Staging cholangiocarcinoma by cholangioscopy

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Abstract
Peroral cholangioscopy (POCS) and percutaneous transhepatic cholangioscopy (PTCS) were first developed in the 1970s, and technical developments and clinical applications have taken place gradually ever since. POCS is used to diagnose small mucosal biliary lesions in non-icteric patients and early malignant changes in patients with persistent primary sclerosing cholangitis (PSC). Although PTCS is a more invasive diagnostic procedure than POCS, it has the advantage of precise diagnosis with mapping biopsy in defining the proximal and distal extension of superficially spreading cholangiocarcinoma (CCA) or mucin-producing CCA, which is predominantly found in papillary type CCA. POCS is significantly superior to ERCP in distinguishing between malignant and benign dominant bile duct stenoses in patients with PSC. The positive rate of PTCS biopsy for CCA is 96%, while morbidity and mortality of PTCS are 9% and 0%, respectively. Although magnetic resonance (MR) cholangiography may replace PTCS in determining the longitudinal spread of infiltrating type hilar CCA, the accuracy of MR cholangiography in papillary type hilar CCA is significantly lower than that of PTCS.

Key Words: Cholangioscopy, Cholangiocarcinoma, Cholangiography

Introduction
Biliary endoscopy has been used as a therapeutic procedure to remove gallstones retained in the common bile duct and intrahepatic duct through a choledochotomy during biliary surgery. And a fiberoptic choledochoscope developed in the 1970s has been used postoperatively through a T-tube sinus tract to remove retained stones [1].

Peroral cholangioscopy was first reported in 1976 [2,3]. Percutaneous transhepatic cholangioscopy was also developed in the 1970s [4], and technical developments and clinical use of this technique have gradually progressed and the value of PTCS for cholangiocarcinoma (CCA) has been reported [5,6].

Indications
Peroral cholangioscopy (POCS) is used to make a definitive diagnosis of extrahepatic CCA and recent development of diagnostic techniques has made it possible to detect a minute lesion in the bile duct of non-icteric patients. Small polyps and small stenotic lesions can be distinguished by endoscopic observation and biopsy [7,8]. Distal extension of the tumor is defined by cholangioscopic biopsy, especially in the case of superficially spreading CCA [6]. Recently, a new imaging technique, “narrow band imaging” (NBI), has been developed providing better visualization of fine mucosal structures and tumor vessels [9]. Although POCS is less invasive than PTCS, proximal extension of the tumor cannot be examined in common types of CCA obstructing the bile duct.

PTCS has also been used to differentiate the biliary strictures and polyps [10–12] and to make a preoperative definitive diagnosis of more difficult CCA located not only in the extrahepatic bile duct but also in the intrahepatic bile duct [6,13,14].

Usefulness
POCS is advantageous in the definitive diagnosis of small mucosal biliary lesions detected in non-icteric patients [8] and helpful in diagnosing early malignant changes in patients with persistent primary sclerosing cholangitis [12]. Although PTCS is a more invasive diagnostic procedure than POCS, it has the advantage of precise preoperative diagnosis in the case of patients with more difficult CCA. Mapping biopsy
for superficially spreading CCA is helpful in defining the proximal and distal extension of the tumor [5,6,14–16] and in designing a type of resection with negative surgical margins. Furthermore, in special cases of mucin-producing intrahepatic CCA, PTBD followed by PTCS is important when evaluating the progress of cancer along the intrahepatic segmental duct and extrahepatic bile duct and in providing an expected type of hepatobiliary resection with or without pancreateoduodenectomy [17–19].

**Results**

POCS by using NBI is significantly more useful than conventional POCS in identifying the surface structure and vessels of the lesions \( (p < 0.01 \) and \( p < 0.05 \) \) [9]. In terms of its sensitivity, specificity, accuracy, positive predictive value, and negative predictive value, POCS is significantly superior to ERCP in distinguishing between malignant and benign dominant bile duct stenosis in patients with primary sclerosing cholangitis [12]. PTCS observation with biopsy offers a high positive rate in malignant biliary diseases. Correct results for bile duct carcinoma have been obtained in 96% of patients (101 from 111), and negative biopsy findings in 10 patients with diffusely infiltrating CCA (Table I). The morbidity and mortality rates of PTBD (501 patients) and PTCS (295 patients) were 9% (46 patients) and 0%, respectively (Table II) [14].

Routine histological examination, including P53 immunostaining and telomerase activity, in cholangioscopic biopsy specimens increases both sensitivity and specificity in determining the spread of CCA [20,21]. Similarly to distal bile duct cancer, hilar CCA also shows several types of morphology and superficially spreading cancer in more than 10% of resected patients. This type of cancer is found predominantly in papillary type CCA [22]. Although MR cholangiography may supersede PTCS in determining the longitudinal spread of infiltrating type hilar CCA, the accuracy of MR cholangiography in papillary type hilar CCA is significantly lower than that of PTCS [23].

**Consensus statement**

- Cholangioscopy should be performed for preoperative staging of CCA when papillary type CCA or mucin-producing CCA is suspected in conventional cholangiography or MR cholangiography, because these types of CCA are predominantly associated with superficially spreading carcinoma, which should be precisely diagnosed with mapping biopsy to design a type of resective surgery.

**References**


<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dislodgement of catheter</td>
<td>9</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>5</td>
</tr>
<tr>
<td>Hemobilia</td>
<td>18</td>
</tr>
<tr>
<td>Perforation of the sinus tract</td>
<td>5</td>
</tr>
<tr>
<td>Cancer seeding in the sinus tract</td>
<td>7</td>
</tr>
<tr>
<td>Arterio-portal shunt</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>46 (9%)</td>
</tr>
</tbody>
</table>

Table II. Morbidity of PTBD and PTCS.


