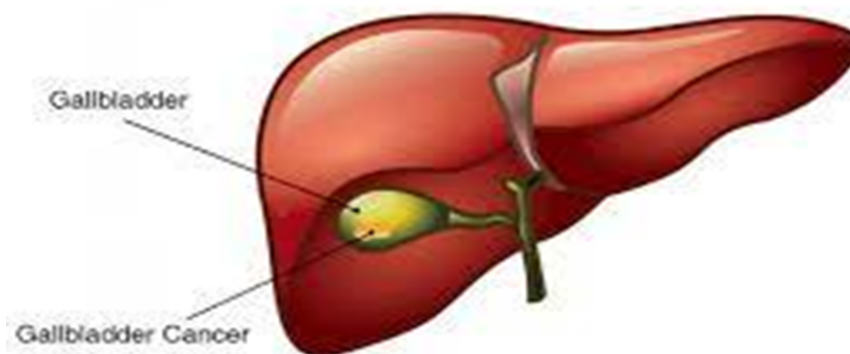




TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Gallbladder Cancer



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Gallbladder cancer

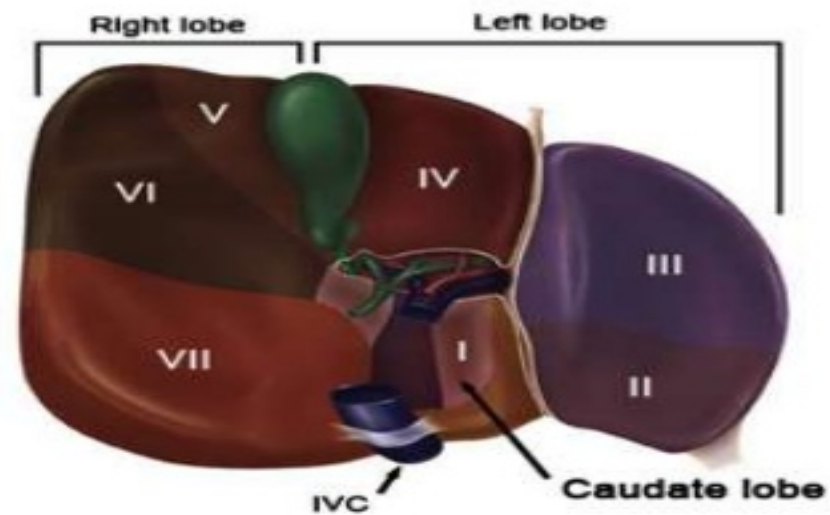
- is an uncommon but highly fatal malignancy; fewer than 5000 new cases are diagnosed each year in the United States.
- The majority (close to 90 %) are adenocarcinoma.
- The majority are found incidentally in patients undergoing exploration for cholelithiasis; a tumor will be found in 1 to 2 % of such cases.
- The poor prognosis associated with GBC is thought to be related to advanced stage at diagnosis, which is due both to the anatomic

- Gallstones are present in 70 -90 % of patients with GBC.
- The risk is higher with larger gallstones (in one study, patients with stones larger than 3 cm had a 10-fold higher risk of GBC compared with those with stones <1 cm) and longer duration of cholelithiasis (particularly over the age of 40 years .

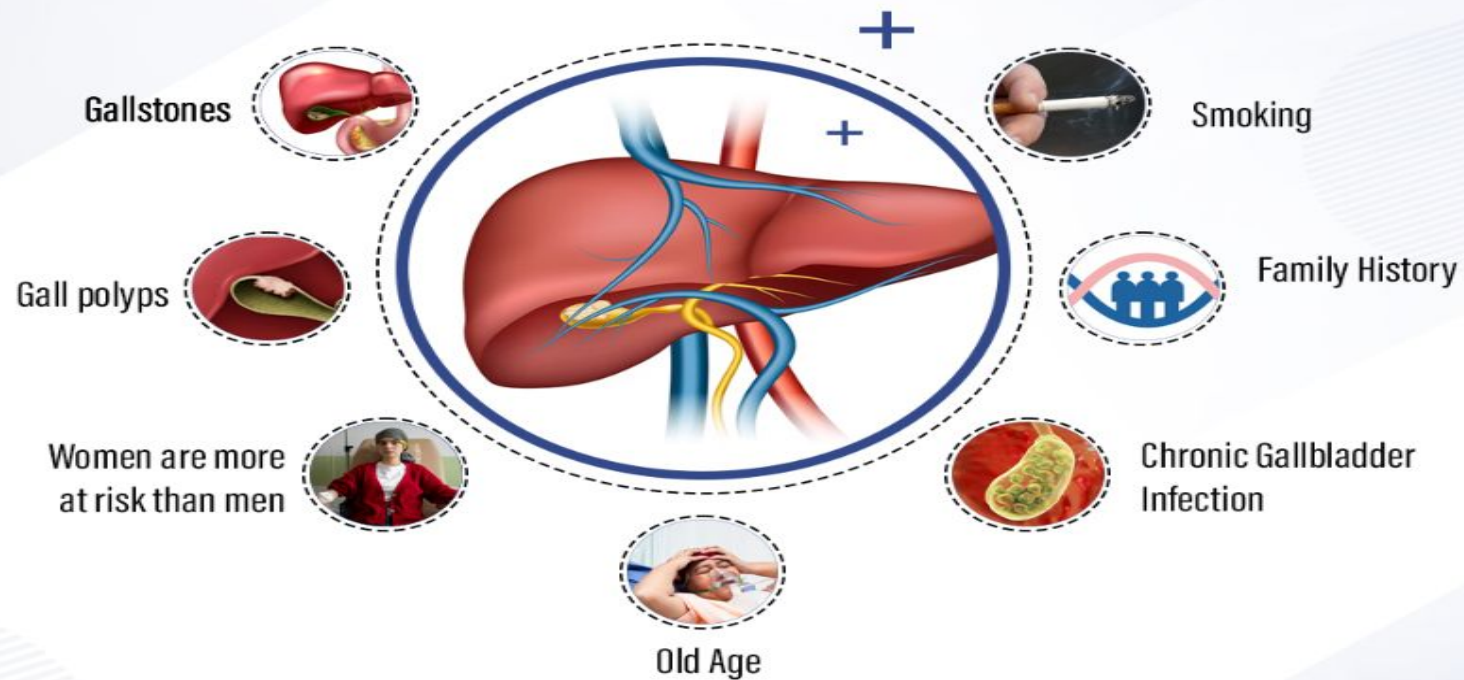
Epidemiology

- Worldwide, there is prominent geographic variability in GBC incidence that correlates with the prevalence of cholelithiasis.
- High rates of GBC are seen in South American countries, particularly Chile, Bolivia, and Ecuador, as well as some areas of northern India, Pakistan, Japan, Korea, and Poland.
- Globally, the burden of gallbladder and other biliary tract cancers has risen over the last 30 years .

- The gallbladder is attached to segments IVb and V of the liver and these segments are involved early in tumors of the fundus and body of the gallbladder → limited segmental resection often possible



Risk Factors of GALLBLADDER CANCER



Clinical presentation and diagnostic evaluation

- Patients with early invasive GBC are most often asymptomatic, or they have nonspecific symptoms that mimic or are due to cholelithiasis or cholecystitis.
- Malignancy diagnosed incidentally on pathologic examination after a simple cholecystectomy is the most common mode of presentation of early stage disease.
- Ultrasound (US) is typically the initial study; however, the overall accuracy of US for staging the local and distant extent of suspected GBC is limited.
- Laboratory studies are generally non diagnostic.

CT or MRI or MRCP is needed for patients who have concerning findings on sonography (calcification, a mass protruding into the lumen, loss of interface between gallbladder and liver, direct liver infiltration, gallbladder polyps ≥ 10 mm, or a thickened gallbladder wall that is not explained by cholecystitis).

In this setting, evaluation of potential resectability is the key factor.

Staging(TNM)

- The spread to nearby lymph **nodes (N)**: Has the cancer spread to nearby lymph nodes and if so, how many?
- The spread (**metastasis**) to distant sites (**M**): Has the cancer spread to distant organs such as the liver, the peritoneum (the lining of the abdominal cavity), or the lungs?

The system described below is the most recent AJCC system, effective January 2018. This system is used to stage cancers of the gallbladder as well as cancers that start in the cystic duct (the tube that carries bile away from the gallbladder).

Primary tumor (T)

Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor invades the lamina propria or muscle layer
T1a	Tumor invades the lamina propria
T1b	Tumor invades the muscle layer
T2	Tumor invades perimuscular connective tissue; no extension beyond the serosa or into the liver
T3	Tumor perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure, such as the stomach, duodenum, colon, pancreas, omentum, or extrahepatic bile ducts
T4	Tumor invades the main portal vein or hepatic artery or invades two or more extrahepatic organs or structures

Regional lymph nodes (N)

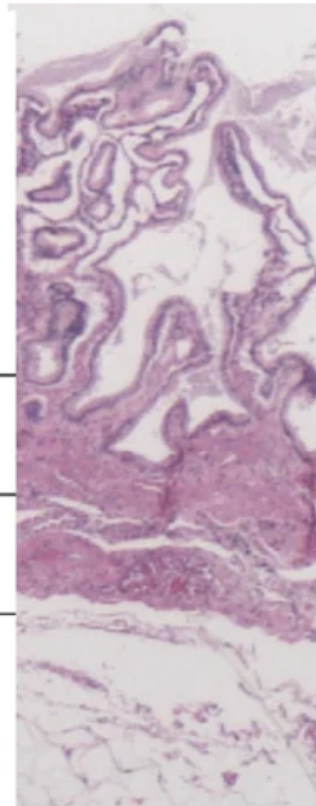
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

Distant metastasis (M)

Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage grouping

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage III	T4	Any N	M0
Stage IV	Any T	Any N	M1



T1a - Lamina Propria

T1b - Muscularis propria

T2 - Perimuscular connective tissue, not beyond serosa

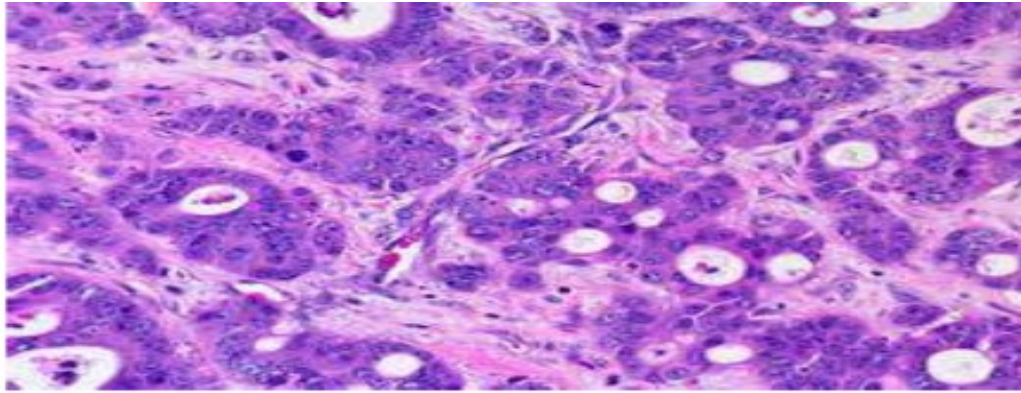
T3 - Perforates serosa and/or liver and/or one other adjacent organ

T4 - Tumor invades portal vein/hepatic artery or other extrahepatic structures

Prognosis

- The prognosis worsens when the tumor invades the deeper layers of the gallbladder. In fact, the 5-year survival rates range from 70% with involvement of the sub-serosa (T2= invasion of peri muscular connective tissue), falling to 0% with the spread to adjacent organs (T3= penetration of the serosa).

The 5-year survival rates start at 80% for stage 0,
50% for stage I
28% for stage II
8%for stage IIIa
7% for stage IIIb, 4% for stage IVa
2% for stage IVb.

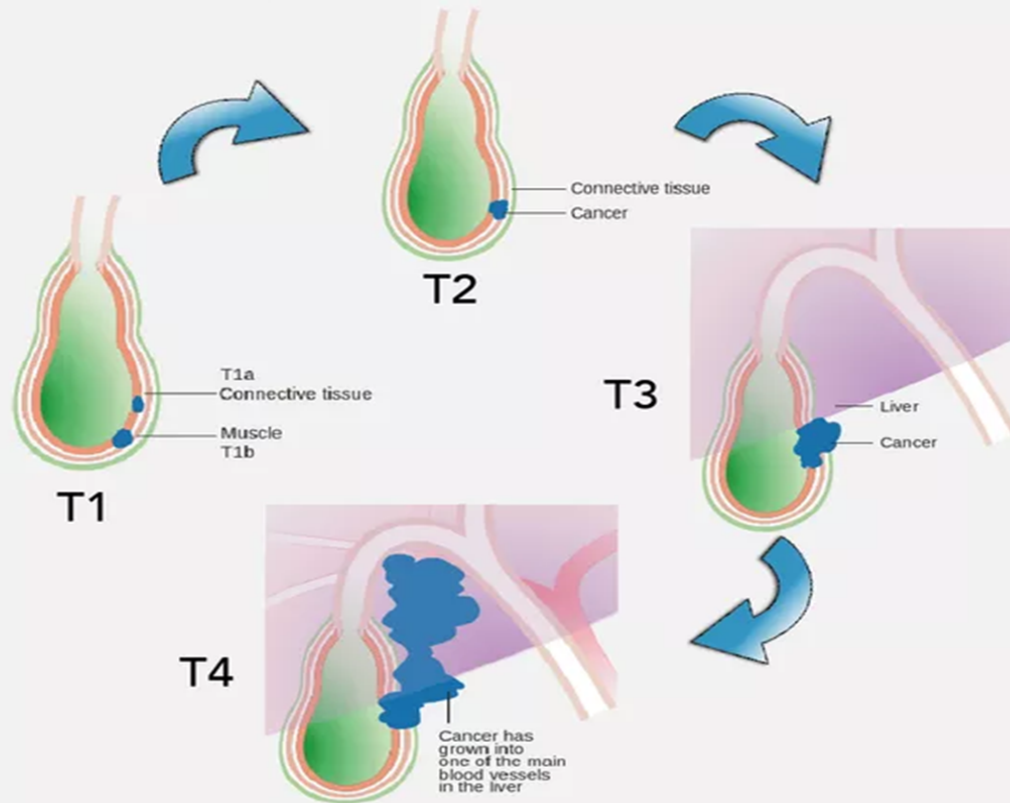


- Histopathological grading
 - G1- well differentiated
 - G3- undifferentiated
 - Majority of patient present with G3 poorly differentiated tumors

Adenocarcinoma is the most frequent histologic type, accounting for 98% of all gallbladder tumors; two-thirds of these are moderately or poorly differentiated.

Treatment

Stages of Gallbladder Cancer



5% 5-year survival rate

2 - 6 times **higher** risk for women

Mutations identified by *Iyer et al*:

ERBB2: Target of the drug Afatinib

KRAS: Confers resistance to treatment

