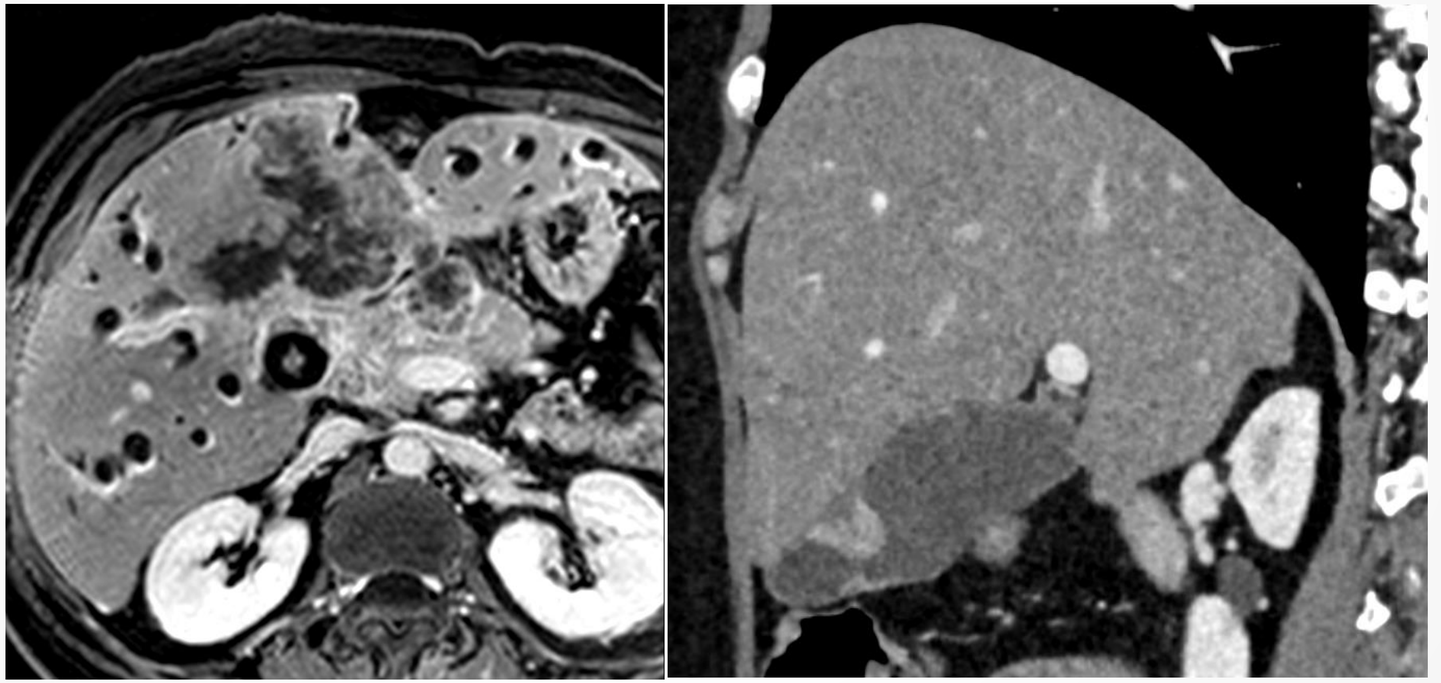
Gall Bladder Polyp to Carcinoma – "The Road to Hell"

Authors: Karthik Ganesan, Shivsamb Jalkote, Ankit Jain, Slesha Bhalja, Shah Alam, Swarup Nellore,
Sir.H.N.Reliance Foundation Hospital and Research Center
Mumbai | India
Email: karthik.s.ganesan@rfhospital.org
drkarthikg@gmail.com



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Presenting Author
Dr.Ankit Jain, MBBS, MD
Sir.H.N.Reliance Foundation Hospital and Research Center
Mumbai | India

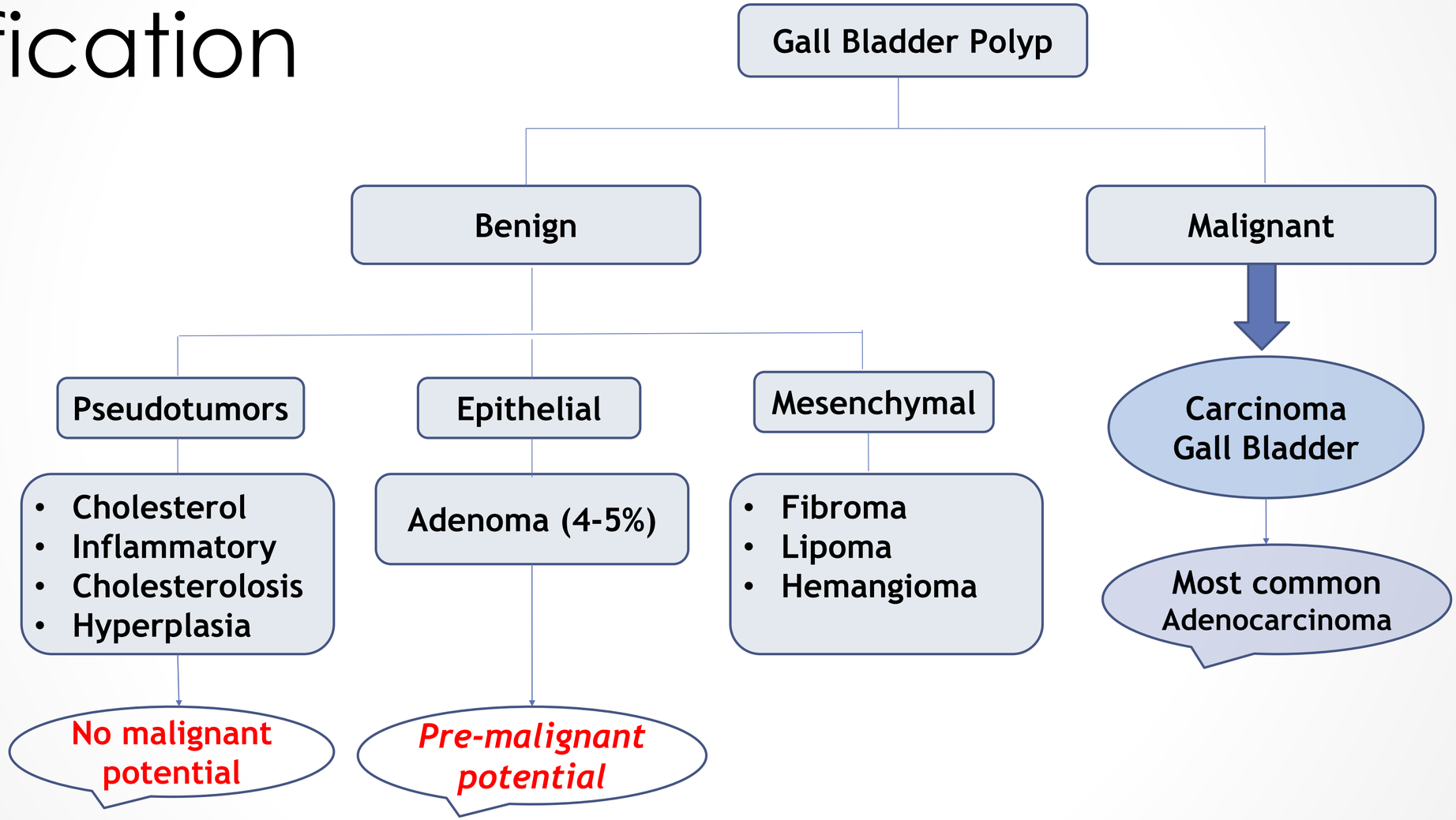
Learning Objectives

- Discuss etiopathogenesis of GB polyps and Cancer.
- Review the joint guidelines for management of GB polyp by ESGAR, EAES, EFISDS and ESGE.
- Discuss key imaging features and pathways of spread of GBC [Gall bladder carcinoma].
- Discuss imaging mimics of GBC.
- Review current guidelines for management of GBC.

Epidemiology

- Gall bladder polyps are considered as elevation of the gallbladder mucosa that protrudes into the gallbladder lumen.
- Common incidentalomas with a reported prevalence of 0.3 – 9.5%.
- Majority of the gallbladder polyps are pseudopolyps [70%] and benign.
- True gall bladder polyps can be benign and malignant.

Classification



- Due to pre-malignant potential of true polyp, and poor prognosis of gallbladder carcinoma, they need meticulous assessment and management.

- ***Need of early diagnosis*** **- Gall bladder carcinoma carries poor prognosis.**

5-year survival rate in Carcinoma gall bladder	
Stage I (confined to the muscularis mucosa)	100%
Stage II (confined to the perimuscular connective tissue)	57-72 %
Stage III (perforates serosa)	< 25%

ESGAR with collaboration of EAES, EFISDS & ESGE sought to develop evidence based consensus guidelines in order to address:

1. Which patients require cholecystectomy?

2. Which patients require USG follow-up?

3. What should be the frequency & duration of follow-up?

- European Society of Gastrointestinal and Abdominal Radiology (ESGAR) , European Association for Endoscopic Surgery (EAES) International Society of Digestive Surgery – European Federation (EFISDS) , European Society of Gastrointestinal Endoscopy (ESGE)

GB Polyp on USG

> 10mm → Cholecystectomy, if not then follow-up

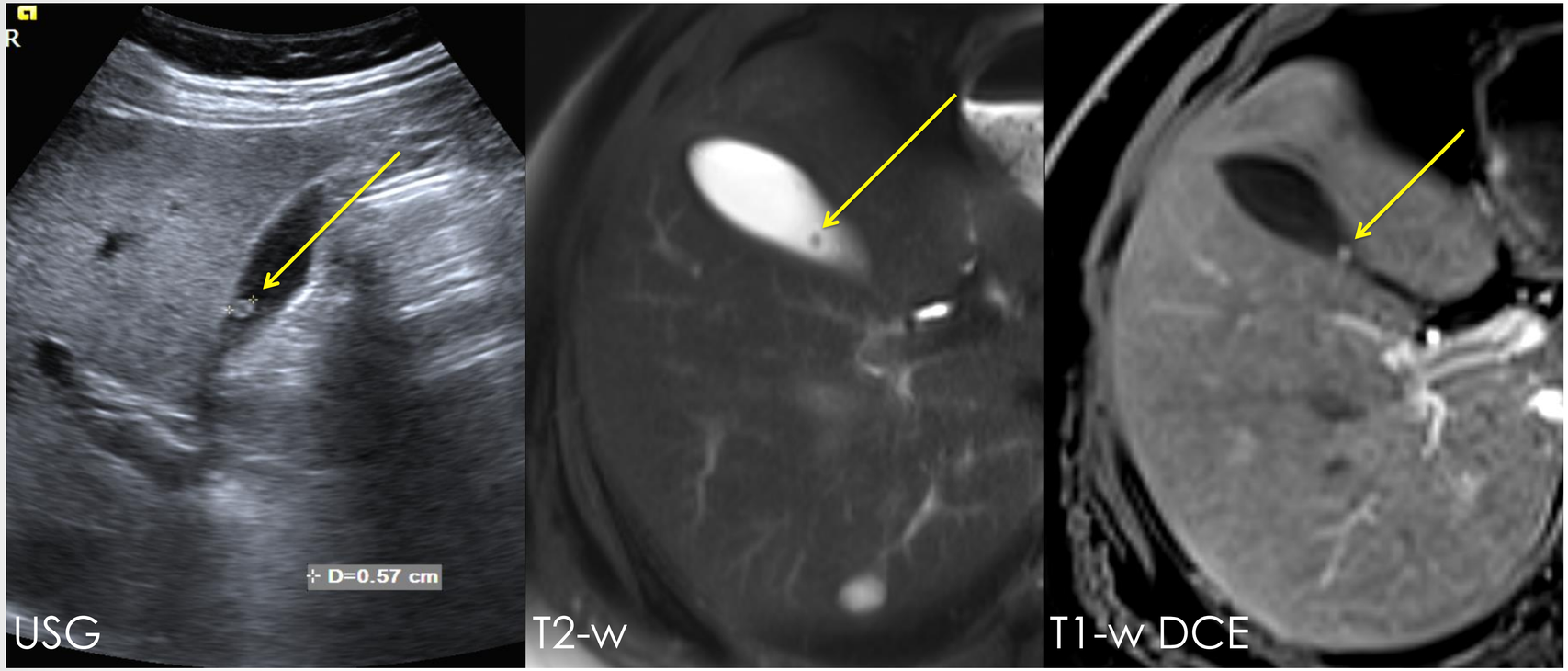
<10mm → Does the pt. have symptoms ?

Yes → Cholecystectomy [no alternative cause of symptoms], if not then follow-up

No → Risk factors for GB malignancy
- Age >50 yrs
- Primary sclerosing cholangitis
- Indian ethnicity
- Sessile polyp (focal wall thickening > 4 mm)

Yes →
- Polyp < 6mm : follow-up USG at 6M/1/2/3/ 4/5 yrs
- Polyp 6-9 mm : cholecystectomy, if not then follow up

No →
- **Polyp < 6mm :** Follow-up USG at 1/3/5 yrs
- **Polyp 6-9 mm :** Follow up at 6M/1/2/3/4/5 yrs



51 year old, Indian ethnicity male patient, with incidentally detected gall polyp of size 5mm.

PEARL – Polyp of <5mm, in an Indian patient requires follow-up.

GB Polyp on USG

< 5 mm

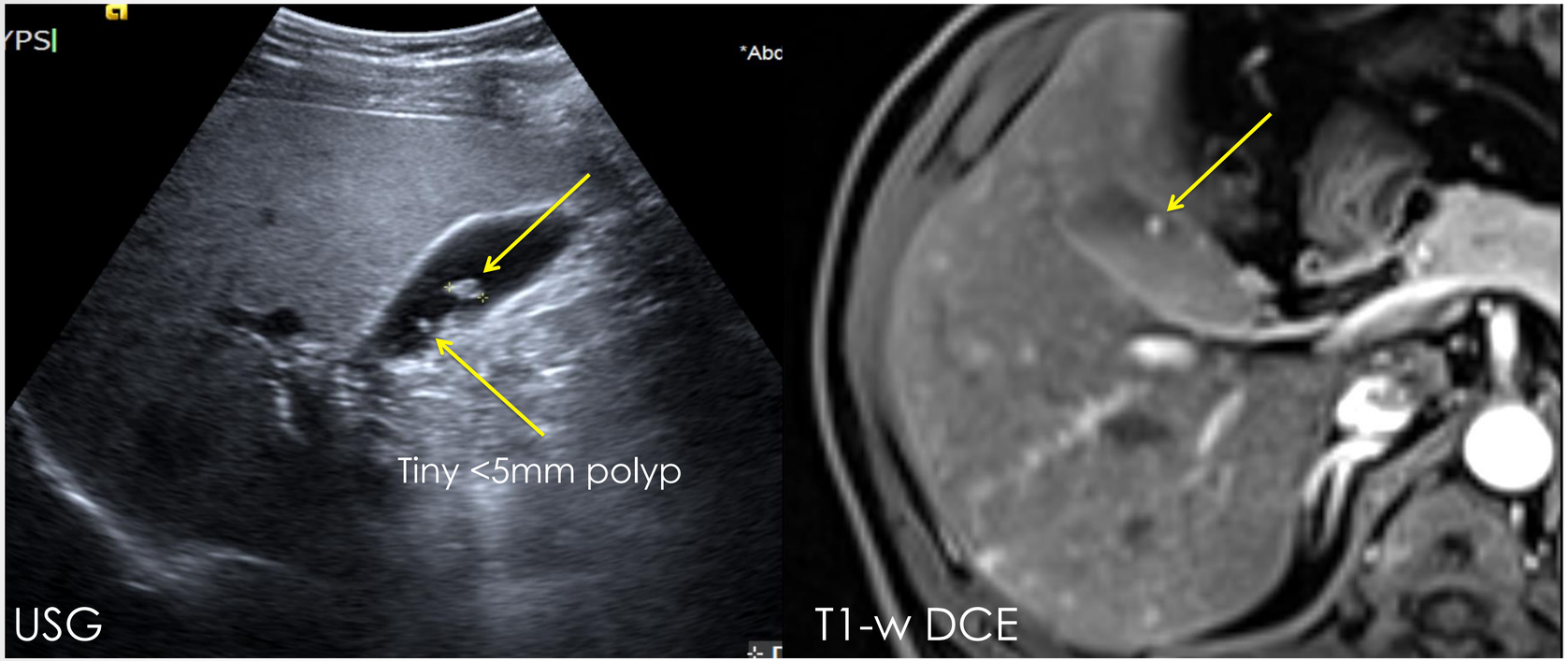
Does the pt. have symptoms ?

No

Risk factors for GB malignancy
- Age >50 yrs
- Primary sclerosing cholangitis
- Indian ethnicity
- Sessile polyp (focal wall thickening >4mm)

Yes

Polyp < 6mm : follow-up USG at 6M/1/2/3/4/5 years



58 year old, Indian ethnicity male patient, with incidentally detected gall polyp of size 7 mm.

PEARL – Polyp of 6-9mm, in Indian patient, cholecystectomy is always preferred.

GB Polyp on USG

< 10 mm

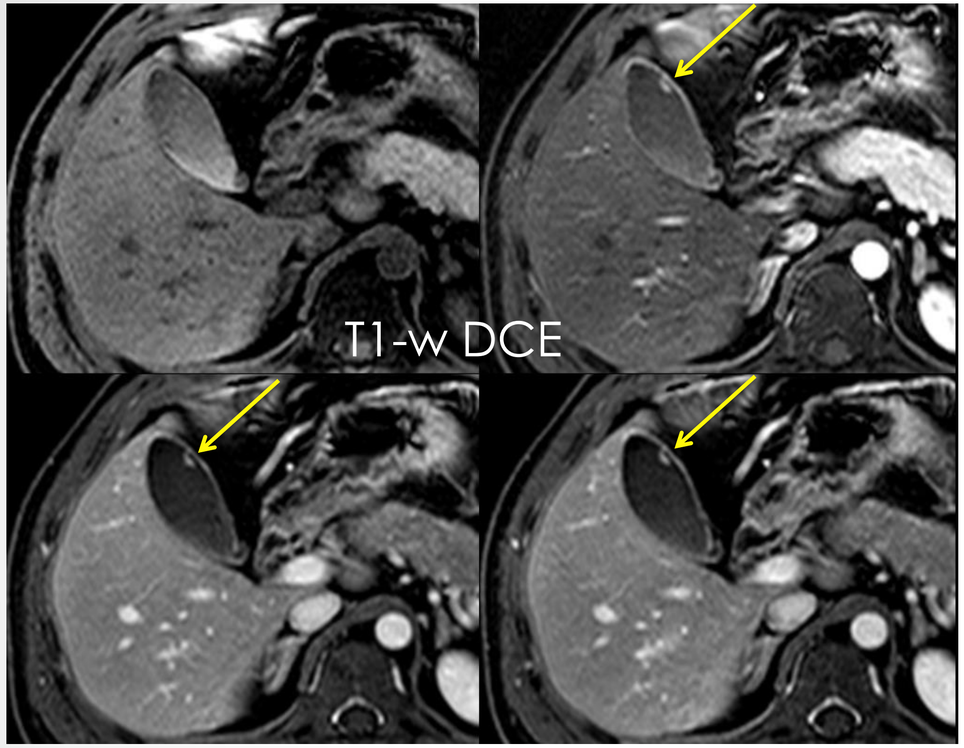
Does the pt. have symptoms ?

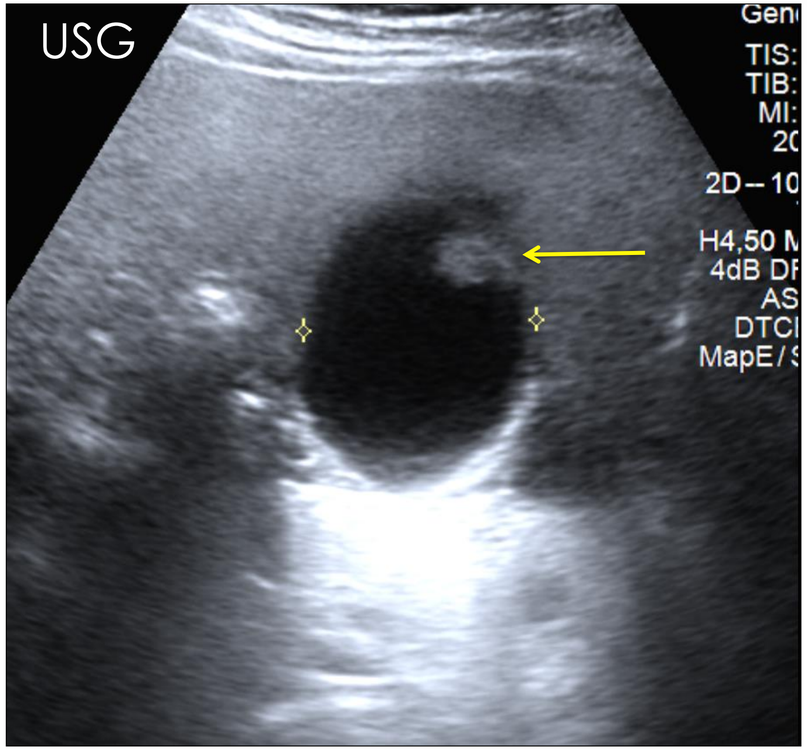
No

Risk factors for GB malignancy
- Age >50 yrs
- Primary sclerosing cholangitis
- Indian ethnicity
- Sessile polyp (focal wall thickening > 4 mm)

Yes

Polyp 6-9 mm : cholecystectomy, if not then follow up





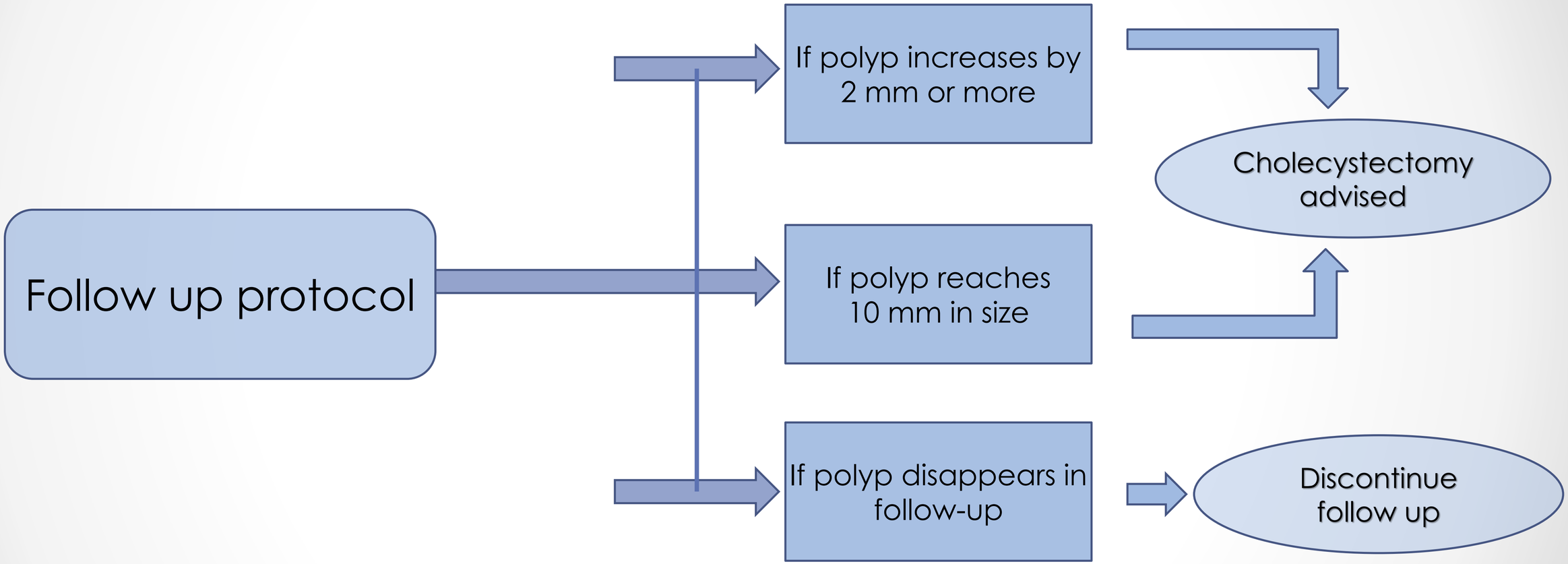
GB Polyp on USG

> 10 mm

Cholecystectomy, if not then follow-up

50 year old, Indian ethnicity male patient, with incidental detected gall polyp of size 11mm.

PEARL – Polyp of 10mm or more, patient directly goes for cholecystectomy, irrespective of risk factors.


Follow up protocol
If polyp increases by 2 mm or more
If polyp reaches 10 mm in size
If polyp disappears in follow-up
Cholecystectomy advised
Discontinue follow up

Risk Factors for Gall bladder Malignancy

Age	Advancing age with 50 years as cut-off for intensive management plan.
Sex	Women > Men, especially in Asian females.
Ethnicity	~ 13 times higher risk in Indian compared to Caucasian population.
Morphology	Sessile polyp
Numbers	Single [frequently malignant], multiple [usually cholesterol polyp].
Primary sclerosing cholangitis	Increase the risk, mainly in polyp > 6mm
Tumor markers [Serum CEA and CA 19-9]	Little role in differentiating benign and malignancy.

Gall bladder carcinoma, although a rare illness, is the most common malignancy of the biliary tract, with traditionally poor outcome because of the following reasons:

- Often minimally symptomatic/ asymptomatic in its early stages.
- Metastasis and invasion often before diagnosis.
- Not sensitive to radiotherapy and chemotherapy.
- 5-year survival rate of less than 5% in advanced stage.

In early-stage disease, a 5-year survival rate of 75%-100% can be achieved

So, the primary goal in the management of gallbladder polyps is to prevent or early detection of the gallbladder carcinoma.

Risk Factors for Gall bladder Malignancy

Demographics

- Advancing age
- Female gender
- Obesity
- Geographical and ethnicity
- Genetic predisposition

Pathologies

- Cholelithiasis
- Porcelain gallbladder
- Gallbladder polyps
- Congenital biliary cysts
- Ductal anomalies

Exposure

- Heavy metals
- Medications: methyldopa, OCP, isoniazid, and estrogen
- Smoking.

Infection

- Salmonella
- Helicobacter

Mechanisms of Initiation of Cancer

Chronic inflammation

↓

Recurrent or chronic inflammation results in detrimental damage of DNA

↓

Tissue repeatedly attempts at restoration and provokes tissue proliferation

↓

Release many cytokines and growth factors, and predispose cells to oncogenic transformation

Principles of Imaging - GB polyps

Abdominal ultrasonography considered as the best modality for diagnosing gallbladder polyps, because of accessibility, low cost, with good sensitivity and specificity.

ULTRASONOGRAPHY

- Best Modality for diagnosis
- Seen As An Elevation Of GB Wall That Protrudes Into The Lumen.
- Should Not Be Mobile Or Demonstrate Posterior Acoustic Shadow

C.T.

- Not sensitive in detecting small gallbladder polyps.
- Larger polyps - soft tissue attenuation projections with similar enhancement as rest of the gallbladder.
- Increased enhancement raise suspicion of malignancy.

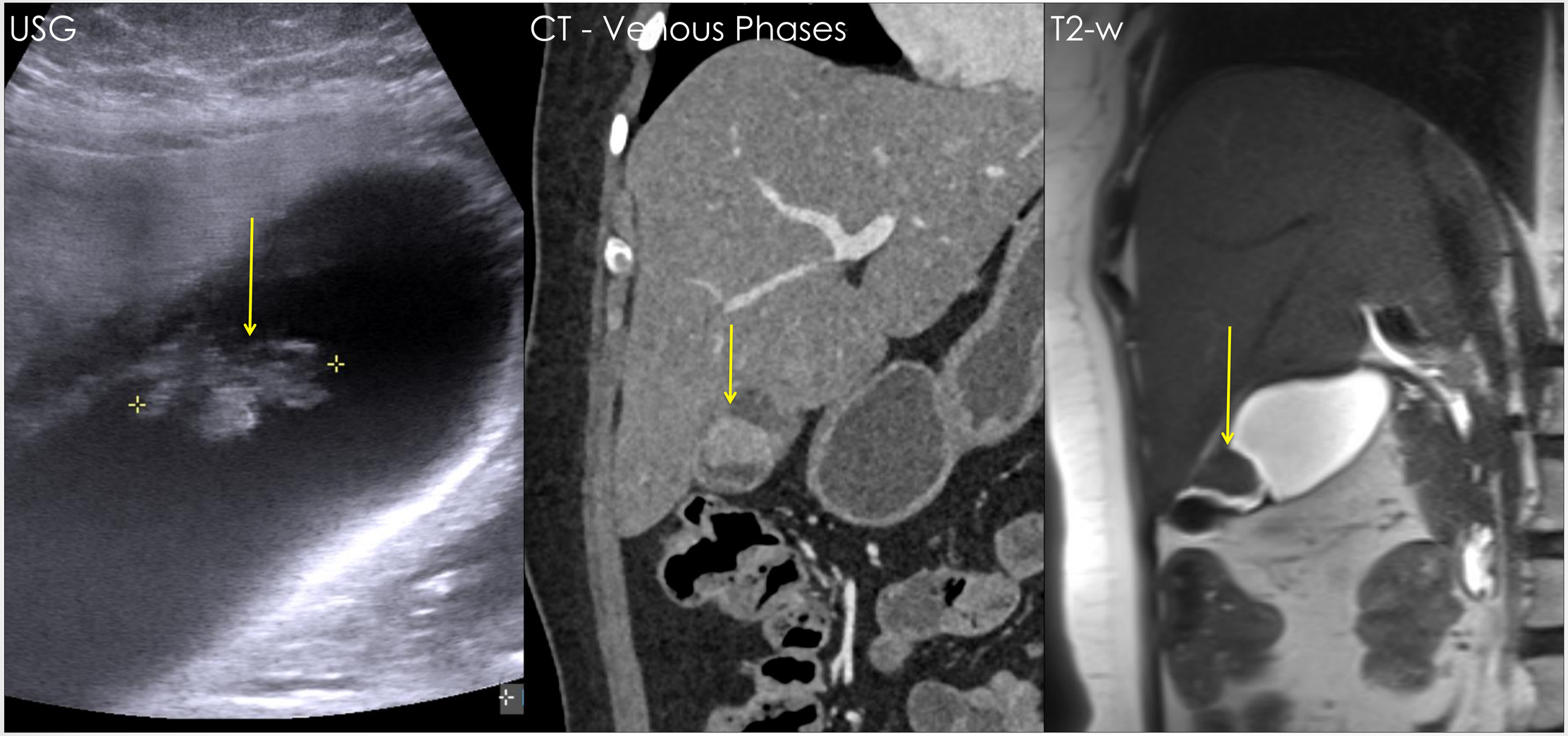
M.R.I

- Not routinely used to evaluate gall bladder polyp.
- Seen as T2 hypointense foci with early enhancement and subsequent washout.
- DWI/ADC – differentiating benign and malignant polypoidal lesions by demonstrating high cellularity in later.

Principles of Imaging - Carcinoma GB

- Cross sectional imaging plays a pivotal role in staging of the gall bladder cancer.
- CECT of abdomen and pelvis / CE-MRI with MRCP sequences with CT chest [contrast / noncontrast] should be performed.
- MRI - Better in evaluating masses within the gall bladder with bile duct involvement.
- Nodal disease should be properly evaluated, specifically the porta hepatis, left gastric and aorto-caval basin.
- PET/CT - limited sensitivity for disease perse. but has high specificity for regional nodal disease, so used in case of equivocal CT/MRI findings.
- Follow up imaging – includes CECT / MRI of abdomen and pelvis with chest imaging.

Ref: – NCCN Guidelines Version 2.2019 Gall Bladder Cancer



-old Male with a 24mm polypoidal lesion with multiple frond-like protuberances [yellow arrows] arising from the GB wall [hepatic
H.P: Papillary Carcinoma of the Gall Bladder

GB Cancer - Imaging techniques

ULTRASONOGRAPHY

- Polypoidal / wall thickening / mass replacing the gall bladder.
- Malignant polyps are sessile, solitary, and >1cm and reveals internal vascularity.
- Easily detect invasion of liver parenchyma with loss of normal tissue interface.
- About 80% accurate in advanced stages

C.T.

- Most common imaging modality for the detection of primary tumor and tumor staging.
- Precisely [85%] detect liver or porta hepatis invasion, lymphadenopathy, and the adjacent organs.
- Four patterns of gallbladder cancer on CT scan:

1. Polypoid mass lesion(15– 25%)
2. Focal wall thickening
3. Diffuse wall thickening (20%)
4. Mass replacing gallbladder (40–65%).

M.R.I

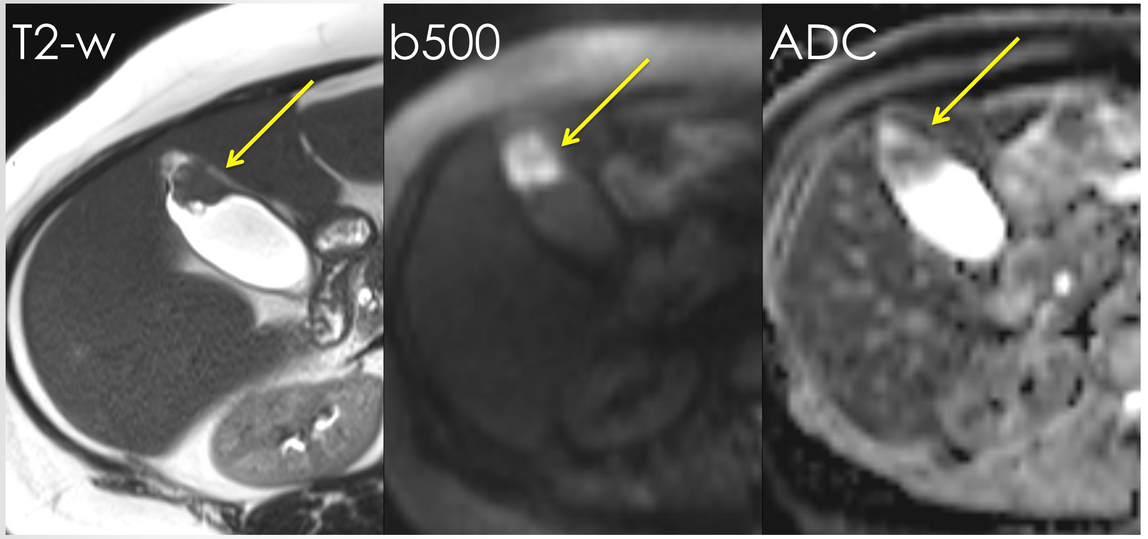
- Superior to CT scan for differentiating T1a lesions from T1b or greater and also biliary involvement.
- Early and prolonged enhancement pattern of malignant lesions varies from the early enhancement with washout of benign masses.
- DWI/ADC – malignancy reveals high restricted diffusivity due to high cellularity and thus aids in differentiation the malignant from benign disease with high sensitivity.

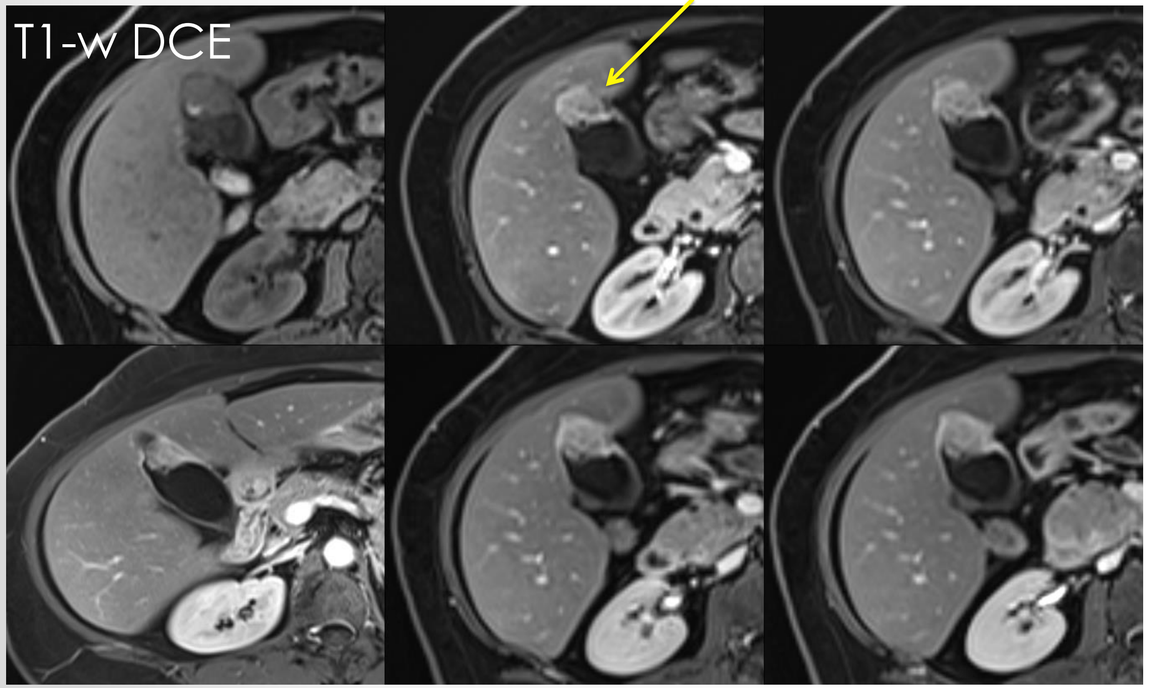
FDG – PET

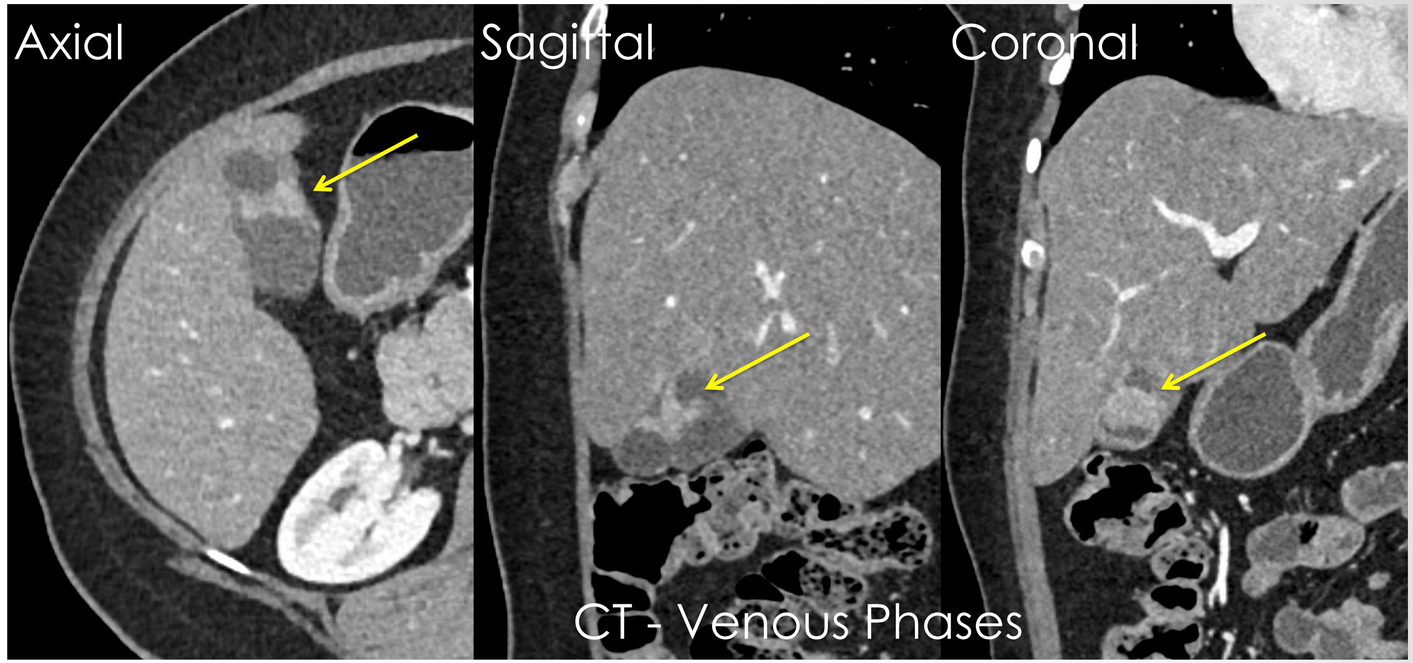
- Problem solving modality.
- Helpful in diagnose the ambiguous primary lesions.
- Residual disease after cholecystectomy are better appreciated with this modality.
- Distant disease not otherwise appreciable by other imaging modalities.

GB Cancer - Staging

Staging of gall bladder cancer.			
Stage I	T1 N0 MO	Confined to the inner layers	→ Confined to GB
Stage II	IIA – T2a N0 M0	Invades the outer layers.	→ Locally invasive
	IIB – T2b N0 M0		
Stage III	IIIA – T3 N0 M0	Invades the near by organs i.e. liver, small intestine, stomach or nodes.	→ Locally advanced
	IIIB – T1-3 N1 M0		
Stage IV	IVA – T4 N0-1 M0	Involving multiple nearby organs or distant areas.	→ Metastatic disease
	IVB – T1-4 N2 M0 or T1-4 N0-2 M1		







Focal Polypoidal subtype of Carcinoma Gall Bladder - Stage T2

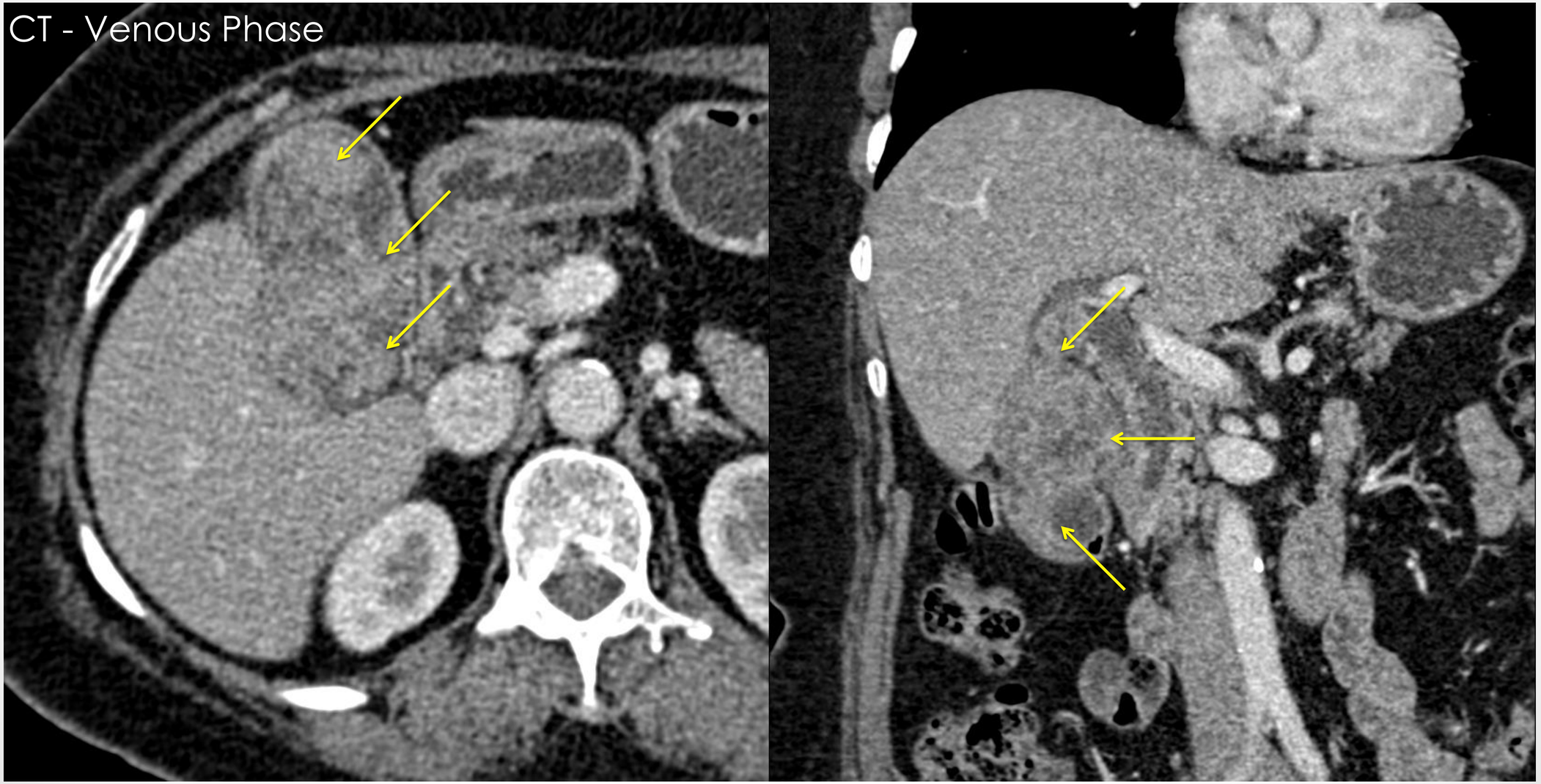
Note, that contrast-enhanced CT and MRI perform similar in detection

Characterization and staging of T2 stage neoplasms.

However, in early

T1 stage neoplasms, MR performs better than CT

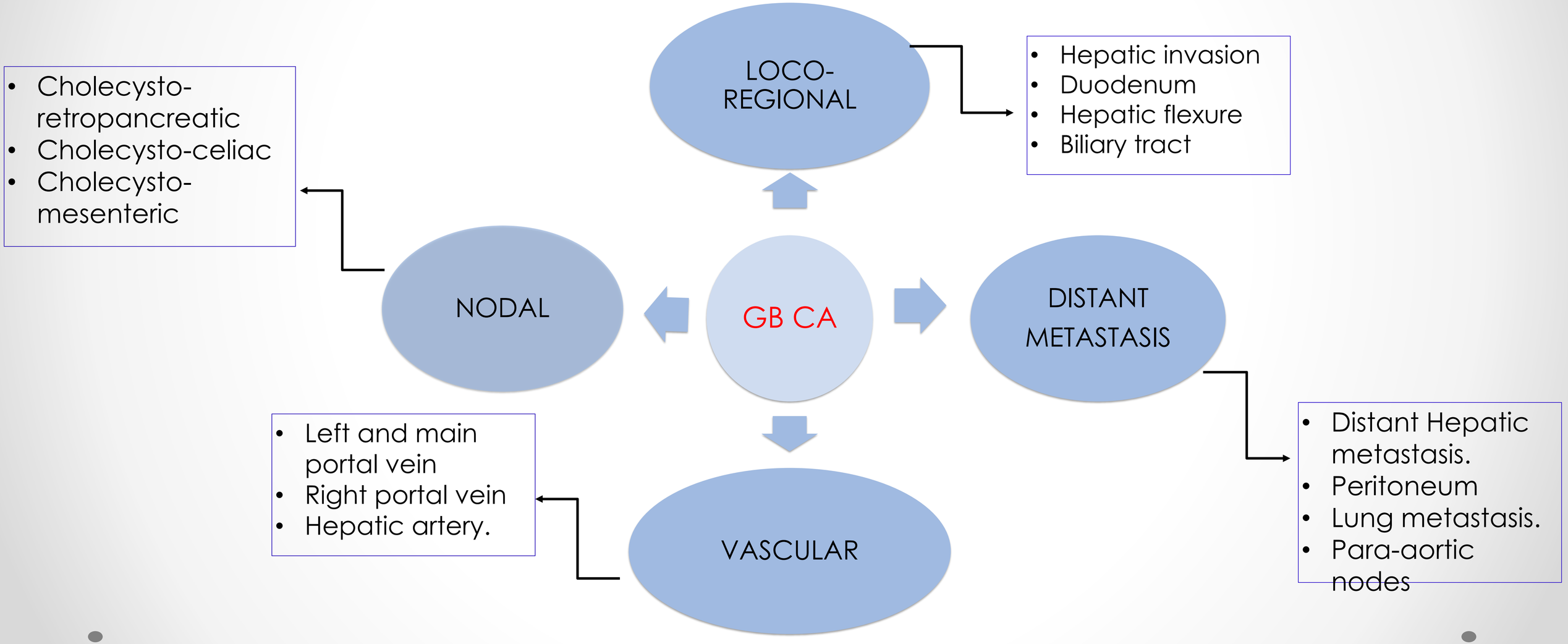
Polypoidal / Papillary subtype of Carcinoma Gall Bladder - Note a large volume proliferative growth near completely occupying the gall bladder lumen with relative paucity of mural invasion

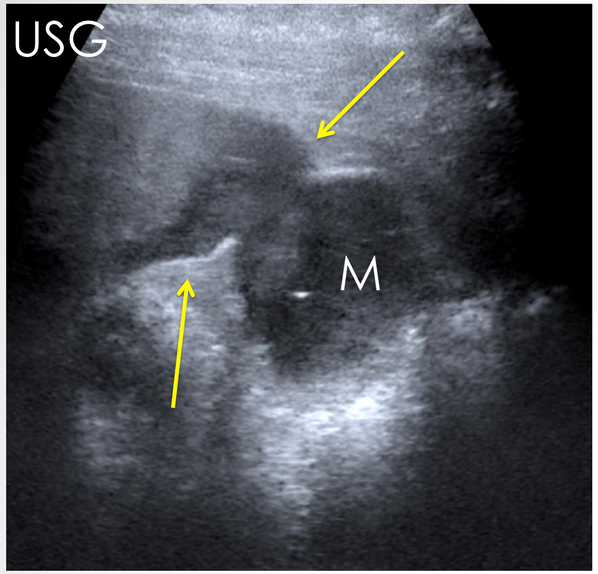


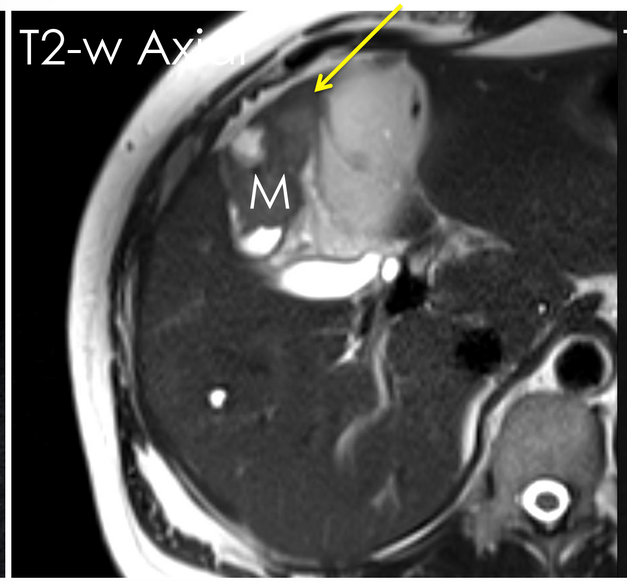
Spread Patterns

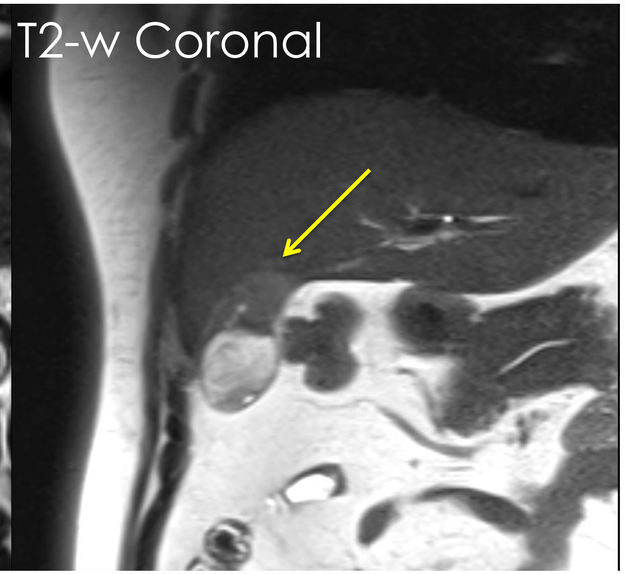
- Locoregional spread *more common* than distant metastasis. Metastases usually occur in liver, lymph nodes, adjacent organs and peritoneum.
- Lymph nodal involvement - 60% of cases
- Hepatic Involvement - 76%-86% cases.
- Intraperitoneal spread - Ascites, omental nodules and peritoneal implants

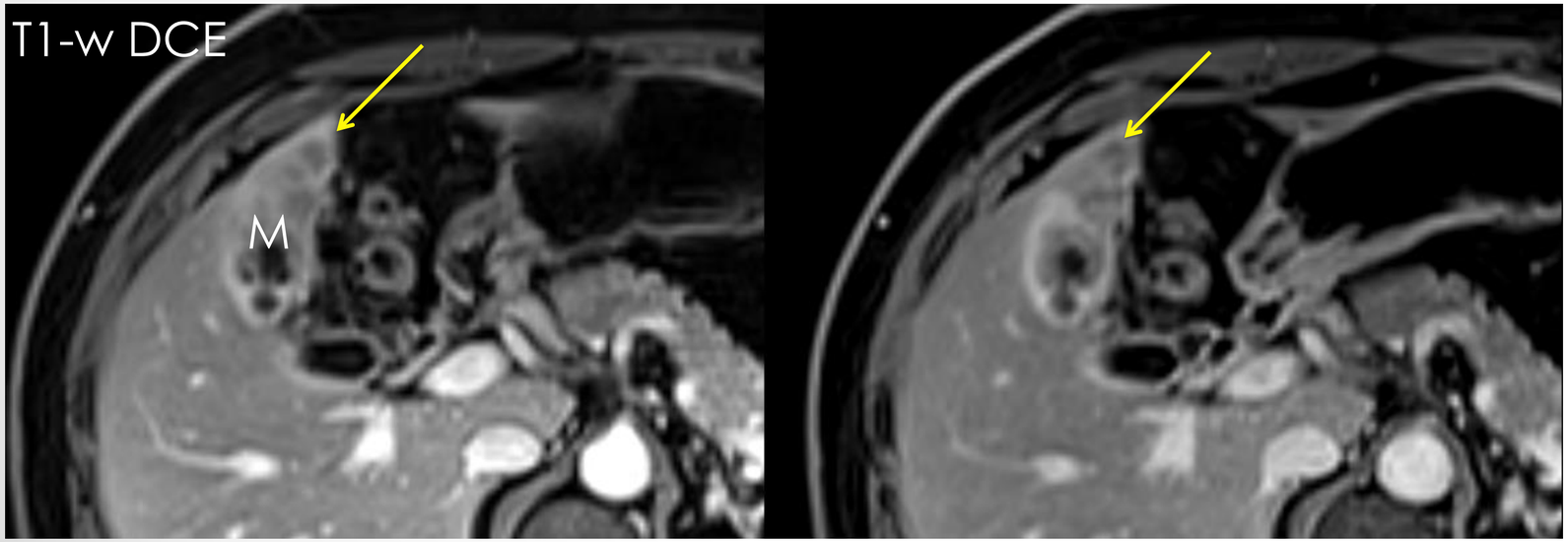
Spread Patterns







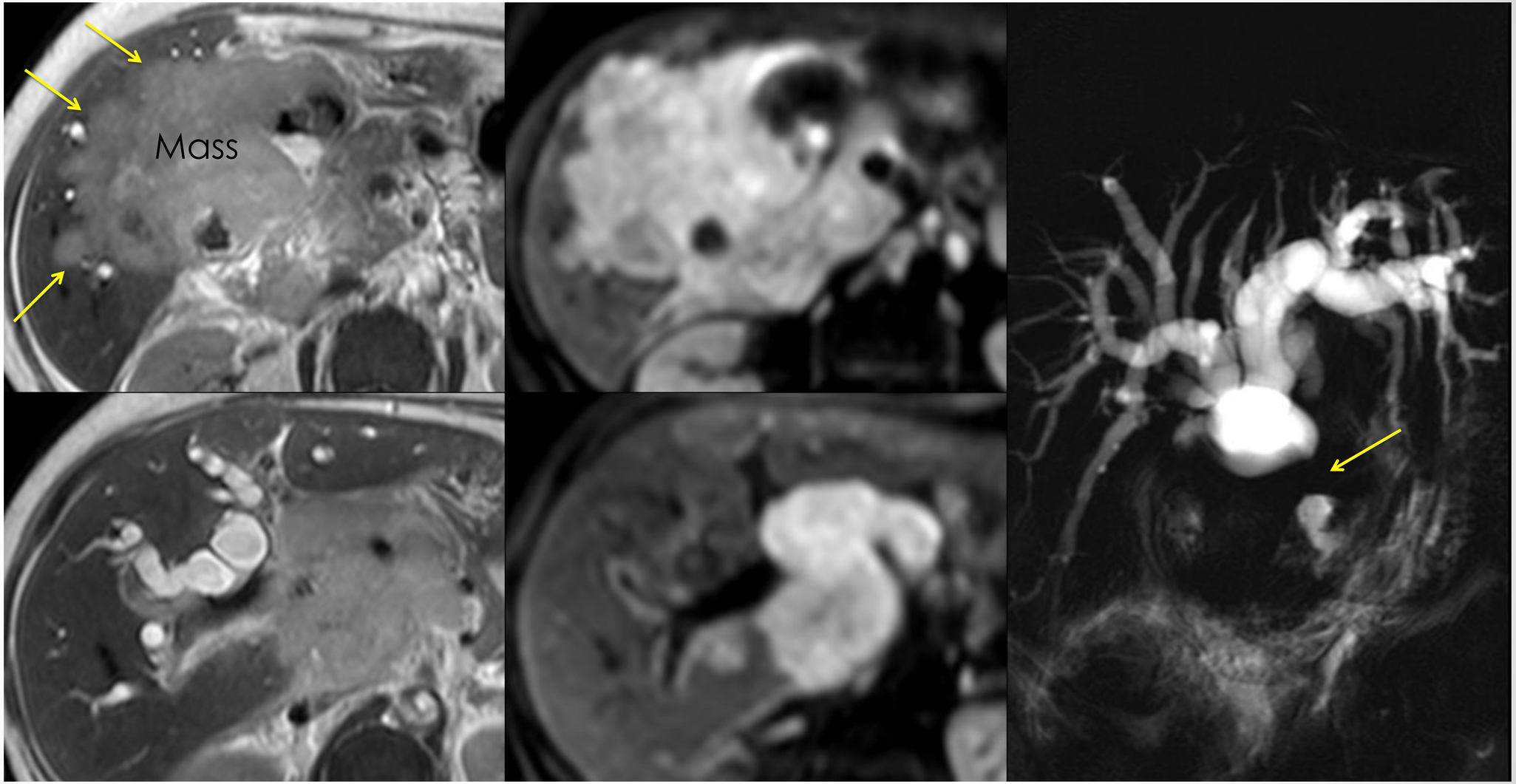




Early Hepatic Plate Infiltration

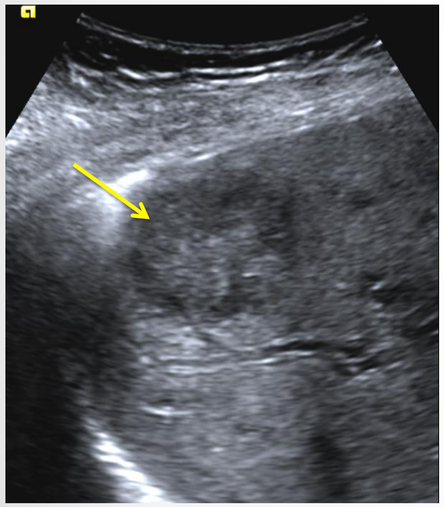
Early Invasion of Hepatic Plate - Stage T3
47/M with a focal proliferative mass in the gall bladder fungus focally invading the hepatic plate in segment IVB [yellow arrows].

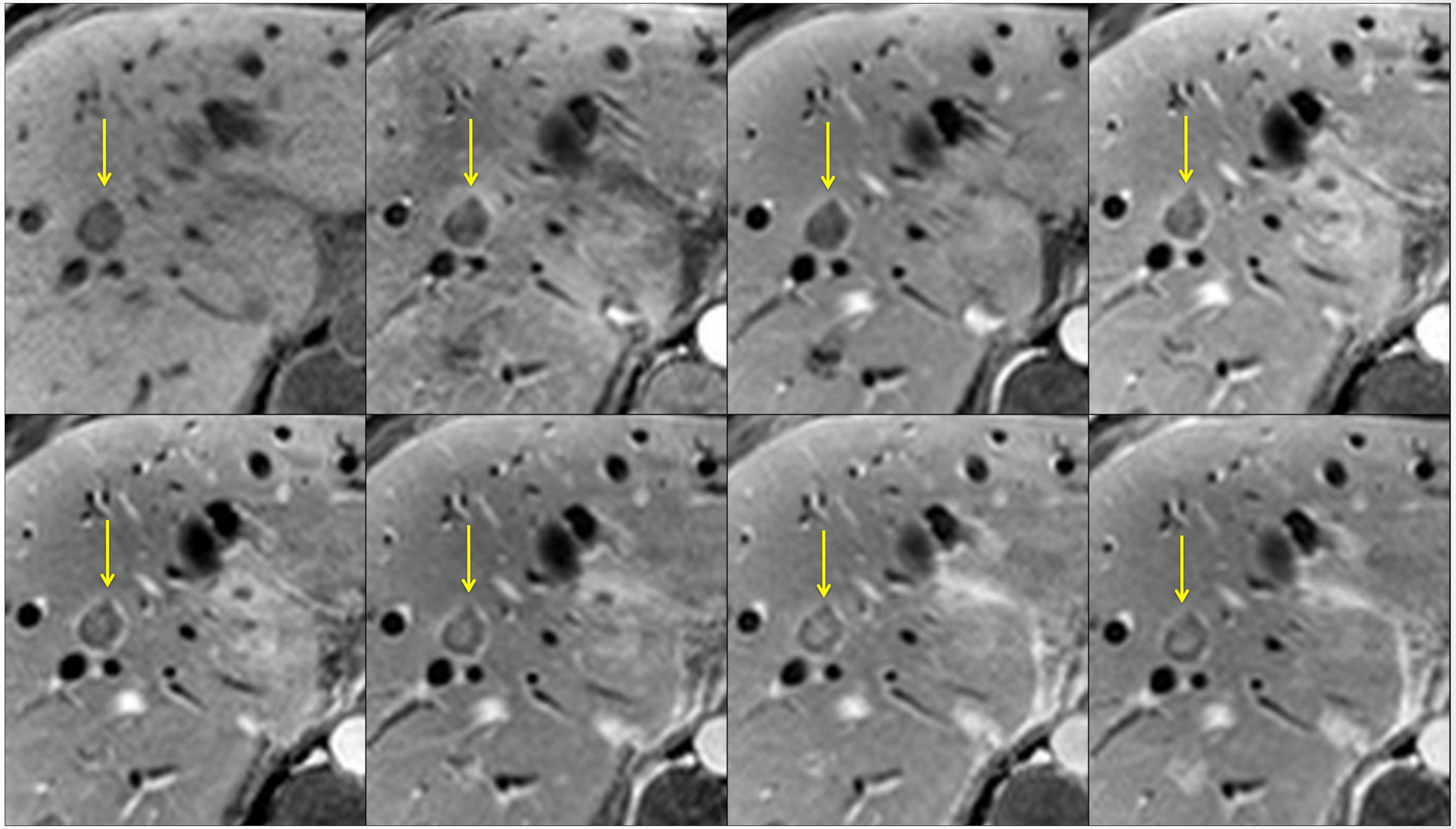
Advanced Hepatic Plate Infiltration



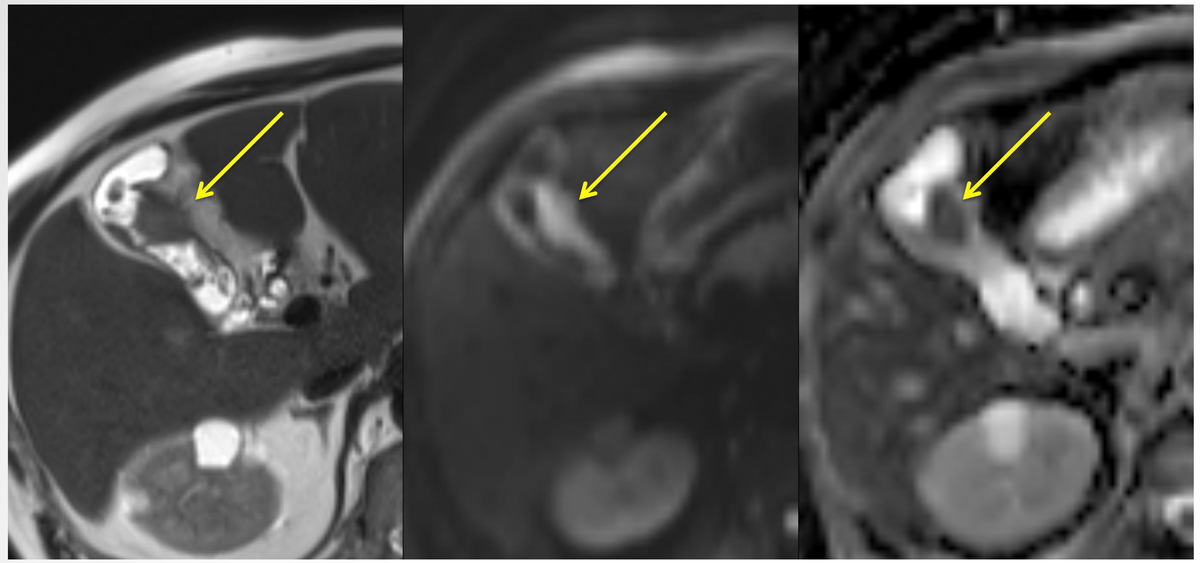
54/F with a large proliferative mass replacing the entire gall bladder [which contains multiple calculi], invading the hepatic plate and porta hepatis with infiltration of the hepatoduodenal ligament and bile duct encasement.

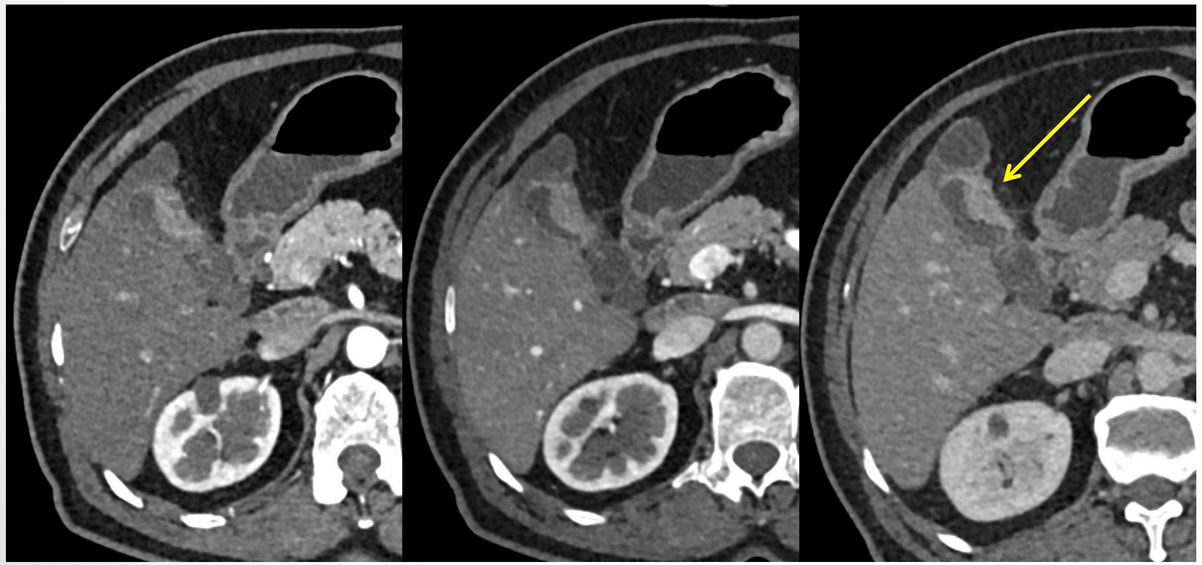
Hepatic Metastases

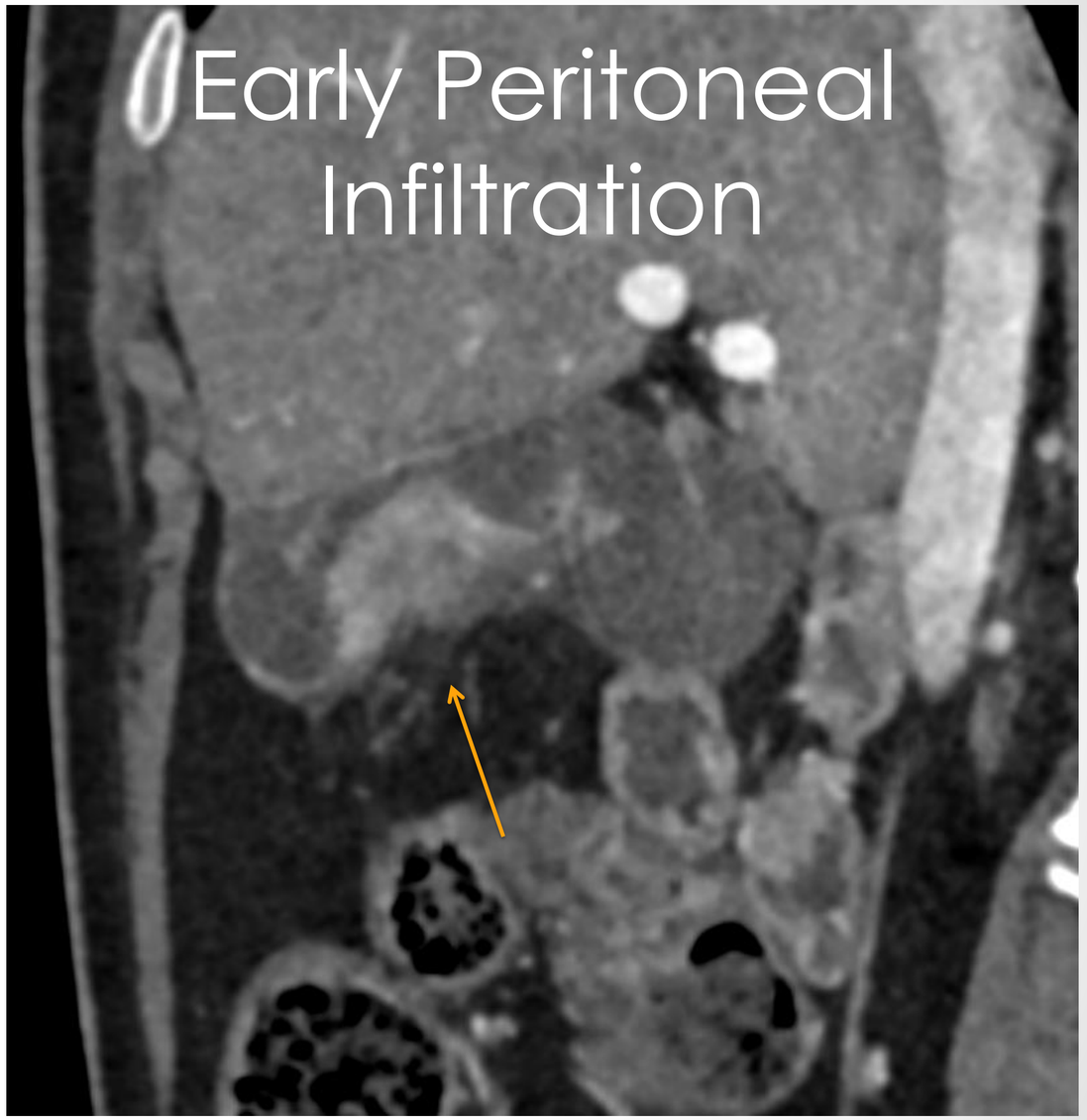




54/F with a large proliferative mass replacing the entire gall bladder with multiple hepatic metastases. Note the targetoid nature of these lesions demonstrating the “peripheral washout sign”.

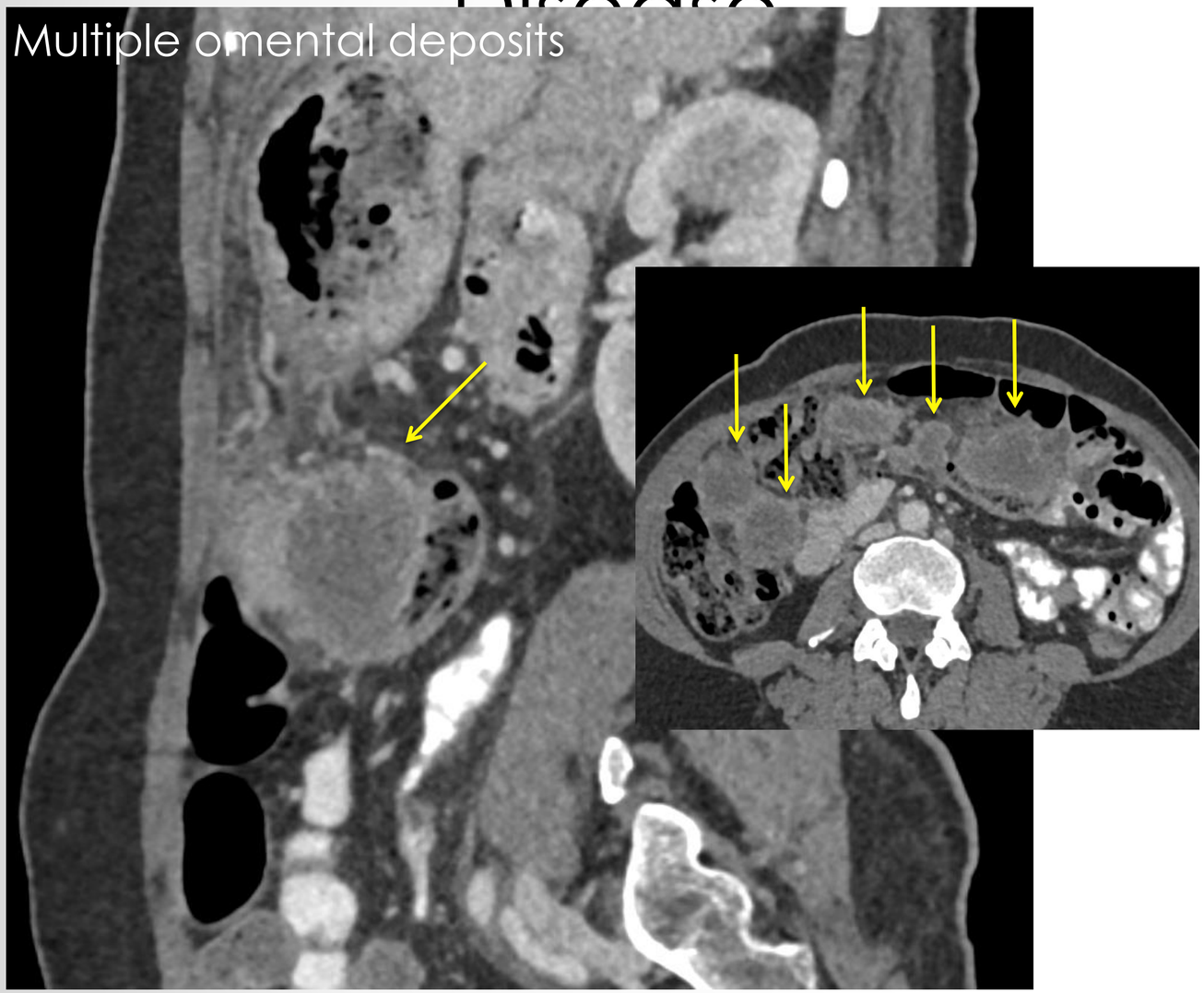


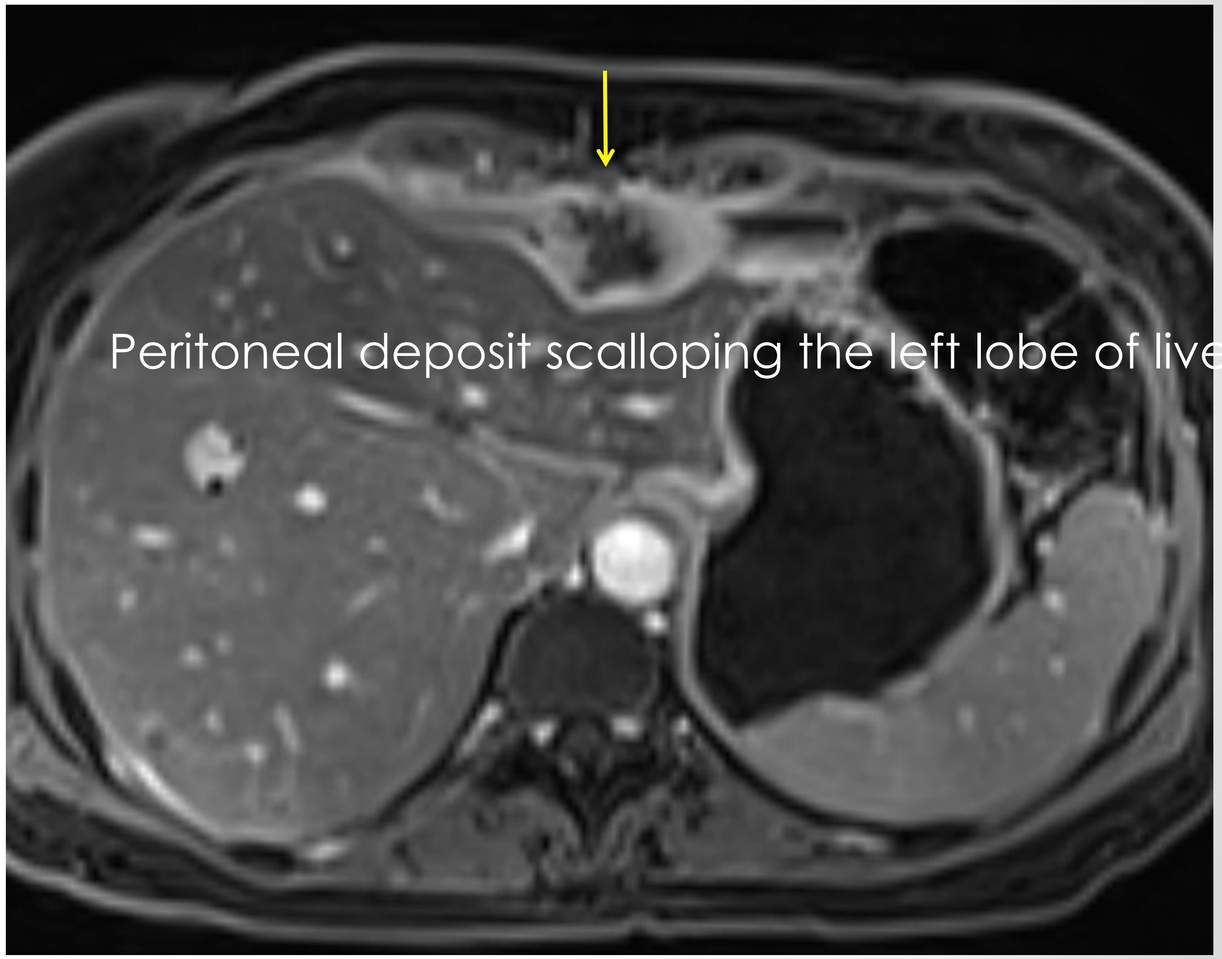




Stage T3 - 60/M with focal eccentric mural thickening [restricted diffusivity], more pronounced along the peritoneal aspect, with transmural invasion and pericholecystic fat infiltration [orange arrow]. Note reserved fat plane with the liver.

Peritoneal & Omental Disease





Nodal Spread Pathways

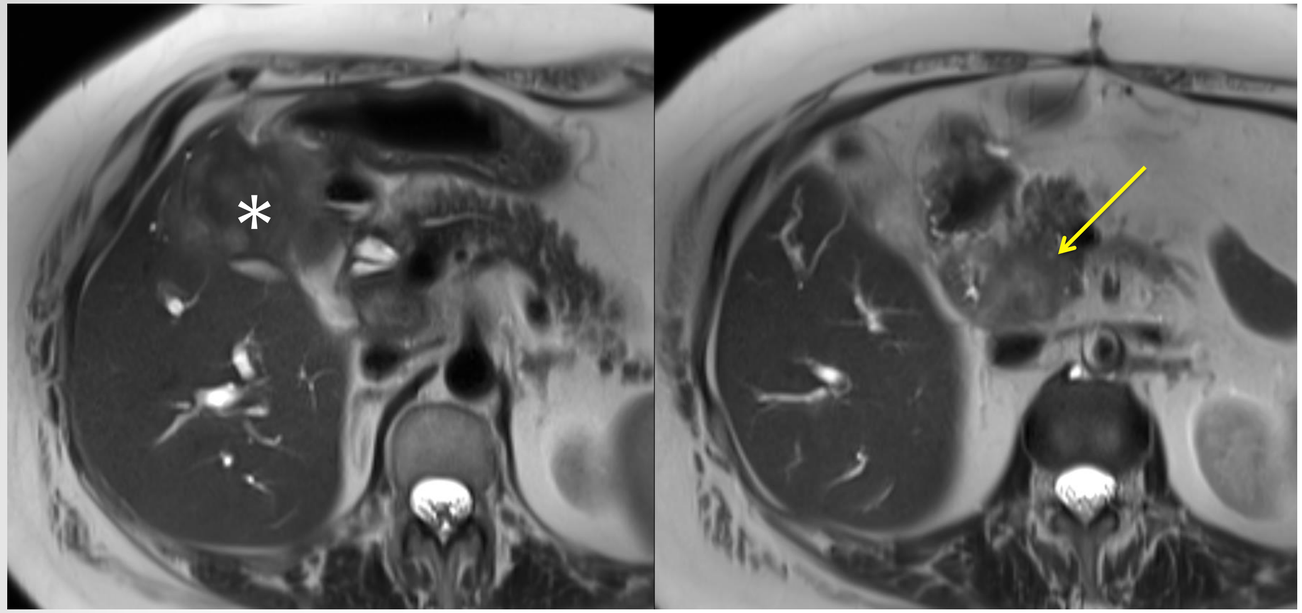
- *Common route of dissemination*.
- Cystic, pericholedochal and hilar nodes are the *first key station* of nodal involvement.
- Ito et al. proposed three common pathways for lymphatic spread of gall bladder cancer:

1) Cholecysto-retropancreatic pathway (*main pathway*).
2) Cholecysto-celiac pathway (accessory pathway).
3) Cholecysto-mesenteric pathway (accessory pathway).

Radical Resection

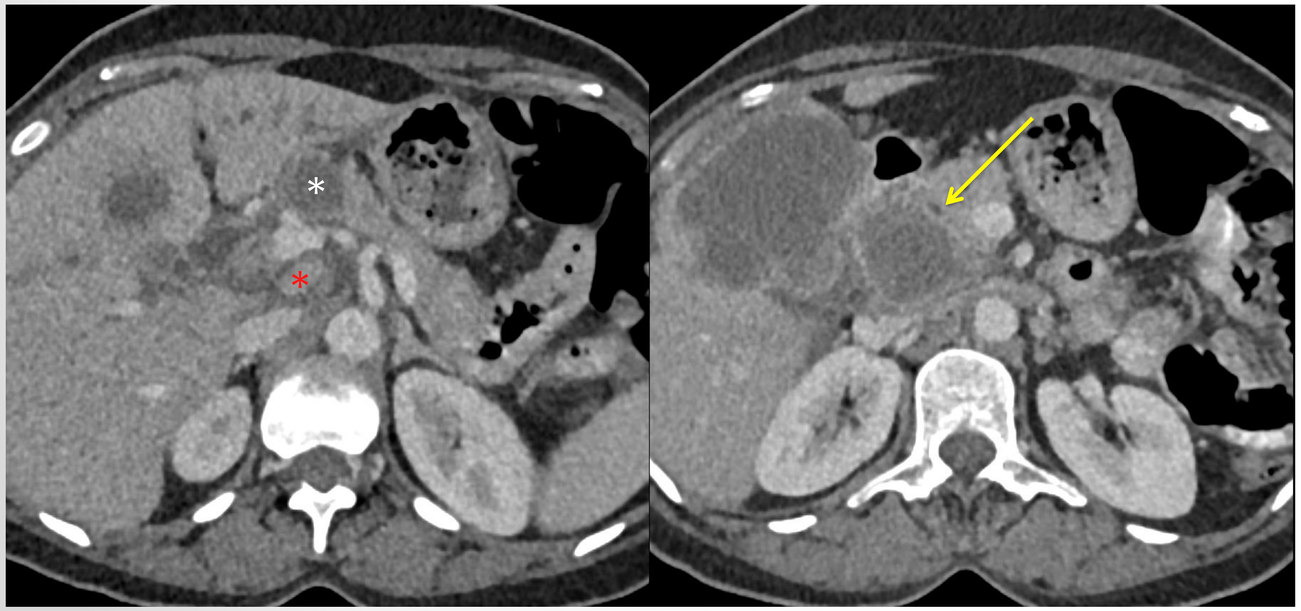
Done for patients with involvement of hepatoduodenal ligaments, posterosuperior pancreaticoduodenal area, and the common hepatic artery

Not advocated for patients with superior mesenteric node, celiac node, and para-aortic lymph node



Cholecysto-retropancreatic pathway

62/F with a primary infiltrative GB mass [white asterix] invading the paraduodenal fat and 1st part of duodenum with an enlarged retropancreatic nodal mass
[yellow arrow].



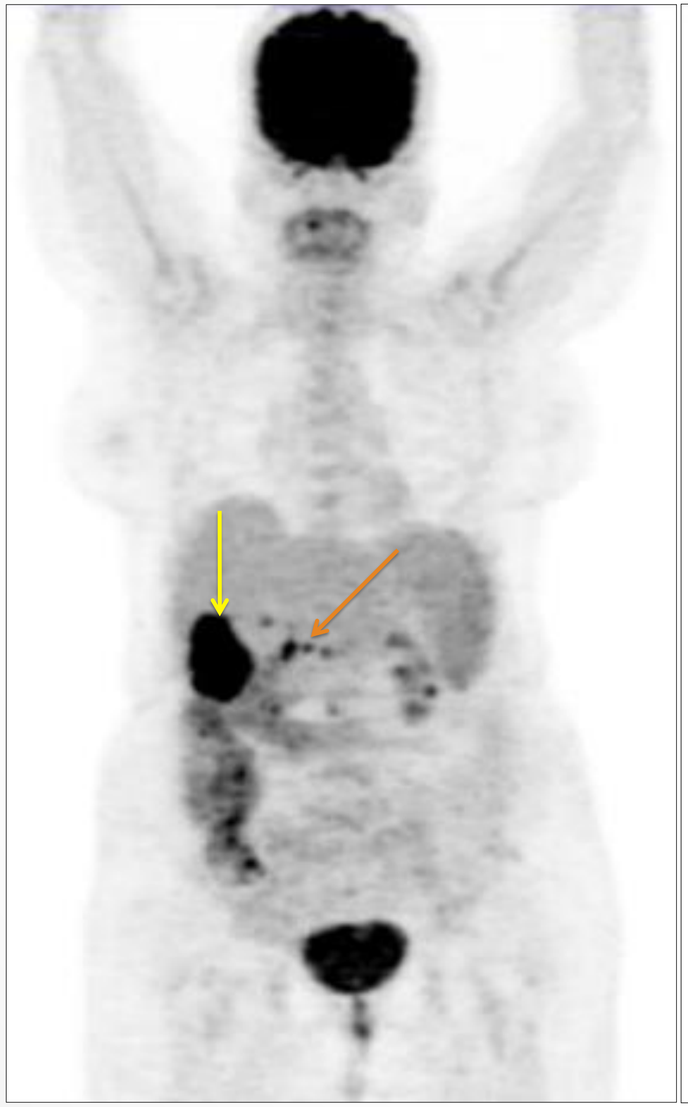
Cholecysto-retropancreatic + Cholecystoceliac pathway

57/F with a large necrotic GB mass invading the liver,
paraduodenal fat and 1st part of duodenum with an
enlarged necrotic node ventral to the CHA [white asterix],
non-necrotic node to the right of the celiac trunk [red asterix] and a large retropancreatic necrotic nodal
mass [yellow arrow].

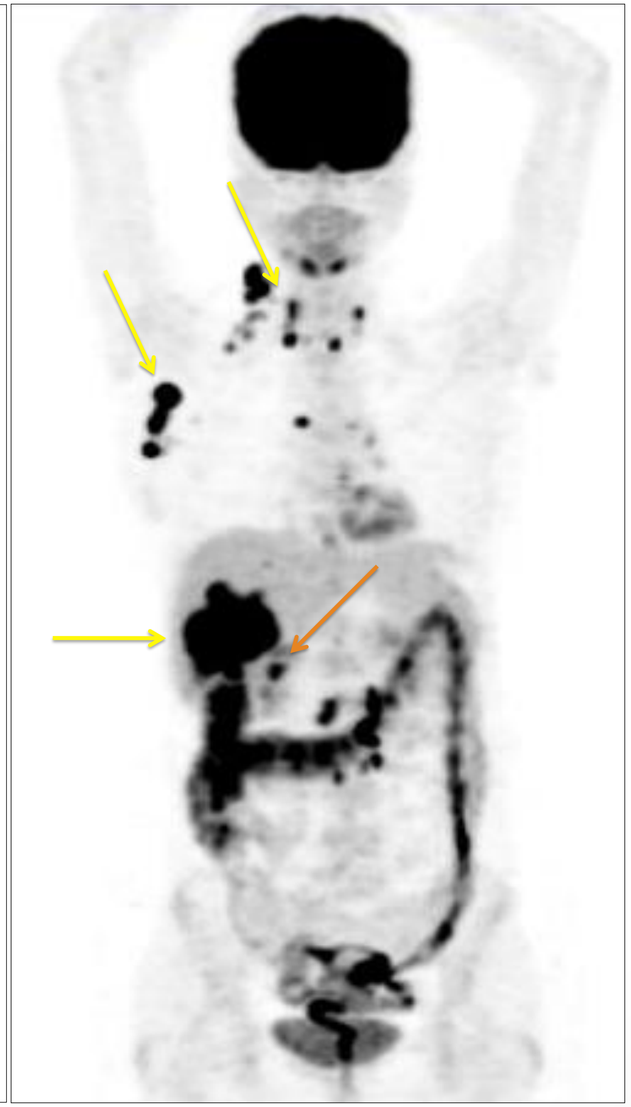
PET/CT

- Primary staging
- Surveillance
- Recurrence Detection

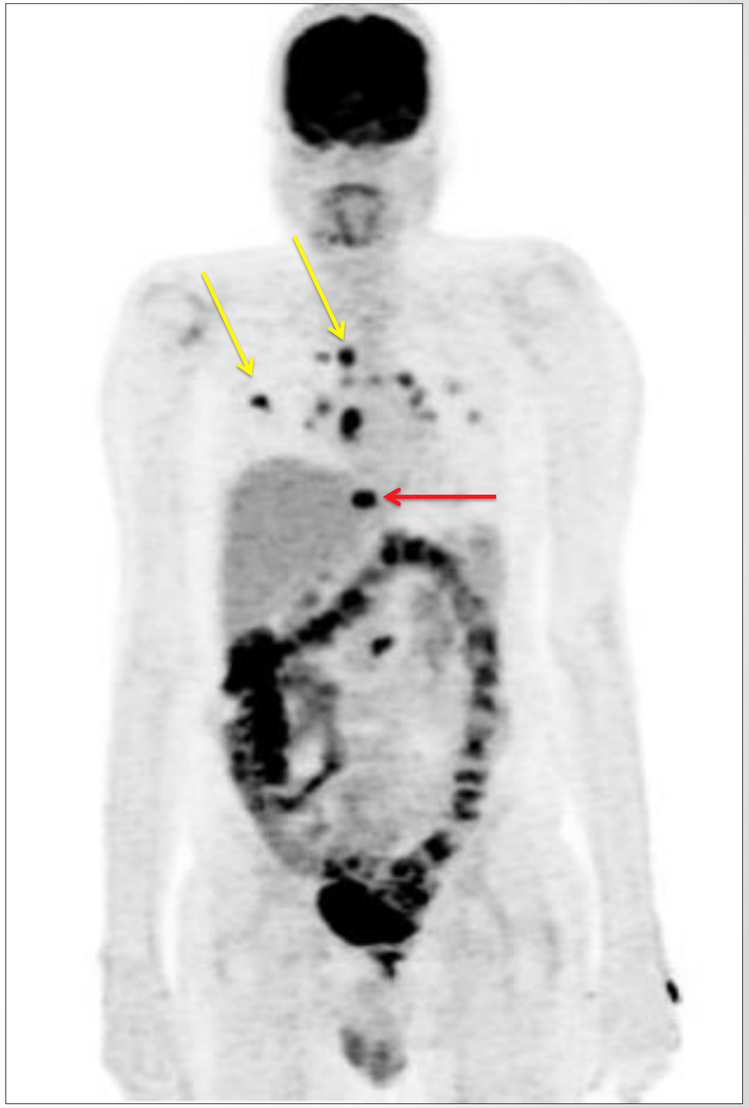
Primary Staging
GB mass with regional nodes



Primary Staging
GB mass with regional and extensive supradiaphragmatic nodes



Elevated Ca 19-9 post surgery
Note recurrent liver and lung lesions and supradiaphragmatic nodes



Management of Ca Gall Bladder

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2019
Gallbladder Cancer

NCCN Guidelines Index
Table of Contents
Discussion

PRESENTATION **WORKUP** **PRIMARY TREATMENT**

Mass on imaging →

- H&P
- Multiphasic abdominal/pelvic CT/MRI with IV contrast[a]
- Chest CT+/- contrast[a]
- Liver function tests (LFTs)
- Surgical consultation
- Assessment of hepatic reserve
- Consider CEA[l]
- Consider CA 19-9[l]
- Consider staging laparoscopy

Resectable[b,c] →
Cholecystectomy[b]
+ en bloc hepatic resection
+ lymphadenectomy ± bile duct excision for malignant involvement
→ See Adjuvant Treatment and Surveillance (GALL-5)

Unresectable → Biopsy
- MSI/MMR testing

→ Options:[e]
- Gemcitabine/cisplatin combination therapy[f] (category 1)
- Fluoropyrimidine-based or other gemcitabine-based chemotherapy regimen[f]
- EBRT with concurrent fluoropyrimidine[g,h]
- Radiation therapy[h]
- Clinical trial
- Best supportive care
- Pembrolizumab[i] (only for MSI-H/dMMR tumors)

Mimics

Mimics	Pattern of presentation	Differentiating features
Adherent stone / sludge	Polypoidal mass	Mobile / immobile, hyperechoic, nonvascular balls
Xanthogranulomatous cholecystitis	Polypoidal mass	Hypodense band around the gallbladder on CT is the most specific finding
Adenomyomatosis	Focal wall thickening	Fluid-filled intramural diverticula (pearl necklace sign)
Metastatic melanoma	Focal wall thickening	Tendency for the serosal surface due to peritoneal implantation
Inflammatory thickening of GB wall	Diffuse wall thickening	Enhancement pattern – homogeneous. *c.f. Two-layer pattern* with strongly enhancing inner layer and weakly enhancing outer layer or *one-layer pattern with heterogeneous enhancement* s/o malignancy.
Primary lymphoma [extremely rare]	Diffuse wall thickening	Submucosal homogenous wall thickening

Summary

- Ca GB is one the most common malignant neoplasm of the biliary tract with poor prognosis because it is usually detected at an advanced stage, with stage-adjusted therapy being cornerstone for improving survival.
- Only potentially curative therapy for Ca GB is surgical resection.
- Abdominal radiologists should understand key imaging features of gall bladder polyps and cancers, which would guide the clinician in appropriate patient management.