Ali holecistektomija vpliva na oddijev sfinkter in ampulo papile vateri?

Does cholecystectomy affect the sphincter of oddi and the ampulla of vater?

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Izvleček

Namen: *Ker ima 20–50 % holecistektomirancev tudi po operaciji žolčnih kamnov nadaljnje dispeptične težave, želim dokazati, da del teh težav ne izvira iz primarne bolezni žolčnika s kamni, ampak so drugega, natančneje duodenalnega izvora.*

Metode: *Z endoskopskim ultrazvokom (EUZ) sem pred operacijo (AOP) žolčnih kamnov pregledal 80 bolnikov. Tri mesece po operaciji (POP3) in 6 mesecev po njej (POP6) sem preiskavo ponovil. 50 operirancev je bilo simptomatskih, 30 pooperativno asimptomatskih. Pri vseh sem opravil analizo papile Vateri (PV) s posebnim poudarkom na analizi vidljivosti sfinkterja Oddi kompleksa (SOK) in ampule papile (AP).*

Rezultati: *Vidljivost SOK je signifikantna v meritvah AOP/POP3 ($p < 0.05$) iz prikazanih sprememb. Prav tako je signifikantna primerjava*

Abstract

Purpose: *About 20–50% of cholecystectomized patients complain of dyspeptic problems after gallstone surgery. I hypothesized that some of these problems do not arise from primary gallbladder disease, but are due to problems of duodenal origin.*

Methods: *I examined 80 patients using endoscopic ultrasound (EUS) before gallstone surgery (AOP). I repeated the examination 3 months (POP3) and 6 months (POP6) after the surgery. Fifty patients who underwent surgery were symptomatic; 30 were asymptomatic. In all patients, an analysis of the papilla of Vater (PV) was carried out with a special focus on the visibility of the sphincter of Oddi complex (SOC) and the ampulla of papilla (AP).*

Results: *The visibility of the SOC was significant in the measurements AOP/POP3 ($p<0.05$). The comparison POP3/POP6 ($p<0.001$) was also*

POP3/POP6 ($p < 0.001$). Vzorec obnašanja AP (AOP/POP3, POP3/POP6, AOP/POP6) v različnih meritvah ni signifikanten ($p > 0.05$). Linearno zvečanje odstotka nevidnih AP (76 %, 78 %, 80 %) kaže na druge mehanizme sprememb, kot sem jih ugotovil pri vidljivosti SOK 52 % (AOP), 72 % (POP3) in 50 % (POP6).

Zaključek: *Holecistektomija očitno deluje incidentalno na vidljivost SOK. To potrjujejo klinične izkušnje v potrebnem rekonvalenscentnem dietetnem režimu nekaj mesecev po operaciji, ki so potrebne za »reprogramiranje SOK–a«. AP, ki se obnaša po svoji embrionalni in histološki zasnovi po duodenalnem vzorcu (SOK po biliarnem), pa kaže počasne nesignifikantne linearne trende zvišane nevidljivosti.*

significant. The behavior pattern of the AP (AOP/POP3, POP3/POP6, AOP/POP6) in various measurements was not significant ($p>0.05$). The linear percentage increase of non–visible AP (76%, 78%, and 80%) indicated different changes in the mechanism with respect to visibility of the SOC; 52% (AOP), 72% (POP3) and 50% (POP6).

Conclusions: *These data showed that cholecystectomy affected the visibility of the SOC. The AP, with its embryological and histological disposition based on a duodenal pattern (SOC is based on a biliary pattern), showed non–significant linear trends of increased non–visibility.*

INTRODUCTION

Langenbuch (1) in 1882 reported that patients who underwent cholecystectomy as therapy for gallstone disease experienced unpleasant effects. Pribram (2) in 1950 described such effects as "post–cholecystectomy syndrome" (PHS). He suggested three possible reasons: immediate consequence of the surgery; biliary symptoms despite surgery; or misinterpret non–biliary symptoms. The main focus of our research is anomalies of the latter.

The prevalence of PHS is 20–50% (3). For disorders that appear with a non–biliary etiology, we can assume that they are partially dependent upon dysfunction of the upper alimentary canal and not with gallbladder removal. Studies in which the gallbladder remained in situ after extracorporeal shockwave lithotripsy (ESWL) showed that the reason for PHS was probably not due to the biliary system. About 20–40% of these patients also report problems related to PHS (4). Rädecke found a significant correlation ($p<0.005$) between preoperative symptoms and outcome (5).

To analyze and comprehend the non–biliary etiology of PHS, it is necessary to understand the specific anatomy of the distal bile duct, sphincter of Oddi, the ampulla of Vater, and the papilla of Vater. The choledochus forms by the junction of the hepatic duct and cystic duct, and is joined by the duct of Wirsung in the pancreatic part. At the point of entry of the duodenal wall, the ampulla of the papilla (AP) is formed, which is a component part of the papilla of Vater (PV). To understand the functioning of the sphincter of Oddi complex (SOC), it is necessary to understand the anatomy of the distal choledochus. The lower choledochal sphincter muscle is formed in the intramural part.

The musculature is progressively weakened when ascending. The muscular meshwork of the upper choledochal sphincter is formed in the distal part of the intrapancreatic choledochus. The duct of Wirsung is also surrounded by muscular layers in the immediate vicinity of the junction, where both musculatures are linked and continue their way towards the AP. This miniature muscle fills the bile duct and the gallbladder in a retrograde fashion; it regulates the flow of bile and secretion of pancreatic fluid (6). An analysis of patients who underwent cholecystectomy demonstrated that the sphincter activates itself irrespective of the intestinal–duodenal musculature (7). It is very important that development of the musculus proprius choledochi in an embryo is 5 weeks after that of the intestinal duodenal musculature (8). The functionality of this valve mechanism on the level of the junction is directly associated with erection of the papilla and the emptying of bile and pancreatic fluid. The SOC is influenced by numerous gastrointestinal hormones and neuroendocrine agents that affect the basal pressure and phase contractions. Abnormal functioning of the SOC causes colic–like pain (9). It is not known if the function of the SOC and the pancreatic duct are independent of each other (10). The sphincter choledochus and the sphincter of Wirsung together form the first portion of the AP. Muscles and their fibres reach into the submucosa, where they entwine with glands and surrounding tissue. They then form the SOC (11). The SOC has a high pressure and is 6 mm from the orifice of the papilla. It covers 10–15 mm of the distal choledochus, and comprises choledochal, pancreatic and ampullary parts. The coordination of these three segments is not known (12). The contractile activity of the SOC is measured using manometry. Pressure in the duodenal wall (pars intramuralis), SOC and the choledochus are recorded. The measurements indicate various pressures and different activity phases (13). Functional manometry confirms the separate activity of the SOC lying in the ampullo–choledochal segment of the PV of the AP, which is the duodenal functional model of embryo development (8, 14). The AP is formed and continues towards the orifice of papilla. Muscular fibers are very rare, and "embrace" glandular structures. The primary structure is the duodenal mucosa. Its epithelium forms the ampullary wall. Brunner's glands and some connective tissue are in the submucosa. The muscularis propria is part of the intestinal musculature. The blood flow of the PV is very specific. Arterial blood flow is low because the median vein diameter of the plexus arteriosus is 0.98 mm (15). As a consequence, all tissue characteristics and physical changes of the SOC and AP have diverse ultrasound (US) echogenicity, impedance, reflectance, diffusion, and this is termed "scattering". Unlike percutaneous US, the accessibility of the subtle organogram of the anatomical structures of the PV with the EUS is considerably more precise and reliable. In health, the size of the PV is between 20–25 mm^2. It has the form of a conventional triangle with a height of 0.6 mm. This form is taken into consideration when calculating the surface area (11). Enlargement of the PV by 2–4–fold has been reported for patients with gallstones (11). The SOC and AP have different embryonic, anatomic and histological genesis. Hence, one would expect different behaviours of the SOC and AP in gallstone disease, during surgery, and the postoperative period. I analyzed the behaviours mentioned above using endoscopic ultrasound (EUS) as a semi–invasive method. This represents normal stress for the patient, just like classical endoscopy (12).

MATERIALS AND METHODS

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, University of Maribor, (Maribor, Slovenia). All patients provided written informed consent to be included in the study.

The study involved 80 cholecystectomized patients with no evidence of choledocholithiasis or cholestasis. Fifty of these patients experienced early atypical complaints such as bloating, distension, nausea, and pain in the upper abdomen. The remaining 30 patients had no symptoms in the same period after cholecystectomy. EUS, as well as visibility of the SOC and

AP lumen was evaluated in all patients. The results were compared with normal values, and parameters of the PV.

Echogenicity (scattering) is dependent upon the impedance between various tissues as well as the velocity and energy of reflected US waves. The greater the reflection of sound waves (scattering) the brighter ("hyperechogenic") the structure will appear. Conversely, the smaller the reflection of sound waves, the less bright ("hypoechogenic") the structure will appear. A mid–point between these extremes is a structure that appears to be iso–echogenic. Echogenicity is not dependent upon tissue thickness (13, 14). Histologically, the SOC and AP comprise epithelium and mucosa. The submucosa consists of various glands, vascular structures, tissue, muscles, and interstitial fluid (15, 16).

I analyzed the sonograms of the PV of 24 healthy subjects who underwent a full medical examination in Maribor (Slovenia) and Zagreb (Croatia). These analyses did not show the PV structures of the SOC and AP. This indicated that the normal PV was EUS isosonic in its isoechogenic substrate (17). Also, the size (20–25 mm^2), height HPV (6 mm), and width (12 mm) of the PV were noted (11).

In addition, no sex–related differences were observed. A GF UM 20 (Olympus Optical, Shibuyaku, Japan) machine was used with a 7.5–MHz ultrasound probe at 360° rotation. When observing the PV, the probe was placed in a perpendicular and axial position in the descending duodenum. I categorized the visibility of the SOC as "well visible", "less visible" or "not visible" in the sonogram of the PV. The height of the papilla (HPV) was measured separately (Figure 1). Description of the appearance of the AP was based on whether the lumen of the ampulla was visible or not (Figure 2).

Statistical analyses was based on the values measured in cholecystectomized patients before cholecystectomy (AOP), 3 months after gallbladder removal (POP 3) and 6 months after gallbladder removal (POP 6). The Mann–Whitney–Wilcoxon non–parametric test and the Stuart x2 test were used. The results were compared with normal values measured in 24 healthy subjects.

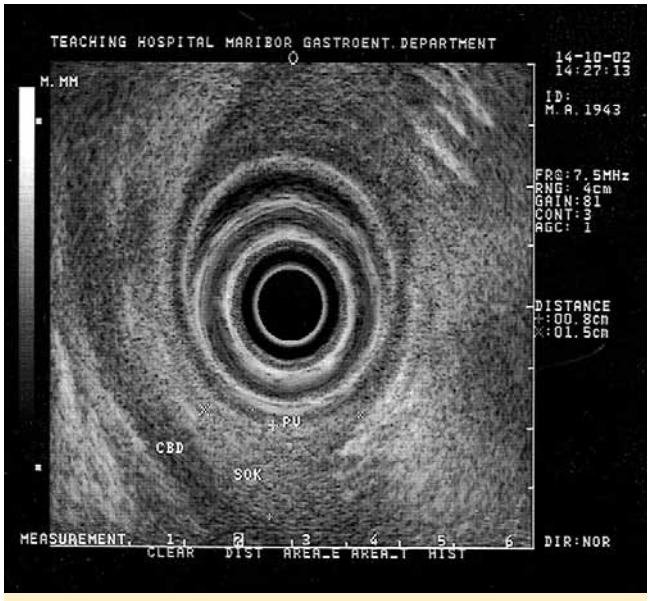

Figure 1. *SOK – Sphincter of Oddi Complex less visible. PV – Papilla of Vateri, CBD Common Bile Duct, +...+ Height of the PV (0.8 cm), x...x Width of the PV (1.5 cm)*

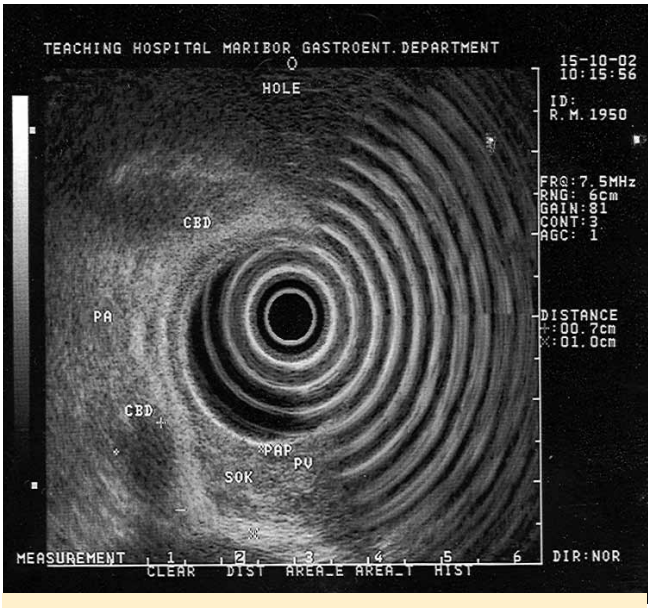

Figure 2. *SOK – Sphincter of Oddi Complex is well visible. PV Papilla of Vateri, CBD Common Bile Duct, +...+ Diameter of CBD (0.7 cm), x...x Height of the PV (1.0 cm), PAP lumen of Ampulla of PV*

RESULTS

The group of 50 patients consisted of 19 men and 31 women. The mean age for men and women were 58 years and 63 years, respectively. The youngest patient was aged 19 years and the oldest 83 years. In the group of 30 asymptomatic patients, 16 were men and 14 women. The mean age for men was 53 years and for women was 61 years. The control group consisted of 11 men and 13 women. The youngest was aged 24 years and the oldest 79 years. The median age was 52 years for men and 57 for women. All our patients were from the region of Maribor (Slovenia) and Zagreb (Croatia).

The differences between men and women in HPV and visibility of the AP lumen were not statistically significant, so the results were analyzed for the sample as a whole. Table 1 shows the calculated HPV in three time periods in 50 symptomatic patients. Table 2 shows the percentage differences in echogenicity of the SOC measured thrice at different time periods. The data in Tables 1 and 2 are for all 50 symptomatic patients. Table 3 and Figures 1 and 2 show the appearance of the SOC of the PV during measurements before surgery as well as 3 and 6 months after surgery. Table 4 shows HPV measurements before cholecystectomy as well as 3 months and 6 months after cholecystectomy in 30 asymptomatic patients. Table 5 shows results of measurements of the SOC of the PV before cholecystectomy as well as 3 months and 6 months after cholecystectomy in 30 asymptomatic patients. The analysis confirmed the non–visibility of the SOC before surgery and 6 months after surgery, whereas visibility was best 3 months after surgery. The

Table 1. *HPV measurement in 50 symptomatic patients*

	X SD	Median	Min	Max	χ^2	p
AOP	9.9 ± 3.4	9.0	6.0	21.0	10.92	< 0.005
POP3	10.8 ± 3.6	10.0	6.0	24.0		
POP6	9.4 ± 2.3	8.5	6.0	16.0		

AOP:POP3 3.05 $p < 0.05$; AOP:POP6 1.26 $p > 0.05$; POP3:POP6 3.67 $p < 0.001$

AOP: prior to surgery; POP3: 3 months after surgery; POP6: 6 months after surgery.

Table 2. *Measurements of the SOC of the papilla of Vater before cholecystectomy as well as 3 months and 6 months after cholecystectomy in 50 symptomatic patients*

	1. Measurement		2. Measurement		3. Measurement	
Visibility	AOP		POP3		POP6	
	n	%	n	%	n	%
Well visible	5	10.0	8	16.0	–	–
Less visible	21	42.0	28	56.0	25	50.0
Not visible	24	48.0	14	28.0	25	50.0

AOP: prior to surgery; POP3: 3 months after surgery; POP6: 6 months after surgery, SOC of the PV after cholecystectomy in 50 symptomatic patients

Table 3. *Appearance of the SOC of the PV according to measurements*

AOP

		Well visible	Less visible	Not visible
POP3	Well visible	5	2	1
	Less visible	0	14	14
	Not visible	0	5	9

(Stuart) $X^2 = 7.12$ $df = 2$ $p < 0.05$

AOP

		Well visible	Less visible	Not visible
POP6	Well visible	0	0	0
	Less visible	5	9	11
	Not visible	0	12	13

(Stuart) $X^2 = 5.04$ $df = 2$ $p > 0.05$

POP3

		Well visible	Less visible	Not visible
POP6	Well visible	0	0	0
	Less visible	8	13	4
	Not visible	0	15	10

(Stuart) $X^2 = 14.37$ $df = 2$ $p < 0.001$

AOP: prior to surgery; POP3: 3 months after surgery, POP6: 6 months after surgery.
df – Degree of Freedom

visibility was significantly low (p<0.001) 6 months after surgery.

Table 6 describes the appearance of the ampulla lumen. It showed a tendency of progressive non–visibility of the linear type in 30 asymptomatic patients. The visibility of the lumen of AP was inversely proportional to the visibility of the SOC. Table 7 shows the visibility of the AP lumen according to measurements in 50 symptomatic patients. Changes in the visibility of the AP lumen were not significant in any measurement (p>0.05).

Table 8 shows the results of the analysis of the HPV as well as the visibility of the SOC and AP lumen. The statistical significance of the HPV and the visibility of the SOC were equal. This confirmed the identity of the anatomical location of the SOC with respect to the HPV: AOP/POP3 (p<0.05), POP3/POP6 (p<0.001). The measurements between AOP and POP6 (p>0.05) were not significant. The HPV in symptomatic and asymptomatic patients was higher than in the normal population (7–9 mm). The results of the visibility of the AP lumen were not significant (AOP, POP3, POP6, p>0.05). There were only minor linear non–visibility trends for the AP (76%, 78%, and 80% at AOP, POP3 and POP6, respectively). The visibility trends of the SOC deviated considerably (52%, 72%, and 50%, respectively) for the three measurements. The visibility of the SOC was significant in the measurements AOP/POP3 (p<0.05) and POP3/POP6 (p<0.001), but not for AOP/POP6 (p>0.05).

Identical changes were also observed in asymptomatic patients, so an unknown agent did not cause the complaints in patients.

DISCUSSION

Despite its small size (PV is 20–25 mm2 in normal subjects), the PV in cholecystectomized patients (75–90 mm2) is very important (18). Furthermore, it is very important to be familiar with structures such as the SOC and AP. For correct interpretation and analyses of EUS findings, a good knowledge of microanatomy is required. In his supplemented edition of embryonic histomorphology, Acosta (19) identified the ampullary choledochal segment of the PV as a functional smooth muscle entity of SOC PV.

Table 4. *HPV measurements before cholecystectomy as well as 3 months and 6 months after cholecystectomy in 30 asymptomatic patients*

	X SD	Median	Min	Max	χ^2	p
AOP	9.8 ± 3.2	9.0	5.9	21.0		
POP3	10.9 ± 3.7	10.0	6.0	23.9	10.73	< 0.005
POP6	9.3 ± 2.2	8.3	6.0	15.9		

AOP:POP3 3.05 $p < 0.05$; AOP:POP6 1.26 $p > 0.05$; POP3:POP6 3.67 $p < 0.001$

AOP: prior to surgery; POP3: 3 months after surgery; POP6: 6 months after surgery.

Table 5. *Measurements of the SOC of the papilla of Vater before cholecystectomy as well as 3 months and 6 months after cholecystectomy in 30 asymptomatic patients*

	1. Measurement		2. Measurement		3. Measurement	
	AOP		POP3		POP6	
	n	%	n	%	n	%
Well visible	3	10.0	5	17.0	1	3
Less visible	13	42.0	16	53.0	14	47.0
Not visible	14	48.0	9	30.0	15	50.0

AOP: prior to surgery; POP3: 3 months after surgery; POP6: 6 months after surgery, SOC of the PV after cholecystectomy in 30 asymptomatic patients.

Table 6. *Measurements of the visibility of the AP lumen of the papilla of Vater before cholecystectomy as well as 3 months and 6 months after cholecystectomy in 50 symptomatic patients*

	1. Measurement		2. Measurement		3. Measurement	
	AOP		POP3		POP6	
	n	%	n	%	n	%
Lumen	7	14.0	5	10.0	1	2
Small lumen	5	10.0	6	12.0	9	18.0
Not visible	38	76.0	39	78.0	40	80.0

AOP: prior to surgery; POP3: 3 months after surgery; POP6: 6 months after surgery, SOC of the PV after cholecystectomy in 30 asymptomatic patients.

Table 7. *Visibility of the AP lumen according to measurements*

AOP

		Well visible	Less visible	Not visible
POP3	Well visible	4	0	1
	Less visible	3	1	2
	Not visible	0	4	35

(Stuart) $X^2 = 1.40$ $df = 3$ $p > 0.05$

AOP

		Well visible	Less visible	Not visible
POP6	Well visible	0	0	1
	Less visible	3	2	4
	Not visible	3	4	33

(Stuart) $X^2 = 4.65$ $df = 3$ $p > 0.05$

AOP

		Well visible	Less visible	Not visible
POP6	Well visible	0	0	0
	Less visible	3	5	2
	Not visible	3	1	36

(Stuart) $X^2 = 6.32$ $df = 3$ $p > 0.05$

AOP: prior to surgery; POP3: 3 months after surgery, POP6: 6 months after surgery.

Moreover, he assigned the ampullo–papillary segment of the AP lumen as having an embryo–duodenal origin. Histologically, the main structures of the SOC are interlaced with the muscularis mucosa of the choledochus, the duct of Wirsung, and part of the ampullary musculature. Most of the histomorphological structures of the ampullo–duodenal segment of the AP belong to submucosal tissue of the duodenal type. This also explains the specific behavior of the PV (8).

Considering the non–visibility of the AP lumen (a normal lumen was not visible), we concluded that there were linear trends of improvements in this part of the papilla (76%, 78%, and 80%). However, the behavior of the proximal choledochal part of the SOC did not show this type of linearity. An explanation for this observation could be due to the arterioles of the submucosal plexus lying towards the orifice of the PV. This vein system is harmonized within its own functional blood flows followed by various vasoactive substances (e.g. hormones) and neural innervation. It is about the flow through the capillary vessel network of the duodenal type. Brunner's mucosal ampullo–papillary glands are activated by the same mechanisms. This could be due to an adenomatous type of stimulation of the AP with major secretion of mucus and non–peptic duodenal papillitis (20). It is probably a form of functional papillitis with characteristics as in functional duodenopathy of non–peptic origin (21). Data on the chronic problems of dyspeptics (22, 23, 24) after a cholecystectomy are in accordance with 20% of visible AP found in the present study.

The SOC consists of three muscles forming the proximal portion of the ampulla. The entire complex is 10–15–mm long. Manometric analyses show synchronous motor activity of the upper alimentary canal (25). The most surprising feature of the activity analysis of the SOC are the pressure waves with a frequency of 4–5 impulses in 4 min with the duration of 4–5–s each. An amplitude height ≤130 mmHg is of great importance, and often exceeds values of systolic blood pressure (yet always exceeds the values of diastolic blood pressure). The strongest phase contractions are manifested 6–8 mm in the distal choledochus. This is also the site of the ampullary choledochal segment of the HPV, where the SOC is positioned. Wave phase sequences are significantly elevated in the form of repeating waves. They are more frequent in cholecystectomized patients, who

Table 8. *Correlation between HPV and the visibility of the SOC and AP lumen*

	HPV	Visibility of the SOC	Visibility of the AP lumen
AOP/POP3	***p<0.005***	***p<0.05***	*p>0.05*
AOP/POP6	*p>0.05*	*p>0.05*	*p>0.05*
POP3/POP6	***p<0.001***	***p<0.001***	*p>0.05*

AOP: prior to surgery; POP3: 3 months after surgery, POP6: 6 months after surgery.

usually have a normal endoscopic retrograde cholangiopancreatography (ERCP) (26).

The present study showed that the SOC and AP lumen are practically invisible in a normal papilla. EUS showed a normal papilla that was iso–echogenic. Various diseases of the biliary tract or surgeries can affect the papilla (27, 28, 29). This leads to changes in EUS echogenicity. The same is true for the visibility of the AP. The AP is visible only if it contains tissue fluids, secreted mucus, and other secretions, which are a result of greater activity of Brunner's glands. The mucous membrane of the AP reacts to duodenal stimulation (30, 31).

In conclusion, the visibility of the SOC and the HPV were significantly correlated, whereas visibility of the AP lumen compared with the SOC and HPV were statistically non–significant. This is the first time that the different behavior of the SOC and AP has been described.

REFERENCES

1. Langenbuch C. Ein Fall von Extirpation der Gallenblase wegen chronischer Choletithiasis. Helung Berl Klin Wochenschr 1882; 48:725–7.
2. Pribram B.O.C. Postcholecystectomy syndromes. JAMA 1950; 142: 1262–9.
3. Bodval B. The postcholecystectomy syndrome. Clin Gastoenterol 1973; 2: 103–26.
4. Wehrmann T, Seifert H, Seipp M, Lembcke B, Caspary WF. Endoscopic injection of botulinum toxin for biliary sphincter of Oddi dysfunction. Endoscopy 1988; 30: 702–7.
5. Rädecke J, Waninger J, Schlotterbeck E, Farthmann EH. Folgezustände nach Cholezystektomie – eine prospektive Studie. Zentralbl Chir 1993; 118: 337–41.
6. Farthmann EH, Rädecke J. Das Postcholecistektomie–Syndrom. Chirurg 1993; 64: 994–9.
7. Stzilvassy Z, Nagy I, Madacsy L, Hajnal F, Velösy B, Takács T et al. Beneficial effect of lovastatin on sphincter of Oddi dyskinesia in hypercholesterolemia and hypertriglyceridemia. Am J Gastroenterol 1997; 92: 900–2.
8. Boyden EA. The anatomy of the choledochoduodenal junction in man. Surg Gynec Obst 1957; 104: 641–52.
9. Neoptolemos JP, Bailey IS, Carr–Locke DL. Sphincter of Oddi dysfunction: Results of treatment by endoscopic sphincterotomy. Br. J. Surg 1988; 75: 454–7.
10. Fazel A, Li SC, Burton FR. Octreotide relaxes the hypertensive sphincter of Oddi: Pathophysiological and therapeutic implications. Am J Gastroenterol 2002; 97: 612–6.

11. Skalicky M, Dajcman D, Hojs R. Effect of cholecystectomy for gallstones on the surface of the papilla of Vater and the diameter of the common bile duct. Eur J Gastroenterol Hepatol 2002; 14 (4): 399–404.
12. Kaw M, Brodmerkel GJ. ERCP, biliary crystal analysis, and sphincter of Oddi manometry in idiopathic recurrent pancreatitis. Gastrointest Endosc 2002; 55: 157–62.
13. Stolte M, Wiessner V, Schaffner O, Koch H. Vaskularisation der Papilla Vateri und Blutungsgefahr bei der Papillotomie. Leber Magen Darm 1980; 10/6: 293–301.
14. Baczako K, Buchler M, Beger HG, Kirkpatrick CJ, Haferkamp O. Morphogenesis and possible precursor lesions of invasive carcinoma of the papilla of Vater. Hum Pathol 1985; 16: 307–10.
15. Keriven O. Patterns of the ampulla of Vater at endoscopic ultrasonography (EUS). Gastrointest Endosc 1993; 39: 320–25.
16. Kimmey MB, Martin RW. Basic principles and fundamentals of endoscopic ultrasound imaging. Gress F, Bhattacharya I, Endoscopic ultrasonography Malden: Blackwell Science 2001; 4–14.
17. Acosta JM, Civantos F, Nardi GL, Castleman B. Fibrosis of the papilla of Vater. Surgery, Gynecology, Obstetrics. 1967; 3: 787–94.
18. Itoh A. Intraductal Ultrasonography for the Examination of Duodenal Papillary Region. J. Ultrasound Med 1994; 13: 679–84.
19. Wolfe MM, Sach G. Acid suppression: Optimizing Therapy for gastroduodenal ulcer healing, gastroesophageal reflux disease, and stress–related erosive syndrome. Gastroenterology 2000; 118:9.
20. Classen M. Endoscopic approach to papillary stenosis (PS). Endoscopy 1981; 13: 154–6.
21. Toouli J. Leading article/What is sphincter of Oddi dysfunction? Gut 1989; 30: 753–6.
22. Neoptolemos JP, Bailey IS, Carr–Locke DL. Sphincter of Oddi dysfunction: Results of treatment by endoscopic sphincterotomy. Br J Surg. 1988; 75: 454–7.
23. Manier JW, Cohen WN, Printen KJ. Dysfunction of the sphincter of Oddi in a postcholecystectomy patient. Am J Gastroenterol 1974; 62:148–52.
24. Shimizu S, Tada M, Kawwai K. Diagnostic ERCP. Endoscopy 1994; 26: 88–92.
25. Rustemovic N, Cukovic–Cavka S, Opacic M, Petrovecki M, Hrstic I, Radic D et al. Endoscopic ultrasound elastography as a method for screening the patients with suspected primary sclerosing cholangitis. Eur J Gastroenterol Hepatol. 2010; 22(6): 748–53.