Postcholecystectomy syndrome

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OBJECTIVES

- ❑ Definition
- ❑ Epidemiology
- ❑ Aetiology
- ❑ Pathophysiology
- ❑ Clinical features
- ❑ Investigations
- ❑ Management

WHAT IS IT

- Postcholecystectomy syndrome(PCS) first described in 1947
- It is the persistence of symptoms following cholecystectomy
  - continuation of symptoms which was thought to be caused by gall bladder
  - developmment of new symptoms usually attributed to gall bladder
  - symptoms due to absence of gall bladder
  - Sometimes, symptoms of extra-biliary disorders mimic biliary symptoms.

EPIDEMIOLOGY

- Average 10-15% of patients develop the symptoms
- Ranging from 5-30% (Jensen 2008) or even as high as 40% (Graefer 2007)
- Incidence is high in patients who didn't have gall stones
- Increased risk of developing PCS with increasing duration of preoperative symptoms
- Also high in emergency surgery patients
- Pre operative secure diagnosis reduce incidence
- Functional disorders are the most common causes
- Can be transient, persistent or lifelong
- More common in younger age and in female(female to male ratio is 1.8:1)

PATHOPHYSIOLOGY

- Due to increase bile flow into upper GI tract
  - bile reflux gastritis and esophagitis (**Billiary phase**)

- Due to bile in the lower GI tract
  - diarrhoea and lower abdominal pain (**Intestinal phase**)

- Other symptoms could be resulting from structures in biliray tree or extra biliary structures

AETIOLOGY

- **Hepato-biliary system**
  - Cystic duct and gall bladder ramnant
  - Stump cholelithiasis
  - Neuroma
- **Biliary tract**
  - Cholangitis
  - Adhesions
  - Strictures
  - Cyst
  - Choledocholithiasis
  - Fistula

AETIOLOGY....

- **Periampullary**
  - Sphincter of Oddi dyskinesia. (**SOD**)
  - Stricture
  - Papilloma
- **Pancreas**
  - Pancreatitis
  - Pancreatic stones
  - Pancreatic cancer

EXTRA BILIARY

- **Oesophagus**
  - Oesophagitis
  - Hiatal hernia
  - Achalasia
- **Stomach**
  - Bile gastritis
  - PUD
  - Cancer
- **Duodenum**
  - Adhesions
  - Diverticulum

OTHER PATHOLOGIES

- Colon
- Mesenteric ischaemia
- IBS

A cause can be identified in upto 95% of patients

EXTRABILIARY ETIOLOGY

- Lasson *et al*. followed 65 patients initially diagnosed with PCS and found 48% with identifiable extrabiliary diseases during 4-13 years of follow up

- Similarly,Filip *et al.* found 27 of 80 patients (34%) evaluated for PCS actually had non-biliary symptoms

- Thus, the first step in evaluating patients with PCS must be a careful history and evaluation to exclude these common and often treatable disorders

ORGANIC BILIARY ETIOLOGY

- New biliary disorders may develop after cholecystectomy, and these must be ruled out through standard laboratory and radiological assessments

- Common bile duct stones and cholangiocarcinoma can arise independently of cholecystectomy

- Filip *et al.* recently published a cohort study demonstrating endoscopic ultrasound was 96.2% sensitive and 88.9% specific for identifying pancreaticobiliary diseases

FUNCTIONAL BILIARY ETIOLOGY:
TRUE POSTCHOLECYSTECTOMY SYNDROME

Sphincter of Oddi dysfunction (SOD)

- When basic evaluation has ruled out both extra biliary disorders and gross biliary obstruction, sphincter of Oddi dysfunction(SOD) is believed to be the most frequently identifiable cause of PCS
- SOD may account for 14% of pain from PCS
- The pathogenesis of SOD remains poorly understood
- Two mechanisms have been proposed: sphincter of Oddi stenosis refers to a structural abnormality resulting from inflammation and scarring of the sphincter

FUNCTIONAL BILIARY ETIOLOGY....

- The second is sphincter of Oddi dyskinesia, referring to a functional abnormality of the sphincter leading to intermittent obstruction, perhaps due to still unknown neuro-hormonal disturbances

- Geenan and Hogan were the first to demonstrate relief of pain after endoscopic biliary sphincterotomy (EBS) in 91% (10 of 11) of cholecystectomized patients with elevated sphincter of Oddi (SO) pressures at 12-month follow up, but no benefit in patients with normal sphincter pressures

FUNCTIONAL BILIARY ETIOLOGY....

- SOD has been historically classified into 3 types according to the modified Milwaukee Criteria, based on the presence or absence of 3 criteria:
  - biliary type abdominal pain
  - elevation of serum transaminases, alkaline phosphatase, or bilirubin to 1.5 times the upper limit of normal with normalization between attacks

    And
  - bile duct dilatation of more than 12 mm on imaging
- Type I is defined as the presence of all 3 criteria, Type II as pain plus one other criteria,and Type III as pain alone
- This classification is useful in identifying the subset of patients with Type I SOD, who have a greater than 90% chance of symptomatic improvement from EBS.

BILIARY MICROLITHIASIS

- Increasing evidence suggests biliary microlithiasis (BM) is another important cause of PCS
- Bile crystals, composed of cholesterol monohydrate crystals (CMC) and calcium bilirubinate granules (CBG), are the precursors to gallstones
- By definition, microlithiasis cannot be directly visualized by conventional trans-abdominal ultrasound or CT
- Bile from duodenal or bile duct aspirates can be examined for the presence of such microlithiasis
- They are considered positive if 3 or more crystals are present in a high power view in a polarized microscope
- Microlithiasis has already been identified as a cause of recurrent idiopathic acute pancreatitis in patients with an intact gallbladder, presumably due to transient obstruction of the ampulla or pancreatic duct

BILIARY MICROLITHIASIS…

- In a recent randomized trial,10% of PCS patients had microlithiasis identified in their bile
- Patients were randomized to receive ursodeoxycholic acid (urso) or placebo for six months
- The results demonstrated statistically significant improvement or resolution of symptoms in the urso group compared to the placebo group
- This positive response to urso strongly suggests BM as a cause of PCS pain

CYSTIC DUCT REMNANT:
RETAINED CALCULI AND NEUROMA

- Both the presence of retained calculi and the development of traumatic neuroma have been identified as the underlying pathology in multiple studies

- By definition, a remnant cystic duct is more than 1cm long and believed to be associated with a higher risk of retained calculi

- Though the incidence is unknown, it appears to be growing in the laparoscopic era where higher rates of bile duct and vascular injuries encourage surgeons to leave behind a longer cystic duct or even part of the gall bladder

- Walsh *et al*. reported patients developing recurrent biliary type pain 14 months to 20 years after either laparoscopic or open cholecystectomy, and 6 out of 7 patients were found to have retained cystic duct calculi on ERCP

- Symptoms were relieved nearly a year after surgical resection of the remnant, extracorporeal shockwave lithotripsy (ESWL), or endoscopic biliary holmium laser lithotripsy
- Milking of the cystic duct before clipping it and routine use of intraoperative cholangiogram have been proposed

CLINICAL FEATURES

- Biliary colic - 90%
- Pain- 75%
- Fever - 38%
- Jaundice- 25%
- Diarrhoea- 35%
- Nausea- 35%
- Bloating

DIAGNOSTICS

- CBC
- LFTs- S.bilirubin,S. alkaline phosphatase
- S.amylase/lipase
- Trans abdominal USG(TUS), Endoscopic USG(EUS)
- Esophagogastroduodenoscopy for examination of the stomach, duodenum and the area major duodenal papilla
- Endoscopic retrograde cholangiopancreatography(ERCP)
- Hepatobiliary iminodiacetic acid(HIDA) scan
- MRCP
- Analysis of biliary sludge obtained through ERCP
- SeHCAT or other test for bile acid diarrhea

DIAGNOSTIC AND THERAPEUTIC APPROACH

- The first step in the evaluation of a PCS patient should be a thorough history and physical examination to rule out common treatable conditions which may have been previously overlooked

- Assessment for *H. pylori* infection,peptic ulcer disease, gastroparesis, amongst other disorders, should be initiated in the right clinical setting

DIAGNOSTIC AND THERAPEUTIC APPROACH....

- The workup for true PCS should begin with differentiating functional pain from biliary pain, and Rome III criteria may be employed in this process

- Having excluded a functional etiology, practitioners should evaluate patients for SOD

- Patients with *definite SOD* can be diagnosed with Modified Milwaukee Criteria with liver function tests and radiography, and should undergo ERCP and EBS

DIAGNOSTIC AND THERAPEUTIC APPROACH....

- MRCP and EUS can be employed to diagnose pathology involving the cystic duct, such as retained stone
- If the workup is negative, a multidisciplinary approach with pain management and psychiatry may be appropriate
- Few studies have looked at the long-term efficacy of medical therapy for PCS or SOD

DIAGNOSTIC AND THERAPEUTIC APPROACH....

- Two small double-blind, placebo controlled, crossover studies have shown that **nifedipine** can reduce the severity and frequency of pain, and need for analgesics compared to the placebo group

- **Nitrates** have been shown to reduce the basal sphincter pressure in asymptomatic volunteers and symptomatic patients with SOD

- **Octreotide** has also been shown to reduce basal sphincter pressures in manometrically proven SOD in a prospective randomized placebo controlled trial

- **Nitroglycerine, spasmolytics, opiate analgesics,** and **corticosteroids** have all been reported to relieve pain from SOD attacks to varying degrees

DIAGNOSTIC AND THERAPEUTIC APPROACH....

- Of note, Cheon *et al*. recently conducted a randomized controlled trial involving cases of suspected SOD: the administration of vardenafil into the duodenum distal to the papilla caused a significant decrease in basal sphincter of oddi pressures on SOM

- In summary, despite the paucity of data for the above treatments, given their relative safety and the benign course of PCS and SOD, experts recommend a trial of medical therapy prior to SOM and BSE

- Collective understanding of postcholecystectomy syndrome is still imperfect

- Future studies are needed to elucidate the pathogenesis of SOD, to develop cost effective and non-invasive methods for evaluating SOD, and to pursue medical therapies as an adjunct or alternative to invasive interventions

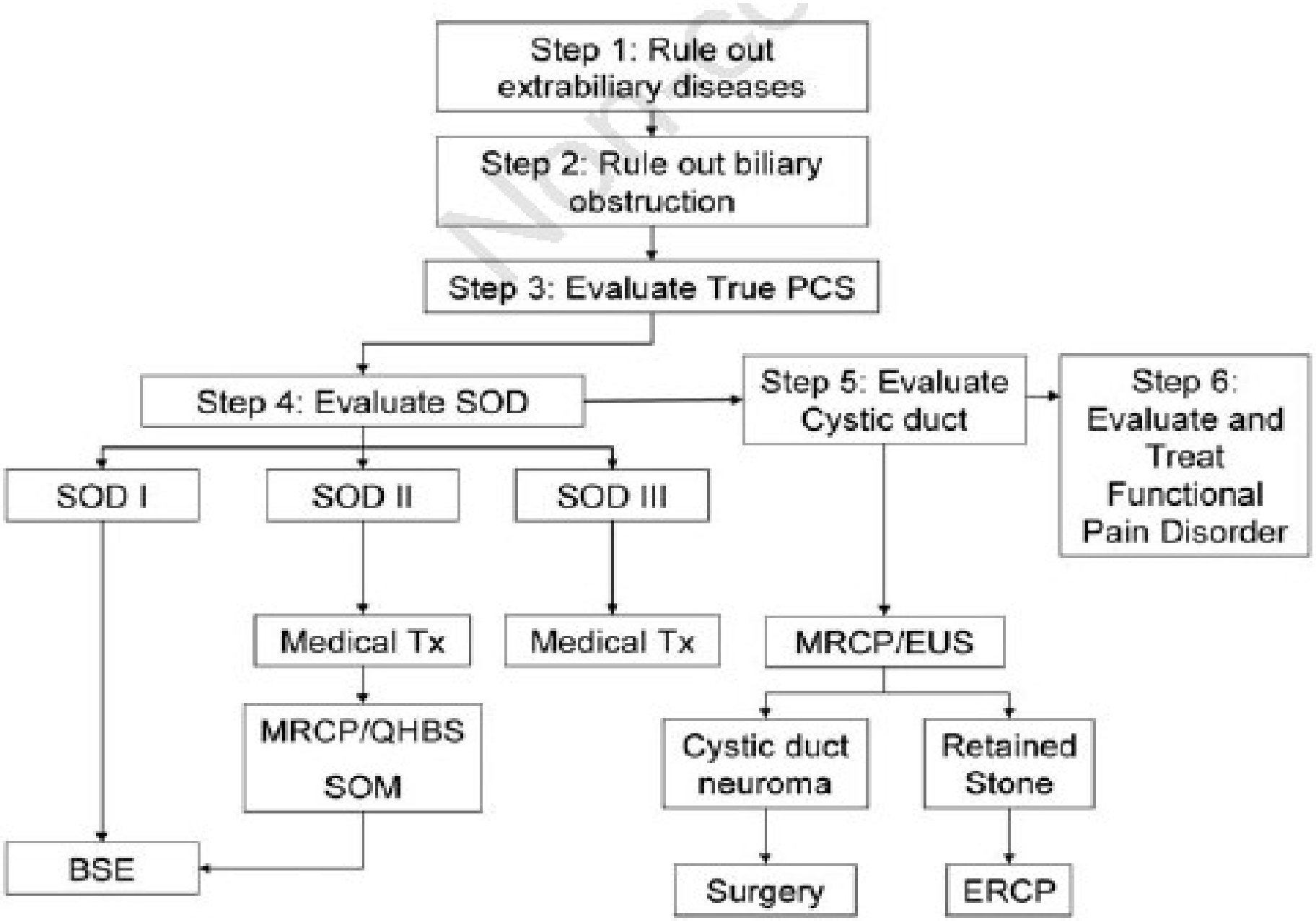

Figure 1. Diagnostic and therapeutic approach to postcholecystectomy syndrome

TREATMENT- Pharmacologic approach

- Dietary modification- reduced fatty food.
- If biliary microlithiasis - oral **ursodeoxycholic acid**
- Bile acid sequestrant therapy (**Cholestyramine**) for bile acid diarrhea
- For functional dyspepsia-- **proton pump inhibitors** and **dopamine antagonists**
- **Tricyclic antidepressants** for nausea, vomiting, early satiety, impaired motility and other related symptoms

GENERAL DIET AND LIFESTYLE REMEDIES

- Avoid overeating
- Eat several small meals a day or eat smaller portions at breakfast, lunch, and dinner
- Going too long without eating is also bad as our bodies signal bile to be released at certain times of the day
- Not eating can lead to bile acid diarrhea and intestinal discomfort after cholecystectomy.
- Don’t eat fast, instead, chew your food thoroughly and take your time
- Eat a low-fat diet especially saturated fats, keeping fat intake under 3 grams per meal and snack

GENERAL DIET AND LIFESTYLE REMEDIES..

- Medium-chain triglycerides (MCT) oils i.e. coconut and palm kernel oil, are better as they do not require bile for digestion
- Beets, apples, and ginger all support bile formation
- Other foods reported to protect the liver and increase bile production are bitter foods such as dandelion and mustard greens, radishes, artichokes, fruits high in vitamin c, and cruciferous vegetables such as broccoli, cauliflower, and cabbage

FOODS THAT CLEANSE THE LIVER

The Farmacy

GRAPEFRUIT

BEETS

CARROTS

GREEN TEA

APPLES

BROCCOLI

LEMONS & LIMES

ARUGULA

WALNUTS

CABBAGE

CAULIFLOWER

AVOCADO

SPINACH

GARLIC

TURMERIC

CONCLUSION

- Cholelithiasis is the most common disease of biliary Tract and

Laparoscopic cholecystectomy(LC) is a safe procedure in trained hands, especially when the procedure is converted early

- In the world literature, the incidence of PCS varies widely, between 5-63%. More than half of patients will have some symptoms after LC.

- Patients with previous attacks of acute cholecystitis and those with co-morbid diseases are more prone to develop persistent symptoms

- A cause can be identified in up to 95% of patients and only patients with persisting symptoms and no obvious cause on investigation should be labelled as PCS

- Early recognition of etiology can be essential to prevent worse outcomes of cholecystectomy. So, interdisciplinary approach with surgeons, gastroenterologists, cardiologists, psychiatrists is necessary

- Internal medicine specialists can play the role of the marshal of this medical war field to best explain the pathophysiology of this syndrome of versatile etiology


Thank You