency and locations are described in **Table 6**. Only one case had multiple lesions while the other 17 cases were solitary lesions. The size of malignant polyps ranged from 0.7 cm to 7cm. Mean size was 3.22 cm. The case with the smallest malignancy consisted of multiple foci of tumor. The tumor presented most frequently in an advanced stage with extension upto peri muscular connective tissue in 9 cases, liver in 2 cases and both liver and sigmoid colon in 2 cases. Lymph node metastasis was seen in 3 cases.

The characteristics of the polypoid malignancies of gallbladder are listed in **table 6**.

Discussion

Cholecystectomy is one of the most commonly performed surgery in our institution and we received 2134 specimens over the last five years. Gallbladder polyps and polypoid lesions were identified in 3.4%, i.e. 72 of all cholecystectomies received in our department. The number is similar to 4% reported by Inzunza et. al from Chile and 2.4% reported by Maciejewski and Strzelczyk from Poland, however some studies report a much higher number i.e. 15.2%.^{1,13,14} There was a female preponderance in the number of polyps with 61.1% cases occurring in females, which was also seen in all the cholecystectomies received in the department. The gender predilection was not statistically significant and thus thought to be by chance only.

There was a significant difference in the age at which different types of polyps occur with a sharp reversal in the number of non-neoplastic and neoplastic polyps after the age of 50. A similar conclusion was found in a number of other studies, including Cha et. al and Lee et. al.¹⁵⁻¹⁷

Table 6. A characterization of malignant polyps of gallbladder.

Characteristics	Category	Number
Site	Neck	0
	Neck + body	2
	Body	6
	Body+fundus	6
	Fundus	4
Size	Mean	3.22
	>1cm	17
	>2cm	15
Type	ICPN with invasion	
	5	
	Adenocarcinoma- Biliary	7
	Adeno carcinoma- Intestinal	2
	Adenocarcinoma- Mucinous	1
	Adenocarcinoma, NOS	3
Extent	Lamina propria	1
	Muscularis propria	4
	Perimuscular connective tissue	9
	Liver	2
	Liver+colon	2
T	T1a	1
	T1b	4
	T2a	6
	T2b	3
	T3	4
N	Nx	6
	N0	9
	N1	3

The best discussed and best-established preoperative factor predicting malignancy is the size of the polyps which is believed to be more than 10mm. In our study also >90% polyps in the range of >1cm were neoplastic. Our ROC curve showed a cutoff of 9mm to be better with a sensitivity of 68.2% and specificity was 89.3% with area under the curve of 0.862 [0.772–0.952, 95% CI]. Our finding was very similar to that of Taskin et. al.¹ However Cha et. al. used a similar method and found a higher cut off of 15mm in their study but they recommended a lower cut off of 10mm in cases older than 65 years of age.¹⁵ Another study by Sung et al. also found a much higher cut off of 14.5mm.¹⁸

Morphological characteristics also provided valuable diagnostic clues. Non-neoplastic polyps were frequently multiple and located predominantly in the body and fundus. In contrast, neoplastic polyps (both benign and malignant) were more likely to be solitary and larger, with malignant lesions commonly involving multiple regions, eg. the body and fundus although these were not strongly supported statistically. A larger number of samples may have provided statistical significance.

Among the associated histological features with the polypoid lesions, the non-neoplastic polyps were frequently found to have cholesterosis. Other such findings were intestinal metaplasia and pyloric gland metaplasia; however, these were found more frequently with benign neoplastic polyps indicating a possible role in pathogenesis of neoplastic changes, and with the small number of cases here we are not able to conclude this statistically. More importantly biliary intraepithelial neoplasia was noted in 3 cases of benign polypoid lesions.

Polypoid lesions can be of a wide variety and can range from non-neoplastic ones like cholesterol polyps and inflammatory polyps to neoplastic ones; And again, within the neoplastic group ranging from benign polyps like intracholecystic papillary neoplasms with varying degrees of dysplasia to adenocarcinomas. In contrast to most studies, we found a greater number of neoplastic polyps than non-neoplastic polyps among our cases. The explanation for this could be that not all polypoid lesions which are diagnosed on ultrasound undergo cholecystectomy, as characterized by their size and other preoperative risk factors. Therefore, patients undergo a triage at preoperative level. Also, the study site being a tertiary care center does more surgeries for neoplastic conditions than most other medical centers. A few studies also mention hemangiomas and lipomas.^{4,18} However, we did not encounter any of these in our study.

There were 2 cases of polypoid pyloric gland metaplasia and 12 cases of pyloric gland adenomas in our study. There has been some debate regarding these terminologies and there is concern that the term adenoma simply implies a neoplastic potential in lesions that don't actually carry such potential. As it stands now, polypoid lesions that are <0.5cm, lack any atypia, or complex architecture and are associated with pyloric gland metaplasia in the surrounding mucosa should be termed polypoid pyloric gland metaplasia rather and not pyloric gland adenoma. Sternberg's Diagnostic Surgical Pathology further suggests a suitable cutoff of 1cm.^{9,19}

Intracholecystic papillary neoplasms make up about half of our benign neoplasms. These lesions have also been discussed extensively regarding their subtypes and their possible outcome. They may have low grade dysplasia or high-grade dysplasia based upon their worst cytological as well as architectural atypia and this is thought to be the most significant predictor of outcome. All but one of our

cases had low grade dysplasia. Subtypes like gastric, biliary, intestinal, and oncocytic are seen and mixed types are also noted. However, they are not believed to be significant in outcome. They may be associated with dysplasia in the surrounding uninvolved gallbladder mucosa. There has also been debate regarding whether Pyloric gland adenoma and other tubular lesions should be incorporated within this group.²⁰ The most important point to note while reporting is to not over-recognize involvement of Rokitsansky Aschoff sinuses as invasive disease.²¹

The next entity, Intracholecystic papillary neoplasm with invasion, in spite of being invasive carcinoma have an incomparably better prognosis than other invasive carcinoma of the gall bladder with a 5 year survival rate of 60%.²¹ In our study, we had 5 such cases. The remaining cases were adenocarcinoma of biliary type, mucinous, intestinal and adenocarcinoma, NOS. In accordance with most existing literature, the commonest site was fundus or involving both the body and fundus. Seventeen out of 18 malignant cases were >1cm in size and 15 were >2cm in size. An important finding was that we had only 5 T1 cases, while we had 9 and 4 cases of T2 and T3 tumors indicating that our patients predominantly presented as advanced lesions when compared to other studies, for example, one by Sung et. al. from Korea, which had the same number of malignant cases as us but 11 T1 cases, 6 T2 cases and only 1 T3 tumor.¹⁸

Gallbladder carcinomas are aggressive carcinomas and their effective treatment depends heavily on early diagnosis. This makes the late presentation of our patients all the more worrisome.²² Finally, we received lymph nodes with only twelve of our malignant cases of which 3 showed metastatic disease. A limitation of our study were that we could not incorporate the radiological findings in these patients. A larger data set would have given us better relevance of some of the parameters such as site of lesion.

Conclusion

Polypoid lesions of the gallbladder were encountered in 3.4% of all cholecystectomy specimens. Age of more than 50 years and size of 9mm are the most useful features to distinguish neoplastic from non-neoplastic from lesion. Malignant polypoid lesion of gallbladder tends to present late in our population.

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