



## Asymptomatic Gallstones: Dilemma, Controversy and Consensus

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### Abstract

**Background:** Cholecystectomy is currently advised only for patients with symptomatic gallstones. However, about 4.1% of patients with asymptomatic gallstones develop symptoms including cholecystitis, obstructive jaundice, pancreatitis, and gallbladder cancer.

**Objectives:** To assess the benefits and harms of surgical removal of the gallbladder for patients with asymptomatic gallstones.

**Material & Methods:** A topic wise search was done in Pubmed, Google-scholar, medIND and other electronic sources for asymptomatic gallstone, silent gallstones and preventive cholecystectomy.

**Conclusion:** There are no randomized trials comparing cholecystectomy versus no cholecystectomy in patients with silent gallstones. Further evaluation of observational studies, which measure outcomes such as obstructive jaundice, gallstone-associated pancreatitis, and/or gall-bladder cancer for sufficient duration of follow-up, is necessary.

But Laparoscopic cholecystectomy may be recommended for asymptomatic gallstones in areas where there is high prevalence of gallbladder stone disease and cancer.

**Keywords:** Asymptomatic gallstone, silent gallstones, preventive cholecystectomy, AsGS, gallbladder carcinoma.

### Introduction

Gallstone disease (GSD) or cholelithiasis is one of the most common medical problems leading to surgical intervention world over. With easy availability of abdominal ultrasound, asymptomatic gallstones (AsGS) are being diagnosed with increasing frequency.

Gallstones develop insidiously, and they may remain asymptomatic for decades. Complications of gall stones include cholecystitis,

choledocholithiasis, cholangitis, pancreatitis, gallstone ileus, empyema of gall bladder, mucocele, pyocele, perforation and rarely Mirizzi syndrome and carcinoma. Asymptomatic Gallstones (AsGS) are gallstones detected incidentally in patients who do not have any symptoms or have symptoms that are not attributable to gallstones. Diagnosis is made during ultrasound for other abdominal conditions or, sometimes, by palpation of the gall bladder at operation.

Patients with gallstones have significantly higher risk of developing gallbladder carcinoma (GBC) as compared to those without gallstones. About 50%-60% of patients with GBC have gallstones. Most patients with GBC have prior symptoms due to gallstones but GBC developing in patients with gallstones that were silent (asymptomatic) is not uncommon. This means that some patients with asymptomatic GS may go on to develop gallbladder carcinoma without having symptoms of cholelithiasis.

One Italian (GREPCO) study reports an annual complication rate of 0.3 - 1.2% if the stones are initially asymptomatic and 0.7 - 2% per annum if the stones are initially symptomatic [1].

The risk of developing gall bladder cancer is 0.3% over 30 years in one study and 0.25% for women and 0.12% for men in another over a similar period. Some studies suggest a much higher cancer risk with stones larger than 3cm size. A gall bladder cancer is rarely found without gallstone in the gall bladder except in the rare condition of adenomatous polyps.

**Materials and Methods**

To conduct this study we have gone through several journals and reports. A topic wise search was done in Pubmed , Google-scholar, medIND, the Cochrane Hepato-Biliary Group Controlled Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL),in The Cochrane Library, MEDLINE, EMBASE, and Science Citation Index Expanded until June 2018 and other sources for asymptomatic gallstone, silent gallstones and preventive cholecystectomy’.

**Aims & Objectives**

The purpose of this article was to examine various argument for and against preventive or prophylactic cholecystectomy for asymptomatic, silent and incidental gallstones with a special emphasis on certain groups of patients in Indian subcontinent context.

**Treatment Options**

From one extreme ( the most conservative) to other (the most aggressive), treatment options are: watchful expectant management; cholecystectomy if and when patient becomes symptomatic; selective cholecystectomy (in a subset of high risk cases) or prophylactic or preventive cholecystectomy (in all asymptomatic cases).Table 1 summaries conditions for selective cholecystectomy in asymptomatic GS harbourers.

**Table 1:** High-risk situations for cholecystectomy for asymptomatic gallstones.

<ul style="list-style-type: none"> <li>• Gallstones &gt;20 mm or &lt;3 mm with patent cystic duct</li> <li>• Gall bladder polyps &gt;10 mm</li> <li>• Non functioning gall bladder and porcelain gall bladder</li> <li>• Diabetes mellitus</li> <li>• Anomalous pancreatico-biliary ductal junction</li> <li>• On waiting list for non-hepatic organ transplant, e.g., heart and kidney</li> <li>• Life expectancy &gt;20 years</li> <li>• Females &lt;60 years</li> <li>• Area or populations with high prevalence of GBC (e.g. North and North-Eastern India)</li> </ul> <p>Source: References [2,3]</p>
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There is a subtle difference between the terms ‘prophylactic’ cholecystectomy (to prevent symptoms and complications of gallstones) and ‘preventive’ cholecystectomy (to prevent GBC, in areas with high incidence rates of GBC such as north and north-eastern India).The advantages and disadvantages of the above three approaches are summarized in Table 2.

**Table 2:** Management strategies compared

Strategies	Benefits	Harms
Watchful expectancy	1.Avoids overtreatment 2.Avoids anesthesia /surgery related complications Avoids unnecessary cost/workload on the health care system	1.Potential for development of a serious complication while waiting 2. Operation is done on an older patient (with co-morbidities) or in an emergency situation leading to extra complications.
Selective Cholecystectomy	1.Looks ideal – only high risk subsets with symptoms and complications would be treated	2.Practically difficult – clear identification of high-risk subjects is not easy and accurate

Prophylactic or Preventive cholecystectomy	1. Definitive cure with freedom from future symptoms and complications. 2. Usually a safe procedure with low morbidity and mortality, because asymptomatic and young subjects are operated.	1. Overtreatment of a large number of patients. 2. Early life morbidity/mortality from anesthesia and surgery
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### Concomitant or Incidental Gallstones

In patients with AsGS who undergo some other abdominal surgery, there is a high incidence of biliary symptoms and/or complications following surgery have been documented. Cholecystectomy is required in up to 40% of these patients within one year of this operation. A concomitant or incidental cholecystectomy is usually advised in such situations<sup>[4]</sup>. It requires planning for incision and is contraindicated when a prosthetic material is being used.

### GBC in India

Gallstone disease is relatively common in northern and northeastern India.<sup>[5,6]</sup> Incidence of GBC in women in northern India is as high as 9 per 100,000 per year as compared to, as low as 1 per 100,000, per year in parts of southern India.<sup>[7]</sup>

Studies from Delhi have reported early onset of gallstones in patients developing GBC, which is typical of high-incidence regions.<sup>[8]</sup> Epidemiological data suggest that the incidence rates in Delhi are the highest in the world.

Like Chile, the northern Indian subcontinent is a high-incidence region that extends from Karachi to Kolkata.<sup>[9,10,11]</sup>

Over 80% of GBC in India are diagnosed in an advanced stage, leading to little chance of cure.<sup>[13]</sup>

Female illiteracy, gender bias and poor public health services contribute to late diagnosis. A large proportion of Indian patients have jaundice when diagnosed.<sup>[12,13]</sup>

One epidemiological characteristic of high-incidence regions is the onset of gallstones at a younger age with increased complication rates and earlier need for cholecystectomy. Because

gallstones develop early in these populations, there is prolonged (several decades) exposure to the risk factor, with an increased risk of GBC.<sup>[14,15]</sup>

Since the carcinogenic progress is asymptomatic, most GBC are diagnosed in advanced stages with very low curability rates. Prophylactic cholecystectomy is said to be justified in this subgroup because a higher percent (3%-5%) develop GBC. Overall median survival for symptomatic GBC is less than 6 months and the overall five-year survival rate for GBC is less than 5%.

### Gallstones and GBC

Gallstones are usually 'silent' in most patients. Many previous follow-up studies have revealed that less than 20% with gallstones develop symptoms over a few decades.<sup>[16,17]</sup>

It requires the removal of 100 gall bladders to prevent one GBC. The standard recommendation therefore had been no prophylactic cholecystectomy for asymptomatic gallstones.<sup>[18,19]</sup>

A ten-year follow up in the GREPCO study revealed opposite findings. The study demonstrates a high incidence of gallstone disease in women belonging to a rural free-living population in Italy and suggests body mass index and parity as possible true risk factors. Moreover, it confirms that a remarkable proportion of asymptomatic patients become symptomatic and eventually undergo cholecystectomy.<sup>[20]</sup> More recent follow-up studies also reveal that silent gallstones are not that innocent. Similarly a population-based Swedish study revealed that intervention is required in 10% of patients in 5 years.<sup>[21]</sup>

### Prevention of Gall Bladder Cancer

The traditional recommendation for asymptomatic gallstones has been expectant observation.

The consensus statements however make an exception to this in high-risk population groups. The risk and complications of laparoscopic cholecystectomy (LC) is low when performed at a younger age as an elective surgery when the gall bladder is not inflamed or complicated. A recent

cost-effectiveness analysis of Chilean women under 40 years old with asymptomatic gallstones revealed that prophylactic LC can benefit the population at a very low incremental cost.<sup>[22]</sup>

It is true that the doing cholecystectomy to treat all patients with asymptomatic gallstones may be impossible in India. But this should not prevent us from offering LC to those who have incidentally detected gallstones in higher incidence regions of India. Large experience from India shows that the morbidity and mortality associated with LC is very low.<sup>[23, 24]</sup>

The fear of increased risk of colorectal cancer (CRC) and other cancers after LC is not proven. Also occurrence of diarrhea after gall bladder removal is also controversial. The following reasons may validate performance of preventive laparoscopic cholecystectomy in north Indian women<sup>[25]</sup>:

1. Elective laparoscopic cholecystectomy in properly trained hands very safe in India.
2. Gender bias, rampant illiteracy create obstacles in healthcare delivery
3. Incidence rate of GBC in Delhi and Kolkata one of the highest in the world.
4. Life expectancy of northern Indian women has increased beyond sixty years
5. Large percentage of women develops gallstones before 50 years age.
6. Lack of medical insurance and health-care facilities hamper regular follow up.
7. Laparoscopic cholecystectomy safe in young patients with uncomplicated gallstone disease.
8. Most women also have other risk factors like early pregnancy and multiple pregnancies.
9. Outcome of clinically diagnosed GBC in India dismal for last 20 years.

### Conclusion

NICE Clinical Guideline 188 on 'Managing asymptomatic gallbladder stones' states: "Reassure people with asymptomatic gallbladder stones found in a normal gallbladder and normal biliary tree that they do not need treatment unless they develop symptoms."

A recent Cochrane Database Systematic Review<sup>[26]</sup> observed "There are no randomized trials comparing cholecystectomy versus no cholecystectomy in patients with silent (asymptomatic) GS. Further observational studies randomised trials, which measures outcomes such as obstructive jaundice, GS associated pancreatitis and/or GBC involving a long follow-up, is necessary in order to evaluate whether cholecystectomy or no cholecystectomy is better for asymptomatic GS.

Cholecystectomy is currently advised only for symptomatic gallstones. However, about 4.1% of patients with asymptomatic gallstones develop complications including, obstructive jaundice, pancreatitis, and gallbladder cancer.

There is no randomised trial comparing cholecystectomy versus no cholecystectomy in silent gallstones. Further evaluation of observational studies, which measure outcomes such as obstructive jaundice, gallstone-associated pancreatitis, and/or gall-bladder cancer for sufficient duration of follow-up is necessary before randomized trials are designed in order to evaluate whether cholecystectomy or no cholecystectomy is better for asymptomatic gallstones. But current opinion is that management of most patients with asymptomatic gallstones should be expectant, although it is still a controversial issue.

In the era of laparoscopic cholecystectomy, a consensus appears to be emerging regarding laparoscopic cholecystectomy in selected groups of patients with asymptomatic gallstones. Laparoscopic cholecystectomy is recommended for asymptomatic gallstones in areas where there is high prevalence of gallbladder cancer. This may be a case for supporting preventive cholecystectomy for GBC in a young (20s or 30s) patient with a large GS in north and north east India but, till today, there is no data or evidence or consensus to support it.

Therefore preventive cholecystectomy for asymptomatic gallstone remains an individual decision taken in consultation with the patient after explaining everything and taking informed consent..

BUT.... 'The availability of laparoscopic cholecystectomy should not expand the indications for gall bladder removal'. [NIH Consensus Conference Report 1993].

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