

## Current Status of Endoscopic Papillectomy for Ampullary Tumors

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Detection of tumors of the ampulla of Vater, including ampullary adenoma, has been improved by routine screening endoscopic procedures and imaging modalities. Endoscopic resection by endoscopic papillectomy is rapidly replacing classic surgical resection and is a less invasive procedure. Endoscopic resection can have a role not only in the final histopathologic diagnosis but also as a definite therapeutic option. However, the indications for endoscopic resection are not fully established, and endoscopic procedures are not standardized. Significant complications, including severe pancreatitis, intractable bleeding and duodenal perforation, are rare but can occur, especially in less experienced hands. Severe pancreatitis is the most feared complication, but it can be prevented by pancreatic duct stent insertion in most cases. However, in some cases, pancreatic stenting can be challenging after resection. Incomplete resections are sometimes performed to avoid complications. Endoscopic surveillance is also important for identifying and managing remnant adenomatous tissue or recurrent lesions. Further technical development is needed to expand the indications for this procedure, minimize complications and ensure a high success rate. (**Gut Liver 2014;8:598-604**)

**Key Words:** Ampullary tumor; Ampullary adenoma; Endoscopic resection; Endoscopic papillectomy

### INTRODUCTION

Detection of tumors of the ampulla of Vater (AV) has improved through increased use of screening upper gastrointestinal (GI) endoscopy, ultrasonography (US), and computed tomography. Ampullary adenoma is the most common ampullary tumor with malignant potential. Traditionally, surgical resection has been the standard method for complete removal of ampullary

tumors. There are two kinds of surgical options for ampullary tumor: standard radical surgical resection by pancreaticoduodenectomy, and surgical ampullectomy as a local surgical excision. Surgical ampullectomy requires technical expertise and has a high recurrence rate. However, surgical resection can be considered over-treatment for a relatively small ampullary lesion. The difficulty of treatment decisions has driven efforts to develop endoscopic alternatives for the removal of ampullary tumors, including adenomas. Endoscopic papillectomy (EP) is a less invasive treatment with less morbidity.<sup>1-3</sup> EP can be the first-line treatment in patients with ampullary adenoma without intraductal invasion with a 81.0% cure rate (Table 1).<sup>4</sup> The method is simple using snaring and resection, as is done with polypoid lesions of the GI tract (Fig. 1). However, it is different from conventional polypectomy in the stomach or colon. Detection of microscopically invading malignant foci in the main adenoma or intraductal invasion can be difficult in some cases before complete resection. Intraductal ultrasound has demonstrated superior accuracy over endoscopic ultrasound for local T-staging and intraductal extension (Fig. 2).<sup>5</sup> The false negative rate of forceps biopsy for the detection of infiltrating carcinomas of the relatively large size of ampullary adenomas is not uncommon. Therefore, EP is required to gain sufficient tissue for complete histopathologic examination to overcome the limitations of forceps biopsy.<sup>6</sup> There are several technically difficult aspects of performing successful endoscopic resection of ampullary tumors without complications, including anatomically difficult locations in the duodenum, the complexity of anatomy of the AV, confluence of the pancreatic and biliary duct orifices, the thin duodenal wall, and the highly vascularized area. Therefore, possible postprocedure complications and incomplete resection of the lesion to avoid complications can lead to hesitancy about performing EP. EP is not a daily endoscopic procedure at an average-volume endoscopic center. Occasional

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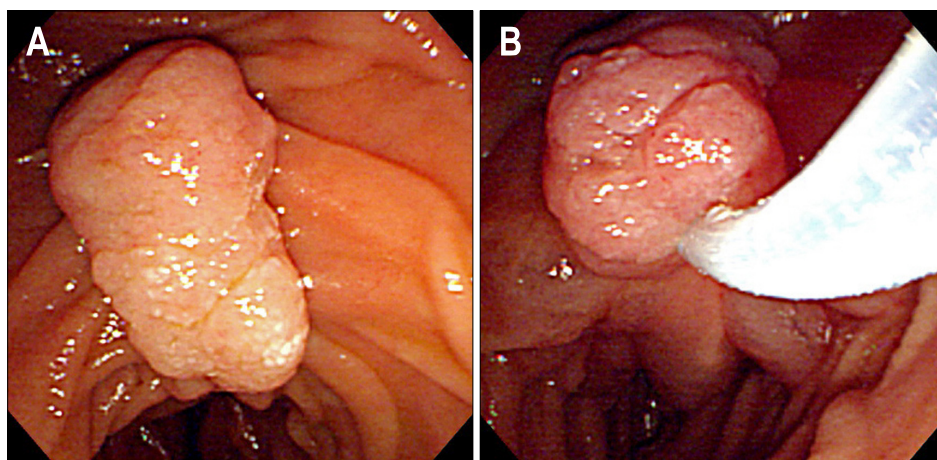
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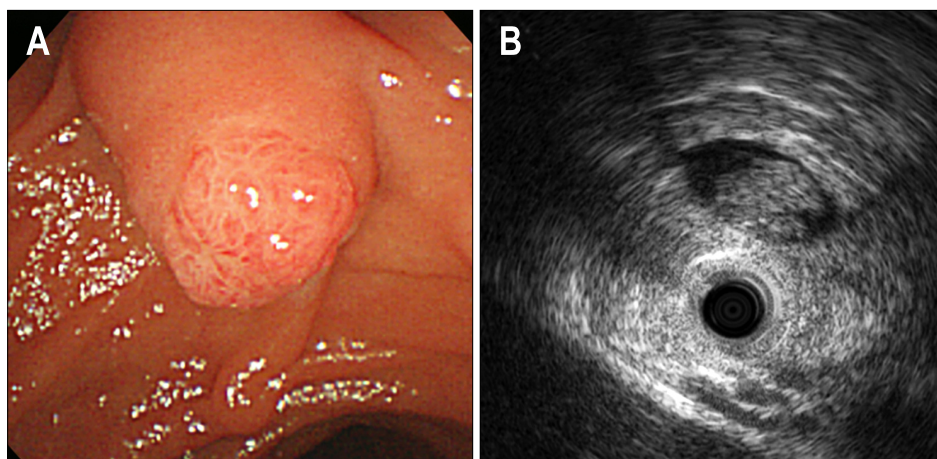
**Table 1.** Outcomes of Endoscopic Papillectomy in Published Studies

Study	No. of patients	Complete resection, no. (%)	Malignant foci	Recurrence, no. (%)	Surgery
Binmoeller <i>et al.</i> <sup>7</sup>	25	23/25 (92)	0/23	6/23 (26)	3/25
Desilets <i>et al.</i> <sup>8</sup>	13	12/13 (92)	0/12	0/12 (0)	1/13
Catalano <i>et al.</i> <sup>20</sup>	103	83/103 (81)	6/83	10/103 (10)	16/103
Cheng <i>et al.</i> <sup>9</sup>	55	39/55 (71)	7/39	9/27 (33)	4/55
Kahaleh <i>et al.</i> <sup>17</sup>	56	30/56 (54)	21/56	NA	12/56
Bohnacker <i>et al.</i> <sup>18</sup>	87	74/87 (85)	NA	15/87 (17)	17/87
Irani <i>et al.</i> <sup>1</sup>	102	86/102 (84)	8/102	8/102 (8)	16/102
Kim <i>et al.</i> <sup>27</sup>	72	65/72 (90)	3/72	5/65 (8)	2/72
Napoleon <i>et al.</i> <sup>4</sup>	79	70/79 (89)	8/79	5/69 (7)	5/79
Riditid <i>et al.</i> <sup>29</sup>	151	107/151 (71)	12/151	16/107 (15)	NA

NA, not available.



**Fig. 1.** Endoscopic papillectomy by snaring. (A) Endoscopic view of adenoma arising from the major duodenal papilla. (B) Endoscopic view of performing papillectomy after grasping the adenoma with a snare.



**Fig. 2.** Intraductal ultrasound. (A) Endoscopic view of ampullary adenoma. (B) Intraductal ultrasound detected tumor extension to the pancreatic duct.

performance of EP by less experienced endoscopists can lead to a relatively high complication or incomplete resection rates. Furthermore, many questions have arisen about aspects of current EP such as indications, standardized technique, prevention and management of complications, and recurrence rate.

#### INDICATIONS FOR ENDOSCOPIC PAPILLECTOMY

The indications for EP are still not fully established. An absolute indication is adenoma confined to just the ampullary region with exposed-type adenoma, absence of extension into

the pancreatic or biliary ducts, no evidence of malignancy, no invasion of the duodenal muscular layer, and size less than 4 cm.<sup>7-9</sup> Early AV cancer confined to the sphincter of Oddi shows good prognosis compared to advanced cases. Theoretically, early AV cancer can be an indication of EP.<sup>10</sup> However, exact diagnosis in an early stage before resection is very difficult, even after performing intraductal ultrasound.<sup>5</sup> Another problem is that there are insufficient data on lymph node metastasis. One Korean group reported that lymphovascular invasion or lymph node metastasis and duct mucosal involvement were not found in 18 patients with focal cancer in the main adenoma after EP.<sup>11</sup> Recurrence of tumor did not occur during a mean 32.2-month follow-up period. The authors concluded that focal cancer in the main adenoma can be an indication for endoscopic resection. However, another study reported different results, showing an 80% (8/10) recurrence rate in patients with high-grade dysplasia on forceps biopsy before EP.<sup>12,13</sup> In two different Korean studies, lymph node metastasis was present in 9% to 10% of patients with even early-stage AV cancer.<sup>14,15</sup> However, in another case series, there was no lymph node metastasis in six patients with the carcinoma *in situ* stage of AV cancer.<sup>15</sup> Hence, determining indications for endoscopic resection of AV cancers, including cancers suspected of being early stage, can be difficult because of the possibility of lymph node metastasis and recurrence. Intraductal growing ampullary adenoma means direct biliary or pancreatic extension of ampullary adenoma. Endoscopic resection for intraductal growing ampullary adenoma is also technically possible using the technique of balloon traction after sphincterotomy.<sup>16</sup> However, problems include a low success rate for complete resection and a high recurrence rate.<sup>17</sup> In a previous case series, the successful endoscopic resection rate was 13 of 31 patients (46%) with intraductal growth of adenoma, having a high surgery rate (37%).<sup>18</sup> Thus, intraductal growing ampullary adenoma cannot be a good indication for EP. Patients with familial adenomatous polyposis show a high incidence of

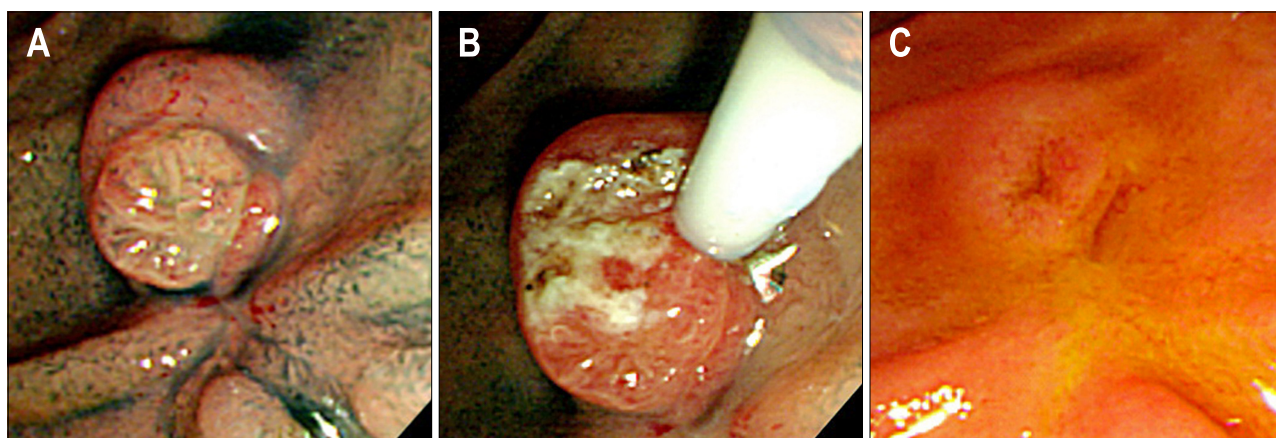
duodenal adenomatosis including ampullary adenoma.<sup>19</sup> The role of EP in patients with familial adenomatous polyposis is still unclear because of the possible development of adenomas on another part of the duodenum, especially the second part. The recurrence rate is also relatively high.<sup>20,21</sup>

## TECHNIQUES OF ENDOSCOPIC PAPILLECTOMY

The best technique of EP is to perform complete resection without complications at one time. The general procedure is endoscopic resection with electrosurgical currents after snaring followed by pancreatic duct stenting. However, a standardized endoscopic technique for EP is still not established. Also, there is no consensus regarding the type of current and power settings for use with electrosurgical units. Before resection, submucosal injection is not generally recommended, except in adenoma cases involving the duodenal wall.<sup>1</sup>

*En bloc* resection is fundamental in endoscopic treatment of neoplastic lesions. It shortens procedure time and requires less electrocautery. Piecemeal resection may lead to a possible reduction in complications, but it needs multiple endoscopic retrograde cholangiopancreatography (ERCP) sessions for complete excision, with possible increased rates of remnant adenoma. Therefore, *en bloc* resection is recommended, but there are no long-term data comparing recurrence rates between *en bloc* and piecemeal resections. After EP by *en bloc* or piecemeal resection, complete histopathological evaluation of all resected specimens is essential for the evaluation of complete resection or malignant foci with invasiveness.

Treatment of remnant adenomatous tissue can be performed with snare resection, removal with biopsy forceps, or thermal ablation. Thermal ablation can be performed by argon plasma coagulation and is useful for destroying residual or recurrent adenomatous tissue and preventing or treating bleeding after EP (Fig. 3). However, there is no consensus regarding settings or



**Fig. 3.** Thermal ablation with argon plasma coagulation. (A) Endoscopic view of recurrent ampullary adenoma. (B) Endoscopic view of thermal ablation using argon plasma coagulation. (C) Follow-up endoscopic view revealing no residual tumor.

power levels for argon plasma coagulation.

## COMPLICATIONS OF ENDOSCOPIC PAPILLECTOMY AND THEIR PREVENTION

The complication rate of EP is up to 25% with a 0.4% mortality rate. Pancreatitis (8% to 15%) and bleeding (2% to 13%) are the most common early complications of EP.<sup>22</sup> Duodenal perforation is rare, about 0% to 4%. Papillary stenosis can occur as a late complication with a 0% to 8% rate (Table 2).<sup>22</sup>

Bleeding is usually mild and on the anal side of the resected margin. Bleeding can be treated endoscopically using injection, clipping, or argon plasma coagulation. However, bleeding after resection can interfere with subsequent pancreatic stenting. Delayed continuous oozing after resection requires cumbersome, time-consuming, and repeated hemostasis.

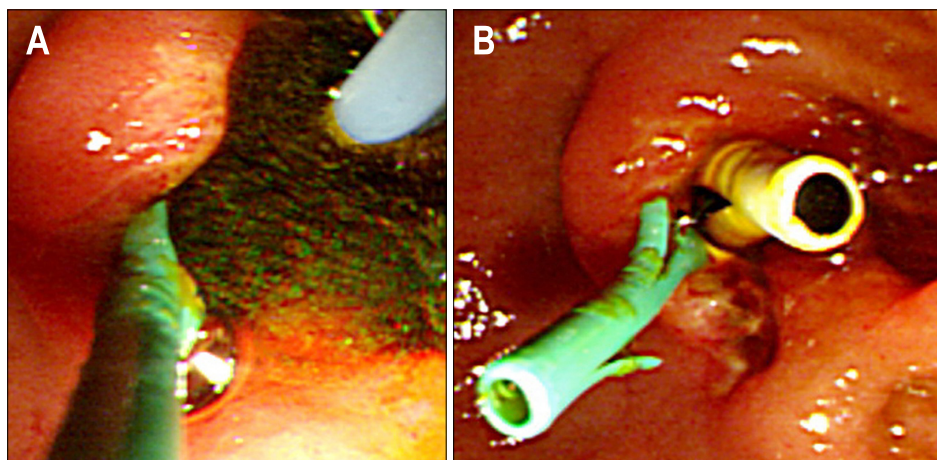
Cholangitis is a rare complication (0% to 2%) that is easily controlled by endoscopic sphincterotomy followed by implantation of a plastic biliary stent (Fig. 4). However, there is no established consensus for prophylactic endoscopic sphincterotomy with biliary stenting to prevent cholangitis after EP.<sup>9</sup>

Pancreatitis is the most common problematic complication. Placement of a prophylactic pancreatic duct stent is highly recommended to reduce the risk of pancreatitis, especially for the severe form.<sup>23,24</sup> There is no established consensus for pancreatic stenting after EP, such as routine or selective placement of a pancreatic stent. The shapes, diameters, and lengths of pancreatic duct stents are not standardized. The removal time of such stents reportedly varies from 2 days to 3 months.<sup>8</sup> Sometimes it is necessary for a pancreatic stent to remain in place longer to protect the pancreatic duct orifice during second procedures for the removal of remnant tissue. Some groups prefer preresection pancreatic stenting to reduce the likelihood of pancreatitis,<sup>8,25</sup> but it can interfere with *en bloc* complete resection. A pre-existing pancreatic stent makes resection difficult and makes EP time-consuming. Postresection pancreatic duct stenting is a common procedure for *en bloc* resection. Usually, pancreatic stenting is possible in the majority of cases after EP. However, it can be very difficult in some cases because of a hidden or deviated orifice within the coagulum after resection or electro-surgery-induced edema. Furthermore, repeated trials for selective cannulation into the pancreatic duct can predispose one to

**Table 2.** Complications Related to Endoscopic Papillectomy in Published Studies

Study	No. of patients	Pancreatitis, no. (%)	Bleeding	Perforation	Cholangitis	Stricture	Mortality
Binmoeller <i>et al.</i> <sup>7</sup>	25	3/25 (12)	2	0	0	0	0
Desilets <i>et al.</i> <sup>8</sup>	13	1/13 (8)	0	0	0	0	0
Catalano <i>et al.</i> <sup>20</sup>	103	5/103 (5)	2	0	0	3	0
Cheng <i>et al.</i> <sup>9</sup>	55	5/55 (9)	4	1	0	2	0
Kahaleh <i>et al.</i> <sup>17</sup>	56	4/56 (7)	2	0	1	0	1
Bohnacker <i>et al.</i> <sup>18</sup>	87	11/87 (13)	18	0	0	0	0
Irani <i>et al.</i> <sup>1</sup>	102	10/102 (10)	5	2	1	3	0
Kim <i>et al.</i> <sup>27</sup>	72	6/72 (8)	12	0	0	0	0
Ridititid <i>et al.</i> <sup>29</sup>	182*	7/182 (4)	23	3	0	7	1

\*Total number including patients with nonadenomatous benign lesions.



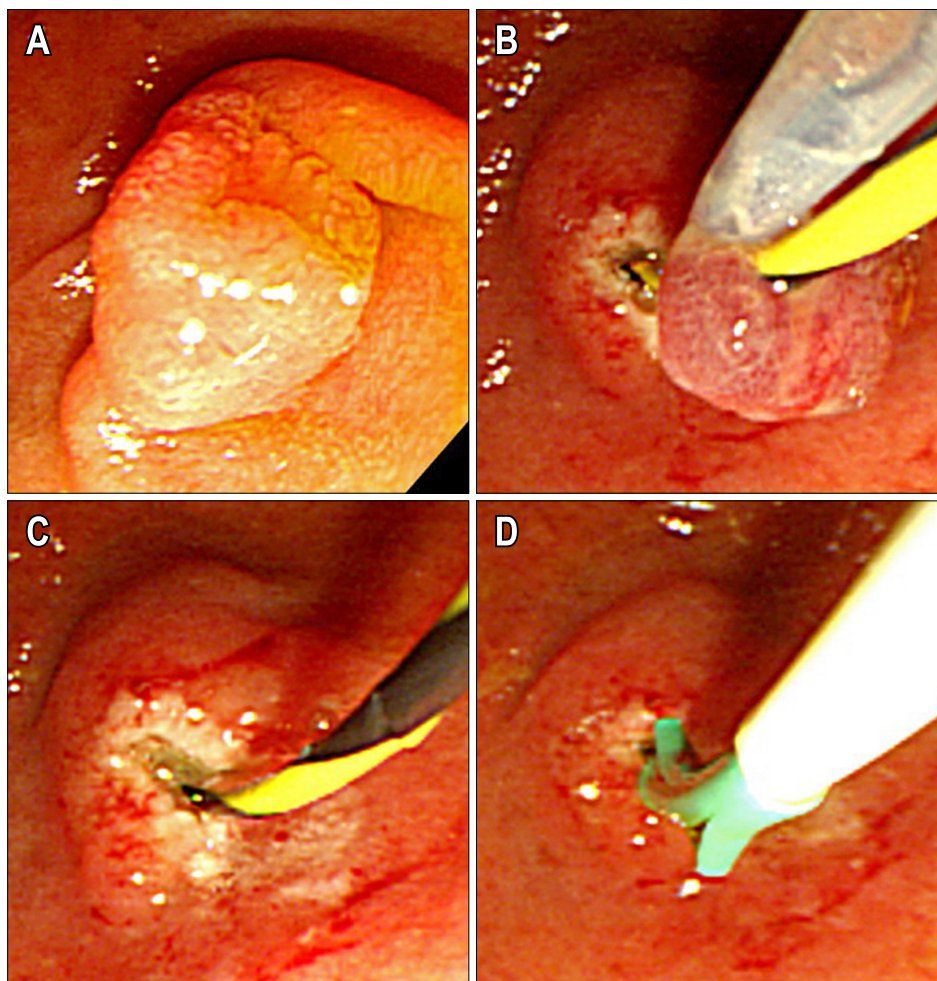
**Fig. 4.** Biliary stenting after endoscopic papillectomy. (A) Endoscopic view showing the drainage of biliary sludge after papillectomy followed by endoscopic sphincterotomy. (B) Endoscopic view of biliary stenting with a plastic stent.

pancreatitis. Pancreatic duct wire-guided EP has been developed to solve the problem of difficult cannulation after EP.<sup>26</sup> It is a simple method for securing a route for pancreatic stent insertion with a guide wire before EP. In brief, after cannulation of the pancreatic duct, a guide wire is inserted into the pancreatic duct. After passing the loop of the snare over the guide wire, tumor snaring and resection are performed. After complete resection, pancreatic stenting through the guide wire is immediately possible (Fig. 5). Kim *et al.*<sup>27</sup> reported the results of pancreatic duct wire-guided EP in 72 patients with ampullary adenoma. Exclusion criteria were suggestion of malignancy at endoscopy, suspicion of invasion into the pancreatic duct and/or the bile duct, histopathologic finding of adenocarcinoma, tendency for bleeding, size greater than 25 mm, and failure of guide wire insertion into the proximal pancreatic duct. *En bloc* resection was performed in 83% of cases, and the complete resection rate was 90%. Pancreatic duct stenting was possible in all cases. Pancreatitis occurred in 8%, but there were no cases of severe pancreatitis. During a mean follow-up period of 23.7 months, five cases recurred, and surgical resection was performed in two cases. Pancreatic stent-related complications after EP can occur, such as intraductal migration of the pancreatic stent or late-

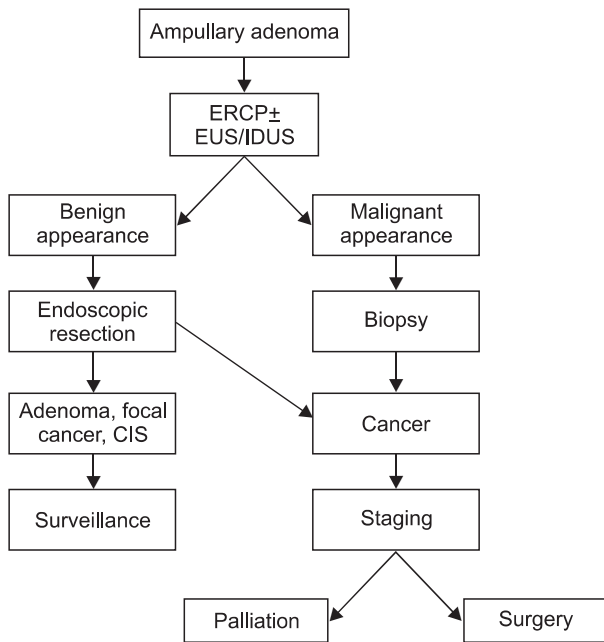
onset indwelling pancreatitis.<sup>26</sup> Yoon *et al.*<sup>28</sup> reported retrieval of intraductally migrated pancreatic stents after EP using wire-guided endoscopic snaring.

### POSTPAPILLECTOMY SURVEILLANCE

Rates of endoscopic success and recurrence after EP have differed in various reports. The endoscopic success rate after EP was 61% to 92%, and the recurrence rate was 0% to 33%.<sup>22</sup> In one study, 73.6% (134/182) had complete resection after EP, and 15% (16/107) developed recurrence up to 65 months after complete resection.<sup>29</sup> In that study, jaundice at presentation, occult malignant foci in the resected specimen, and intraductal involvement were risk factors for a lower rate of complete resection. However, a high success rate was achieved with a second endoscopic treatment, even in cases with recurrence. Postpapillectomy surveillance is also important after EP, but there is no consensus about the interval, modality, and method of post-EP surveillance. In cases with complete resection of ampullary adenoma, follow-up endoscopy with ERCP and multiple biopsies is recommended at 1, 3, 6, and 12 months after resection, and then at yearly intervals for 5 years on obtaining a negative



**Fig. 5.** Pancreatic duct wire-guided endoscopic papillectomy. (A) Endoscopic view of ampullary adenoma. (B) Endoscopic view depicting a guide wire in the pancreatic duct, a snare sheath introduced over to the guide wire and the papillary adenoma grasped with a snare. (C) Endoscopic view after papillectomy showing a guide wire inserted into the pancreatic duct. (D) Endoscopic view of pancreatic stenting through the guide wire.



**Fig. 6.** Proposed algorithm for the management of ampullary adenoma.

ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; IDUS, intraductal ultrasonography; CIS, carcinoma *in situ*.

biopsy.<sup>20</sup> In cases with incomplete excision, or those in which thermal ablation is performed, endoscopic examination should be performed every 1 to 3 months until complete resection is proven. Cases in which resection shows that patients have focal cancer in the main adenoma or carcinoma *in situ* can be followed with cautious routine endoscopic surveillance.<sup>11,15</sup> However, cases with incomplete resection of cancer should be considered for radical surgery because of the risk of lymph node metastasis (Fig. 6).

## CONCLUSIONS

EP can be a primary effective therapy for ampullary adenoma. Pancreatic stent insertion is highly recommended to prevent severe pancreatitis, a most dangerous complication. Postprocedure endoscopic surveillance is important to ensure complete resection and decrease the likelihood of recurrence. Techniques of endoscopic removal of ampullary adenoma should be standardized for complete removal and to minimize complications. With further technical development, the indications for EP can be expanded.

## CONFLICTS OF INTEREST

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

## ACKNOWLEDGEMENTS

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