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Duodenogastric Reflux after Cholecystectomy: Evaluation, Esophageal Carcinogenesis

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Abstract:

Cholecystectomy is the most common gastrointestinal surgery today. Most surgeons believe that this is a mundane operation and that most patients will go through quite well.

However, the phenomenon of duodenal fluid regurgitation into the stomach, Duodeno gastric reflux (DGR), occurs naturally even in healthy people in the early morning and after eating.

However, people who have undergone biliary surgery such as cholecystectomy or biliary reconstruction often have symptoms due to DGR such as nausea, biliary vomiting, and epigastric pain. This time, we will report on cholecystectomy and DGR, DGR evaluation method, DGR and esophageal carcinogenesis with literature and my experimental data.

Key Words: cholecystectomy; duodenogastric reflux; esophageal cancer

Introduction

Cholecystectomy remains one of the most frequent abdominal surgeries worldwide. The course is usually fine, but 20-40% of patients continue to have various gastrointestinal symptoms. Causes have been diagnosed as residual common bile duct stones, common bile duct stenosis, papillary tumors, residual cystic ducts, dysfunction of the oddi sphincter, and ulcers.

However, among the complaints of postoperative cholecystectomy, there are cases in which the obvious cause is unknown. They may result from cholecystectomy itself. Gastric pH has been reported to shift to alkaline in symptomatic patients after cholecystectomy.

There are numerous clinical and experimental studies that increase duodenogastric reflux (DGR), a phenomenon in which duodenal fluid regurgitates into the stomach after cholecystectomy.

Here, we discuss the relationship between cholecystectomy and DGR, the evaluation method of DGR, and the effect of DGR on the esophagus, focusing on the literature review with our experimental data.

1. Cholecystectomy and Duodenogastric Reflux

Duodenogastric Reflux (DGR), a phenomenon in which duodenal fluid flows back into the stomach, is a phenomenon that occurs naturally even in healthy people in the early morning and after eating. However, people who have undergone biliary surgery such as cholecystectomy or biliary reconstruction often have symptoms due to DGR such as nausea, biliary vomiting, and epigastric pain. Cholecystectomy is the most common gastrointestinal surgery today. Most surgeons believe that this is a mundane operation and most patients will go through quite well. It is difficult to answer the question of how the gallbladder works.

Frequently after surgery, patients have symptoms such as nausea and pain. However, these usually resolve over time. It is especially important to understand the pathophysiology that may result from cholecystectomy in asymptomatic patients.

The mechanism of gallbladder function is very complex and controlled by numerous hormones and nerves. In general, the gallbladder accumulates and concentrates the bile secreted by the liver, and when fatty food enters the duodenum, cholecystokinin (CCK)

is secreted from the duodenum. CCK contracts the gallbladder and at the same time relaxes the papillary sphincter so that bile and fat components are well mixed and digested. The nerve to the gallbladder is very thick and can often be mistaken for an artery by a young surgeon. Experienced surgeons ask them questions and enjoy, "Why this nerve is so thick and what is this doing? "We usually believe that the nerve is important in coordinating the drainage of bile from the gallbladder and the peristaltic movement of the papillary sphincter. The function of the normal papillary sphincter has a role as a gate keeper. Papilla sphincter helps to fill the gallbladder with bile during the interdigestive phase. And the peristaltic movement of the duodenum helps bile to drain from the papilla sphincter. It is interesting that the duodenum and the papilla sphincter move in concert together.

There appears to be a neural mechanism for the coordination of bile drainage from the papilla sphincter and duodenal movement. I think cholecystectomy directly alters pyloric, pyloric sphincter, and duodenal motor function

In a dog experiment by Haruma et al [1], bile acids content in the gastric juice of cholecystectomized dogs was significantly higher than that of non-cholecystectomized dogs. The frequency of pyloric relaxation during phase Ⅱ of the migrasting motor complex was significantly increased after cholecystectomy. After cholecystectomy, bile flows continuously into the duodenum rather than intermittently due to the loss of bile reservoir function in gallbladder, and a lack of coordination of antroduodenal motility exacerbates DGR.

These findings are consistent with increased gastric bile acid levels and decreased pyloric motility during fasting in humans. Hinder et al [2]. performed 24h pH monitor and 24h antroduodenal manometry in 16 cholecystectomy and 19 healthy group, the antral phase III frequency after cholecystectomy was 2.5 ± 0.09 cycle / min compared to 3.2 ±. 0.08 cycle / m in healthy group. Moreover, propagation of the phase Ⅲ front in the duodenum was significantly slowed to 0.14 ± 0.02 cm / s after cholecystectomy compared to 0.27±0.02 cm/s in healthy control.

The duration of the phase Ⅲ in the proximal duodenum after cholecystectomy was also decreased to 4.3±0.27 min compared to 5.9±0.35 min in healthy group. They concluded that the presence of significant DGR and associated gastric pH changes after cholecystectomy occurred due to altered antroduodenal motility Demeester et al [3]. report that exposure to gastric alkali after cholecystectomy is increased, even in asymptomatic patients. This is especially noticeable in the supine position. However, it is even higher in symptomatic patients. Symptomatic patients also appear to have superficial gastritis on endoscopy.

From the above data, it seems that cholecystectomy increases DGR. DGR is an interesting phenomenon that can have serious consequences and we need to fully advise patients on the implications of cholecystectomy.

2. The Evaluation Method of DGR

Objective physiological measurement of DGR is difficult and until recently most of the methods used for measuring DGR have required intubation, which in addition to being an invasive technique may itself promote DGR.

A: Evaluation by biliary scintigraphy [4]: That method can evaluate bile reflux physiologically and non-invasively.

We used Yokogawa Medical Starcam 3000 and after intravenous injection of 99mTc-PMT, Dynamic Scan was performed. The anterior abdominal images were taken at 5-min intervals for 60 min. The grade classification of Duodenogastric reflux is based on the classification of Thomas WEG [5], 0: no regurgitation to the stomach is observed, 1: regurgitation to the pylorus is observed, 2: regurgitation to the gastric body is observed. 3: regurgitation to the gastric body and gastric pylorus was observed, and 4: regurgitation to the esophagus was observed.

It should be noted that this method has a drawback that it cannot be quantitatively evaluated because it only recognizes the regurgitation to the pylorus and the body of the stomach in terms of image analysis. On the other hand, Fountos et al [6] evaluated by duodenogastric reflux index (DGR) = St / A0 × 100 A0: Tc concentration in the entire abdomen St: Maximum Tc concentration in the stomach, and 20% or more had DGR. Quantitative evaluation was performed.

It was reported that the frequency of DGR was significantly increased by cholecystectomy and choledochoduodenostomy. However, it does not mention the relationship with Helicobacter pylori, which has been attracting attention in recent years.

B. Histological Determination of Bile reflux Sobala et al [7] endoscopically biopsied the body and pylorus of the stomach and histologically classified the degree of regurgitation of bile into the gastric mucosa. In this system, an index is derived based on the presence/severity of certain histological parameters:

Lamina propria edema (E), intestinal metaplasia (IM), chronic inflammation (CI), and recent increase in gastroesophageal reflux after eradication of Helicobacter pylori have also been noted, and infection of Helicobacter pylori into the stomach. Classify into 0, mild 1, moderate 2, and marked 3), and create Biliary reflux index (BRI) = (7 × E) + (3 × IM) + (4 × CI) — (6 × Hp). BRI> 14 indicate DGR. Kulan et al [8] report that there are significantly more cases of BRI (+) in choledochoduodenostomy and transduodenal sphincteroplasty than cholecystectomy alone.

C. Billitec ^{R}2000, In 1993 Bechi et al [9] validated system for ambulatory detection of bile reflux by fiber optic spectrophotometer system (Billiltec^{R} 2000, Synectics, and Stockholm,Sweden). Billitec has a spectrophotometer sensor at the tip of the tube and has been reported to be useful in detecting bilirubin. The measurement requires a nasal insertion of the tube into the esophagus. Although it is the best instrument for measuring bilirubin levels in the esophagus, there are opinions that the interpretation of bilirubin levels in the stomach is more complex and not as accurate in this setting.

3. Impact of DGR on the Esophagus

A search from the 1965-1997 Swedish Cancer Registry in Sweden, Freedman et al [10] stated that after cholecystectomy, the frequency of DGR was high and the lower esophagus could be more likely to develop esophageal adenocarcinoma.

We also performed a total gastrectomy in rats to create an esophageal duodenal anastomosis with total gastrectomy, and created a regurgitation model of duodenal fluid (bile, pancreatic fluid). 33% of squamous carcinoma (SCC) and 30% of adenocarcinoma (ADC) were observed [11]. In our experiments, we predicted that most cancers might be ADC, but as mentioned above, in reality, SCC was found in 33% and ADC was found in 30%.

Conventionally, in humans, SCC is often caused by tobacco and alcohol, while ADC is caused by reflux of gastroduodenal fluid. In this experiment, histologically, the associated reflux esophagitis was more prominent in the ADC group than in the SCC group. ADC was abundant near the anastomotic site, and SCC was abundant in the middle to lower part slightly away from the anastomotic site.

It was speculated that this was a tissue feature, namely whether ADC and SCC depended on the amount of duodenal fluid regurgitation, a small amount of regurgitation caused SCC, and a large amount of regurgitation caused ADC. Further studies are needed in the future.

In addition, COX2, PGE2, PCNA labeling index in the lower esophageal tissue showed high values, that is, PGE2, COX2, a metabolite of Arachidonic acid generated by chronic stimulation by duodenal fluid reflux, was found to be an important mediator of esophageal carcinogenesis.

Esophageal cancer has an insidious and apparently painless onset, superficial lesions are completely asymptomatic and discovered accidentally during endoscopic examination. For these reasons, special attention should be paid in the early detection [12].

Conclusion

1. Biliary scintigraphy and BRI seemed to be reliable, reproducible and good evaluations for DGR evaluation.
2. After cholecystectomy, DGR occurs at a considerable frequency and when the gastric mucosa and esophageal mucosa are exposed to duodenal fluid for a long period of time, dysplasia and cancer may occur at the esophagus and stomach. Therefore, sufficient follow-up of the stomach and esophagus is required.

Abbreviations: Duodenogastric Reflux (DGR), Adenocarcinoma (ADC), Squamous cell carcinoma (SCC), Biliary reflux index (BRI)

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