

## Original Research Article

## Outcome and Evaluation of Laparoscopic Cholecystectomy of Chronic Gall Stone Disease with Mucosal Changes in Gall Bladder: A Prospective Multicenter Study in Rajshahi, Bangladesh

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**Abstract: Background:** Gallstones, also widely recognized as cholelithiasis, cause histological changes including chronic inflammation, glandular hyperplasia, granulomatous inflammation, metaplasia dysplasia and anaplasia (Carcinoma). As more than just a result, the goal of this system was also to evaluate how gallstones mucosal changes limit the amount and number of stones in cholecystectomy patients. **Methods:** At Rajshahi Medical College Hospital and Private Hospital in, a multicenter non-randomized experimental prospective study comprising  $n=264$  patients with symptomatic cholelithiasis who were scheduled to have laparoscopic cholecystectomy with written and informed consent between 2014 and 2020 was conducted. All of the patients underwent a preoperative biochemical profile, as well as a complete abdominal ultrasound, was performed by surgeons who were very trained and experienced. The morphologic profiles of gallstones were documented and examined. The mucosal tissues from the gallbladder were transported to a general pathology lab for analysis. All gallbladder mucosal specimens were histopathological typed, and the number and type of gallstones were correlated. **Results:** A total of  $n=264$  gallbladder specimens were collected, with 192 (73%) from female patients and 72 (27%) from male patients (M: F ratio 2:6.4). Patients were on average 42.5 years old (range 22-70). In 57 patients (21.52%), the outer gallbladder surface was clogged, the wall thickness was raised in 86 (32.57%), and mucosal abnormalities were discovered in 121 individuals (45.91%). On microscopy, 155 specimens (58.36%) had epithelial hyperplasia, 44 (16.85%) had antral metaplasia, 41 (15.57%) had intestinal metaplasia, 22 (8.52%) had dysplasia, and one had cancer in situ 2 (0.7%). We have found the satisfactory (Excellent and good) result 96.24% and unsatisfactory (Post Cholecystectomy Syndrome) was 3.76%. When the amount and kind of stones were linked with the gallbladder mucosal response, non-significant findings were obtained. **Conclusions:** Gall stones and mucosal alterations in the gall bladder could be linked. The findings of this study do not provide an etiologic or effective correlation; one conceivable mechanism is that a gallstone continuously erodes the gall bladder wall over time, creating a risk. Non-significant results were obtained when the number and kind of stones were linked with the mucosal response of the gallbladder.

**Keywords:** Gallbladder, Laparoscopic cholecystectomy, Mucosal, Cholelithiasis, Dysplasia, Hyperplasia, Metaplasia, Rajshahi Medical College, Bangladesh.

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## INTRODUCTION

The gallbladder is an essential component of the biliary system. The liver, with its blood supply, the gall bladder, the common hepatic duct, and the common bile duct make up the biliary system. The biliary system has both intrahepatic and extrahepatic components. The gall bladder is part of the biliary system's extrahepatic component [1-3]. The gall bladder's primary role is to retain and concentrate bile. Gallstone disease or cholelithiasis causes a wide range of histopathological abnormalities. Acute inflammation, chronic

inflammation, and autoimmune inflammation are just a few examples [4, 5]. Granulomatous inflammation, cholesterol is, dysplasia, and cancer are all examples of glandular hyperplasia. Gallstones have a variety of components. Cholesterol, pigment and mixed stones are just a few examples. 6 As a result, the current study was designed to evaluate gallbladder mucosal changes in individuals having laparoscopic cholecystectomy, as well as their relationship to the quantity and types of stones.

## METHODS

Between 2014 and 2020, Rajshahi Medical College Hospital conducted a prospective observational study as part of a multicenter non-randomized experimental prospective study. The study comprised n=264 patients who had preoperative ultrasonography-proven symptomatic gall stone disease were over 22 years old, had normal liver function tests and blood amylase and lipase levels and agreed to have elective laparoscopic cholecystectomy and participate in the study. The following exclusion criteria were used: less than 6 weeks had passed since the last attack of acute cholecystitis; >72 hours had passed since the most recent attack of acute cholecystitis; acute cholecystitis with elevated serum amylase and lipase levels; and the patient was deemed unfit for surgery. Under the supervision of qualified and experienced surgeons, laparoscopic cholecystectomy was performed using the 04-port technique while the patient was under general anesthetic. Gallstones' morphologic profile was documented and analyzed. The mucosal tissues of the gallbladder were transferred to a general pathology department for investigation. Gall bladder mucosa histopathology was recorded and associated with gallstone type. We kept track of our findings in a Microsoft Excel spreadsheet. The results were analyzed using SPSS software. When the p-value was less than 0.05, it was considered significant.

### Investigations

All of the patients n=264 had routine hematological and biochemical tests with ERCP done n=17, and post-operative patients Progress report USG hepatobiliary system with another parameter will be normal. n=06 (2.3%) CT Cholangiogram, PET-CT done n=03 (1.46%), (Post Cholecystectomy syndrome).

### Ultrasound

All patients had their abdomens scanned with ultrasound. 264 patients had gallbladder stones, and 13

patients had stones in both the gallbladder and the CBD and open cholecystectomy was done. Pre-operative Assessment For the surgery, a hemoglobin level of 10gm/dl was required. Blood transfusions were administered to a subset of patients in order to boost hemoglobin levels below gm/dl. Acute cholecystitis was treated conservatively in 10 cases with IV fluids, nasogastric aspiration, antibiotics, and analgesics. These patients were treated conservatively for 6 weeks before being offered surgery. During the pre-operative period, all diabetic patients received insulin injections. Before bringing the patient to surgery, any associated medical illness was treated appropriately.

### Pre-operative evaluation

For the surgery, a hemoglobin level of 10% was required. Blood transfusions were administered to a subset of patients in order to boost hemoglobin levels. Acute cholecystitis was treated conservatively in 10 cases with IV fluids, nasogastric aspiration, antibiotics, and analgesics. These patients were treated conservatively for 6 weeks before being offered surgery. During the pre-operative period, all diabetic patients received insulin injections. Before bringing the patient to surgery, any associated medical illness was treated appropriately.

### Complications

Total 2 (0.7%) patients in the current study had wound infection. 4(1.41%) patients experienced post-operative bile leaks, which were treated conservatively and the patients recovered. 4 (1.65%) patients had TB.

### Histopathology report

The current study included 229 (86.96%) patients with chronic cholecystitis, 31 (11.39%) patients with acute cholecystitis, and no cases of malignancy. 4 (1.65%) had growth Contamination with Mycobacterium Tuberculosis.

**Table-1: Correlation of gallbladder mucosal response with the type of stones according to histopathological study (n=264)**

Diagnosis	No. of stones			Total	Chi-square value	P-value
	Single	Two	Multiple			
Chronic Calculous Cholecystitis with Normal mucosa	46	38	74	158		
Chronic Calculous Cholecystitis Hyperplasia	8	22	14	44		
Chronic Calculous Cholecystitis with Metaplasia	18	15	8	41	2.65	0.05
Chronic Calculous Cholecystitis with Dysplasia	6	5	8	19		
Chronic Calculous Cholecystitis with anaplasia G-I (Carcinoma in situ)	1	0	1	2		
Total	79	80	105	264		

**Bile culture**

Bile cultures were performed on all patients, and 180 (68.25%) had no growth, 38 (14.52%) had growth of Escherichia coli, 12 (4.36%) had growth of Klebsiella, and 34 (12.87%) patients each had growth of Staphylococcus aureus and Pseudomonas. These findings matched those of Mathur et al., Goswitz et al., and Battacharya et al.

**Follow-up**

There were no complications during the follow-up period in any of the patients.

**STATISTICAL ANALYSIS**

All the observations were recorded on an excel sheet and were evaluated with ‘SPSS’ software. The Chi-square test was used for the assessment of the level of significance. A P-value of less than 0.05 was taken as significant.

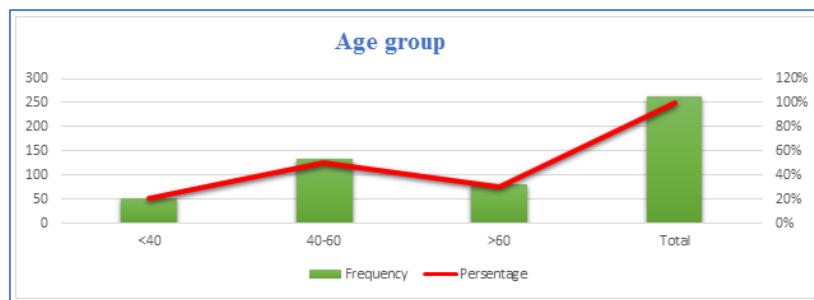
**RESULTS**

We looked at n=264 gallstone patients in our research. The average age of the patients in this study

was 45.5 years, with 50% of them being between 40 and 60 years old. In 57 patients (21.52%), the outer gallbladder surface was clogged, the wall thickness was raised in 86 (32.57%), and mucosal abnormalities were discovered in 121 individuals (45.91%). On microscopy, 155 specimens (58.36%) had epithelial hyperplasia, 44 (16.85%) had antral metaplasia, 41 (15.57%) had intestinal metaplasia, 22 (8.52%) had dysplasia, and one had cancer in situ 2 (0.7%). We have found the satisfactory (Excellent and good) result 96.24% and unsatisfactory (Post Cholecystectomy Syndrome) was 3.76%. When the amount and kind of stones were linked with the gallbladder mucosal response, non-significant findings were obtained.

**Table-2: Distribution of subjects according to age group (n=264).**

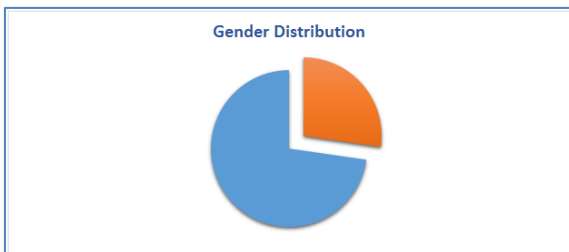
Age group (years)	Frequency	%
<40	52	20
40-60	132	50
>60	80	30
Total	264	100



**Fig-1: Bar diagram showing the age distribution (n=264)**

**Table-3: Distribution of subjects according to gender (n=264)**

Gender	Frequency	%
Females	192	73
Males	72	27
Total	264	100



**Fig-2: Pie diagram showing the gender distribution (n=264)**

The following microscopic diagnostic criteria were used

- Pseudostratification of epithelium, nuclear crowding, tall columnar cells, and occasional mitotic patterns are all signs of hyperplasia.

- Pseudostratification of the epithelium, nuclear crowding, some loss of architecture, disarray of the epithelium, and nuclear atypia are all symptoms of dysplasia.
- Goblet cells are seen in intestinal metaplasia.
- In the lamina propia, antral metaplasia is characterized by branched tortuous glands [2].
- Large vesicula on hyperchromatic nuclei with one or more conspicuous nucleoli, eosinophilic cytoplasm, clear or mucous secreting, occasional gigantic cells, lack of cell polarity, abnormal mitotic patterns, and absence of stromal invasion characterize carcinoma in situ.

**GROSS FEATURES**

The gallbladder's serosal surface was found to be normal in 188 patients (71.54%) and congested in 76 patients (28.46%). Gallbladder wall thickness was normal (less than 3 mm) in 151 patients (57.52%) and thickened (more than 3 mm) in 113 individuals (42.48%). The mucosa was normal in 118 specimens (44.63%), hemorrhagic in 20 specimens (7.52%), strawberry-like in 17 specimens (6.43%), atrophic in 75

specimens (28.72%), and somewhat nodular in 34 specimens (12.7%). Symptomatic individuals had higher gallbladder wall congestion and thickness, although mucosal changes were equal in both symptomatic and asymptomatic gallbladders. The number and type of stones had little effect on the overall alterations. Out of n=264 specimens, only one

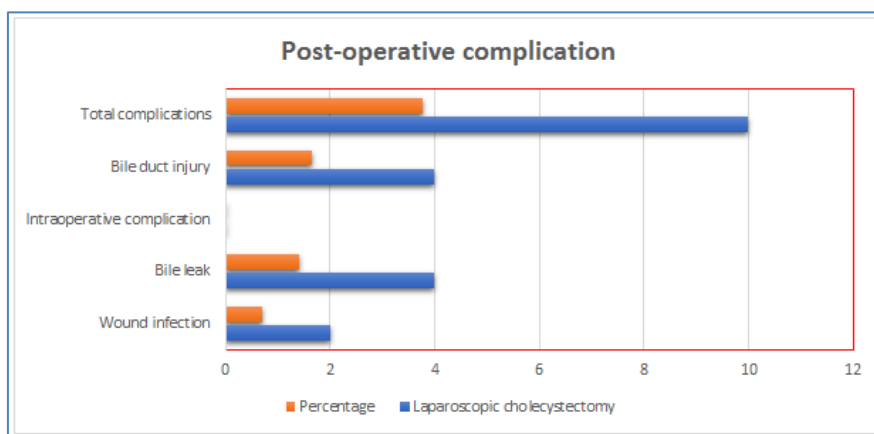
case of carcinoma in situ was discovered (0.7%). Invasive gallbladder cancer was not found in any of the 264 patients who had cholelithiasis surgery. These histological alterations were found in both symptomatic and asymptomatic gallstone patients. There was no difference in epithelial alterations based on the number of gallstones or their characteristics.

**Table-4: Gross features in resected gallbladders (n=264)**

Gross features		Number of cases	Percentage
Serosal surface	Normal	188	71.54
	Congested	76	28.46
Wall	Normal (<3 mm)	151	57.52
	Thickened (>3 mm)	113	42.48
Mucosa	Normal	118	44.63
	Hemorrhagic	20	7.52
	Strawberry	17	6.43
	Atrophic	75	28.72
	Nodular	34	12.7

**Table-5: Complications (n=264)**

Post-operative complication	Laparoscopic cholecystectomy	Percentage
Wound infection	2	0.7
Bile leak	4	1.41
Intraoperative complication	Laparoscopic cholecystectomy	Total
Bile duct injury	4	1.65
Total complications	10	3.76



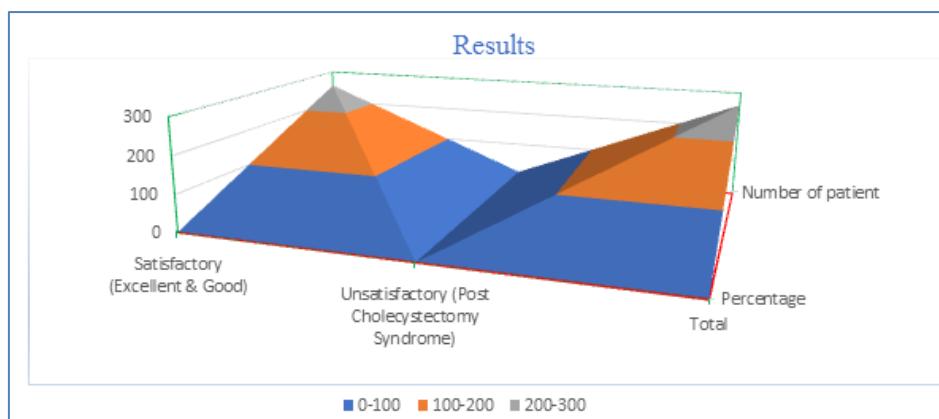
**Fig-3: Bar diagram showing the post-operative complication (n=264)**

**Table-6: Bile culture (n=264)**

Organism Isolated	No. of cases	Percentage
Staphylococcus aureus and Pseudomonas pyocyanus	34	12.87
Escherichia coli	38	14.52
Klebsiella	12	4.36
No growth	180	68.25

**Table-7: Distribution of the results according to the final outcomes (n=264)**

Result	Number of patients	Percentage
Satisfactory (Excellent & Good)	254	96.24
Unsatisfactory (Post Cholecystectomy Syndrome)	10	3.76
Total	264	100



**Fig-4: The Surface Showing results according to the final outcomes (n=264)**

## DISCUSSION

The gallbladder is a prominent organ in the human body with a bad prognosis for related cancers. Moreover, both quantity and quality screening tools are scarce for the early identification of gallbladder cancer, according to current statistics. According to one notion detailed in the literature, the existence of a long-term chronic inflammatory response contributes significantly to the progression of gallbladder cancer [7, 8]. Furthermore, a link has been discovered between the process of cancer growth and the inflammatory response. The cystic duct occlusion or malfunction of the gallbladder's emptying mechanism is the main pathophysiological mechanisms that cause gallstone disease [9, 10]. Gallstones are made up of a variety of substances, including bilirubin ate and cholesterol. Pathologic conditions such as sickle cell disease increase the risk of cholecystitis and cholelithiasis. Due to the accelerated breakdown of red blood cells in sickle cell disease, more bilirubin is produced, making these individuals more susceptible to pigmented stones forming inside the gall bladder. Metaplastic changes are common in chronic cholecystitis patients [11, 12]. This led to a study that looked at gallbladder mucosal changes as well as the number and type of stones in patients undergoing laparoscopic cholecystectomy. The average age of the patients in this study was 45.5 years, with 50% of them being between 40 and 60 years old. The results we obtained were comparable to those obtained by Baig et al. In their study, this study also reported similar demographic findings [13, 14]. Baig et al. investigated the relationship between gallstone composition and histopathology of the mucosal response in their study. In their study, they included a total of 264 patients with gallstone disease, 192 of who were females and the remaining were 72 males. In all patients, histopathology of all gall bladder specimens and chemical analysis of gall stones were obtained [16-18].

In their study, Cholecystitis was discovered in 121 individuals' cases (45.91%). Hyperplasia was observed in 44(16.85%) of the cases, cholecystitis with metaplasia in 41 (15.57%) of the cases, and carcinoma

in 2(0.7%) of the cases. Our findings were consistent with those obtained by Mathur et al. in this study [19, 20]. Total 264 patients with symptomatic gall stones underwent open cholecystectomy in this study. The chemical composition of these stones was determined. 156 (59 percent) of patients had mixed type stones; 66 (25 percent) had combined stones. 24 (9 percent) of patients had a pigment stone, and 18 (7%) had a cholesterol stone. According to the findings of this study, as the weight of the stone, the volume of the stone, or size of the stone increases, the changes were seen in the gall bladder mucosa range from acute inflammation to chronic inflammation, glandular hyperplasia, granulomatous inflammation, cholesterol is, dysplasia, and carcinoma [21, 22]. In a previous study, Goyal et al. assessed the relationship of different types of mucosal responses to different gall stone variables. Total 264 patients with symptomatic cholelithiasis underwent cholecystectomy in this study. Gall bladder specimens were sent for histopathological analysis, while stones were chemically analyzed. The number and size of the stones were counted. Males exhibited the most inflammatory changes. Females were the had GB hyperplasia, intestinal metaplasia, and cancer [23, 24]. When the question of whether mucosal changes are related to the size and type of stone was addressed, it was discovered that there are possible links between some histological alterations of GB and cancer [25].

## CONCLUSION

There is some evidence that constant irritation of the gallstone mucous membranes by gall stones causes mucosal changes. Non-significant results were achieved whenever the gallbladder mucosal response was correlated with the number and type of stones. However, additional research is needed to confirm this.

## REFERENCES

1. Al-Hadeed, S.Y., Moorhead, R.I., Leaper, D.J. (1991). Wong Gallbladder carcinoma: a diagnostic challenge *Edin J Coll Surg*, 36; 174-7.
2. Lewis, J. T., Talwalkar, J. A., Rosen, C. B., Smyrk, T. C., & Abraham, S. C. (2007).



- Prevalence and risk factors for gallbladder neoplasia in patients with primary sclerosing cholangitis: evidence for a metaplasia-dysplasia-carcinoma sequence. *The American journal of surgical pathology*, 31(6), 907-913.
3. Roa, I., De Aretxabala, X., Araya, J. C., & Roa, J. (2006). Preneoplastic lesions in gallbladder cancer. *Journal of surgical oncology*, 93(8), 615-623.
  4. Tazuma, S., & Kajiyama, G. (2001). The development of malignant gallbladder lesions. The consequences of chronic inflammation and gallstones. *Lagenbecks Arch Surg*, 386; 224-9, 2001.
  5. Yamagiwa, H., & Tomiyama, H. (1986). Intestinal metaplasia- dysplasia- carcinoma sequence of the gallbladder. *Pathology International*, 36(7), 989-997.
  6. Kayahara, M., & Nagakawa, T. (2007). A study of 4770 patients revealed recent trends in gallbladder cancer in Japan. *Cancer Res*, 110; 572-80.
  7. Sheth, S., Bedford, A., & Chopra, S. (2000). Recognizing risk factors for primary gallbladder cancer and the role of prophylactic cholecystectomy. *American Journal of Gastroenterology*, 95; 1402-10.
  8. Albores-Saavedra, J., Molberg, K., & Henson, D. E. (1996, November). Unusual malignant epithelial tumors of the gallbladder. In *Seminars in diagnostic pathology* (Vol. 13, No. 4, pp. 326-338).
  9. Gourgiotis, S., Kocher, H. M., Solaini, L., Yarollahi, A., Tsiambas, E., & Salemis, N. S. (2008). Gallbladder cancer. *The American Journal of Surgery*, 196(2), 252-264.
  10. Roa, I., De Aretxabala, X., Araya, J. C., & Roa, J. (2006). Preneoplastic lesions in gallbladder cancer. *Journal of surgical oncology*, 93(8), 615-623.
  11. Silk, Y. N., Douglass Jr, H. O., Nava, H. R., Driscoll, D. L., & Tartarian, G. A. B. R. I. E. L. (1989). Carcinoma of the gallbladder. The Roswell Park experience. *Annals of surgery*, 210(6), 751.
  12. Arora, V. K., Kumar, S., Singh, N., & Bhatia, A. (2005). Intraoperative bile cytology of the dysplasia-carcinoma in situ sequence of gallbladder carcinoma. *Cancer Cytopathology*, 105(5), 277-281.
  13. Baig, S. J., Biswas, S., Das, S., Basu, K., & Chattopadhyay, G. (2002). Histopathological changes in gallbladder mucosa in cholelithiasis: correlation with chemical composition of gallstones. *Tropical gastroenterology: official journal of the Digestive Diseases Foundation*, 23(1), 25-27.
  14. Mathur, S. K., Duhan, A., Singh, S., Aggarwal, M., Aggarwal, G., Sen, R., & Garg, S. (2012). Correlation of gallstone characteristics with mucosal changes in gall bladder. *Tropical gastroenterology*, 33(1), 39-44.
  15. Goyal, S., Singla, S., & Duhan, A. (2014). Correlation between gallstones characteristics and gallbladder mucosal changes: A retrospective study of 313 patients. *Clinical Cancer Investigation Journal*, 3(2), 157.
  16. Shukla, H.S., Avasthi, K., & Naithani, Y.P. (1981). Are the authors of this paper. A clinicopathological investigation of gallbladder carcinoma. *Indian Journal of Cancer*, 18;198-201.
  17. Albores-Saavedra, J., Alcantra, A., Cruz, H., Ortiz, & Herera, R. Goepfer. (1980). The lesions that precede invasive gallbladder carcinoma. Atypical hyperplasia, hyperplasia, and carcinoma in situ. *Cancer*; 45; 919-27.
  18. Mohandas, K.M., Dhir, V. (1999). In India, the epidemiology of digestive tract cancers is being studied. *Indian Journal of Gastroenterology*, 18; 24-8.
  19. SY Al-Hadeedi, Moorhead, R.I., Leaper, R.I., & J. (1991). Wong Gallbladder carcinoma: A diagnostic challenge. *Edin J Coll Surg*, 36; 174-7.
  20. Driscoll, D.L., Silk, Y.N., Douglas, H.O., Nava, H.R. (1989). Gallbladder carcinoma is a type of cancer that affects the gallbladder. *Ann Surg*, 210; 751-752.
  21. Albores-Saavedra, J., Molberg, K., & Henson, D. E. (1996). Gallbladder malignant epithelial tumors that is unusual. *Semin Diagn Pathol*, 13(3); 326-38.
  22. Yamigava, H., & H. (1986). Tamiyama Dysplasia carcinoma sequence of the gallbladder - Dysplasia carcinoma sequence of the gallbladder - Dysplasia carcinoma sequence of the gallbladder - Dysplasia carcinoma sequence of the gallbladder. *Jpn Acta Pathol*, 36; 989-97.
  23. Martinez-Guzman-e and, J. (1998). De-la Rosa-Bayan Gallbladder neoplasms and dysplasias, and their relationship to lithiasis a pathological study in a case-control clinic. *Mexican Journal of Gastroenterology*, 63; 82-8.
  24. Yamamoto, Y.M., Nakajo, S., & Tahara, E. (1989). Gallbladder carcinoma: The relationship between histogenesis and prognosis, 414:83-90 in *Virchows Arch Pathol Anat*.
  25. Duarte, I., Llanos, O., Domke, H., Harz, C., & Valdivieso, V. (1993). Metaplasia and precursor lesions of gallbladder carcinoma. Frequency, distribution, and probability of detection in routine histologic samples. *Cancer*, 72(6), 1878-1884.

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