



# Diagnosis and Treatment of Perihilar Cholangiocarcinoma: A National Survey from the Korean Pancreatobiliary Association

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**Background/Aims:** Based on their anatomy, cholangiocarcinomas (CCAs) are classified into intrahepatic, hilar, and distal CCAs. Although the diagnosis and treatment of each type of CCA are thought to be different, real-world data studies on the current practice are limited. Therefore, this study was designed to capture the current practice of diagnosing and treating perihilar CCA in Korea.

**Methods:** We conducted a survey using an online platform. The questionnaire consisted of 18 questions designed to evaluate the current practice of diagnosing and treating perihilar CCA in Korea. The targets of this survey were biliary endoscopists who are members of the Korean Pancreatobiliary Association.

**Results:** In total, 119 biliary endoscopists completed the survey. Of the respondents, 89.9% thought that the use of the International Classification of Diseases, 11th Revision (ICD-11) system is necessary to classify CCA. Approximately half of the respondents would recommend surgery or chemotherapy until patients were 80 years of age. For the pathological diagnosis of CCA, endoscopic retrograde cholangiopancreatography with biopsy was the most preferred modality. Routine preoperative biliary drainage was performed by 44.5% of the respondents. For operable CCAs, 64.7% of the respondents preferred endoscopic biliary drainage using plastic stents. For palliative biliary drainage, 69.7% of the respondents used plastic stents. For palliative endoscopic biliary drainage using metal stents, 63% of the respondents preferred the stent-in-stent method.

**Conclusions:** A new coding system using the ICD-11 is needed for classifying CCAs. Guidelines for diagnosing and treating CCA based on the clinical situation in Korea are needed. (*Gut Liver* 2024;18:174-183)

**Key Words:** Cholangiocarcinoma; Diagnosis; Treatment; Surveys and questionnaires

## INTRODUCTION

Cholangiocarcinoma (CCA) is a malignant tumor that

occurs in the epithelium of the bile duct and is classified into intrahepatic CCA (iCCA), perihilar CCA (pCCA), and distal CCA (dCCA) according to its location.<sup>1</sup> The



most common type of CCA is pCCA (50% to 60%), followed by dCCA (20% to 30%) and iCCA (10% to 20%).<sup>2</sup> CCA accounts for approximately 3% of all gastrointestinal malignancies. However, its incidence is increasing globally.<sup>2</sup> The incidence of CCA is much higher in Eastern countries than in Western countries.<sup>3</sup> According to the Annual Report of Cancer Statistics 2018 announced by the Korea Central Cancer Registry in 2021, the incidence of CCAs and gallbladder cancers was 3,840 cases (crude incidence rate 15/100,000) for men and 3,339 cases (crude incidence rate 3.6/100,000) for women, ranking 9th in the overall cancer incidence.<sup>4</sup> The 5-year relative survival rate was 28.8%, which showed a poor prognosis compared with other gastrointestinal cancers, such as gastric (77%) and colon (74.3%) cancers.<sup>4</sup>

Each CCA type has distinct characteristics. Therefore, the diagnosis, treatment, and prognosis are thought to be different.<sup>5,6</sup> However, few studies have focused on this issue. One reason is the lack of a separate code for the most common type of CCA (i.e., pCCA) in the 10th revision of the International Classification of Diseases (ICD-10).<sup>3</sup> The

ICD-10 divides CCAs into intrahepatic (C22.1) and extrahepatic (C24.0) CCAs. For this reason, pCCAs are sometimes misclassified as iCCA. Although several guidelines on the diagnosis and treatment of CCAs have been published,<sup>7-9</sup> few real-world data studies on the clinical practice of diagnosing and treating pCCA have been conducted. Therefore, this study was designed to capture the current practice in diagnosing and treating pCCA in Korea.

## MATERIALS AND METHODS

### 1. Study design and contents of the questionnaire

A national online survey was organized by the Committee on Bile Duct Diseases of Korean Pancreatobiliary Association. An 18-item online questionnaire was developed and revised through three meetings after drafting by the committee members. The questionnaire was divided into five categories: (1) demographic characteristics of the respondents, (2) CCA classification, (3) treatment of CCA in elderly patients, (4) diagnosis of pCCA, and (5) biliary drainage in pCCA. E-mails with direct links to the web survey were sent four times to the members of the Korean Pancreatobiliary Association between May 2021 and September 2021.

### 2. ICD and Korean Standard Classification of Disease and Cause of Death (KCD)

Endorsed by the World Health Organization in 1990 and first used in 1994, the ICD-10 is currently the most widely used medical classification coding system (Table 1).<sup>10</sup> The disease code for CCA in Korea follows the KCD-8, which is based on the ICD-10 and the 3rd International Classification of Diseases for Oncology (Table 2).<sup>11</sup> Therefore, the disease code for CCA in Korea also divides CCAs into intrahepatic (C22) and extrahepatic (C24) CCAs. The

**Table 1.** International Classification of Diseases, 10th Revision (ICD-10)

Code	Code description
C22	Malignant neoplasm of liver and intrahepatic bile ducts Exclusion: biliary tract NOS [C24.9] secondary malignant neoplasm of liver [C78.7]
C22.0	Liver cell carcinoma - Hepatocellular carcinoma - Hepatoma
C22.1	Intrahepatic bile duct carcinoma - Cholangiocarcinoma
C22.2	Hepatoblastoma
C22.3	Angiosarcoma of liver - Kupffer cell sarcoma
C22.4	Other sarcomas of liver
C22.7	Other specified carcinomas of liver
C22.9	Liver, unspecified
C24	Malignant neoplasm of other and unspecified parts of biliary tract Exclusion: intrahepatic bile duct [C22.1]
C24.0	Extrahepatic bile duct - Biliary duct or passage NOS - Common bile duct - Cystic duct - Hepatic duct
C24.1	Ampulla of Vater
C24.8	Overlapping lesion of biliary tract - Malignant neoplasm involving both intrahepatic and extrahepatic bile ducts - Malignant neoplasm of biliary tract whose point of origin cannot be classified to any one of the categories C22.0-C24.1
C24.9	Biliary tract, unspecified

NOS, not otherwise specified.

Data from: <https://icd.who.int/browse10/2019/en#/C15-C26>.<sup>10</sup>

**Table 2.** Korean Standard Classification of Disease and Cause of Death, 8th Revision [KCD-8]

Code	Code description
C22.1	Malignant neoplasm of intrahepatic bile duct carcinoma
C22.10	Malignant neoplasm of cholangiocarcinoma
C24.0	Extrahepatic bile duct, malignant neoplasm
C24.00	Biliary duct or passage NOS, malignant neoplasm
C24.01	Common bile duct, malignant neoplasm
C24.02	Cystic duct, malignant neoplasm
C24.03	Hepatic duct, malignant neoplasm
C24.1	Ampulla of Vater, malignant neoplasm
C24.8	Overlapping lesion of biliary tract, malignant neoplasm
C24.80	Malignant neoplasm involving both intrahepatic and extrahepatic bile ducts
C24.9	Biliary tract, unspecified malignant neoplasm

NOS, not otherwise specified.

Data from: <http://kssc.kostat.go.kr/>.<sup>11</sup>

**Table 3.** International Classification of Diseases, 11th Revision (ICD-11)

Code	Code description
2C12	Malignant neoplasms of liver or intrahepatic bile ducts
2C12.0	Malignant neoplasm of liver
2C12.1	Malignant neoplasm of intrahepatic bile ducts 2C12.10 Intrahepatic cholangiocarcinoma 2C12.1Y Other specified malignant neoplasms of intrahepatic bile ducts
2C12.Z	Malignant neoplasms of liver or intrahepatic bile ducts, unspecified
2C14	Malignant neoplasms of proximal biliary tract, cystic duct
2C14.0	Adenocarcinoma of proximal biliary tract, cystic duct
2C14.1	Mucinous cystic neoplasm with associated invasive carcinoma of cystic duct
2C14.2	Neuroendocrine neoplasms of cystic duct
2C14.Y	Other specified malignant neoplasms of biliary tract, cystic duct
2C14.Z	Malignant neoplasms of proximal biliary tract, cystic duct, unspecified
2C15	Malignant neoplasms of biliary tract, distal bile duct
2C15.0	Adenocarcinoma of biliary tract, distal bile duct
2C15.1	Mucinous cystic neoplasm with associated invasive carcinoma of distal bile duct
2C15.2	Neuroendocrine neoplasms of distal bile duct
2C15.Y	Other specified malignant neoplasms of biliary tract, distal bile duct
2C15.Z	Malignant neoplasms of biliary tract, distal bile duct, unspecified
2C17	Malignant neoplasms of other or unspecified parts of biliary tract
2C18	Malignant neoplasms of perihilar bile duct
2C18.0	Hilar cholangiocarcinoma
2C18.1	Mucinous cystic neoplasm with associated invasive carcinoma of perihilar bile duct
2C18.2	Neuroendocrine neoplasm of perihilar bile duct
2C18.Y	Other specified malignant neoplasms of perihilar bile duct
2C18.Z	Malignant neoplasms of perihilar bile duct, unspecified

Data from: <https://icd.who.int/browse11/l-m/en>.<sup>12</sup>

11th revision of the ICD (ICD-11) came into effect on January 1, 2022 and categorizes CCAs into iCCA (2C12), pCCA (2C18), and dCCA (2C14 and 2C15) (Table 3).<sup>12</sup>

### 3. Statistical analysis

Categorical variables were presented as proportions. Univariate analysis was performed using the chi-square test for categorical variations. p-values of less than 0.05 were used to denote statistical significance. All statistical analyses were performed using Statistical Package for the Social Sciences, version 26 (IBM Corp., Armonk, NY, USA).

## RESULTS

### 1. Demographic characteristics of the respondents

Of the 209 certified pancreatobiliary endoscopists, 119 completed the survey (56.9%). Among them, 113 were male doctors and six were female doctors. Fig. 1 shows the demographic characteristics of the respondents in this survey. Twenty respondents (16.8%) were in their 30s, 55 (46.2%) in their 40s, 34 (28.6%) in their 50s, and 10 (8.4%) in their 60s (Fig. 1A). The experience on endoscopic retrograde cholangiopancreatography (ERCP) was >10 years in 65 endoscopists (54.6%), 7 to 9 years in 13 endoscopists (10.9%), 3 to 6 years in 23 endoscopists (19.3%), <3 years in 18 endoscopists (15.1%) (Fig. 1B). Most endoscopists (107/119, 89.9%) worked in tertiary hospitals (Fig. 1C). The number of ERCP procedures per month in the hospitals where the respondents are working was >100 in 43 (36.2%), 50 to 99 in 43 (36.1%), and <50 in 33 (27.7%) (Fig. 1D).

### 2. Classification of CCA

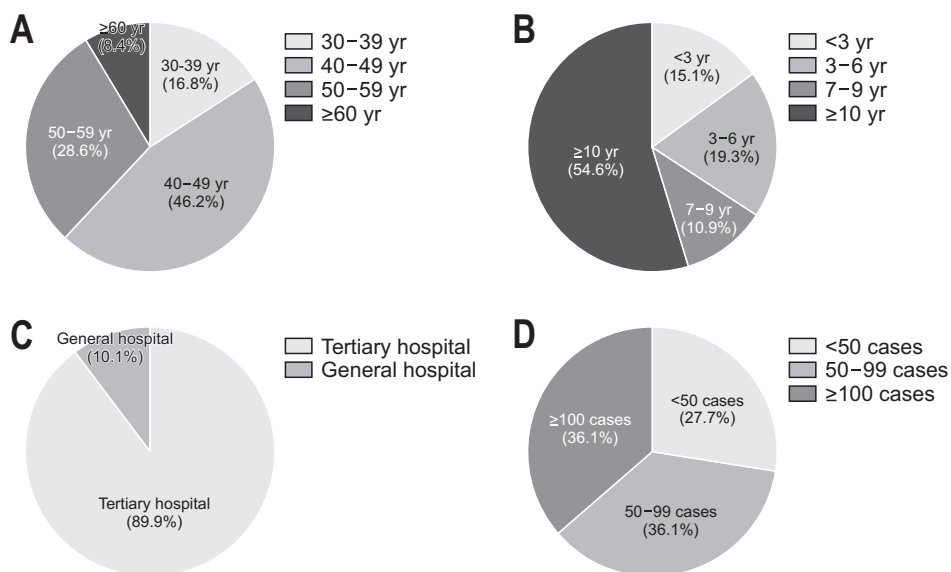
Most respondents (98/119, 82.4%) used separate codes for iCCA and extrahepatic CCA (eCCA) at the time of diagnosis. However, 20 respondents (16.8%) did not use distinguished codes for iCCAs or eCCAs (Fig. 2A). Most respondents (107/119, 89.9%) thought that the replacement of ICD-10 by ICD-11 is needed (Fig. 2B).

### 3. Treatment of CCA in the elderly patients

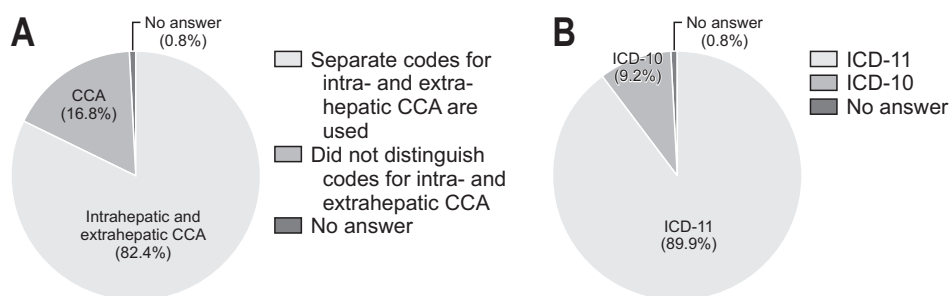
The maximum age of the patients at which the respondents would recommend surgery was 80 years in 62 (52.1%), followed by 85 years in 29 (24.4%), 75 years in 17 (14.3%), >85 years in nine (7.6%), and 70 years in two (1.7%) (Fig. 3A). Moreover, the maximum age of the patients at which the respondents would recommend chemotherapy was 80 years in 57 (47.9%), followed by 85 years in 46 (38.7%), 75 years in 10 (8.4%), >85 years in five (4.2%), and 70 years in one (0.8%) (Fig. 3B).

### 4. Diagnosis of pCCA

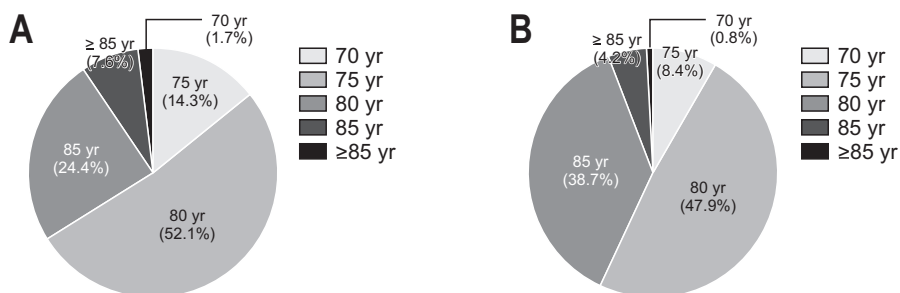
For the pathological confirmation of pCCA, most respondents (114/119, 95.8%) preferred using ERCP with biopsy and cytology as the initial diagnostic method (Fig. 4A). If the first biopsy result showed atypia and curative resection is possible, most respondents (100/119, 84%) thought that a second biopsy would be unnecessary (Fig. 4B). Overall, 102 endoscopists (85.7%) chose ERCP with re-biopsy as the next diagnostic method for the pathological confirmation of unresectable pCCA. Twelve endoscopists (10.1%) used cholangioscopy, three (2.5%) used percutaneous transhepatic biliary drainage (PTBD) with bile juice cytology, and two (1.7%) used endoscopic ultra-



**Fig. 1.** Demographic characteristics of the respondents. (A) Age. (B) Personal experience in endoscopic retrograde cholangiopancreatography (ERCP). (C) Types of respondent hospitals. (D) Monthly ERCP cases at each respondent's hospital.



**Fig. 2.** Classification of cholangiocarcinoma. (A) Actual coding of cholangiocarcinoma at the time of diagnosis. (B) The need for the ICD-10 versus the ICD-11. ICD, International Classification of Diseases; CCA, cholangiocarcinoma.



**Fig. 3.** Treatment of cholangiocarcinoma in elderly patients. (A) What is the maximum age at which you recommend surgery? (B) What is the maximum age at which you recommend chemotherapy?

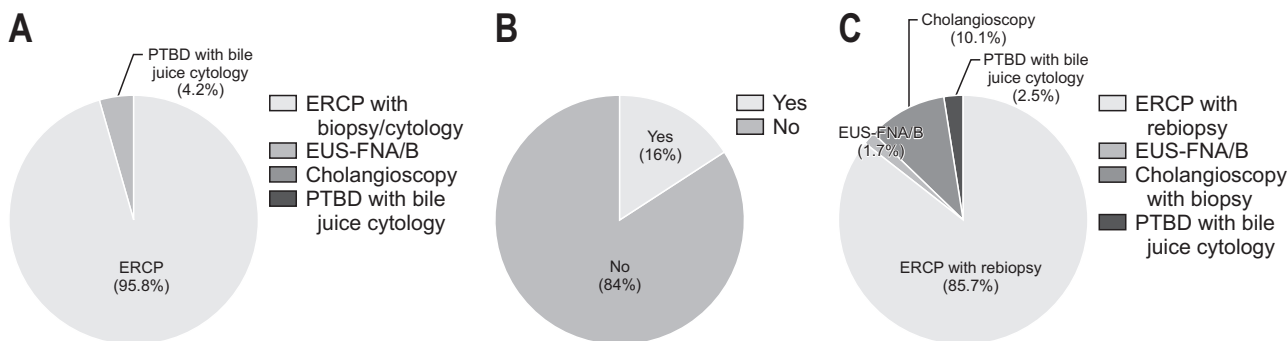
sound-guided fine-needle aspiration/biopsy (EUS-FNA/B) as the second diagnostic method (Fig. 4C).

### 5. Biliary drainage in pCCA

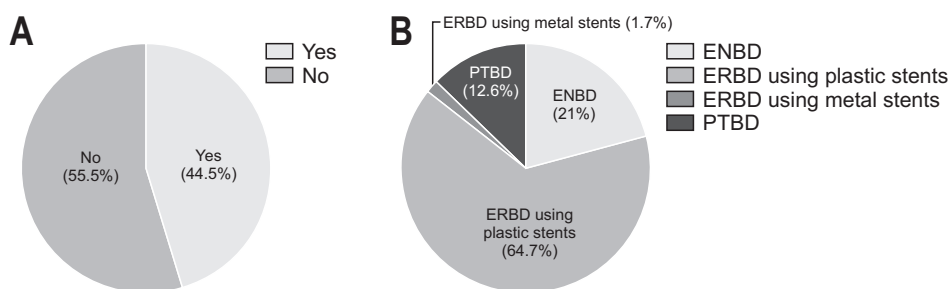
For preoperative biliary drainage, 66 respondents (55.5%) performed biliary drainage in selected patients, whereas 53 (44.5%) performed routine preoperative biliary drainage (Fig. 5A). Regarding the preoperative biliary

drainage method, 77 respondents (64.7%) preferred performing endoscopic retrograde biliary drainage (ERBD) using plastic stents, followed by endoscopic nasobiliary drainage in 25 (21.0%), PTBD in 15 (12.6%), and ERBD using metal stents in two (1.7%) (Fig. 5B).

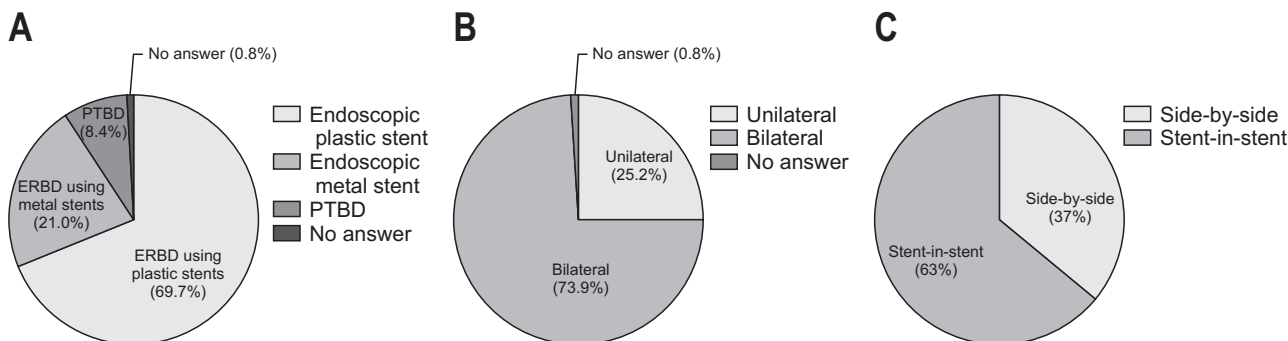
For palliative biliary drainage in inoperable pCCAs, ERBD using plastic stents was the most preferred primary method (83/119, 69.7%), followed by ERBD using metal



**Fig. 4.** Diagnosis of perihilar cholangiocarcinoma (pCCA). (A) What is the first diagnostic modality used for the pathological diagnosis of suspected pCCA? (B) Do you think that preoperative pathological confirmation is necessary in case of curative pCCA if the first biopsy result shows atypia? (C) What is the second diagnostic method for the pathological confirmation of inoperable pCCA? ERCP, endoscopic retrograde cholangiopancreatography; EUS-FNA/B, endoscopic ultrasound-guided fine-needle aspiration/biopsy; PTBD, percutaneous transhepatic biliary drainage.



**Fig. 5.** Preoperative biliary drainage in perihilar cholangiocarcinoma (pCCA). (A) Do you routinely perform preoperative biliary drainage in patients with operable pCCA? (B) What is the most preferred method for preoperative biliary drainage in pCCA? ENBD, endoscopic nasobiliary drainage; ERBD, endoscopic retrograde biliary drainage; PTBD, percutaneous transhepatic biliary drainage.



**Fig. 6.** Palliative biliary drainage in inoperable perihilar cholangiocarcinoma (pCCA). (A) Which is the preferred initial method for palliative biliary drainage in pCCA? (B) When endoscopic palliative biliary drainage is required in pCCA, which method is preferred, unilateral or bilateral drainage? (C) If endoscopic bilateral metal stenting is performed for palliative biliary drainage in pCCA, which method would you prefer, side-by-side or stent-in-stent? ERBD, endoscopic retrograde biliary drainage; PTBD, percutaneous transhepatic biliary drainage.

stents (25/119, 21.0%) and PTBD (10/119, 8.4%) (Fig. 6A). When endoscopic biliary drainage was performed, most endoscopists (88/119, 73.9%) preferred bilateral drainage over unilateral drainage (Fig. 6B). When endoscopic bilateral metal stenting was performed, the stent-in-stent (SIS) method was preferred (75/119, 63%) over the side-by-side (SBS) method (Fig. 6C).

### 6. Differences in the diagnosis and treatment of CCA according to age group

Table 4 shows the difference in the diagnosis and treatment of CCAs among four age groups of respondents. No significant differences in the coding of CCA, the treatment of CCA in the elderly patients, the initial method for the pathological confirmation of CCA, and the need for preoperative pathological confirmation were found among the four age groups. However, a significant difference in the

**Table 4.** Differences in the Diagnosis and Treatment of Cholangiocarcinoma According to the Endoscopists' Age Group

Variable	Age group, No. [%]				p-value
	30–39 yr (n=20)	40–49 yr (n=55)	50–59 yr (n=34)	60–69 yr (n=10)	
<b>Coding of CCA</b>					
Separate codes for iCCA and eCCA	17 (85)	46 (83.6)	27 (79.4)	8 (80)	0.938
Need for ICD-11	20 (100)	46 (83.6)	32 (94.1)	9 (90)	0.465
<b>Treatment of CCA in the elderly</b>					
Maximum age of surgery					0.816
70 yr	0	2 (3.6)	0	0	
75 yr	3 (15)	10 (18.2)	2 (5.9)	2 (20)	
80 yr	11 (55)	28 (50.9)	18 (52.9)	5 (50)	
85 yr	4 (20)	11 (20.0)	12 (35.3)	2 (20)	
>85 yr	2 (10)	4 (7.3)	2 (5.9)	1 (10)	
Maximum age of chemotherapy					0.794
70 yr	0	0	1 (2.9)	0	
75 yr	2 (10)	6 (10.9)	2 (5.9)	0	
80 yr	11 (55)	25 (45.5)	18 (52.9)	3 (30)	
85 yr	6 (30)	22 (40.0)	12 (35.3)	6 (60)	
>85 yr	1 (5)	2 (3.6)	1 (2.9)	1 (10)	
<b>Diagnosis of pCCA</b>					
Initial method for pathological confirmation					0.597
ERCP	19 (95)	54 (98.2)	32 (94.1)	9 (90)	
PTBD with bile juice cytology	1 (5)	1 (1.8)	2 (5.9)	1 (10)	
Preoperative pathological confirmation in curative pCCA necessary					0.249
Yes	3 (15)	12 (21.8)	2 (5.9)	2 (20)	
No	17 (85)	43 (78.2)	32 (94.1)	8 (80)	
Second method for pathological confirmation					<0.05
ERCP with re-biopsy	16 (80)	49 (89.1)	32 (94.1)	5 (50)	
EUS-FNA/B	2 (10)	0	0	0	
Cholangioscopy	2 (10)	4 (7.3)	2 (5.9)	4 (40)	
PTBD with bile juice cytology	0	2 (3.6)	0	1 (10)	
<b>Treatment of pCCA</b>					
Routine preoperative biliary drainage					0.146
Yes	9 (45)	27 (49.1)	16 (47.1)	1 (10)	
No	11 (55)	28 (50.9)	18 (52.9)	9 (90)	
Preferred preoperative biliary drainage method					<0.05
ENBD	4 (20)	11 (20.0)	10 (29.4)	0	
ERCP using plastic stents	14 (70)	38 (69.1)	17 (50.0)	8 (80)	
ERCP using metal stents	0	0	0	2 (20)	
PTBD	2 (10)	6 (10.9)	7 (20.6)	0	
Palliative biliary drainage method					0.712
ERBD using plastic stents	16 (80)	37 (67.3)*	24 (70.6)	6 (60)	
ERBD using metal stents	4 (20)	13 (23.6)	5 (14.7)	3 (30)	
PTBD	0	4 (7.3)	5 (14.7)	1 (10)	
Palliative endoscopic drainage					0.171
Bilateral	2 (10)*	14 (25.5)	12 (35.3)	2 (20)	
Unilateral	17 (85)	41 (74.5)	22 (64.7)	8 (80)	
Bilateral metal stenting method					0.630
Side-by-side	9 (45)	19 (34.5)	11 (32.4)	5 (50)	
Stent-in-stent	11 (55)	36 (65.5)	23 (67.6)	5 (50)	

CCA, cholangiocarcinoma; iCCA, intrahepatic CCA; eCCA, extrahepatic CCA; pCCA, perihilar CCA; ICD, International Classification of Diseases; ERCP, endoscopic retrograde cholangiopancreatography; PTBD, percutaneous transhepatic biliary drainage; EUS-FNA/B, endoscopic ultrasound-guided fine-needle aspiration/biopsy; ENBD, endoscopic nasobiliary drainage.

\*No response (n=1).

second method for the pathological confirmation of pCCA (p<0.05) was observed among the four age groups. Furthermore, >80% of the respondents in the age 30 to 59-year

group preferred ERCP with re-biopsy as the second diagnostic method. In contrast, only 50% of the respondents in their 60s favored ERCP with re-biopsy. EUS-FNA/B was chosen

by the respondents in their 30s only. Cholangioscopy was preferred in 40% of the respondents in their 60s. A trend where preoperative biliary drainage was preferred more by respondents in their 60s than by the respondents of the 30 to 59-year group was noticed (90% vs 50.9%–55%), although this difference was statistically insignificant ( $p=0.146$ ). Furthermore, the respondents of the 60 to 69-year group exclusively preferred ERCP using plastic or metal stents as the preoperative biliary drainage method ( $p<0.05$ ). No significant differences in the palliative biliary drainage method were observed among the four age groups.

## DISCUSSION

This study represents the first survey on the current practices of Korean pancreatobiliary endoscopists in diagnosing and treating pCCA.

In this survey, 82.4% of the respondents used separate diagnostic codes for iCCA and eCCA. However, 16.8% of the respondents did not use distinguished codes. There may be several reasons for this. First, certain KCD-8 codes are ambiguous; for example, clinicians might think that “C22.10 Malignant neoplasm of cholangiocarcinoma” refers to any type of CCA. It is the same code as “C22.1 malignant neoplasm of intrahepatic bile duct carcinoma,” which refers to iCCA. Furthermore, “C24.9 Biliary tract, unspecified malignant neoplasm” might seem to refer to any type of CCA, but it exclusively refers to eCCA. Second, some clinicians may not feel the need to use appropriate diagnostic codes. Most clinicians focus hard on the correct diagnosis and treatment. However, some may not pay as much attention to the coding itself. Improper coding of CCA may result in accumulation of inaccurate data on the prevalence, incidence, or mortality of each CCA type.

Therefore, a new Korean coding system with clearly defined codes is required. Approximately 90% of the respondents thought that using the ICD-11 instead of the ICD-10 was necessary. Hence, a new coding system must include separate codes for each CCA type. Furthermore, educating clinicians on the use of appropriate KCD-8 codes is essential. Until a new Korean coding system is developed, we suggest using C22.1 (malignant neoplasm of intrahepatic bile duct carcinoma) and C22.10 (malignant neoplasm of CCA) for iCCA and C24.0 (extrahepatic bile duct, malignant neoplasm), C24.00 (biliary duct or passage NOS, malignant neoplasm), and C24.01 (common bile duct, malignant neoplasm) for dCCA and pCCA should be used. Tailored codes for the three types of CCA might provide more accurate and meaningful epidemiological data.

According to the Annual Report of Cancer Statistics

2018, the incidence rate of CCA increases with age, peaking at >85 years.<sup>4</sup> The life expectancy in South Korea is 80.3 years for males and 86.1 years for females, which ranks Korea 3rd in the world life expectancy.<sup>13</sup> These data suggest that the number of elderly patients with CCA requiring surgery or chemotherapy will increase. Few reports have investigated the efficacy and safety of curative surgery for CCA in elderly patients. Sumiyoshi *et al.*<sup>14</sup> reported no significant difference in the overall 5-year survival rate between elderly patients ( $\geq 75$  years) with pCCA and younger patients with pCCA ( $< 75$  years) (42.4% vs 51.3%,  $p=0.718$ ). Furthermore, Akashi *et al.*<sup>15</sup> reported that curative surgery can be performed with low mortality and better long-term survival in octogenarians. To the best of our knowledge, no report has been published on the efficacy and safety of chemotherapy in elderly patients with CCA. However, many reports suggest that chemotherapy prolongs the survival of the elderly.<sup>16,17</sup> In this survey, approximately half of the respondents showed that the maximum age of the patients at which the respondents would recommend surgery and chemotherapy was 80 years. The second preferred age limit was 85 years. Given that healthy life expectancy is increasing, more octogenarians may benefit from surgery or chemotherapy in the future.

Most biliary strictures are malignant (70% to 80%), and only 10% to 40% of patients with pCCA can undergo curative surgical resection.<sup>18</sup> The incidence of benign disease after the resection of suspected pCCA is 3.1% to 46%.<sup>19</sup> Therefore, pathological diagnosis is needed in many cases to avoid unnecessary surgery. In this survey, approximately 95% of the respondents preferred ERCP with biopsy and cytology as the first diagnostic method for the pathological confirmation of pCCA. ERCP with biopsy and cytology is considered a standard diagnostic method for the pathological confirmation of pCCA.<sup>18,20</sup> However, the diagnostic yield of this test remains low, with its sensitivity and specificity ranging from 18% to 60%.<sup>20</sup> In cases where the first biopsy result shows atypia and curative resection is possible, 84% of the respondents replied that they would go straight to surgical resection rather than re-biopsy. Potential reasons for this may be that further invasive diagnostic procedures would result in complications, such as cholangitis or pancreatitis, and surgical delays. This practice agrees with a recent guideline, which suggests that preoperative biopsy is not essential in resectable pCCA if the index of suspicion is high.<sup>21</sup>

Surprisingly, >85% of the respondents preferred ERCP with re-biopsy as the second diagnostic method for the pathological confirmation of unresectable pCCA. However, no data showed that repeated ERCP with biopsy significantly increases the diagnostic yield. Furthermore, other diagnostic methods have superior diagnostic yields, such as

cholangioscopy and EUS-FNA/B. The reported sensitivity and specificity of cholangioscopy were 72% to 94% and 87% to 99%, respectively.<sup>18</sup> The diagnostic accuracy of cholangioscopy was reported to be 85%–96%.<sup>22</sup> Additionally, the sensitivity and diagnostic accuracy of EUS-FNA/B were reported to be 75%–94% and 79%–94%, respectively.<sup>18</sup>

There may be some reasons for the unpopularity of cholangioscopy (10.1%) and EUS-FNA/B (1.7%) as the second diagnostic method for the pathological confirmation of CCA. The high cost of these procedures may be one reason. Single-operator cholangioscopy (SpyGlass DS, Boston Scientific) has been covered by the Korean national health insurance only since July 2021, when the survey was being conducted. Moreover, EUS-guided procedures are currently not covered by the national health insurance. Another reason may be that certain procedures require that endoscopists should have more experience or familiarity. Interestingly, EUS-FNA/B was chosen only by the respondents in their 30s, whereas cholangioscopy was preferred in 40% of the respondents in their 60s ( $p < 0.05$ ). The significant difference in these results suggests that there are some age or generational differences in endoscopic procedural preference among endoscopists in Korea.

Although more respondents (55.5%) performed preoperative biliary drainage in selected cases, still many respondents (44.5%) performed routine biliary drainage. A trend where respondents in their 60s (90%) preferred selective preoperative biliary drainage more than the other age groups (50.9% to 55%) was noted, although this difference was statistically insignificant ( $p = 0.146$ ). Most guidelines recommend against routine preoperative biliary drainage in pCCA.<sup>7,9,21,23</sup> Meta-analyses have concluded that routine preoperative biliary drainage is associated with increased morbidity, postoperative infection complications, prolonged hospital stay, and increased cost.<sup>24,25</sup> The suggested indications for preoperative drainage are obstructive cholangitis, intractable pruritus, long-lasting or severe jaundice (total bilirubin  $> 15$  mg/dL), or patients who are eligible for neoadjuvant chemotherapy, portal embolization, or major hepatic resection.<sup>7,9,21,23</sup> Given the possible side effects of biliary drainage procedures, more efforts should be made to perform preoperative biliary drainage in selected patients.

Moreover, 64.7% of the respondents preferred ERBD using plastic stents as the preoperative biliary drainage method, followed by endoscopic nasobiliary drainage (21%), PTBD (12.6%), and ERBD using metal stents (1.7%). This wide variety of clinical practice may be because there is no single superior preoperative biliary drainage method. Studies on the optimal preoperative biliary drainage method had controversial results. A multicenter European study reported no differences in postoperative mortality

between percutaneous and endoscopic approaches.<sup>26</sup> In a Japanese multicenter study, ERBD was not associated with increased adverse events, unplanned re-interventions, or a poor prognosis compared with endoscopic nasobiliary drainage.<sup>27</sup> A meta-analysis reported that postoperative complications were fewer in the PTBD group than in the endoscopic group,<sup>28</sup> whereas another study showed that the incidence of seeding metastasis in patients undergoing endoscopic drainage was reduced compared with that in patients undergoing percutaneous drainage.<sup>29</sup>

For palliative biliary drainage in inoperable pCCA, ERBD using plastic stents was the most preferred modality (69.7%), followed by ERBD using metal stents (21%) and PTBD (8.4%). Biliary obstruction in pCCA is often complex and requires multi-segment biliary drainage. Generally, endoscopic biliary drainage is preferred in Bismuth type I-II pCCA.<sup>30</sup> However, no single drainage method appears superior to another in Bismuth type III-IV pCCA. In a meta-analysis and systematic review, PTBD showed higher rates of successful biliary drainage and lower rates of cholangitis than ERBD.<sup>31</sup> However, ERBD showed lower bleeding complications than PTBD.<sup>31</sup> Recent randomized prospective multicenter studies on endoscopic biliary drainage in advanced pCCA showed clinical success rates of 84.9% to 91.4%.<sup>32,33</sup> Therefore, the optimal biliary drainage method may depend on the patient's biliary obstruction status, experience and skills of the endoscopist or radiologist, and the hospital's facilities.<sup>34</sup>

More respondents preferred plastic stents over metal stents for endoscopic biliary drainage. A possible reason for this practice may be the frequent need for re-intervention in patients with pCCA. Patients with pCCA might undergo re-intervention for re-biopsy or recurrent cholangitis, and re-intervention has been shown to be easier using plastic stents.<sup>35</sup>

When endoscopic biliary drainage is performed, most respondents (73.9%) preferred bilateral drainage over unilateral drainage. This finding was probably influenced by a Korean multicenter, prospective, randomized study.<sup>33</sup> In this study, Lee *et al.*<sup>33</sup> reported that bilateral metal stenting had a similar technical success rate, but with fewer re-interventions and more stent patency in patients with advanced pCCA. In a recent retrospective multicenter study which compared bilateral and trisegment drainage using metal stents in Bismuth type III-IV pCCA, clinical success rates with re-intervention were higher in the trisegment drainage method.<sup>36</sup> Moreover, the drainage of  $> 50\%$  of the liver volume, which frequently requires bilateral stenting, was shown to have survival gain in patients with pCCA.<sup>37</sup>

Regarding bilateral metal stenting, more respondents (63%) preferred the SIS method over the SBS method.

Several studies have shown that the performance of the SIS and SBS methods are comparable.<sup>32</sup> In a Korean prospective, randomized, multicenter study, total adverse events, technical and clinical success, stent patency, and survival were similar between the SIS and SBS methods.<sup>32</sup> In a recent meta-analysis study, the SIS method had higher technical success and lower complication rates, whereas the SBS method was associated with longer stent patency.<sup>38</sup> Further research is needed to develop good selection criteria for the SIS and SBS methods.

This study has several limitations. The data in this study were collected through a survey, which is prone to recall bias. Furthermore, the respondents might have selected what they thought to be the “correct” answer rather than their real-life practice. Finally, selection bias could not be avoided. All respondents in this survey worked in tertiary or general hospitals. However, the diagnosis and treatment of pCCA are almost exclusively performed in tertiary and general hospitals in Korea, where a multidisciplinary approach is possible. Moreover, >99% of ERCP procedures are performed in these hospitals in Korea. Therefore, the findings of this survey could represent the current practice of diagnosing and treating pCCA in Korea.

In conclusion, a new tailored coding system for CCA is needed for more accurate and meaningful epidemiological data. Guidelines for diagnosing and treating CCA according to the clinical situation in Korea are needed.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

## AUTHOR CONTRIBUTIONS

Study concept and design: H.J.K. Data acquisition: E.C. Data analysis and interpretation: S.J.C., M.K.J., B.J.S., J.M.P., J.K., W.S.P., J.K.P., S.M.W. Drafting of manuscript: E.C., S.H.K. Critical revision of manuscript for important intellectual content: S.H.K., M.K.J., J.M.P. Statistical analysis: E.C. Approval of final manuscript: all authors.

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