Hepatolithiasis

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Definition
Calculi or concretions located proximal to the confluence of the Left and Right hepatic ducts

Epidemiology
Most common in East Asia:
Taiwan: 50%
Hong Kong: 3.1%
Japan: 2.2%
Singapore: 1.7%
Western countries less than 1%

Incidence
Equal gender distribution
Type I present in 5th to 6th decades of life
Type IE present in 7th to 8th decades of life

Classification
Most recent system: Nakayama in 1982
- intra-hepatic bile ducts: I
- extra-hepatic bile ducts: E
- intra&extra hepatic bile duct: IE

By locations in liver:
- Right side: type R
- Left side: type L
- Both side: type LR
- Caudate lobe: type C

Most stones appear as brown pigment stones (calcium bilirurate)
Left duct involvement > Right ducts
Left duct courses horizontally in relation to the CHD as compared to the right duct forming an acute angle

Pathology
Bile stasis & mucin producing activity
Bacterial infection
- *Escherichia coli*
- *Clostridium*
- *Bacteroides*
Helmintic infestation
- *Ascaris lumbricoides*
- *Clonorchis sinensis*
Natural history

122 patients with CT & CT-Cholangiography 14/122 became symptomatic at
mean 3.4 yrs
Symptoms: Recurrent abdominal pain, hepatic abscesses, lobar atrophy, cholangitis & cholangiocarcinoma
Lobar atrophy: Major role in development symptoms
- 13/14 (93%) of symptomatic group
- 14/108 (13%) of asymptomatic group
Liver atrophy:
- Hepatolithiasis that associated with CHCA found liver atrophy 90.4%
- Destruction of hepatocyte → chronic inflammation
- CHCA found at atrophic and irregular duct about 22.7%
- Found in developing symptom group = 92.9%
Recurrence of HL in the atrophic liver causes persistent chronic inflammation which leads to formation of strictures and more HL and possibly cholangiocarcinoma
Lobar atrophy is a risk factor for cholangiocarcinoma & hepatectomy is indicated
If left untreated Hepatolithiasis leads to
- Recurrent pyogenic cholangitis
- Progressive biliary strictures
- Formation of liver abscesses
- Atrophy of the affected liver
- Secondary biliary cirrhosis
- Portal Hypertension
- Cholangiocarcinoma
12% develop symptoms in 9 months – 7 years
CCA develops in 10% of IHD stones in Japan
Hepatolithiasis is a risk factor for cholangiocarcinoma from 2.3-10%
Proposed mechanism of CCA:
- Prolonged irritation of biliary epithelium by calculi
- Long term exposure to bile & its products
- Repeated infections
- Metabolic byproducts of bacteria in the biliary tree
- Dynamic irritation by unstable bile flow
- Bile Stasis, reflux & turbulence
Conclusion:
“Closed observation is an alternative management in asymptomatic group except liver atrophy and migrate to extrahepatic part”
Clinical Manifestation & Investigation

Signs & Symptoms
- Abdominal Pain: RUQ or upper abdomen, most common, 70%
- Jaundice & Fever (Cholangitis): 10-30%, Tend to recur, chronic
- Resulting sepsis
- Liver abscess
- Cholangiocarcinoma
  - 25% cause of death in IHD stone patients
  - 5.2% associated with biliary tract carcinoma
  - Intrahepatic cholangiocarcinoma most common
  - In cholangiocarcinoma, associated with IHD 5.7-17.5%
- Abdominal discomfort
- Vomiting
- Asymptomatic: Increased to 16.1%, because of advanced in diagnostic imaging & check-up
  - Hx of previous biliary surgery = 42.1%
    - 22.2% had 2 or more operation = Intractable course of disease

Investigation
- Aim:
  - Diagnosis of IHD stone
  - Evaluate precise location of stones
  - Stricture of bile ducts
  - Concurrent cholangiocarcinoma

Ultrasonography
- Noninvasive, reliable, inexpensive
- First study when suspected hepatolithiasis, Screening tools
- Biliary obstruction: ductal dilatation
- Stone in biliary system: Hyperechoic lesions with acoustic shadows
- Liver abscess
- Ca bilirurate stone: Marked biliary dilatation peripheral to stone
- Cholesterol stone: Limited dilatation at stone location
- Pneumobilia: No shadow, Postural migration, supine & knee-elbow position

Equipment- & operator-dependent

CT scan
- Provide location, type of stone, lobe atrophy, liver parenchyma, anatomic details for deciding treatment
- Single most cost-effective study
- Ca bilirurate stone: round, oval high density in dilated ducts
- Cholesterol or pigmented stone: hard to detect, false negative rate
- Look in noncontrast film first
- Dilated bile ducts: Low-density, tubular, tortuous, branching structures on contrast-enhanced film
- Liver lobar atrophy
- Liver abscess
Cholangiocarcinoma
Portal hypertension
Biliary cirrhosis

CT cholangiography
Slow IV infusion of meglumine iotroxate, Excrete in bile, fill in biliary system
Higher sensitivity than plain CT (92%)
Impaired hepatic function → contrast not excrete in bile duct
Liver atrophy → defect of biliary tree

MRI & MRCP
Non-invasive, no nephrotoxic, no ionizing radiation
Not suitable when therapeutic intervention is planned
Stone location
Obstructed intrahepatic segmental ducts
Bile duct diameter calculation
Abscess: cystic mass variable intensity in T2
Stones: defective low-intensity areas

MRI & MRCP
Evaluation of bile duct stricture or dilatation
96-100% accuracy for level of obstruction
90% accuracy for cause of obstruction

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<th>Detecting</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>IHD stones</td>
<td>97%</td>
<td>99%</td>
<td>98%</td>
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<tr>
<td>strictures</td>
<td>93%</td>
<td>97%</td>
<td>97%</td>
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Limitation:
- Concurrent intraductal cholangiocarcinoma
- Difficult in certain patients: claustrophobia, pacemakers, implants

Percutaneous transhepatic imaging
Especially if stones in Rt lobe or both lobes
More precise information about segmental & subsegmental anatomy of IHD & strictures
Percutaneous transhepatic biliary drainage (PTBD), tube cholangiography
Percutaneous transhepatic cholangiography (PTC)
Percutaneous transhepatic cholangioscopy (PTCS), Selective cholangiography

PTC vs PTBD, PTCS
- Not always adequate visualized
- Impacted stones, mud or mucin in IHD
- Tube cholangiography via PTBD or selective cholangiography by PTCS better
  Image obtained after decompression
  Before & after remove impacted stone
Various projection : RAO, LAO, Rt lat, Lt lat
Biliary stricture with proximal duct dilatation
  - Ca bilirubinate stone more frequently than others
  - False positive: narrow space between stones and bile duct wall, disappear after PTCS lithotomy
  - Localized unchange diminution of bile duct caliber
  - Cause stone formation or result from stones & repeated infection?
Cholangiocarcinoma
  - Difficult by cholangiography
  - Stones & stricture obscure visualization of entire IHD
  - Diagnostic clues
    Persistent filling defects & obliteration of involved IHD
    Mucobilia & mucosal change in PTCS

**ERCP**
Operator-dependent
Morbidty 1-7%, Unsuccessful cannulation 3-10%
Sensitivity 90-96% & Specificity 98% in CBD stone
Frequently misdiagnosis in IHD stone
IHD peripheral to stones or strictures poorly visualized
Risk of cholangitis: Esp. multiple intrahepatic stones
MRCP better than ERCP
Therapeutic role: extract stone, biopsy, stenting

**Planning definitive treatment**
Aim:
  - To eliminate source of recurrent sepsis by removal ductal stone
  - Bypass or resect stricture part
  - Resection of chronic infective useless hepatic segment
  - Preserving functioning liver parenchyma
Detection and localization of ductal stone
  - Combination of cholangiography, ultrasonography, CT
Imaging of liver volume and parenchymal involvement
  - Ultrasonography, CT or MRI
Evaluation of portal hypertension
  - Doppler US, MR angiography
During Acute Exacerbation
Ultrasonography:
  - Accesses the location of biliary obstruction
  - Diagnosis of abscess
  - Percutaneous drainage
PTC or ERC for biliary obstruction that need drainage
CT:
  - Indicated in patient with persistent sepsis
  - The source of which cannot be satisfactorily elucidate by US or PTC and ERC
CT guide drainage
MRI: not recommend

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<th>Diagnostic imaging</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<tr>
<td>CT</td>
<td>50.0</td>
<td>97.6</td>
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<tr>
<td>MRT1-GE</td>
<td>77.8</td>
<td>97.6</td>
</tr>
<tr>
<td>MRCP</td>
<td>66.7</td>
<td>100</td>
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<tr>
<td>MRI (MRCP + MRT1)</td>
<td>94.4</td>
<td>97.6</td>
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**Management**
If asymptomatic: no treatment, F/U
Treatment: when
1) symptomatic
2) stone in extrahepatic duct
3) liver atrophy
4) suspicious malignant
Aims of treatment:
- Prevention of liver damage by early clearance of stones and elimination of bile stasis
  - Removal of stones
  - Removal of strictured bile ducts
  - Providing good drainage of bile
- Minimizing bacterial infection
  - Resection of source of recurrent infection & biliary stasis
  - Removal of cholangiocarcinoma
  - Removal of atrophic liver
  - Removal of hepatic abscess
- Residual stones should be able to spontaneously enter the GI tract

**Conclusion Goals:**
- To eliminate the source of recurrent sepsis by removal of ductal stones
- Management of stricture duct
- Resection of chronic infective useless hepatic segment
- Preserving functioning liver parenchyma

**Treatment**
“Combination of different treatment modalities is necessary to improve the outcome of hepatolithiasis”
**Stone removal group**
Cholangioenterostomy: Residual stone 56%
Percutaneous transhepatic cholangioscopic lithotomy (PTCSL)
Complete clearance 82%; recurrent rate 32-40%

**Liver resection group**
- Hepatectomy + hepaticosubcutaneous jejunostomy
  - Complete clearance 98%; recurrent rate 9%

**Percutaneous Transhepatic Placement of Metallic Stents**
- No recurrent strictures or formed calculi were found in the six patients during follow-up periods of up to 64 months.
- Metallic stents are a well-tolerated and promising alternative in the management of refractory intrahepatic long-segment biliary strictures with hepatolithiasis.

**Hepatic resection VS PTCSL**

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<th>Otani et al</th>
<th>Treatments for Hepatolithiasis</th>
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<tbody>
<tr>
<td>Table 2. Comparison of Treatment Results</td>
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<tr>
<td>Result</td>
<td>Hepatic resection</td>
<td>PTCSL</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Final clearance rate of stones</td>
<td>25/26</td>
<td>96.2</td>
</tr>
<tr>
<td>Bile duct strictures at treatment</td>
<td>22/26</td>
<td>84.6</td>
</tr>
<tr>
<td>Remaining bile duct strictures after treatment</td>
<td>4/22</td>
<td>18.2</td>
</tr>
<tr>
<td>Complications</td>
<td>10/26</td>
<td>38.5</td>
</tr>
<tr>
<td>Mortality</td>
<td>1/26</td>
<td>3.8</td>
</tr>
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NS, not significant; PTCSL, percutaneous transhepatic cholangioscopic lithotomy.

**PTCSL**
- Poor surgical risk patient with previous biliary surgery
- Stone distribution in multiple segments
- Refuse surgery

Stone clearance rate of up to 95% reported when combined with ERCP and Electrohydraulic lithotripsy.

High recurrent rate especially in patient with bile duct stricture (p=0.026)

"PTCSL is effective for treating primary hepatolithiasis in selected case."

Resection the dominant segment followed by PTCSL is recommended for bilateral stones.
Endoscopic Retrograde Approach
- Removal of both Intra & Extrahepatic biliary stones
- Introduction of basket/balloon catheters
- Avoids injury to the hepatic parenchyma
- Difficult technique with high failure rates

Hepatectomy for hepatolithiasis
Seem to be the most definite approach for hepatolithiasis due to:
- Remove the stones and biliary stricture
  - Reduce recurrent stone and cholangitis
- Remove useless liver parenchyma
  - Reduce risk of cholangiocarcinoma and cholangitis

Immediate clearance 86 - 90%
Final outcome up to 98%
Recurrent rate : 9%
Morbidity 16 - 28% (most common = wound infection)
Factors that significant to postoperative complication
   - Hyperbilirubinemia (p=0.038)
   - Right hepatectomy (p=0.006)
Biliary stricture : main cause of recurrent stone
CCA : an independent prognostic factor of survival
Cholangiocarcinoma with hepatolithiasis
5 – 7 %
Should be suspect if:
- CEA > 4.2
- Higher level of serum alkaline phosphatase
- A long history of hepatolithiasis with weight loss
- Age > 40 yrs
Imaging’s suspect:
- filling defect with mucobilia or mucosal change from endoscope
- portal vein thrombosis

Hepatectomy
Depend on: Location of stone and liver parenchyma (liver atrophy)
- Biliary stricture site
- Coexist with CHCA
“Need combination procedures”
Liver resection
  Left lateral segmentectomy
  Left hepatectomy
  Right hepatectomy
Endoscopic treatment: choledoscopy
Surgical bypass or resection for good drainage of bile
  Hepaticojejunostomy
Placement of access loops

Indications for Hepatic Resection
- Advantage
  - Removal of all stones along with pathologic bile ducts including the carcinomatous bile ducts
  - Atrophic & Fibrotic / Abscess of a liver segment or lobe
    - Left > Right
  - Possibility of concomitant cholangiocarcinoma
  - Localized intrahepatic calculi with irreversible biliary strictures

Stone locate one lobe without stricture
- Parenchymal change
  Hepatectomy and choledoscopy + T tube
  ? Hepatico-enterostomy
- Parenchymal unchange
  Choledoscopy with stone removal + T tube
  PTCSL
  ? Hepatectomy ? hepatico-enterostomy

Stone locate both lobes without hilar stricture
  Cholangiography, choledoscopy
  Remove IHD stones
  T-tube
  + Bypass (hepaticojejunostomy with subcutaneous access limb)
  + Hepatectomy and with hepatico-subcutaneous jejunostomy

Stone locate both lobe with hilar stricture
  Hepatectomy and hilar resection with hepatico-subcutaneous jejunostomy
  Hepatectomy and quadrate lobe resection and hilar bile duct plasty with hepaticojejunostomy
  PTCSL with dilatation and stent

Access Loop Procedures
  - Provide continuous postoperative access to the biliary tree for residual/recurrent stone retraction
  - Percutaneous/Cutaneous
- Permanent cutaneous access
  - Hepaticocutaneous jejunosotomy
- Interposition jejunal segment between hepatic hilum & duodenum
- Side to side Roux-en-Y jejuno-duodenal access loop

**Survival**
Overall 5 years 82 - 93 %
5 year survival with CHCA 9 %