Controversy

Cholecystectomy in patients with asymptomatic gallstones to prevent gall bladder cancer – the case against

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Gallstones (GS) are common in northern India. GS are the most important risk factor for gall bladder cancer (GBC). Data from the West, however, indicate that the risk of GBC in persons with asymptomatic GS is very small and does not warrant prophylactic cholecystectomy. Can these recommendations be applied to northern India where incidence rates of GBC are one of the highest in the world? Not all persons with asymptomatic GS require cholecystectomy. There may, however, be a case for offering cholecystectomy to a young woman in northern India with a large GS or a gall bladder packed with GS, though there is no evidence to support this recommendation. Type of stone, tumor markers and genetic markers need to be investigated to identify those with asymptomatic GS who are at the highest risk of developing GBC so that they can selectively be offered pre-emptive cholecystectomy to prevent GBC. [IndianJ Gastroenterol 2006;25:152-154]

Gallstones (GS) are common in northern India. The overall prevalence in women in Kashmir was 4%; as many as 16% and 29% of women above the age of 40-49 years and 50-59 years, respectively, had GS. For every patient with symptomatic gallstone disease (GSD) there are many with asymptomatic GS; Khan, in a review of 9,332 post-mortem reports over 10 years, found that only 14% of those with GS had undergone cholecystectomy, indicating that up to 86% were asymptomatic. These asymptomatic GS are being more frequently detected incidentally as ultrasonography (US) has become a routine investigation.

Cholecystectomy is the treatment of choice for GSD. With an extrapolated prevalence rate of 4%, the state of Uttar Pradesh, with a population of 150 million, will have 6 million persons with asymptomatic GS. If one center were to perform five laparoscopic cholecystectomies (LC) a day for 200 working days in a year, we will need 600 such centers to perform only LC for 10 years to treat all these persons. With a 0.5% risk of bile duct injury (BDI) during LC, this will result in 30,000 BDI. Cholecystectomy also increases the risk of colon cancer; in a study comparing 55,960 patients who underwent cholecystectomy with 574,668 who did not, the incidence ratio of colon cancer was 1.3 (1.2-1.5). Patients may also develop duodeno-gastric reflux and diarrhea after cholecystectomy.

Patients with GS have higher risk of developing GBC as compared to those without GS. A majority (60%-70%) of patients with GBC have GS. Most patients with GBC have prior symptoms of GSD but GBC developing in patients with GS that were silent (asymptomatic) is not uncommon. This means that some patients with asymptomatic GS may go on to develop GBC without having symptoms of GSD.

The natural history of asymptomatic GS for development of GBC has been well studied. Ransohoff and Gracie reviewed 1,000 persons with asymptomatic GS followed up for 7,000 patient years; none developed GBC. The Group for Epidemiology and Prevention of Cholelithiasis (GREPCO) in Italy followed up 118 persons with asymptomatic GS for 10 years; only one developed GBC and died. Maringhini followed up 2,583 patients with gallstones; only 5 (0.2%) developed GBC. Various studies have thus indicated that a very small number of persons with asymptomatic gallstones develop GBC over years. Prophylactic cholecystectomy to prevent GBC is, therefore, not recommended for asymptomatic GS. Can recommendations from the West where GBC is uncommon apply to northern India where GBC is common? Also, the follow up in these studies ranged from 7-25 years; can these recommendations apply to young persons in their 20s and 30s who have 50-70 years of life ahead?

There are, admittedly, some indications for prophylactic cholecystectomy in patients with asymptomatic GS to prevent GBC. These include

1. Age: GS in children and young adults, even if asymptomatic, as the cumulative lifetime risk of developing GBC may be higher.
2. Thick-walled gall bladder (GB) (wall thickness >3 mm on US), as one-half of these GB are likely to have xanthogranulomatous cholecystitis, and the risk of an incidental GBC in them is higher.
3. Large stones: persons with stones larger than 3 cm have ten times higher risk of developing GBC as compared to those with stones smaller than 1 cm. GB packed with stones (high stone / GB volume ratio) are more likely to have GBC. 

4. Associated conditions such as porcelain GB, large sessile polyp, anomalous pancreatico-biliary ductal union, all of which have higher risk of GBC.

5. Race and geographical location: the incidence rates of GBC show great variations amongst various races and in different geographical areas. Native American Indians have a very high risk of GBC in the presence of GS. Lowenfels performed a case-control study in 139 patients with GBC and 2,399 without GBC; the 20-year cumulative risk of developing GBC was 1.5% in native American females (versus 0.1% in black males). One GBC could be prevented by performing only 67 cholecystectomies in the high-risk population (versus 769 cholecystectomies in the low-risk group).

The incidence of GBC is very high (more than 5 per 100,000 per year as compared to less than 1 per 100,000 per year in USA and UK) in central and south America, central and eastern Europe, and Japan. In India, incidence rates in females in the north are very high (AAR 9.8) as compared to those in the south. Indians, as a race, may be at higher risk to develop GBC because Indian migrants to the UK, Australia, Fiji, Kuwait and Singapore have higher incidence / mortality from GBC as compared to native populations in these areas. Prophylactic cholecystectomy may be indicated in these races and in these geographical areas. Surgeons in Chile recommend prophylactic cholecystectomy for all women with GS, though without much supporting evidence.

6. High parity and first childbirth before 25 years of age, as these factors are also associated with higher risk of GBC.

Any person with asymptomatic GS who is advised to undergo prophylactic cholecystectomy should be fully motivated for surgery and must be very clearly and explicitly told about the possible risks and complications, particularly BDI, the risk of which is unfortunately higher after laparoscopic than after open cholecystectomy. As opposed to cholecystectomy for symptomatic GSD, there are no immediate benefits from the operation.

If persons with asymptomatic GS are not operated on, what advice should be given to them? Follow up with frequent US? But how frequent? Is an annual US enough to detect GBC in the early resec-

Table stage? Probably not. In Niigata, Japan, when annual US screening was performed for persons above 40 years of age, 3 of 4 GBC that were detected were in advanced stages.

Cholecystectomy will prevent GBC but all persons with asymptomatic GS need not, cannot and should not be advised to have prophylactic cholecystectomy to prevent GBC. Those who have a higher risk of developing GBC need to be identified and probably offered ‘pre-emptive’ cholecystectomy. This will take age, geography, race, size of stone and stone / GB volume ratio into account. Tumor markers and genetic markers may also help to identify these persons. We are presently analyzing the stones obtained from patients with GBC and GSD to find out if they are different and if these differences can be detected in vivo using nuclear magnetic resonance, computed tomography and bone densitometry.

The wise surgeon may read Rabindranath Tagore but should use his (her) discretion and judgment in a given case.

References

12. Lowenfels AB, Lindstrom CG, Conway MJ, Hastings PR.
A 52-year-old man presented with recent onset of exertional dyspnea and dyspepsia. There was no history of gastrointestinal bleeding. Physical examination was normal except for pallor.

Investigations: hemoglobin 7.5 g/dL, total leukocyte count 5,600/mm$^3$, platelets 210,000/mm$^3$. Peripheral smear showed microcytic hypochromic anemia. Fecal occult blood test was positive. Endoscopy showed multiple punctate hemorrhagic areas in the antrum with slender, short, reddish worms in the same location (Fig). The worms were attached to the mucosa and showed active movement. No worms were seen in the first or second part of duodenum. Under light microscope, the worms were identified as *Ancylostoma duodenale* and the crushed specimens showed ova of hookworms. The patient was treated with albendazole 400 mg single dose followed by hematinics.

Two months later, the patient has improved, stool occult blood test was negative, and hemoglobin was 12.2 g/dL.

Hookworms develop into adult worms in the upper small intestine and attach to the small intestinal mucosa. Very rarely, they are retrieved from ectopic sites like the stomach and cecum. Ectopic localization in the antrum of the stomach has been attributed to jejuno-duodeno-gastric reflux.

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**References**


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