Extrahepatic biliary obstruction after percutaneous tumour ablation for hepatocellular carcinoma: aetiology and successful treatment with endoscopic papillary balloon dilatation

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Background and aims: Percutaneous tumour ablation (PTA), such as ethanol injection and radiofrequency ablation, is now recognised as a primary treatment for hepatocellular carcinoma (HCC). Although PTA is a relatively safe procedure, it can cause biliary obstruction as a rare complication. As patients with cirrhosis undergoing surgery or endoscopic retrograde cholangiopancreatography/sphincterotomy have a high mortality rate from bleeding, we adopted the use of endoscopic papillary balloon dilatation (EPBD) in these patients and now report the results. We retrospectively analysed the incidence of biliary obstruction after PTA and the efficacy of treatment with EPBD.

Patients and methods: A total of 1043 patients with HCC were treated by PTA, of whom 538 were treated with transarterial embolisation with up to eight years of follow up.

Results: There were 17 (1.6%) cases of hilar obstruction due to tumour progression and 35 (3.4%) cases of extrahepatic obstruction. Apart from the expected causes of biliary obstruction (haemobilia $n=11$, gallstones $n=11$, and three miscellaneous causes), we found that 10 patients had obstruction due to biliary casts. This is the first description of biliary casts after percutaneous tumour ablation therapy. Extrahepatic biliary obstruction by procedure related haemobilia occurred within three days of PTA while other causes occurred between 0 and 17 (average 4.9) months. Biliary casts occurred more frequently after ethanol injection than after radiofrequency ablation. EPBD successfully dissipated biliary obstruction in 33 of 35 cases, while two died due to hepatic failure despite successful drainage.

Conclusions: Extrahepatic biliary obstruction is an uncommon complication after PTA for HCC, and can be safely and effectively treated with EPBD, despite impaired liver function.

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide, usually occurring in patients with cirrhosis due to chronic viral hepatitis.^{1–3} In spite of advances in safety, surgical resection of HCC is still frequently contraindicated because of poor liver function.⁴ Percutaneous tumour ablation (PTA), such as percutaneous ethanol injection therapy (PEIT) and radiofrequency ablation (RFA), is frequently performed as a primary treatment for HCC.^{5–7} PTA is applicable even for those with impaired liver function and its safety in general has been well documented. However, several complications are well recognised.⁷ Haemorrhage is the most frequent complication of PTA and is usually treated conservatively.⁸ However, it can lead to biliary obstruction and deterioration in liver function and death. Biliary damage, including haemobilia, is reported to occur in up to 1% of cases treated with PTA.^{7–10} However, most of these reports covered short term complications during the periprocedural period. There were no reports of obstructive jaundice in a large series of patients after PTA for HCC.

Biliary obstruction is known to occur in patients with HCC due to tumour infiltration or compression of the bile duct, biliary tumour thrombi, spontaneous HCC haemorrhage, and choledocholithiasis.^{11–16}

However, endoscopic facilitation of biliary drainage may be life saving in patients with acute suppurative cholangitis and biliary obstruction.^{17–23} However, patients with HCC have an

increased risk of bleeding due to liver dysfunction, and a mortality of up to 50% for surgery and up to 22% for endoscopic sphincterotomy (EST) has been reported for patients with cirrhosis and coagulopathy.^{19–22} A potentially safer alternative to EST is endoscopic papillary balloon dilatation (EPBD) in which complications such as severe bleeding are rare, even in patients with advanced cirrhosis.^{24–27} Thus we adopted EPBD as the firstline treatment for extrahepatic biliary obstruction occurring in patients with HCC. In this article, we describe our results.

When treating patients with HCC and biliary obstruction who had undergone PTA, we began to recognise that biliary obstruction was frequently caused by biliary casts that were morphologically and histologically distinguishable from haemobilia, tumour thrombi, and common bile duct stones, and were similar to those reported as a complication of liver transplantation.^{28–33} This paper is the first description of biliary casts that occurred in the course of HCC treated by PTA.

Abbreviations: PTA, percutaneous tumour ablation; HCC, hepatocellular carcinoma; EPBD, endoscopic papillary balloon dilatation; PEIT, percutaneous ethanol injection therapy; RFA, radiofrequency ablation; EST, endoscopic sphincterotomy; US, ultrasonography; CT, computed tomography; TAE, transarterial embolisation; ERC, endoscopic retrograde cholangiography; ERCP, endoscopic retrograde cholangiopancreatography; γ -GTP, gamma-glutamyl transpeptidase

Table 1 Profile of all patients with hepatocellular carcinoma treated by percutaneous tumour ablation and that of patients with obstructive jaundice

	Patients (n)	Age (y) (mean)	Sex (M/F)	Child-Pugh (A/B/C)	Prothrombin time (%) (mean)	Platelet count ($\times 10^4/\mu\text{l}$) (mean)
All patients	1043	36–90 (66)	731/312	699/323/21	35.0–100 (73.0)	4.0–43.4 (10.7)
Extrahepatic bile duct obstruction	35	43–88 (66)	29/6	5/22/8	27.1–97.2 (61.5)	3.2–32.5 (13)
Hilar bile duct obstruction	17	51–75 (66)	14/3	1/11/5	54.5–96.7 (72.8)	5.8–37.9 (14)

MATERIALS AND METHODS

Patients

A total of 1043 consecutive patients with HCC were admitted to Tokyo University Hospital from January 1995 to December 2002. They received 8807 sessions of PTA therapy (6322 PEIT, 467 percutaneous microwave coagulation therapy, and 2018 RFA).^{5–7} These 1043 patients consisted of 312 women and 731 men, with a mean age of 66.4 years (range 36–90 years). Eighty five per cent of the patients had cirrhosis, with a Child-Pugh classification of A in 67%, B in 31%, and C in 2% (table 1). The aetiology of liver disease was hepatitis B, hepatitis C, alcohol, and other causes in 11%, 82%, 3%, and 4%, respectively. The diagnosis of HCC was confirmed by percutaneous needle biopsy and histology in 898 of 1043 (86%) patients. The remaining 145 patients were diagnosed as having HCC based on abdominal ultrasonography (US), computed tomography (CT), magnetic resonance imaging, and/or hepatic arterial angiography, together with measurement of α -fetoprotein levels. Also, 538 patients (52%) were treated by transarterial embolisation (TAE) in addition to PTA. All patients treated with PTA were followed up until recurrence or another occurrence of HCC, with monthly clinical examinations and blood tests, and every three months by abdominal US and/or CT scan, primarily to survey for recurrence of HCC.

Biliary obstruction, when and if it occurred, was diagnosed radiologically and patients were classified as having either extrahepatic biliary or hilar bile duct obstruction. Patients with extrahepatic biliary obstruction underwent endoscopic retrograde cholangiography (ERC) to evaluate the cause of obstruction, and plan for a subsequent EPBD, if indicated. Informed consent for both procedures was obtained from each patient. All patients, except two with extrahepatic bile duct obstruction, were treated by EPBD. EPBD was not used in two cases because one patient had a history of papilloplasty and the other had duodenal obstruction.

The causes of biliary obstruction were classified as: (1) casts, (2) stones, and (3) haemobilia, and the underlying clinical features, such as plasma biochemistry or complications, was determined (see table 2). Associated gallbladder abnormalities, including stones and "haemobilia sign", suggesting bleeding into biliary duct trees,³⁴ and the presence of strictures along the biliary tract, were recorded. The immediate results after EPBD are also described in table 2.

Endoscopic treatment

EPBD was performed as previously described, with minor modifications^{24–25} after June 1999 to reduce the risk of pancreatitis. In particular, maximum pressure and duration for full balloon dilatation were decreased from routine 8 atm to maximum 8 atm (most often between 3 and 4 atm) and from two minutes to 15 seconds, respectively. Briefly, diagnostic ERC was performed using a side view endoscope and a standard catheter, through which a 0.035 inch guidewire was inserted into the bile duct. A 5 Fr balloon tipped catheter for bile duct dilation (PET dilator; balloon 3 cm long $\times$ 8 mm wide, or 2 cm long $\times$ 6 mm wide; Bard Interventional Products, CR Bard Inc., Tewksbury,

Massachusetts, USA) was then exchanged over the guidewire and positioned across the papilla of Vater. Under endoscopic and fluoroscopic control, the balloon was gradually inflated with diluted contrast material until the sphincter was adequately dilated under pressure (maximum 8 atm) and the "waist" in the balloon had completely disappeared. The fully inflated balloon was maintained at the same pressure for 15 seconds before it was deflated and removed.

After papillary dilation, further interventions were performed through the dilated papilla, such as extraction of biliary stones, casts, coagulation debris, or biliary drainage. When complete clearance of the extrahepatic bile duct could not be obtained, a plastic tube stent was placed temporarily, usually for less than a week, in the common bile duct until the next endoscopic treatment was performed. The plastic stents were 7–8.5 Fr, 5–8.5 cm, Tannenbaum (Wilson-Cook Medical, Inc., Winston-Salem, North Carolina, USA), Solopass, or Flexima (Microvasive/Boston Scientific Corp., Watertown, Massachusetts, USA), depending on the timing of the stenting. Endoscopic nasobiliary drainage was also performed in cases of severe cholangitis or persistent biliary haemorrhage using a 7 Fr nasobiliary drainage tube (Wilson-Cook Medical, Inc.).

RESULTS

Hilar bile duct obstruction

Forty seven of 1043 (4.5%) patients with HCC treated with PTA over eight years presented a total of 52 episodes of obstructive jaundice (table 1). There were 17 cases of hilar bile duct obstruction. Five of these 17 patients had a history of successful treatment of extrahepatic biliary obstruction. Hilar or intrahepatic obstruction of the bile duct were primarily treated by percutaneous transhepatic biliary drainage as many had multiple intrahepatic bile duct occlusions. The cause of biliary obstruction in all of these cases was either direct invasion of HCC or tumour thrombi into the bile duct.^{11–13}

Extrahepatic bile duct obstruction

Cases of extrahepatic bile duct obstruction

There were 35 cases of extrahepatic biliary obstruction (table 1). Extrahepatic biliary obstruction was due to choledocholithiasis in 11 cases, biliary casts in 10, haemobilia in 11, and miscellaneous causes in three (table 2). One of the novel observations of this study was the finding of casts in the biliary tree. Casts were composed of sludge that had become confluent and had assumed a shape conforming to the biliary trees.³³ Typical cholangiographic and endoscopic appearances of the casts in our series are shown in fig 1. Analysis of the casts performed for three of the 10 patients showed that they mainly consisted of acellular biliary material with or without bacterial colonies, fragments of bile duct epithelium, or collagen tissue. These findings were similar to those observed in previous reports of casts from patients after liver transplantation.^{28–29–32} Haemobilia was characterised as vague irregular margins by cholangiography, and was frequently distributed within multiple intrahepatic bile ducts.³⁵ The remaining three cases of biliary obstruction

Table 2 Cholangiographic and clinical variables among different categories of extrahepatic bile duct obstruction

Variable	Cast (n = 10)	Stones (n = 11)	Haemobilia (n = 11)	
			PTA related (n = 8)	HCC related (n = 3)
Period after initial PTA (months)	7–72 (32)	0–88 (27)	0–42 (7.8)	30–99 (55)
Period after latest PTA (months)	0–12 (3)	0–17 (6.5)	0	2–10 (5.3)
T bilirubin (mg/dl)	0.5–4.1 (2.0)	1.0–15.9 (4.3)	1.7–26.3 (7.9)	8–29 (19.3)
Alkaline phosphatase (IU/l)	146–1485 (553)	248–1065 (417)	229–787 (470)	448–965 (625)
γ -GTP (IU/l)	51–952 (268)	34–253 (110)	53–649 (267)	111–494 (309)
Abdominal pain	4/10 (40%)	6/11 (55%)	4/8 (50%)	3/3 (100%)
Pancreatitis	0/10 (0%)	3/11 (27%)	0/8 (0%)	0/3 (0%)
Liver abscess	5/10 (50%)	2/11 (18%)	0/8 (0%)	0/3 (0%)
Gallstone	2/10 (20%)	10/10 (100%)	3/8 (40%)	0/2 (0%)
“Haemobilia sign”	1/10 (10%)	0/11 (0%)	8/8 (100%)	1/2 (50%)
Biliary strictures	9/10 (90%)	2/11 (18%)	1/8 (13%)	1/3 (33%)
Type of PTA (PEIT/PMCT/RFA)	10/2/1	9/1/2	8/0/0	3/0/0
History of TAE	8/10 (80%)	6/11 (55%)	2/8 (25%)	1/3 (33%)
Size of HCC (cm)	0–8.5 (2.9)	0–7.5 (3.2)	1.5–6 (3.4)	2
PVTT	1/10 (10%)	1/11 (9%)	2/8 (25%)	1/3 (33%)
Additional therapy	None	None	TAE 1	Surgery for HCC 2, PTA 1
Immediate prognosis				
Recovered	10/10 (100%)	11/11 (100%)	6/8 (75%)	3/3 (100%)
Died			2/8 (25%)	

PTA, percutaneous tumour ablation; HCC, hepatocellular carcinoma; T bilirubin, total bilirubin; PEIT, percutaneous ethanol injection therapy; PMCT, percutaneous microwave coagulation therapy; RFA, radiofrequency ablation; TAE, transarterial embolisation; PVTT, portal vein tumour thrombus; γ -GTP, gamma-glutamyl transpeptidase.

were due to chronic pancreatitis, bile duct stenosis secondary to local ethanol injection, and one case was undetermined. The clinical backgrounds of the patients were similar, regardless of the cause of biliary obstruction, and there were no differences in terms of age, sex, Child-Pugh score, prothrombin time, or platelet count (data not shown). It was noted that biliary casts and haemobilia occurred more frequently in men (that is, nine males and one female for casts, and 10 males and one female for haemobilia), although this was not statistically significant ($p = 0.3$ and 0.19 , respectively; Fisher's exact test).

Characteristics of clinical parameters

The average time from the last PTA to the development of biliary obstruction was approximately six months for patients with stones and about three months for patients with casts. Haemobilia generally occurred immediately after percutaneous tumour ablation (eight of 11 patients). It was probably due to procedure related bleeding, such as puncture of vessels in or around the HCC with the bile duct. However, haemobilia was also observed 2–10 months (average 5.3 months) after percutaneous tumour ablation and was probably due to spontaneous bleeding from a HCC (table 2).

The concentration of serum bilirubin was noticeably higher in the haemobilia group, although there was considerable variation from patient to patient. Pancreatitis was observed in 3/11 patients with bile duct stones. Liver abscess occurred in 5/10 (50%) patients with biliary casts. Gallstones were common in all groups (20% of those with casts and 30% of those with haemobilia), being especially prominent in patients with bile duct stones (100%). The “haemobilia sign” on US scan, in which echogenic material appears in the gallbladder immediately after biliary bleeding,³⁴ occurred almost exclusively in the haemobilia group, except for one patient who subsequently developed a biliary cast. Biliary strictures existed most frequently (9/10, 90%) in patients with biliary casts but were always benign on brushing cytology, and the strictures were resolved by endoscopic dilatation. There were no differences in terms of size of HCC, presence of portal vein tumour thrombus, or type of PTA. A history of TAE was highest (8/10, 80%) in the biliary cast group although this was not statistically significant ($p = 0.06$; Fisher's exact test) (table 2).

Efficacy of endoscopic treatment

Thirty three of the 35 cases with extrahepatic bile duct obstruction were treated by endoscopic balloon dilatation. The clinical backgrounds are outlined in table 2. No patient received blood products before EPBD and prophylactic antibiotics were used routinely prior to EPBD.

EPBD was successfully performed in all 33 cases, regardless of liver cirrhosis and including those with an advanced condition. After EPBD, stones, biliary casts, or haemobilia in the bile duct were removed using such devices as a basket catheter (FG-22Q; Olympus Optical Co., Tokyo, Japan) and a retrieval balloon catheter (Zeon Medical Inc., Tokyo, Japan). Temporary plastic stents and nasobiliary drainage tubes were used in five (four cases, stents; one case, drainage tube) of 11 cases with choledocholithiasis, in two (one and one) of 10 cases with biliary casts, and in seven (0 and seven) of 11 cases with haemobilia, respectively, and left for approximately one week. In two cases with haemobilia, nasobiliary drainage was continued for up to one month. In one biliary cast case, two plastic stents (one in the common bile duct and the other in the gallbladder) were placed for two years, exchanging them every three months, because of the presence of fistulas between the liver abscess, gallbladder, and lung, and also because of biliary stricture in the common bile duct. These complicated fistulas were relieved by stenting, and there was no recurrence after their removal. All cases with biliary stones and casts were treated successfully without complications, except for one with bleeding that required blood transfusion and additional interventional therapy for haemostasis, including TAE of the branches of the posterior superior pancreaticoduodenal artery. This patient did not have severe thrombocytopenia or coagulopathy (platelet count $8.3 \times 10^4/\mu\text{l}$, prothrombin time 72.8%). The common bile duct stone in this patient was a maximum of 20 mm in diameter and had a sharp margin that damaged the papilla during extraction. There were no other bleeding complications in the remaining patients treated with EPBD. Serious complications, such as perforation or severe pancreatitis, did not occur. The only other complication was a case with mild pancreatitis according to Cotton's criteria.³⁶

Of eight patients with haemobilia related to PTA, three suffered from persistent haemorrhaging into the bile duct after extracting coagulated blood into the duodenum by

Figure 1 A typical case of biliary cast. (A) Endoscopic retrograde cholangiopancreatography findings: biliary cast occupying the extrahepatic bile duct. (B) Endoscopic view: biliary cast removed endoscopically. (C) Biliary cast after extraction.

basket catheter and balloon retrieval. TAE was successfully performed in one of these cases, but liver function was too poor to perform TAE in the remaining two and they died of hepatic failure 25 and 40 days after EPBD. Autopsies of these two cases suggested that the invading HCC itself had caused the haemorrhage spontaneously.

DISCUSSION

Obstructive jaundice in HCC patients is usually due to extrahepatic obstruction or hilar bile duct obstruction. Hilar bile duct obstruction is a relatively rare but well known complication of HCC, usually caused by direct infiltration or compression by the tumour. There were 17 (1.6%) cases of hilar obstruction among our 1043 patients, an incidence comparable with the previously reported 2–3%.^{12–37} In addition, we found 35 (3.4%) cases of extrahepatic biliary obstruction, most of which were not caused by direct invasion of the HCC. Causes were divided almost equally into three categories: biliary cast, choledocholithiasis, and haemobilia.

Biliary casts were composed of sludge that had become confluent and assumed a shape conforming to the biliary tree. Although pathological confirmation was available in only three of the 10 cases, we assumed that the remaining seven cases had casts based on their typical cholangiographic and endoscopic appearance. Biliary cast formation had been previously reported mainly as a sequel of liver transplantation, occurring up to several months after the procedure.^{28–32} A similar interval between PTA and the development of biliary cast obstruction was observed in this study. A connection was suggested between ischaemia and cast formation after liver transplantation.^{28–30, 32} Ischaemia of the bile duct was also reported in patients with HCC after TAE,^{38, 39} and the majority of patients showing bile casts had a history of TAE prior to PTA. Therefore, TAE appears to be a cause of bile cast formation. However, although TAE has been a commonly used procedure, there have been no reports on biliary cast formation in these patients. This suggests that PTA itself may have played a role in bile cast formation. One possibility is that the ablation material, ethanol, may have leaked into the bile duct and triggered cast formation, possibly by damaging the bile duct epithelium. Indeed, most of the patients with bile casts had undergone PEIT as the modality of PTA (table 2).

Biliary obstruction due to haemobilia occurred either immediately after percutaneous tumour ablation or after a long interval. Immediate haemobilia is the most common—it is associated with percutaneous tumour ablation. Great care is taken not to penetrate the portal vein with the ablation needle, and haemorrhage became less with increased clinical experience. On the other hand, haemobilia occasionally occurs late after percutaneous tumour ablation, is secondary to tumour growth, and carries a poor prognosis. It was not related to the procedure but rather to the growth of HCC, presenting a poor prognosis.

Gallstone formation is a common complication in cirrhosis,^{14–16} and biliary obstruction due to gallstones is unlikely to be related to PTA. Nevertheless, subsequent obstructive suppurative cholangitis, sometimes associated with pancreatitis, is an extremely serious problem, especially in cirrhotic patients,^{17–18} and a high mortality has been reported after treatment by surgery as well as after EST. However, we were able to successfully remove the common bile duct stones in all of our patients.

Tumour fragments or tumour casts have been reported to cause biliary obstruction in HCC patients but there was no such case in the present series. Tumour casts are reported to be soft, grayish-white, and resemble chicken fat,¹² in contrast with the amorphous, dark brownish, or black coloured biliary cast.

In the present study, all patients with extrahepatic biliary obstruction treated by EPBD had impaired liver function. Twenty eight patients (85%) were assessed as Child-Pugh grade B or C, with the most prolonged prothrombin activity (34.5%), the lowest platelet count (37 000/ μ L), and the highest bilirubin concentration (29 mg/dl), all of whom

would have been considered as having a poor prognosis with more invasive treatments. There were no complications, except for one case of ensuing mild pancreatitis and one of moderate bleeding.

In conclusion, the major causes of extrahepatic biliary obstruction after PTA were biliary casts, haemobilia, and common bile duct stones. The biliary cast appeared to be a complication specific to PTA, and PEIT in particular. All cases were successfully treated with EPBD in spite of impaired liver function.

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REFERENCES

- Shiratori Y, Shiina S, Imamura M, et al. Characteristic difference of hepatocellular carcinoma between hepatitis B- and C-viral infection in Japan. *Hepatology* 1995;21:1027-33.
- Taylor-Robinson SD, Foster GR, Arora S, et al. Increase in primary liver cancer in the UK, 1979-1994. *Lancet* 1997;350:1142-3.
- Hashem BE, Andrew CM. Rising incidence of hepatocellular carcinoma in the United States. *N Engl J Med* 1999;340:745-50.
- Poon RT, Fan ST, Tsang FH, et al. Locoregional therapies for hepatocellular carcinoma: a critical review from the surgeon's perspective. *Ann Surg* 2002;235:466-8.
- Shiina S, Teratani T, Obi S, et al. Percutaneous ethanol injection therapy for liver tumors. *European J Ultrasound* 2001;13:95-106.
- Teratani T, Ishikawa T, Shiratori Y, et al. Hepatocellular carcinoma in elderly patients: beneficial therapeutic efficacy using percutaneous ethanol injection therapy. *Cancer* 2002;95:816-23.
- Shiina S, Teratani T, Obi S, et al. Nonsurgical treatment of hepatocellular carcinoma: from percutaneous ethanol injection therapy and percutaneous microwave coagulation therapy to radiofrequency ablation. *Oncology* 2002;62:64-8.
- Di Stasi M, Buscarini L, Livraghi T, et al. Percutaneous ethanol injection in the treatment of hepatocellular carcinoma. A multicenter survey of evaluation practices and complication rates. *Scand J Gastroenterol* 1997;32:1168-73.
- Mulier S, Mulier P, Ni Y, et al. Complications of radiofrequency coagulation of liver tumors. *Br J Surg* 2002;89:1206-22.
- Livraghi T, Solbiati L, Meloni MF, et al. Treatment of focal liver tumors with percutaneous radio-frequency ablation: Complication encountered in a multicenter study. *Radiology* 2003;226:441-51.
- Kojiro M, Kawabata K, Kawano W, et al. Hepatocellular carcinoma presenting as intrabiliary duct tumor growth: a clinicopathologic study of 24 cases. *Cancer* 1982;49:2144-7.
- Lau WY, Leung JW, Li AK. Management of hepatocellular carcinoma presenting as obstructive jaundice. *Am J Surg* 1990;160:280-2.
- Chen MF, Jan YY, Jeng LB, et al. Obstructive jaundice secondary to ruptured hepatocellular carcinoma into the common bile duct. Surgical experiences of 20 cases. *Cancer* 1994;73:1335-40.
- Bouchier IA. Postmortem study of the frequency of gallstones in patients with cirrhosis of the liver. *Gut* 1969;10:705-10.
- Dario C, Mirella F, Fabio F, et al. Close relation between cirrhosis and gallstones: Cross-sectional and longitudinal survey. *Arch Intern Med* 1999;159:49-52.
- Koda M, Murawaki Y, Idobe Y, et al. Is choledocholithiasis a late complication of nonresectional therapies for hepatocellular carcinoma? *Hepatogastroenterology* 1999;46:3091-4.
- Gigot JF, Lesse T, Dereme T, et al. Acute cholangitis. Multivariate analysis of risk factors. *Ann Surg* 1989;209:435-8.
- Lai EC, Mok FP, Tan ES, et al. Endoscopic biliary drainage for severe acute cholangitis. *N Engl J Med* 1992;326:1582-6.
- Chijiwa K, Kozaki N, Naito T, et al. Treatment of choice for choledocholithiasis in patients with acute obstructive suppurative cholangitis and liver cirrhosis. *Am J Surg* 1995;170:356-60.
- Sirinek KR, Burk RR, Brown M, et al. Improving survival in patients with cirrhosis undergoing major abdominal operations. *Arch Surg* 1987;122:271-3.
- Sugiyama M, Atomi Y, Kuroda A, et al. Treatment of choledocholithiasis in patients with liver cirrhosis. Surgical treatment or endoscopic sphincterotomy? *Ann Surg* 1993;218:68-73.
- Freeman ML, Nelson DB, Sherman S, et al. Complication of endoscopic biliary sphincterotomy. *N Engl J Med* 1996;335:909-18.
- Van Os EC, Kamath PS, Gostout CJ, et al. Gastroenterological procedures among patients with disorders of hemostasis: evaluation and management recommendations. *Gastrointest Endosc* 1999;50:536-43.
- Kawabe T, Komatsu Y, Tada M, et al. Endoscopic papillary balloon dilatation in cirrhotic patients: Removal of common bile duct stones without sphincterotomy. *Endoscopy* 1996;28:694-8.
- Komatsu Y, Kawabe T, Toda N, et al. Endoscopic papillary balloon dilatation for the management of bile duct stones: Experience of 226 cases. *Endoscopy* 1998;30:12-17.
- Bergman JGHM, Rauws EAJ, Fockens P, et al. Randomized trial of endoscopic balloon dilation versus endoscopic sphincterotomy for removal of bile duct stones. *Lancet* 1997;349:1124-9.
- Fujita N, Maguchi H, Komatsu Y, for the JESD study group, et al. Endoscopic sphincterotomy and endoscopic papillary balloon dilatation for bile duct stones: a prospective randomized controlled multicenter trial. *Gastrointest Endosc* 2003;57:151-5.
- Waldram R, Williams R, Calne Y. Bile composition and bile cast formation after transplantation of the liver in man. *Transplantation* 1975;19:382-7.
- Chen CH, Wang KL, Chuang JH, et al. Biliary sludge-cast formation following liver transplantation. *Hepatogastroenterology* 1988;35:22-4.
- Ward EM, Kiely MJ, Maus TP, et al. Hilar biliary strictures after liver transplantation: Cholangiography and percutaneous treatment. *Radiology* 1990;177:259-63.
- Sheng R, Ramirez CB, Zajko AB, et al. Biliary stones and sludge in liver transplant patients: A 13-year experience. *Radiology* 1996;198:243-7.
- Shah JN, Haigh WG, Lee SP, et al. Biliary casts after orthotopic liver transplantation: clinical factors, treatment, biochemical analysis. *Am J Gastroenterol* 2003;98:1861-7.
- Baron TH, Yates RM iii, Morgan DE, et al. Biliary cast syndrome: Successful endoscopic treatment. *Gastrointest Endosc* 2000;52:78-9.
- Obi S, Shiratori Y, Shiina S, et al. Early detection of haemobilia associated with percutaneous ethanol injection for hepatocellular carcinoma. *Eur J Gastroenterol Hepatol* 2000;12:285-90.
- Joo YE, Kim HS, Choi SK, et al. Haemobilia caused by liver abscess due to intrahepatic duct stones. *J Gastroenterol* 2003;38:507-11.
- Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 1991;37:383-93.
- Lau WY, Leung KL, Leung TW, et al. A logical approach to hepatocellular carcinoma presenting with jaundice. *Ann Surgery* 1997;225:281-5.
- Tarazov PG, Polysalv VN, Prozorovsky KV, et al. Ischemic complications of transcatheter arterial chemoembolization in liver malignancies. *Acta Radiol* 2000;41:156-60.
- Yu JS, Kim KW, Park MS, et al. Bile duct injuries leading to portal vein obliteration after transcatheter arterial chemoembolization in the liver. CT findings and initial observations. *Radiology* 2001;221:429-36.