Hepatic cyst reduction surgery and its significance for polycystic liver disease

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Abstract

Purpose.
Although there have been many studies on polycystic liver disease (PCLD), most have not considered the effectiveness of computed tomography volumetry for liver resection as part of reduction surgery. In this study, we report the techniques used for liver resection in reduction surgery for PCLD and describe the theoretical basis.

Methods.
We performed clinical and imaging investigations in five patients with PCLD whose chief complaints were abdominal distention and early satiety.

Results.
The average plasma indocyanine green retention at 15 min (ICG R15), which indicates hepatic functional reserve, was 11.3 ± 6.7%, indicating moderate liver damage. The average galactosyl human serum albumin uptake during single photon emission tomography uptake for assessing asialoscintigraphy was 50.6% ± 17.8%, indicating slightly decreased uptake. The disease was present in both lobes of the liver in all patients except one, in whom PCLD was localized in the left lobe. Because multiple cysts were present in the hepatic radial margin, we only resected cysts without the surrounding parenchyma when possible. The cyst walls were comparatively tough and firm. Because Glisson’s capsule was present between the cysts, resection was performed with double or triple ligation with transfixing sutures to prevent suture failure and postoperative biliary leakage. Only one patient reported symptom recurrence because of enlargement of cyst remnants.

The average preoperative and postoperative total liver volumes were 4644 ± 1813 cm³ and 2698 ± 1615 cm³, respectively, indicating a significant decrease (p < 0.01). The average preoperative cyst volume was 3765 ± 1780 cm³, which decreased to 1894 ± 1546 cm³ after surgery, indicating a significant 35% decrease in cyst volume (p < 0.01). The average preoperative and postoperative noncystic volumes were 880 ± 80 cm³ and 805 ± 173 cm³, respectively, indicating no significant loss of liver parenchyma.

Conclusion.
The goal of liver resection in PCLD is bulk reduction to alleviate abdominal distention and early satiety. All patients in this study were alive at the time of publication, indicating that the surgery allows patients to survive beyond a few years.

Key term: polycystic liver disease, reduction surgery, liver regeneration, computed tomography volumetry
Introduction

Adult polycystic liver disease (PCLD) is a benign disease that causes the liver to swell gradually, resulting in increasing feelings of distention and abdominal pain. In addition, patients often eventually present with cyst infection, cyst rupture, portal hypertension, and other conditions [1].

Numerous treatments have been used for PCLD. Approaches in internal medicine involve cyst aspiration and injections with ethanolamine oleate and other drugs [2]. In addition, surgical treatment options include liver resection, cyst fenestration, and liver transplantation [3, 4]. Liver transplantation is considered a radical treatment, but most cases in Japan involve living donor transplantation. Because family members often have the same disease, the number of potential donors is limited, making liver transplantation more difficult than other transplantations. Recent studies have focused on laparoscopic liver resection.

Although there are many studies on PCLD, few have reported on the significance of liver resection using computed tomography (CT) volumetry or have provided details of the surgical technique used [3]. In this study, we report the techniques used for liver resection in reduction surgery for PCLD and outline the theory behind these techniques.

Patients and Methods

We enrolled five patients with PCLD who underwent liver resection at Yamagata University Hospital First Department of Surgery between 2002 and 2012. We recorded their age, sex, liver function, liver reserve function as indicated by indocyanine green retention at 15 min (ICG R15), and asialoscintigraphy findings. PCLD was described using Gigot’s classification as follows [6]. Type I patients had less than 10 cysts measuring ≥10 cm. Type II patients had medium-sized cysts distributed diffusely in the liver, with large areas of normal residual liver parenchyma. Type III patients had diffuse distribution of cysts with very little normal residual liver parenchyma. We obtained a large biochemical sample of intracystic fluid from one patient.

Liver resection for the reduction of hepatic cysts was performed to alleviate the chief complaints of abdominal distention and early satiety and allow patients to return to a normal life. Therefore, rather than resecting all cysts, we resected only those in select regions of the liver where several cysts were concentrated with little or no normal residual liver parenchyma. At the same time, we left areas of normal liver parenchyma untouched.

Because the cyst walls were comparatively tough, we used Rochester Pean forceps and Kelly forceps (Leibinger, Germany) to open them, but considerable pressure was required to pierce the walls. Normally, we use an electrosurgical knife to dissect cyst walls.

Multiple cysts were present in the hepatic radial margin, and Glisson’s capsule was present between the cysts. Therefore, we performed resection with double or triple ligation using transfixing sutures, with 5 to 10 mm between the ligations and the margin to prevent suture failure and loosening and consequent postoperative biliary leakage.

CT volumetry was conducted by tracing all CT images, calculating the cystic and noncystic regions, and calculating the total of all the sections.

Results

The average age of the patients was 55.6 years (range, 51-68 years) and the ratio of males to females was 2:3 (Table 1). The chief complaints were epigastric distention and pain. Three patients presented with concurrent polycystic kidney disease (PCKD).

The average ICG R15 was used as an indicator of liver reserve function and was 11.3 ± 6.7%, indicating moderate liver damage. However, the
average 99mTc-GSA SPECT uptake was 50.6% ± 17.8%, indicating a slight decrease (Table 1).

PCLD was located in both lobes (Fig. 2 a-c) in all patients except one, in whom it was located mainly in the left lobe (Fig. 1 a, b). According to Gigot’s classification, there was one Type I and Type II patient each and were three Type III patients (Table 1).

We used a variety of surgical techniques, as shown in Table 1. However, most surgeries were performed peripherally, rather than in the center of the liver (Table 1).

Biochemical tests were performed on cyst fluid

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Chief complaint</th>
<th>PCLD ICG %</th>
<th>GSA R15</th>
<th>Gigot’s class</th>
<th>Location</th>
<th>Surgical technique(s)</th>
<th>Complication(s)</th>
<th>Prognosis</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>F</td>
<td>Abdominal distention</td>
<td>Yes</td>
<td>8%</td>
<td>Type II</td>
<td>Both lobes</td>
<td>Lateral segmentectomy</td>
<td>Slight bile leakage</td>
<td>Good</td>
</tr>
<tr>
<td>2</td>
<td>51</td>
<td>M</td>
<td>Abdominal distention</td>
<td>Yes</td>
<td>11%</td>
<td>Type III</td>
<td>Both lobes</td>
<td>S7, 8 resection S4, 2, 6 fenestration</td>
<td>Slight bile leakage</td>
<td>Good</td>
</tr>
<tr>
<td>3</td>
<td>52</td>
<td>F</td>
<td>Epigastric distention</td>
<td>Yes</td>
<td>22%</td>
<td>Type III</td>
<td>Both lobes</td>
<td>Lateral segmentectomy S6 partial resection</td>
<td>None</td>
<td>Cyst enlargement in remnant liver</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>F</td>
<td>Abdominal pain</td>
<td>No</td>
<td>4%</td>
<td>Type I</td>
<td>Mainly L. lobe</td>
<td>L. lobe resection, S7 fenestration</td>
<td>Hemorrhage into drain</td>
<td>Good</td>
</tr>
<tr>
<td>5</td>
<td>68</td>
<td>M</td>
<td>Epigastric distention</td>
<td>No</td>
<td>11%</td>
<td>Type III</td>
<td>Both lobes</td>
<td>S3, 5, 6 partial resection</td>
<td>Bile leakage</td>
<td>Bile leakage ceased after 2.5 years</td>
</tr>
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</table>

**Fig. 1a.** Dominant left lobe resection in a Type I patient according to Gigot’s classification (Table 1; Patient 4)

**Fig. 1b.** Disappearance of epigastric pain after surgery

**Fig. 2a.** Type III patient according to Gigot’s classification (Table 1; Patient 5)

**Fig. 2b.** S5 and S6 resection was done for Type III patient.

**Fig. 2c.** An intraoperative view showing pericystic infection proximal to S6 resection revealed that the fluid within the cysts was bile. The patient experienced prolonged postoperative bile leakage.
collected from 34 locations in a single participant (Fig. 3 case). All cyst fluid samples had a total bilirubin count of <0.1 mg/dL. The average carcinoembryonic antigen (CEA) level was 29.8 ± 73.3 ng/mL (range, 0.4-357.6), and 25 cysts (73.5%) had CEA values of ≥3 ng/mL. The carbohydrate antigen 19-9 (CA19-9) level was ≥9999 U/L in all samples.

Bile was present inside the peripheral hepatic cysts of two patients. One of the patients with cysts containing bile required drain placement for 2 years and 6 months. In another patient, we identified areas of bile flow by observing Glisson’s capsule between many of the cysts. We sutured these areas using PDS® II 4-0 sutures (Ethicon, Japan) and observed no postoperative bile leakage.

Patients were discharged from the hospital by an average of 33.2 ± 8.8 days after surgery (range, 24-44 days). The abdominal symptoms disappeared in all patients. In patient 3, gastric distention due to PCLD was relieved and nutritional intake improved after resecting the left lateral segment of the liver. CT performed on an outpatient basis indicated no enlargement in the hepatic parenchyma and few cysts (Fig. 4 a-e). Enlargement of hepatic cysts was observed in the remnant liver in only one of the five patients.

In patient 2, preoperative aspartate aminotransferase and alanine transaminase were elevated at 72 U/L and 63 U/L, respectively, but they returned to normal levels (24 U/L and 23 U/L, respectively) after surgery. Currently, 4 of the 5 patients have no symptoms and are being observed as outpatients. The cysts in the right lobe of the remnant liver have enlarged in the patient who underwent lateral segment and S6 resection.

We performed CT volumetry in all patients. The average preoperative and postoperative total hepatic volumes were 4644 ± 1813 cm³ and 2698 ± 1615 cm³, respectively, indicating a significant

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**Fig. 3a.** Resections of the lateral segment and posterior segment were done for Type II patient according to Gigot’s classification (Table 1; Patient 1).

**Fig. 3b.** A decrease in postoperative cyst volume and an increase in noncystic liver parenchyma

**Fig. 3c.** Preoperative asialsctintigraphy is useful for determining the scope of liver resection to preserve the functional red areas.

**Fig. 3d.** Because of the large number of preoperative cysts, resection was performed mainly in the posterior and the lateral segments.

**Fig. 3e.** The main cysts were resected and the central portion of the liver, where there were few cysts, was preserved.
decrease in total hepatic volume ($p < 0.01$) (Table 2). The average preoperative cystic volume was 3765 ± 1780 cm$^3$, decreasing to 1894 ± 1546 cm$^3$ after surgery. The average decrease was approximately 35%, and cystic volume significantly decreased by up to 49.7% of the preoperative volume ($p < 0.01$). The average preoperative and postoperative noncystic volumes were 880 ± 80 cm$^3$ and 805 ± 173 cm$^3$, respectively, indicating that there was no significant loss of parenchymal volume.

In all patients, the chief preoperative complaints of abdominal distention and early satiety were alleviated. The patients are able to lead comfortable lives because of increased appetite and improved nutrition.

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<tbody>
<tr>
<td>1</td>
<td>3918 cm$^3$</td>
<td>1204</td>
<td>3167</td>
<td>459</td>
<td>752</td>
<td>746</td>
</tr>
<tr>
<td>2</td>
<td>7307</td>
<td>4610</td>
<td>6352</td>
<td>3582</td>
<td>955</td>
<td>1028</td>
</tr>
<tr>
<td>3</td>
<td>3985</td>
<td>3180</td>
<td>3046</td>
<td>2255</td>
<td>938</td>
<td>925</td>
</tr>
<tr>
<td>4</td>
<td>2542</td>
<td>852</td>
<td>1663</td>
<td>115</td>
<td>879</td>
<td>737</td>
</tr>
<tr>
<td>5</td>
<td>5472</td>
<td>3646</td>
<td>4597</td>
<td>3059</td>
<td>875</td>
<td>587</td>
</tr>
<tr>
<td>Average</td>
<td>4644 ± 1813</td>
<td>2698 ± 1615</td>
<td>3765 ± 1780</td>
<td>1894 ± 1546</td>
<td>880 ± 80</td>
<td>805 ± 173</td>
</tr>
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</table>

Decrease rate of cystic volume: (preoperative cyst volume-postoperative cyst volume)/preoperative cyst volume = (3765-1894)/3765 = 49.7%
Discussion

PCLD is divided into childhood and adult types. The frequency of the adult type is reported to be 0.05% to 0.13% \(^8,9\). The incidence is 4 to 5 times higher in women than in men. PCLD is often complicated by autosomal dominant polycystic kidney disease \(^10\). However, PCLD is not observed in patients with autosomal dominant polycystic liver disease \(^11\). The leading cause of death in PCLD is kidney failure caused by advanced disease.

When cysts enlarge, the patient experiences a feeling of pressure that can be concentrated in the gastric region after meals \(^12\). PCLD can be complicated by cyst infection, which is difficult to treat \(^13\). It has been reported that positron emission tomography-computed tomography is useful for the diagnosis of cyst infection \(^14\) and that high serum CA19-9 levels are useful indicators \(^15\). Other complications include cholangiocarcinoma, cyst rupture, and massive ascites due to inferior vena cava occlusion \(^16\).

Medical approaches include shrinkage of the cysts via the administration of molecular targeting drugs and lanreotide (Somatuline\(^®\)) \(^16\). It is believed that the mammalian target of rapamycin (mTOR) inhibitor sirolimus is effective; however, its use is not yet established \(^17\). Transcatheter arterial embolization (TAE) is also reported to be effective for patients who are not suitable for surgical treatment \(^18\).

Because gene therapy is not currently available, the only radical approach is liver transplantation \(^19-21\). In Europe, the 5-year survival rate in 584 liver transplantations was reportedly 84% \(^22\). In Japan, where living donor liver transplantation is practiced, donors are usually family members. However, it is highly likely that nongtous relatives have the same genetic makeup \(^23\). PCLD patients often have associated PCKD, making kidney failure a common cause of death. Therefore, only hepatorenal transplantation, rather than liver transplantation alone, can rightfully be called a true radical therapy \(^24,25\). Therefore, liver resection with cyst fenestration has been proposed as a therapeutic approach for PCLD, primarily because it is a less invasive alternative to liver transplantation and does not require postoperative immunosuppression \(^26-30\). A French group reported that in patients with PCLD without end-stage renal failure in whom noncystic hepatic parenchyma occupies ≥30% of the total liver, resection is preferred over transplantation \(^31\). The Mayo group has also reported that the 5-year survival rate for liver resection with cyst fenestration is 92%, while that for liver transplantation is 60% \(^4\). Recently, fenestration has been performed laparoscopically \(^11,32\). On the basis of Gigot’s classification, type I patients are considered good candidates for laparoscopic fenestration \(^6\). In addition, extended fenestration is considered effective for patients with type II disease, although long-term observation is recommended. However, patients with type III disease have poor prognoses and are contraindicated.

During liver resection in our patients with PCLD, we noted thin sections of liver parenchyma extending to the edges of the cyst surfaces. The resection line should not include this thin brown extension of the liver parenchyma. Resection only up to the white cyst walls is important to prevent postoperative bile leakage.

In conventional liver resection, the Pean fracture method is used to resect the liver parenchyma. Then, the liver parenchyma is fragmented using a Cavition\(^®\) ultrasonic surgical aspirator (CUSA) and the remaining blood vessels and Glisson’s capsule are ligated. However, because the resection margin in most PCLD patients is at the tough cyst walls, it is difficult to use a CUSA because the liver parenchyma remains between the cysts. In liver resection, this margin is normally sutured once, but this is risky in PCLD patients because the sutures may break or loosen because of the tough cyst walls. Also, the presence of Glisson’s capsule between the cyst walls increases the concern of bile leakage after surgery. Therefore, we performed double suturing with nonabsorbable transfixing sutures (Ticron, Covidien, Tokyo), maintaining a distance of 5-10 mm between each ligation and the resected area to prevent subsequent tearing or loosening. It is important to prevent bile leakage from the liver parenchyma and Glisson’s capsule.
between the cyst walls. It has been reported that bile duct stents implanted using endoscopic retrograde cholangiopancreatography (ERCP) are effective for bile leakage after liver resection for PCLD [33].

Our approach to PCLD is to resect areas of the liver with high concentrations of cysts and fenestrate the larger remaining cysts. In our investigation, we found that both total liver volume and cyst volume decreased significantly after liver resection. In addition, there was no significant difference between the preoperative and postoperative volumes of relatively unaffected noncystic liver parenchyma. Therefore, despite the presence of cysts that affect liver function in PCLD patients, resection of the main cyst-containing areas can preserve normal noncystic liver parenchyma by preferentially reducing cyst volume.

Reduction of cyst bulk caused the disappearance of the chief complaints in all patients and allowed them to lead normal lives. The goal of liver resection in PCLD is bulk reduction to alleviate abdominal bloating and early satiety. All patients in this study were alive at the time of publication, indicating that the surgery allows patients to survive beyond a few years.

Authors’ Contributions
Study conception and design: Kimura W
Acquisition of data: Hirai I, Sugawara S
Analysis and interpretation of data: Kimura W, Hirai I
Drafting of manuscript: Kimura W, Hirai I
Critical revision of manuscript: Watanabe T, Tezua K

References