

Gallstone disease

Bibble class 11.04.2018

Gallstones epidemiology

- overall prevalence - 10-15 %
- higher risk - White, Hispanics, Native US
 - > Mexican American woman - 27 %
- lower risk - Eastern European, Coloured, Japanese
 - > black men - 5 %

Risk factors

- female
- forty - age
- fertile - pregnancy
- fat - obesity
- family
- fair
- rapid weight loss and liver cirrhosis

Pregnancy pathophysiology

- bile supersaturated with cholesterol
 - estrogen-induced - more cholesterol secretion
 - progesterone-induced - less bile acid secretion
- qualitative change in bile acid synthesis
 - reduced ability to solubilize cholesterol
- progesterone-induced slowing of gallbladder emptying - causing bile stasis

Bariatric patients

- high incidence of greater than 30 %
- mechanism incompletely understood
- bile mucin content increased massively, also bile calcium concentration
- patients more likely symptomatic
- prophylaxis with UDCA effective
- some centers combine bariatric surgery with cholecystectomy

Liver cirrhosis

- major risk factor for gallstones
- overall prevalence - 29.5 %
- reduced hepatic synthesis and transport of bile salts
- high estrogen levels
- impaired gallbladder contraction

Rare risk factors

- Diabetes mellitus
- gallbladder stasis - TPN, prolonged fasting
- clofibrate - reduced bile acid secretion
- ceftriaxone - biliary excretion -> stasis
- Crohn's disease - twice as frequent

Gallstone disease

- no symptoms - incidental gallstones
- typical symptoms - no complications
- atypical symptoms - gallstones on imaging
- typical symptoms - no gallstones

Incidental gallstones

- 20% develop symptoms over 15 years
- symptomatic patients will have recurrent problems in about 70% within two years
- complications around 2-3% per year
- further, more severe complications 30% /a
- prophylactic cholecystectomy NOT indicated

Symptomatic - clinical features

- biliary colic - constant, dull pain in RUQ
- typically 30min – 6h
- nausea and vomiting
- physical examination normal - not inflamed
- lab normal

- common trigger - fatty meal

Investigation

- abdominal ultrasound - operator dependant
- CT - less sensitive
- negative U/S - consider EUS
- sequence - sludge, microlithiasis, stones
- bile microscopy/collection - time consuming

Differential diagnosis

- esophageal chest pain
- reflux disease
- PUD
- nonulcer dyspepsia
- hepatitis
- functional GB disorder
- SOD
- chronic pancreatitis
- IBS
- ischemic heart disease
- pyelonephritis
- ureteral calculi
- complications of gallstone disease

Complications

- acute cholecystitis
- CDL with or without cholangitis
- biliary pancreatitis

Acute cholecystitis

- most common complication
- persistent RUQ pain - Murphy's sign
- fever
- elevated infection parameters, LFT's, bilirubin
- typical abdominal ultrasound

- NICE - surgery within 72 hours

Choledocholithiasis

- 5-20% of all gallstone patients
- 10% primary choledocholithiasis - bile stasis
 - older patients, dilated CBD, periamp. diverticular
 - extra- and intrahepatic stones -> often cholangitis
- 5% after cholecystectomy
- 21-34% of CBD stones migrate spontaneously

Symptoms

- RUQ and epigastric pain
- intermittent pain - transient blockage
- nausea and vomiting

- RUQ tenderness, Courvoisier's sign
- elevated LFT's -> cholestatic picture

- but clinic and lab might be normal

Abdominal ultrasound

- poor stone sensitivity, especially distal CBD
- stone probability according to CBD diameter
- 4-6 mm - 9.4%
- 6-10 mm - 30%
- >10 mm - 50%

EUS

- previous gold standard - ERCP with possible intervention, but cost of higher complications
- EUS least likely examination to miss small stones – sensitivity 90-94%, specificity 95%
- early ERCP in biliary pancreatitis NOT beneficial without jaundice -> EUS-guided
- failed ERCP -> interventional EUS offers treatment options

Cholangitis

- acute Cholangitis -> Charcot's triad
 - fever, RUQ pain and jaundice
 - with sepsis and confusion -> Reynold's pentad
- longstanding cholestasis -> biliary cirrhosis
- lab tests and abdominal ultrasound
- MRCP or EUS - < 5mm stones EUS better

- septic cholangitis – urgent ERCP with biliary drainage – stone extraction later
- acute cholangitis and pancreatitis -> early ERCP within 72h
- only pancreatitis - always EUS first

TABLE 2. A proposed strategy to assign risk of choledocholithiasis in patients with symptomatic cholelithiasis based on clinical predictors

Predictors of choledocholithiasis^{13,14,29,31,32}

Very strong

CBD stone on transabdominal US

Clinical ascending cholangitis

Bilirubin >4 mg/dL

Strong

Dilated CBD on US (>6 mm with gallbladder in situ)

Bilirubin level 1.8-4 mg/dL

Moderate

Abnormal liver biochemical test other than bilirubin

Age older than 55 y

Clinical gallstone pancreatitis

Assigning a likelihood of choledocholithiasis based on clinical predictors^{12-14,28,29,31,32}

Presence of any very strong predictor High

Presence of both strong predictors High

No predictors present Low

All other patients Intermediate

Pregnancy

- gallstones more common during pregnancy
- decreased gallbladder motility
- increased cholesterol saturation of bile
 - estrogen more cholesterol
 - progesteron less bile acid secretion and slows gallbladder emptying
- changes normalize 1-2 months after delivery

Incidence

- 3200 women first trimester no stones
- 7.1% with sludge during second and 7.9% at third trimester
- only 1.2% developed any symptoms
- postpartum sludge resolved in 61%

pregnancy DD

- severe preeclampsia – urine, hypertension
- HELLP syndrome – low platelets
- acute fatty liver – hypoglycemia
- abruptio placentae – lower abdominal pain
- uterine rupture – laboring women
- intra-amniotic infection – fever, uterine contractions, maternal and fetal tachycardia

non-pregnancy DD

- reflux
- PUD
- hepatitis
- right-sided pneumonia
- appendicitis

Treatment

- recurrent biliary colic -> cholecystectomy during second or early third trimester
- avoid surgery near term – reassess after birth
- UDCA not useful
- ERCP in case of complications possible
- prompt surgery for complicated cholecystitis at any time

Acalculous cholecystitis

- 10% of all cholecystitis cases
- high morbidity and mortality rates
- gallbladder stasis and ischemia causes a local inflammatory response

Risk factors

Ampullary stenosis
Bone marrow transplantation
Burns
Cardiopulmonary resuscitation
Childbirth
Choledochal cyst
Cholesterol emboli
Coronary heart disease
Cystic duct obstruction by a percutaneous transhepatic catheter in the bile duct
Diabetes mellitus
End-stage renal disease
Heart failure
Hemobilia
Immunosuppression
Infections
Major trauma
Mechanical ventilation
Medications (eg, opiates, sunitinib)
Metastases to porta hepatis
Multiple transfusions
Nonbiliary surgery
Sepsis/hypotension

Infections predisposing to acalculous cholecystitis

Ascaris lumbricoides
Brucella species
Campylobacter jejuni
Candida species
Coxiella burnetii
Cryptosporidium
Cytomegalovirus
Echinococcus granulosus
Epstein-Barr virus
Flavivirus
Hepatitis A and B
Isospora
Leptospira species
Mycobacterium tuberculosis
Plasmodium species
Salmonella species (S enterica, S typhi)
Vibrio cholerae

Acalculous cholecystitis

- 10% of all cholecystitis cases
- high morbidity and mortality rates
- gallbladder stasis and ischemia causes a local inflammatory response
- often secondary infections
- hospitalized and critically ill patients
- highest incidence with up to 4% after bone marrow transplantation

- up to 1% in vascular patients
- male preponderance - 40-80%
- unexplained fever

- gangrene and perforation as complication
- U/S abdomen or CT scan

Treatment

- imperative!!
- around 30% mortality
- mortality rises with delayed treatment of up to 75%
- emergency cholecystectomy
 - gallbladder necrosis
 - emphysematous cholecystitis
 - gallbladder perforation

ASGE guidelines

- intraoperative ERCP
- small EST followed by balloon dilatation
- failed ERCP - interventional EUS!!
- altered anatomy - interventional EUS!!

- old guidelines, EUS undervalued