

# Hepatolithiasis: A Turkey experience

## Intrahepatik taş: Türkiye deneyimi

Burçak KAYHAN<sup>1</sup>, Meral AKDOĞAN<sup>2</sup>, Erkan PARLAK<sup>2</sup>, Ersan ÖZARSLAN<sup>1</sup>, Burhan ŞAHİN<sup>2</sup>

Department of <sup>1</sup>Gastroenterology, Ankara Numune Education and Training Hospital, Ankara

Department of <sup>2</sup>Gastroenterology, Türkiye Yüksek İhtisas Hospital, Ankara

**Background/aims:** The aim of this study was to report our experience of hepatolithiasis, diagnosed in 55 patients between June 1995 and March 2003. **Methods:** Fifty-five patients who underwent endoscopic retrograde cholangiopancreatography for hepatolithiasis between June 1995 and March 2003 at our institution were evaluated. Diagnosis of hepatolithiasis was based on cholangiography, ultrasonography and computed tomography. Patients with hepatolithiasis were classified according to Tsunoda classification. **Results:** Fifty-five patients with hepatolithiasis (22 female, 33 male; mean age: 48.2 ± 14.9, range: 22-83) were included in this study. The major causes of hepatolithiasis were previous bilio-digestive surgery and Caroli disease, with rates of 49% and 14.5%, respectively. While 37 of 55 patients (67.3%) presented with only intrahepatic lithiasis, 18 patients (32.7%) had intrahepatic lithiasis associated with common bile duct (16/18, 29%) or gallbladder (2/18, 3.6%) stones. According to Tsunoda classification, 4 patients were classified as type I, 32 type II, 9 type III and 10 type IV. Patients with types I and II had significantly better stone clearance rates in comparison to those with types III and IV (p<0.05). Complete eradication of stones in the patients with proximal strictures was significantly lower than in the patients with distal strictures (p<0.01). While complete clearance of stones was achieved in 22 cases (40%), incomplete clearance was achieved in 17 cases (30.9%) with endoscopic retrograde cholangiopancreatography. Mean number of endoscopic retrograde cholangiopancreatography procedures for clearance of stones was 4 (ranges: 1-9). **Conclusion:** The etiology of hepatolithiasis in our patients is similar to that observed in Western populations and endoscopic approach appears to be an effective alternative to surgery.

**Key words:** Liver, hepatolithiasis, endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, hepatic hydatid disease

**Amaç:** Kliniğimizde Haziran 1995- Mart 2003 yılları arasında intrahepatik taş tanısı alan 55 olguyu sunduk. **Yöntem:** Haziran 1995-Mart 2003 yılları arasında, intrahepatik taş nedeniyle endoskopik retrograde kolanjiopankreatografi yapılam 55 olgu değerlendirildi. İntrahepatik taş tanısı abdominal ultrasonografi, kolanjiografi ve bilgisayarlı tomografi ile kondu. Tsunoda sınıflamasına göre hastalar sınıflandırıldı. **Bulgular:** Elli beş (22 kadın, 33 erkek, ortalama yaş: 48.2 ± 14.9, sınırlar: 22-83) intrahepatik taş olgusu çalışmaya alındı. İntrahepatik taşın en önemli nedenleri, geçirilmiş safra yolları cerrahisi ve Caroli hastalığıydı, sırasıyla %49, %14.5. Olguların 37 (%67.3)'sinde sadece intrahepatik taş varken, 18'inde (%32.7) intrahepatik taşla birlikte koledok (%29) ve safra kesesinde de (%3.6) taş vardı. Tsunoda sınıflamasına göre 4 olgu tip I, 32 olgu tip II, 9 olgu tip III ve 10 olgu tip IV'dü. Tip I ve II'de taşların tamamen temizlenme oranı tip III ve IV'e göre anlamlı olarak daha yüksekti (p<0.05). Proksimal darlıklarda başarı, distal darlıklara göre daha düşüktü (p<0.01). Endoskopik retrograde kolanjiopankreatografi ile 22 (%40) olguda taşlar tamamen temizlenirken, 17 (%30.9) olguda kısmi başarı sağlandı. Taşların temizlenmesi için yapılan ortalama endoskopik retrograde kolanjiopankreatografi sayısı 4'tü (sınırlar: 1-9). **Sonuç:** Olgularımızda intrahepatik taş etyolojisi Batı toplumuna benzer iken, endoskopik yaklaşım cerrahi tedaviye alternatif gibi gözükmektedir.

**Anahtar kelimeler:** Karaciğer, intrahepatik taş, endoskopik retrograd kolanjiopankreatografi, perkütan transhepatik kolanjiografi, karaciğer hidatik kisti

## INTRODUCTION

Intrahepatic lithiasis (IHL), a rare entity in Europe but highly prevalent in East Asia, causes long-term complications (1-3). In the West, hepatolithiasis is mainly associated with bile stasis caused by postoperative strictures, sclerosing cholangitis (to

a lesser degree), choledochal cyst, Caroli disease and neoplasm, whereas oriental cholangitis is the most common cause of hepatolithiasis in the Far East (4, 5). Postoperative strictures due to hepatic hydatid disease (HHD) surgery are not uncommon

**Address for correspondence:** Burçak KAYHAN  
Department of Gastroenterology, Ankara Numune Education and Training Hospital, Ankara, Turkey  
Phone: +90-312 310 30 30/3301 • Fax: +90 312 427 24 83  
E-mail: burkaygastro@hotmail.com

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in Turkey and surgery is difficult in these cases because strictures are multiple, long and proximally located. Endoscopic therapy is a viable option for the management of these patients (6).

In this study, we investigated a group of IHL patients in the Turkish population in reference to etiology, the nature of stricture, and efficacy of endoscopic treatment in comparison to Asian and European populations.

## MATERIALS AND METHODS

This study was conducted in Türkiye Yüksek İhtisas Hospital, Ankara, which is a reference center for endoscopic retrograde cholangiopancreatography (ERCP) in Turkey. Between June 1995 and March 2003, we detected 55 patients (22 female, 33 male; mean age  $48.16 \pm 14.9$ , range: 22-83 years) with hepatolithiasis out of 11,065 ERCP patients.

Patients with intrahepatic stones were divided into four types according to the Tsunoda classification (7): type I, no marked dilatation or strictures of intrahepatic bile ducts; type II, diffuse dilatation without intrahepatic strictures and often a stricture of the distal common bile duct (CBD); type III, unilaterally solitary or multiple cystic intrahepatic dilatation, which was frequently accompanied by stenosis of the left or right intrahepatic bile ducts; type IV, same as type III but with bilateral involvement of hepatic lobes. Strictures were classified into two types based on the sites as proximal or distal.

For patients who presented with acute cholangitis or pancreatitis, endoscopic sphincterotomy was performed at the discretion of the endoscopist. Extraction of stones was performed with the use of a Dormia basket or balloon. Stent or nasobiliary drains (NBD) were placed to secure drainage if extraction of stones failed. When a stricture was seen, dilatation was performed using balloon or bougie dilators. Hepatic resection was considered if the stones and strictures were localized to a single atrophic liver segment or lobe.

The results were expressed as mean  $\pm$  standard error. Statistical analyses were performed with the chi-square and the Student *t* tests. Probability difference of .05 was considered significant.

## RESULTS

Fifty-five patients (22 female, 33 male; mean age:  $48.16 \pm 14.9$ , range: 22-83 years) with hepatolithi-

asis were evaluated in this study. The diagnosis was confirmed in all patients by cholangiography (ERCP or percutaneous transhepatic cholangiography, PTC), whereas ultrasonography (USG) was done in 52 (94.5%) and computed tomography (CT) in 32 patients (58.2%).

Thirty-seven of 55 cases (67.3%) presented with the sole finding of intrahepatic lithiasis, while 18 cases (32.7%) had associated findings in the CBD (16, 29%) or gallbladder (2, 3.7%) (Figure 1).



**Figure 1.** Marked dilatation of the left hepatic duct with multiple stones

The causes of IHL were Caroli disease in 8 (14.5%), previous biliary surgery in 28 (50.9%) cholecystectomy and no biliary drainage procedure in 13 (23.6%), cholecystectomy and biliodigestive anastomosis in 7 (12.7%), hydatid cyst operation and biliodigestive anastomosis in 8 (14.5%), liver trauma in 1 (1.8%), cirrhosis in 1 (1.8%), hereditary spherocytosis in 1 (1.8%), multiple myeloma in 1 (1.8%), Oddi fibrosis in 1 (1.8%), primary



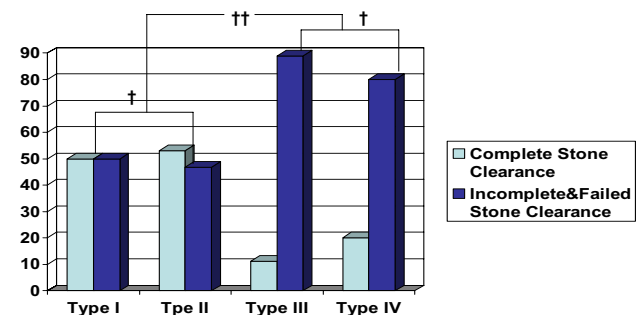
**Figure 2.** Nasobiliary drainage was placed on the left intrahepatic duct

sclerosing cholangitis (PSC) in 1 (1.8%), and bilioenteric fistula in 2 (3.6%). In 12 (21.8%) patients, the etiology could not be determined (Figure 2).

We achieved complete clearance of stone in 22 cases (40%) and incomplete clearance in 17 cases (30.9%) with ERCP. Endoscopic stenting and NBD were performed in 10 and 4 patients, respectively. Both ERCP and PTC were performed in 3 cases. Endoscopic therapy failed in 16 (29%) patients (10 had proximal, 4 had distal strictures and 2 had Caroli disease). Mean number of ERCP procedures for clearance of stones was 2 (ranges: 1-7).

Surgery was inevitable in 5 of these 16 (31.2%) patients (left lobectomy in 2, segmentectomy in 3). Six of 11 patients with failed therapy were treated conservatively including NBD and/or administration of antibiotics. One patient was listed on the liver transplantation program. One patient expired due to cholangiocarcinoma (diagnosed concurrently with IHL). Three patients were lost to follow-up.

According to Tsunoda classification, among the 55 patients, 4, 32, 9 and 10 were classified as having type I, II, III and IV, respectively. The stone clearance rate in the patients with type I was the same as in type II. However, types I and II patients fared better than those with types III and IV ( $p<0.05$ ). Moreover complete removal of stones in the patients with type II was significantly higher than in the patients with types III and IV. There was no difference between the patients with types III and IV ( $p>0.05$ ). The success rates in those patients were very low (18.8% vs. 52.8% in types I and II). Stone clearance rate was significantly lower in the patients with proximal versus distal strictures (20% vs. 68.2%,  $p<0.01$ ) (Figure 3).



† $p>0.05$ , †† $p<0.05$

**Figure 3.** Treatment outcomes in patients with hepatolithiasis according to Tsunoda classifications

Patients had prospective evaluation with USG and/or CT every six months. On follow-up, 15 patients with complete or partial removal of stone (15/39, 38.5%) had recurrent stones in a three-year period (mean:  $2.73\pm 2.18$ , range: 1-7).

A 33-year-old man with diagnosis of Caroli disease developed cholangiocarcinoma during the follow-up period and died six months after diagnosis. Another patient with alveolar cyst hydatid operation developed secondary biliary cirrhosis and expired six years later. Four of 6 patients who failed therapy were lost to follow-up. The patients who underwent surgery did not have any recurrence within the two-year follow-up period. Twenty-two patients with recurrent cholangitis (15 with recurrent stones, 7 failed therapies) were treated conservatively including administration of antibiotics and/or by performing repeat ERCP or PTC.

## DISCUSSION

Intrahepatic stones have a prevalence of 4-52% in East Asia, in contrast to 0.6-1.3% in the West (8). Comparative data between Eastern (9, 10) and Western (11, 12) studies and the present study are shown in Table 1. It is known that oriental cholangiohepatitis is the most common cause of hepatolithiasis in the Eastern populations (4). Although *Ascaris lumbricoides* is widespread in this country, hepatolithiasis is mainly associated with bile stasis secondary to biliary surgery and/or Caroli disease as in the Western populations (11, 13). Caroli disease is a relatively common etiology of hepatolithiasis in Western countries when compared to the East (13). The frequency of Caroli disease in our hepatolithiasis patients is similar to that observed in Western populations. Hepatolithiasis due to previous surgery for hydatid disease is more common in our population in comparison to the East and West.

In the present study, the complete and partial stone clearance rate was 70.9%. Proximal stricture resulted in high rates of residual stones and unsatisfactory results (failed therapy in this group was 80%). Thirty-three patients who had type I and type II had higher complete stone clearance and lower rates of stone recurrence compared to the patients with types III and IV. To date, studies have revealed a recurrence rate of hepatolithiasis ranging from 8% to 35% after endoscopic treatment (10). Our rate of 38.5% was slightly higher.

The most difficult aspect of treatment is the association of hepatolithiasis with intrahepatic biliary stricture, which may limit the eradication of stones and pose a propensity for recurrence (16). Placement of plastic stents in patients with stenosis of the CBD and changing them every three to six months is an essential part of our endoscopic treatment protocol and is commensurate with previous studies (15). The association between cholan-

**Table 1.** Patient characteristics in different geographic areas

Parameters	East		Turkey	West	
	n = 96 <sup>(7)</sup>	n = 190 <sup>(8)</sup>	n = 55	n = 20 <sup>(9)</sup>	n = 55 <sup>(10)</sup>
Age (mean)	59.5 (21-87)	46 (28-80)	48.16 (22-83)	45 (19-83)	61 (22-88)
Sex (male/female)	46/50	75/115	33/22	6/14	13/42
Etiology-previous biliary surgery	54 (56%)	NR	28 (50.9%)	6 (30%)	NA
-Caroli disease	-		8 (14.5%)	4 (20%)	
-Others	42 (44%)		7 (12.8%)	10 (50%)	
-Unknown			12 (21.8%)		
Presentations -acute cholangitis	57 (59%)	NA	38 (69.1%)	16 (80%)	23 (41.8%)
-abdominal pain	29 (30%)		11 (20%)	4 (20%)	8 (14.5%)
-jaundice	10 (10%)		6 (10.9%)		24 (43.6%)
-others					
Locations of stones					
-left IHD	31	70	16	9 (45%)	23
-right IHD	8	87	11	5 (25%)	10
-left and right IHD	10	33	10	6 (30%)	6
-left or right IHD&common duct			16		16
-left or right IHD&gallbladder	42		2		
Recurrence	3 (3%)	24 (15%)	15 (38.5%)	2 (10%)	NA

NR: Not reported, NA: Not available, <sup>7</sup>55 patients in 245 who underwent surgery had complete recovery; 190 patients with failed surgery included in this study

Our choice of treatment for hepatolithiasis was endoscopic methods rather than surgery for patients with Caroli disease or for patients with liver resection for hydatid disease. As explained previously, the reason for this is the difficulty of the surgery in these patients. Among the factors that make the surgery difficult in recurrent hepatolithiasis are extensive adhesions, distorted anatomy and scarring of the CBD due to previous operations (5, 15).

giocarcinoma and hepatolithiasis is well recognized, and prevalence of cholangiocarcinoma in patients with hepatolithiasis ranges from 2.36% to 10% (14, 17). Hepatic resection is the treatment of choice for cholangiocarcinoma due to hepatolithiasis if it is resectable (18). In our study, cholangiocarcinoma developed in 1 patient (1/46, 2.2%) during the follow-up period and another patient was diagnosed with hepatolithiasis and cholangiocarcinoma in the same investigation.

In conclusion, the incidence and etiology of hepatolithiasis in Turkey, despite some differences, seem to be similar to the disease profile seen in Eu-

rope. Endoscopic retrograde cholangiopancreatography is a safe and relatively effective means of managing this group of patients.

## REFERENCES

1. Sheen-Chen SM, Cheng YF, Chen FC, et al. Ductal dilatation and stenting for residual hepatolithiasis: a promising treatment strategy. *Gut* 1998; 42: 708-10.
2. Balasegaram M. Surgical treatment of hepatic calculi. In: Okuda K, Nakayama F, Wong J, eds. *Intrahepatic Calculi*. New York: Liss, 1984; 283-301.
3. Pausawasdi A, Watanapa P. Hepatolithiasis: epidemiology and classification. *Hepatogastroenterology* 1997; 44: 314-6.
4. Leung JW, Yu AS. Hepatolithiasis and biliary parasites. *Bailliere's Clin Gastroenterol* 1997; 11: 681-703.
5. Huang MH, Chen CH, Yen CM, et al. Relation of hepatolithiasis to helminthic infestation. *J Gastroenterol Hepatol* 2005; 20: 141-6.
6. Eickhoff A, Schilling D, Benz CA, Riemann JF. Endoscopic stenting for postoperative biliary strictures due to hepatic hydatid disease: effectiveness and long-term outcome. *J Clin Gastroenterol* 2003; 37: 74-8.
7. Tsunoda T, Tsuchiya R, Harada N, et al. Long-term results of surgical treatment for intrahepatic stones. *Jpn J Surg* 1985; 15: 455-62.
8. Cheung KL, Lai EC. The management of intrahepatic stones. *Adv Surg* 1996; 29: 111-29.
9. Liu CL, Fan ST, Wong J. Primary biliary stones: diagnosis and management. *World J Surg* 1998; 22: 1162-6.
10. Cheng YF, Lee TY, Sheen-Chen SM, et al. Treatment of complicated hepatolithiasis with intrahepatic biliary stricture by ductal dilatation and stenting. *World J Surg* 2000; 24: 712-6.
11. di Carlo I, Sauvanet A, Belghiti J. Intrahepatic lithiasis: a western experience. *Surg Today* 2000; 30: 319-22.
12. Adamek HE, Schneider ARJ, Adamek MU, et al. Treatment of difficult intrahepatic stones by using extracorporeal and intracorporeal lithotripsy technique: 10 years' experience in 55 patients. *Scand J Gastroenterol* 1999; 11: 1157-61.
13. Ros E, Navorro S, Bru C, et al. Ursodeoxycholic acid treatment of primary hepatolithiasis in Caroli's syndrome. *Lancet* 1993; 342: 404-6.
14. Lee SK, Seo DW, Myung SJ, et al. Percutaneous transhepatic cholangioscopic treatment for hepatolithiasis: an evaluation of long-term results and risk factors for recurrence. *Gastrointest Endosc* 2001; 53: 318-23.
15. Jeng KS, Sheen IS, Yang FS. Are expandable metallic stents better than conventional methods for treating difficult intrahepatic biliary strictures with recurrent hepatolithiasis? *Arch Surg* 1999; 134: 267-73.
16. Jeng KS. Treatment of intrahepatic biliary stricture associated with hepatolithiasis. *Hepatogastroenterology* 1997; 44: 342-51.
17. Chijiwa K, Ohtani K, Noshiro H, et al. Cholangiocellular carcinoma depending on the kind of intrahepatic calculi in patients with hepatolithiasis. *Hepatogastroenterology* 2002; 49: 96-9.
18. Chu KM, Lo CM, Liu CL, Fan ST. Malignancy associated with hepatolithiasis. *Hepatogastroenterology* 1997; 44: 352-7.