

Management of Simple Hepatic Cyst

Tetsuya Shimizu, Masato Yoshioka, Yohei Kaneya, Tomohiro Kanda, Yuto Aoki, Ryota Kondo, Hideyuki Takata, Junji Ueda, Youichi Kawano, Atsushi Hirakata, Akira Matsushita, Nobuhiko Taniai, Yasuhiro Mamada and Hiroshi Yoshida

Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, Tokyo, Japan

Simple hepatic cysts are typically saccular, thin-walled masses with fluid-filled epithelial lined cavities. They arise from aberrant bile duct cells that develop during embryonic development. With the development of diagnostic modalities such as ultrasonography (US), CT, and MRI, simple hepatic cysts are frequently detected in clinical examinations. US is the most useful and noninvasive tool for diagnosis of simple hepatic cysts and can usually differentiate simple hepatic cysts from abscesses, hemangiomas, and malignancies. Cysts with irregular walls, septations, calcifications, or daughter cysts on US should be evaluated with enhanced CT or MRI, to differentiate simple hepatic cysts from cystic neoplasms or hydatid cysts. Growth and compression of hepatic cysts cause abdominal discomfort, pain, distension, and dietary symptoms such as nausea, vomiting, a feeling of fullness, and early satiety. Complications of simple hepatic cysts include infection, spontaneous hemorrhage, rupture, and external compression of biliary tree or major vessels.

Asymptomatic simple hepatic cysts do not require treatment. Treatment for symptomatic simple hepatic cysts includes percutaneous aspiration, aspiration followed by sclerotherapy, and surgery. The American College of Gastroenterology clinical guidelines recommend laparoscopic fenestration because of its high success rate and low invasiveness. Percutaneous procedures for treatment of simple hepatic cysts are particularly effective for immediate palliation of patient symptoms; however, they are not generally recommended because of the high rate of recurrence. Management of simple hepatic cysts requires correct differentiation from neoplasms and infections, and selection of a reliable treatment.

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Key words: simple hepatic cyst, fenestration, aspiration, diagnosis, management

Introduction

Simple hepatic cysts are typically thin-walled masses with fluid-filled, epithelium-lined cavities. They arise from aberrant bile duct cells that develop during embryonic development^{1,2}. Now that diagnostic modalities such as ultrasonography (US), CT, and MRI are widely available, simple hepatic cysts are frequently detected during clinical examination. However, these are rarely treated and often overlooked. Enlarged simple hepatic cysts are associated with symptoms such as abdominal distension and pain, and mechanical compression of adjacent structures may cause organ dysfunction. Treatment is indicated for symptomatic hepatic cysts, and this review fo-

cuses on management of simple hepatic cysts.

Epidemiology

Before the widespread appearance of diagnostic modalities, hepatic cyst was diagnosed intraoperatively. In 1974, Sanfelippo et al.³ reported that the incidence of hepatic cystic lesions was 17 per 10,000 explorations. With the increased use of diagnostic modalities, including US and CT, hepatic cyst is diagnosed easily and encountered frequently in medical examinations. The prevalence of simple hepatic cyst ranges from 3% to 5% on US to as high as 18% on CT⁴. Large hepatic cysts are more frequent in women older than 50 years, and the female to male ratio is 4:1⁵.

Correspondence to Tetsuya Shimizu, MD, Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

E-mail: tetsuya@nms.ac.jp

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Clinical Presentation

On radiographic imaging, hepatic cysts can be solitary or multiple and range from small to large. Simple hepatic cysts measure from <1 cm to 30 cm and are more frequent in the right hepatic lobe^{5,6}. The presence of more than 20 hepatic cysts is defined as polycystic liver disease (PLD). Simple hepatic cyst is usually easy to differentiate from PLD.

On microscopic examination, simple hepatic cysts have an outer layer of thin fibrous tissue and an inner layer of cuboid or columnar epithelium lining resembling biliary epithelium without mesenchymal stroma or cellular atypia^{4,6}. The diameter of hepatic cysts gradually increases because of continuous production of fluid by secretory epithelial cells, and enlarged hepatic cysts cause symptomatic or complicated disease. The mortality rate for simple hepatic cysts is very low but increases when cyst-related complications develop^{3,7}.

Most patients with simple hepatic cysts do not have common symptoms. Although complications are rare, growing hepatic cysts may cause symptoms. Patients with a large hepatic cyst may have a palpable abdominal mass or hepatomegaly and increased abdominal girth on physical examination⁶. Clinical symptoms occur in 5% of patients and are caused by progressive enlargement or compression of adjacent structures⁸. Symptomatic hepatic cysts are more frequent in women (female to male ratio, 9:1)⁶. Hepatic cysts do not usually impair liver or other organ function; however, mechanical compression of the biliary tract, vessels, and gastrointestinal tract causes liver dysfunction or passage disorder of the blood supply and intestine. While not specific, patient complaints caused by growth and compression of hepatic cysts include abdominal discomfort, pain, distension, and dietary symptoms such as nausea, vomiting, a feeling of fullness, and early satiety^{9,10}.

Complications of simple cysts include infection¹¹⁻¹³, spontaneous hemorrhage^{14,15}, rupture into the peritoneal cavity^{8,16}, and external compression of biliary tree or major vessels^{7,17}.

Patients with intracystic bleeding usually complain of sudden, severe right upper quadrant and shoulder pain¹⁸. Intracystic bleeding resolves on its own, and pain gradually resolves in a few days.

The cause of intracystic hemorrhage is unclear; however, three hypotheses have been proposed¹⁹.

I. High intracystic pressure causes necrosis and sloughing of the cyst's epithelial lining and injures fragile blood capillaries in the cystic wall²⁰.

II. Rapid enlargement of a hepatic cyst causes rupture of vessels, hemangioma, and vascular malformation on the cystic wall or near the cyst²¹.

III. Traumatic direct external pressure injures the cyst wall or vessels near the cyst²².

Spontaneous rupture of hepatocellular carcinoma has occurred occasionally; however, spontaneous rupture of hepatic cysts appears to be a rare complication of non-parasitic hepatic cysts²³⁻²⁵. Salemis et al.⁸ described an extremely rare case of spontaneous rupture of a large hepatic cyst in a patient with clinical manifestations of acute abdomen. They suggested that prophylactic treatment should be considered for large, symptomatic, non-parasitic hepatic cysts with a considerable risk of serious complications.

Complications of vessel compression are rare but severe. Long et al.⁷ reported a case of acute liver failure in which an enlarged hepatic cyst obstructed hepatic venous flow and caused Budd-Chiari syndrome. Taguchi et al.²⁶ described a large, free-floating inferior vena cava thrombus caused by an enlarged, solitary hepatic cyst.

Simple hepatic cysts are thought to be congenital exclusions of hyperplastic bile duct that lack communication with biliary duct^{5,27}. However, they reportedly communicate with the biliary tree in rare case^{28,29}. Conversely, simple liver cysts were reported to occasionally disappear spontaneously, without symptoms^{30,31}.

Diagnosis

Most simple hepatic cysts are detected incidentally and tend to follow a benign course. Laboratory findings are mostly normal and generally nondiagnostic. However, liver enzymes may be elevated; elevations of alkaline phosphatase and gamma-glutamyl transferase are the most common findings^{8,9}. These findings are commonly attributable to anatomical location of the cyst in the hilar region, which can affect biliary tree or major vessels.

US—the most useful and noninvasive diagnostic modality for diagnosis of simple hepatic cyst—typically shows a saccular, homogeneous, anechoic, fluid-filled lesion with thin-walled smooth margins and posterior acoustic enhancement (**Fig. 1A**). Simple hepatic cysts can usually be differentiated from abscesses, malignancies, hemangiomas, and hamartomas by US alone.

CT shows a saccular, smooth, well-demarcated, fluid-filled lesion with water attenuation within a cystic lesion and no internal structure. Contrast-enhanced CT is negative for enhanced internal structure of the cystic lesion (**Fig. 1B**). Similarly, MRI shows a homogeneous, well-

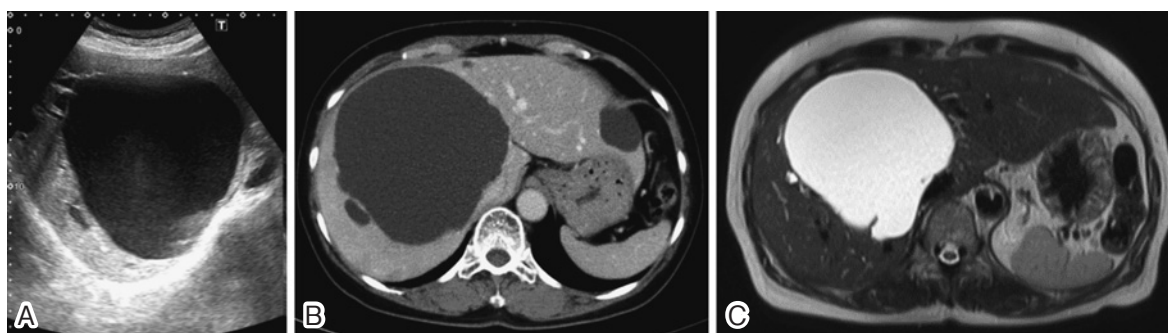


Fig. 1 A: US reveals an anechoic, fluid-filled sacular lesion with thin-walled smooth margins and posterior acoustic enhancement.
 B: CT shows a round, smooth, well-demarcated, and fluid-filled lesion without internal structure.
 C: MRI shows a homogeneous, well-defined, and spherical lesion with high signal intensity on T2-weighted images.

defined, spherical lesion with high signal intensity on T2-weighted images (Fig. 1C) and low signal intensity on T1-weighted images without contrast enhancement.

Differential diagnosis with cystic lesion of the liver is often difficult. The differential diagnosis includes malignancies such as biliary cystadenocarcinoma, cystic metastases from primary cystic tumors, and cystic necrosis of large solid neoplasms. Differential diagnosis excluding neoplasms includes PLD and hydatid cysts resulting from infection by the tapeworms *Echinococcus granulosus* or *Echinococcus multilocularis*⁵.

Cysts with irregular walls, intracystic septations, calcifications, or daughter cysts on US screening should be examined with enhanced CT or MRI for differential diagnosis of cystic neoplasm and hydatid cysts.

Cystadenomas represent 1% to 5% of all hepatic cystic lesions and up to 10% of cysts larger than 4 cm^{5,32}. Cystadenoma has the potential for malignant transformation into cystadenocarcinoma, as surgical samples for most cystadenocarcinomas have coexisting components of cystadenoma³³⁻³⁶. A malignant transformation rate for cystadenoma of 5% to 30% has been reported, and biliary cystadenocarcinoma accounts for 0.41% of malignant hepatic epithelial tumors^{35,37,38}. Cystadenoma is classically characterized in imaging studies as a multilocular, low-density, thick-walled cystic mass with mural nodules and internal septum. However, Labib³⁹ et al. reported no significant difference in average cyst size or radiological features in differential diagnosis between simple hepatic cyst and cystadenoma. They also reported that patients with cystadenoma were more likely to have a single cyst than simple hepatic cysts on imaging. With current imaging techniques, differentiating between cystic neoplasm and simple hepatic cyst is challenging. Recent studies

have described cystadenomas as synonymous with mucinous cystic neoplasms (MCN)³⁹. The World Health Organization redefined cystadenoma as an MCN or intra-ductal papillary neoplasm of the bile duct (IPN-B), depending on the presence of ovarian stroma and bile duct communication, respectively⁴⁰.

Differentiation of simple hepatic cyst is more difficult if the internal fluid contains blood. Hemorrhagic hepatic cysts may also appear nodular with septations on US and weighted MRI, because of the presence of intracystic blood clots^{41,42}. Internal bleeding in simple hepatic cysts tends to have a heterogeneous appearance and to be mistaken for complex lesions such as abscesses, cystadenomas, cystadenocarcinomas, or hydatid cysts^{33,43}. Aspiration of intracystic fluid for cytology is not recommended for diagnosis of simple hepatic cysts. However, if aspiration of a hepatic cyst is performed for treatment, intracystic tumor marker concentrations, cytology, and bacterial culture can be evaluated.

Marnierite and Alan studied carcinoembryonic antigen (CEA) and CA19-9 levels in cystic lesions and found elevated CEA (>600 µg/L) in fluid from biliary cystadenoma, cystadenocarcinoma, and pseudocystic metastatic carcinoma^{44,45}. However, increased CA19-9 and CEA concentrations in internal fluid may also be detected in patients with simple hepatic cysts. Fuks et al.⁴⁶ reported that intracystic fluid concentrations of CEA and CA19-9 were greater than the maximum serum reference values in 7% and 88% of patients with simple hepatic cysts, respectively. They also showed that the cut-off values for differentiating between simple hepatic cyst and mucinous cystic lesion were 30 ng/mL for CEA and 15,000 units/mL for CA19-9⁴⁶. However, because of the lack of specificities and accuracies of intracystic CEA and CA19-9

levels in differentiating simple hepatic cyst from cystic neoplasm, conventional screening of cystic fluid tumor markers is unhelpful for differential diagnosis. In a recent report, high intracystic concentrations of tumor-associated glycoprotein (TAG-72) were detected in cystic neoplasms. Thus, TAG-72 may be a promising tool for differential diagnosis of simple hepatic cyst and cystic neoplasm^{33,46}.

Serum CA19-9 level was not helpful for differential diagnosis⁴⁷. CEA and CA19-9 are expressed by the epithelial cells of normal biliary tract. Therefore, serum CEA and CA19-9 levels were not correlated with malignant potential³³.

Aspiration cytology is rarely helpful and does not provide adequate information. Microbiological analysis is of value only in rare cases when the lesion is hydatid in origin^{33,39,46}. Preoperative intracystic aspiration cytology and fine-needle biopsy for mural nodules or papillary projections are not recommended, because of subsequent development of peritoneal or pleural dissemination in the case of malignancy³³.

Management of Simple Hepatic Cyst

The lack of randomized controlled trials and long-term follow-up for management of simple hepatic cyst make it difficult to establish evidenced-based recommendations with strong support from the literature⁵.

Asymptomatic simple hepatic cysts encountered incidentally by abdominal imaging do not require treatment or follow-up^{5,48}. Likewise, a simple hepatic cyst found incidentally during abdominal surgery should be managed with observation²⁸.

For symptomatic simple hepatic cysts, treatment is indicated. The most feasible treatment is percutaneous aspiration; however, this does not yield a permanent therapeutic benefit. Ultrasonographic-guided percutaneous aspiration is particularly effective for immediate palliation of symptoms of large hepatic cysts. However, recurrence is unavoidable, as the aspirated hepatic cyst refills within several days. Percutaneous aspiration is also a good therapeutic test to confirm whether abdominal symptoms are caused by a hepatic cyst. If abdominal symptoms are not improved by aspiration, other causes of abdominal pain should be investigated^{28,49}.

To improve the effect of percutaneous management and achieve permanent ablation, aspiration of intracystic fluid followed by instillation of sclerosing agents into the cyst can reduce cystic volume and destroy the inner cyst epithelium. A systematic review of percutaneous aspira-

tion and sclerotherapy for symptomatic hepatic cysts reported excellent outcomes, with symptoms persisting in less than 4% of patients, and complication and recurrence rates were each <1%⁵⁰. The most commonly used sclerosing agent is ethanol¹. However, ethanolamine oleate³⁶, polidocanol⁵¹, minocycline hydrochloride^{52,53}, and bleomycin⁵⁴ have also been used. Yoshida et al.⁵³ found that sclerotherapy with minocycline hydrochloride yielded hepatic cyst regression without recurrence.

Surgical options, including open or laparoscopic fenestration and hepatic resection, provide long-term relief in up to 90% of patients with symptomatic hepatic cysts^{4,55}. After fenestration of hepatic cyst was first reported by Lin et al.⁵⁶ in 1968, 'deroofting' or 'marsupialization' have been used as synonymous terms. Regardless of which term is used, the principle of treatment is to remove the roof of the hepatic cyst as a part of the liver surface and allow it to drain freely into the peritoneal cavity. The fluid produced on the wall is reabsorbed by the peritoneum⁵⁷.

Fabiani et al.⁵⁸ introduced laparoscopic fenestration of hepatic cysts in 1991. Since then, the approach has been widespread, with most surgeons adopting laparoscopic fenestration as the preferred therapeutic option because of its success rate and the reductions in morbidity and duration of hospital stay, as compared with open procedures^{32,59}. The American College of Gastroenterology (ACG) clinical guidelines⁵ recommend that symptomatic simple hepatic cysts should be managed by laparoscopic fenestration rather than by percutaneous aspiration and sclerotherapy. ACG clinical guidelines also note that percutaneous procedures may be appropriate for patients who are not candidates for surgery⁵. The anatomical suitability of hepatic cysts for laparoscopic deroofting depends on operator experience and confidence. Careful mapping of the liver cysts with three-dimensional CT may be useful in evaluating the feasibility of laparoscopic surgery. However, for hepatic cysts that are very large, or in locations where laparoscopic access may make complete excision of the cyst wall difficult, open fenestration is probably prudent³².

Reported recurrence rates, including repeated asymptomatic cysts, vary from 0% to 36% after laparoscopic fenestration^{29,32}. The main reason for cyst recurrence after fenestration is reconstitution of the cyst with the adjacent organ or diaphragm forming part of the cystic wall⁶⁰. To prevent hepatic cyst recurrence, wide fenestration of hepatic cyst, omental transposition flap⁶¹, or electrocoagulation ablation of the remnant hepatic cyst epithelium⁵⁹ have

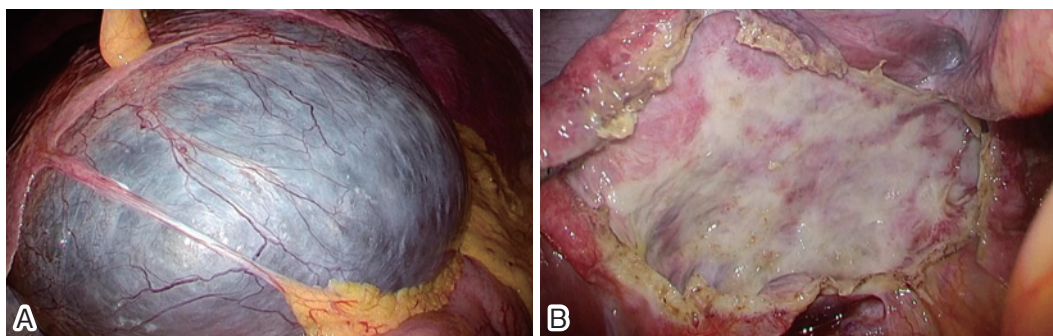


Fig. 2 Intraoperative findings

A: A large fluid-filled simple hepatic cyst before laparoscopic fenestration.

B: Wide fenestration and electrocoagulator ablation of remnant hepatic cyst epithelium.

been introduced (Fig. 2A and B). Recurrence rates of 0% have been reported for total excision and lobe resection³².

Despite technological advances in imaging modalities, the presence of cystobiliary communication is difficult to identify preoperatively⁶². In the case of biliary communication with a hepatic cyst, ligation or running suture to disrupt biliary communication within the hepatic cyst should be attempted^{28,62}. Incomplete separation between the biliary tree and cyst will cause postoperative biloma or biliary peritonitis. Roux-en-Y cystoenterostomy was reported as a treatment for cystobiliary communication but was associated with high risks of sepsis and ascending cholangitis⁶²⁻⁶⁴. Tocchi et al.⁶⁵ reported a case of repeat cholangitis after cystoenterostomy, which required hepatectomy.

When the diagnosis of a hepatic cystic lesion is uncertain, surgical intervention is necessary in order to allow histological examination, particularly for exclusion of hepatic neoplasm. However, for suspected neoplasms, complete surgical excision of the cystic lesion, without spillage of intracystic fluid, is required⁴². Procedures such as complete excision of the hepatic cyst, segmentectomy, or lobectomy are associated with higher morbidity and mortality risks, as compared with fenestration⁵⁷. Because of this increased morbidity risk, hepatic resection should be reserved for recurrence after deroofing, diffuse hepatic involvement, and multiple hepatic cysts⁶⁶.

Liver transplantation is not indicated for patients with simple hepatic cysts. However, in Gigot type III PLD with diffuse liver enlargement and small cysts not suitable for deroofing or resection, detailed evaluation for liver transplantation should attempt to balance the risk of surgery, quality of life, and the possible benefits of a combined renal implant with polycystic kidney disease⁶⁶.

Conclusion

Effective management of simple hepatic cyst requires differentiation from neoplasm and infection and selection of a reliable treatment that reduces the risk of recurrence in patients with symptomatic simple hepatic cysts.

Conflict of Interest: The authors have no conflicts of interest to declare.

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