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ENDOLUMINAL SURGERY

# New experience of endoscopic papillectomy for ampullary neoplasms

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## Abstract

**Aim** To establish the clinical value of endoscopic papillectomy for duodenal papillary tumor based on endoscopic and clinical characteristics.

**Patients and methods** This single-center, retrospective study included 110 patients with duodenal papillary tumor who underwent endoscopic papillectomy between January 2006 and April 2017 at the gastrointestinal endoscopic center of the Chinese PLA General Hospital. Clinical data, postoperative pathology, procedure-related complications, and therapeutic outcomes were analyzed.

**Results** Endoscopic papillectomy was technically feasible in all patients, and was mainly performed by four experienced endoscopists. The primary success rate of endoscopic papillectomy for ampullary neoplasms was 78.2%. A total of 13 patients experienced recurrence during a mean follow-up period of 16.28 months (range 6–132 months), the predictive factors that were related to recurrence were complete resection (53.8% vs. 94.2%; $P=0.001$), and final pathology findings ($P=0.001$). Delayed hemorrhage, the most common procedure-related complication, occurred in 20% (22/110) of patients and was significantly related to intraoperative bleeding ($P=0.042$). Pancreatitis was the second most common complication, which was closely related to intraoperative bleeding requiring intervention ($P=0.040$) and larger tumor size ($P=0.044$). Histology, type of resection, stent placement, sphincterotomy, and duration of procedure were not related to post-procedure hemorrhage or pancreatitis. Older age ($63.7\pm13.5$ vs. $57.4\pm12.2$; $P=0.033$), jaundice (47.8% vs. 13.8%; $P=0.001$), endoscopic forceps biopsy diagnosis of high-grade intraepithelial neoplasia (82.6% vs. 14.9%; $P=0.001$), tumor size $\geq 2$ cm (60.9% vs. 34.5%; $P=0.022$), and dilation of the bile duct (34.8% vs. 9.2%; $P=0.006$) were clinical features for ampullary carcinoma. The rate of complete resection (52.2% vs. 92.0%; $P=0.001$) and recurrence (34.8% vs. 6.8%; $P=0.001$) were also related to the diagnosis of ampullary carcinoma at final pathology.

**Conclusions** Endoscopic papillectomy is a feasible and reasonable option for both diagnosis and treatment of tumors of the duodenal papilla in properly selected patients.

**Keywords** Endoscopy · Duodenal papilla · Neoplasm · Lesion · Pathology

Ampullary neoplasms are uncommon among digestive tract neoplasms [1], and can be asymptomatic. However, with the wider application of esophagogastroduodenoscopy (EGD) and other advanced imaging techniques, duodenal papillary tumors are now more frequently identified at an early stage [2]. Ampullary adenomas with malignant potential are among the most common types of tumors that may arise in the ampullary region [3], and because of their malignant potential, they should be removed quickly. The traditional treatment of duodenal papillary tumors has been laparotomy, including local resection or pancreaticoduodenectomy (Whipple procedure) [4]. While complete removal is possible with these techniques, they are invasive and have been associated with relatively high mortality and morbidity rates [5, 6]. Endoscopic papillectomy is now accepted as a relatively safe and minimally invasive alternative to surgery for the treatment of duodenal papillary tumors in select patients [7, 8]. However, the indication for endoscopic papillectomy is not uniformly established, and the proper selection of patients may be confounded by endoscopic forceps biopsy,

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which has been criticized as inaccurate. The diagnostic accuracy rate of endoscopic forceps biopsy ranges from 62 to 85%, with a relatively high false-negative rate [9–13], which may lead to the erroneous choice of endoscopic papillectomy for the treatment of some ampullary adenomas. Currently, there are few studies that discuss the factors related to malignancy in the endoscopic papillectomy specimen after a biopsy diagnosis of benign. Significantly, the indications for endoscopic papillectomy can be well established by studying the clinical features related to malignancy in the endoscopic papillectomy specimen.

In the present study, we aim to investigate the clinical value of endoscopic papillectomy for duodenal papillary tumor based on endoscopic and clinical characteristics and follow-up results, with a particular emphasis on the pathological findings and risk factors for complications and recurrence, providing a basis for the uniform clinical application of endoscopic papillectomy.

## Patients and methods

### Patients

Between January 2006 and April 2017, a total of 110 patients with duodenal papillary tumor underwent endoscopic papillectomy at the Gastrointestinal Endoscopic Center of the Chinese PLA General Hospital. These cases were reviewed retrospectively. Patients were diagnosed with duodenal papillary tumor by clinical manifestations, laboratory tests, computed tomography (CT), magnetic resonance cholangiopancreatography, endoscopy, endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP), and biopsy, and histopathologic results. Patients with these indications (1) the surface of the papilla is smooth and the pathology is benign, regardless of size and (2) the surface is not smooth, but looks like a villous tubular adenoma, and is pathologically confirmed, regardless of size, were included. All of the patients were aware of the option for endoscopic or surgical treatment, and patients with surgical indications but who refused surgery were also included in the study. EUS or intraductal ultrasound and ERCP were performed before endoscopic papillectomy to assess the location, extent and depth of tumor, and depth of ductal invasion of the tumor before endoscopic papillectomy. Patients with lesions deemed unresectable because of the tumor extends into the biliary common duct for more than 10 mm, lymph node invasion, distant metastasis, or coagulopathy were excluded. Clinical data and therapeutic outcomes were analyzed. Ethical approval was received from the Regional Ethics Committee of the Chinese People's Liberation Army General Hospital, and written informed consent was obtained from all patients.

### Endoscopic papillectomy

Endoscopic papillectomy was mainly performed by four experts who were experienced in ERCP. Prophylactic antibiotics were given to all patients, and all papillectomies were performed with patients under intravenous anesthesia. The duodenoscope (TJF-240/TJF-260V; Olympus, Tokyo, Japan) was advanced to the descending portion of the duodenum, and the morphology of the duodenal papilla was inspected carefully. Where necessary, dilute epinephrine (1:10,000) was injected into the submucosa to elevate the lesion before resection. A snare device (SD-7P-1/SD-221L-25; Olympus, Tokyo, Japan) was inserted via the endoscopic biopsy port, and then, the endoscopist adjusted the snare to securely grasp the lesion, which was then excised by using standard electrocautery. The goal was en bloc removal, but if this failed, a piecemeal approach was used and argon plasma coagulation (APC) or a polypectomy multipolar probe was used to remove any suspicious residual tissue after resection. A basket or grasper was used to extract the resected specimens. Bleeding at the surgical site was treated with APC (50–60 W) or local injection of 1:10,000 epinephrine, and larger exposed blood vessels and active bleeding sites were clamped with hemostasis clips. Prophylactic pancreatic or biliary stents were inserted at the discretion of the treating endoscopist, and ERCP was then used to ensure adequate pancreatobiliary drainage. Additional surgical treatment was recommended for patients with unresectable residual lesions or final pathology diagnoses of malignancy. Close follow-up was necessary when the final diagnosis was malignancy if the patients do not receive additional surgery, and the choice of treatment ultimately belonged to the patient.

### Follow-up

All patients who were treated by endoscopic papillectomy received follow-up. Reexamination by duodenoscopy and biopsy at 3, 6, 12 months, and every year after endoscopic papillectomy was planned. Related complications, tumor recurrence, and treatment received after recurrence were included in the follow-up. When recurrence was detected in patients with malignancies, surgery was recommended, while repeat endoscopic excisions were recommended for recurrence of nonmalignant tumors, unless the lesions were unresectable because of extensive intraductal involvement.

### Definitions

Tumor classification after endoscopic forceps biopsy and endoscopic papillectomy was based on the Vienna classification of gastrointestinal epithelial neoplasia [14]. TNM stage

of ampullary carcinoma was recorded according to the classification of the eighth edition AJCC cancer staging manual. Complete resection of ampullary adenomas was confirmed when no residual tissue was found at the 3-month follow-up endoscopy and endoscopic forceps biopsy. Endoscopic success was defined as complete resection of the lesion was achieved without residual tumor tissue and when no recurrence was evident at the 6-month follow-up after endoscopic papillectomy. Recurrence was defined as discovery of a lesion after the most recent negative surveillance endoscopy or endoscopic biopsy. Post-endoscopic papillectomy pancreatitis was defined as a threefold increase in pancreatic enzymes with abdominal pain [15], and delayed hemorrhage was defined by hematemesis or hematochezia with a progressive decrease in hemoglobin when patients returned to the ward after finishing endoscopic papillectomy.

### Statistical analysis

All statistical analyses were performed with the Statistical Package for the Social Sciences version 19.0 (SPSS 19.0). Mean and standard deviation was used to describe continuous variables and simple proportions were used to describe dichotomous variables. Clinical feature and risk factors of adenoma combined with carcinoma, complication, and recurrence were evaluated by independent Student's *t* test, Chi square test, and if appropriate, Fisher's exact test was used. A statistically significant difference was indicated by $P < 0.05$.

## Results

The baseline characteristics of patients are presented in Table 1. A total of 110 patients (79 men and 31 women) with a mean age of 58.7 ± 12.7 years (range 32–89) were included.

**Table 1** Baseline characteristics of patients

| | *N* (%) (*n* = 110) |
|---|---|
| Age, mean (± SD) (years) | 58.7 ± 12.7 (32–89) |
| Gender, male/female | 79:31 |
| Clinical presentation | |
| Incidental finding | 32 (29.1%) |
| Abdominal discomfort | 55 (50%) |
| Jaundice | 23 (20.9%) |
| Associated diseases | |
| History of cholecystectomy | 9 (8.2%) |
| Cardiovascular disease | 37 (33.6%) |
| Diabetes | 14 (12.7%) |
| Duration of hospital stay (day) | 16.28 ± 6.67 (1–36) |
| Follow-up period (month) | 57.72 ± 41.60 (6–132) |

Ampullary neoplasms were asymptomatic in 32/110 (38%) patients and were found incidentally during EGD for other reasons. Predominant symptoms were abdominal discomfort and jaundice, reported in 55 (50%) and 23 (20.9%) patients, respectively. The mean length of hospital stay and mean follow-up period were 16.28 ± 6.67 (1–36) days and 57.72 ± 41.60 (6–132) months. Endoscopic papillectomy was performed successfully in all of the patients. En bloc resection was achieved in 83 patients (75.5%) and piecemeal resection was performed in 27 (24.5%). Prophylactic pancreatic duct stent was placed in 33 (30%) patients, biliary plastic stent was placed in 24 (21.8%) patients, and combined stents were placed in 15 (13.6%) patients; there was no stent placement in 38 (34.5%) cases. Intraoperative bleeding occurred in 64 cases (58.2%) and was mainly controlled by endoscopic clip placement, followed by injection therapy, thermal therapy, or a combination. The majority of excised tumors were exogenous (96/110; 87.3%), and the mean tumor size was 18.9 ± 9.0 mm (range 5–55 mm) (Table 2).

### Clinical feature for malignancy

The final histopathological diagnosis was adenoma with low grade intraepithelial neoplasia in 58 patients (52.7%),

**Table 2** Endoscopic therapy

| | *N* (%) (*n* = 110) |
|---|---|
| Types of resection | |
| En bloc | 83 (75.5%) |
| Piecemeal | 27 (24.5%) |
| Complete resection | 88 (80.0%) |
| Sphincterotomy | 50 (45.5%) |
| Hemostasis | |
| Titanium clip | 45 (40.9%) |
| APC | 21 (19.1%) |
| Epinephrine injection | 21 (19.1%) |
| Stents implantation | |
| Pancreatic stent | 33 (30.0%) |
| Biliary stent | 24 (21.8%) |
| Double stents | 15 (13.6%) |
| The mean size of tumor (mm) | 18.9 ± 9.0 (5–55) |
| Pathological findings | |
| Inflammation | 2 (1.8%) |
| Adenoma with LIGN | 58 (52.7%) |
| Adenoma with HIGN | 24 (21.8%) |
| Carcinoma | 23 (20.9%) |
| Others | 3 (2.7%) |

Others include one case of angiolymphoma and two cases of neuroendocrine tumor, respectively.

*APC* argon plasma coagulation, *LIN* low grade intraepithelial neoplasia, *HIN* high-grade intraepithelial neoplasia

adenoma with high grade intraepithelial neoplasia in 24 (21.8%), carcinoma in 23 (20.9%), hyperplastic polyp in 2 (1.8%), neuroendocrine tumor in 2 (1.8%), and one case of lymphangioma. Based on these results, the diagnostic accuracy of endoscopic forceps biopsy before endoscopic papillectomy was 68.2% (75/110), with underestimated diagnosis in 30.9% (34/110) (Table 3). The mean age of patients with malignant tumors was higher than that of patients with benign lesions (63.7 ± 13.5 vs. 57.4 ± 12.2; $P = 0.033$). Patients with tumor size ≥ 2 cm had a higher rate of malignancy (60.9% vs. 34.5%, $P = 0.022$). Patients who presented with jaundice (47.8% vs. 13.8%; $P = 0.001$) and dilated bile duct (34.8% vs. 9.2%; $P = 0.006$) were also more likely to have malignancy in the endoscopic papillectomy specimen (Table 4). Furthermore, the diagnostic accuracy rate by endoscopic forceps biopsy before endoscopic papillectomy were improved up to 89.5% when the pathologic diagnosis were combined with these factors (Table 5). The rates of complete resection (52.2% vs. 92.0%; $P = 0.001$) and recurrence (34.8% vs. 6.8%; $P = 0.001$) were significantly different between patients with malignant and benign lesions. There was no correlation between malignancy and gender, post-endoscopic papillectomy complications, length of hospital stays, or procedure time (Table 4).

**Table 3** Comparison of pathologic results between first endoscopic biopsy and final diagnosis

| Endoscopic forceps biopsy | Final pathologic results | | |
|---|---|---|---|
| | Inflammation (2) | Adenoma (82) | Carcinoma (23) |
| Inflammation (12) | 1 | 9 | 2 |
| Adenoma (94) | 1 | 73 | 20 |
| Carcinoma (1) | 0 | 0 | 1 |

**Table 5** Analysis of pathological diagnosis coincidence rate combined with clinical feature of carcinoma

| | Pathological diagnosis | |
|---|---|---|
| | Diagnostic accuracy ($n = 75$) | Underestimated diagnosis ($n = 34$) |
| Age (years) | | |
| ≥ 65 | 22 (57.9%) | 15 (39.5%) |
| < 65 | 53 (73.6%) | 19 (26.4%) |
| Jaundice | | |
| Yes | 10 (43.5%) | 12 (52.2%) |
| No | 65 (74.7%) | 22 (25.3%) |
| Bile duct dilatation | | |
| Yes | 4 (25.0%) | 12 (75.0%) |
| No | 71 (75.5%) | 22 (23.4.5%) |
| Size (mm) | | |
| ≥ 20 mm | 25 (56.8%) | 18 (40.9%) |
| < 20 mm | 50 (75.8%) | 16 (25.2%) |
| Combination of age, jaundice, bile duct dilatation, size | | |
| Yes | 41 (56.9%) | 30 (41.7%) |
| No | 34 (89.5%) | 4 (10.5%) |

## Complications

Procedure-related complications occurred in 39/110 (35.5%) patients. Delayed bleeding was the most common adverse event, occurring in 22 patients (20.0%), including 19 who required endoscopic hemostasis and 3 who required conservative treatment only. Pancreatitis was the second most common complication (13/110; 11.8%), followed by

**Table 4** Univariate analysis of final pathological findings of adenoma combined with carcinoma' risk factors

| | Final pathological findings | | *P* |
|---|---|---|---|
| | Malignancy ($n = 23$) | Benign ($n = 87$) | |
| Age, mean (± SD) (years) | 63.7 ± 13.5 (33–83) | 57.4 ± 12.2 (32–89) | 0.033 |
| Gender (M:F) | 15:8 | 64:23 | 0.429 |
| Jaundice | 11 (47.8%) | 12 (13.8%) | 0.001 |
| Bile duct dilatation | 8 (34.8%) | 8 (9.2%) | 0.006 |
| Preprocedural HGIN | 19 (82.6%) | 13 (14.9%) | 0.001 |
| Size (mm) | | | 0.022 |
| < 20 | 9 (39.1%) | 57 (65.5%) | |
| ≥ 20 | 14 (60.9%) | 30 (34.5%) | |
| Complete resection | 12 (52.2%) | 80 (92.0%) | 0.001 |
| Postoperative complications | 8 (34.8%) | 31 (35.6%) | 0.940 |
| Operation time | 45.5 ± 31.5 (20–155) | 36.0 ± 16.8 (10–90) | 0.187 |
| Hospital stays | 16.6 ± 6.9 (5–27) | 16.1 ± 6.7 (5–36) | 0.756 |
| Recurrence | 8 (34.8%) | 6 (6.8%) | 0.001 |

*HGIN* high-grade intraepithelial neoplasia

**Table 6** Complications of endoscopic papillectomy and management

| | *N* | Management |
|---|---|---|
| Short-term complication | | |
| Pancreatitis | 13 (11.8%) | Drug |
| Bleeding | 22 (20%) | 3 drug/19 endoscopic hemostasis |
| Perforation | 3 (2.7%) | 1 surgery/2 endoscopic treatment |
| Cholangitis | 8 (7.3%) | Drug |
| Long-term complication | | |
| Papillary stenosis | 2 (1.8%) | Balloon dilation & stent placement |
| Mortality | 0 (0%) | |

**Table 7** Univariate analysis of endoscopic papillectomy complications' risk factors

| | Bleeding (*P*-value) | Pancreatitis (*P*-value) |
|---|---|---|
| Age | 0.762 | 0.229 |
| Gender | 0.767 | 0.721 |
| Type of resection | 1.000 | 0.251 |
| Pancreatic stent | 0.149 | 0.817 |
| Sphincterotomy | 0. 125 | 0.070 |
| Hemostasis | 0.042 | 0.040 |
| Tumor size | 0.117 | 0.044 |
| Final pathological findings | 0.210 | 0.359 |
| Hospital stays | 0.002 | 0.132 |
| Operative time | 0.147 | 0.586 |

cholangitis (8/110; 7.3%), and all of these patients recovered with conservative management. Two patients (1.8%) developed papillary stenosis and were treated by endoscopic stent implantation or balloon dilation and one patient had a perforation that required surgical management. There was no mortality (Table 6). There was no correlation between postoperative hemorrhage and pancreatitis with age, gender, pathology, sphincterotomy, type of resection, or time of procedure ($P > 0.05$). Delayed bleeding was associated with intraoperative bleeding ($P = 0.042$) and length of hospital stay ($P = 0.002$), with delayed bleeding occurring in up to 77.3% of patients who had intraoperative bleeding. Interestingly, interventions for intraoperative hemorrhage were also closely related to pancreatitis ($P = 0.040$). Furthermore, pancreatitis was not related to the use of pancreatic duct stent ($P = 0.817$) but was related to the specimen size ($P = 0.044$) (Table 7).

### Recurrence and related risk factors

The primary success rate of endoscopic papillectomy for duodenal papillary tumors was 78.2%. Eleven patients had additional surgery after endoscopic papillectomy because of pathological findings of adenocarcinoma or because the tumor could not be completely removed with endoscopic papillectomy. Among the 99 remaining patients, 3 had residual tumor treated with APC. A total of 13 patients experienced recurrence during a mean follow-up period of 16.28 months (range 6–132 months), 92.3% of them occurred before the first 3-year (Table 8). The factors that showed significant correlation with post-endoscopic papillectomy recurrence were un-completed resection ($P = 0.001$) and final pathology diagnosis ($P = 0.001$), but not the gender, age, alcohol or tobacco use, tumor size, jaundice, or type of resection. Preprocedural biopsy detected high-grade intraepithelial neoplasia in 53.8% of patients with recurrence, much more than in the non-recurrence group, but the difference was not statistically significant (Table 9). 8 of the 13 patients with recurrence underwent surgical resection and 5 had repeat endoscopic treatment. Among the 23 patients who were finally diagnosed as carcinoma, a total of 8 patients received additional surgery after endoscopic papillectomy, including 2 patients with stage T1a, one patient with stage T1b and 5 patients with stage T2. The other 15 patients rejected immediate surgery and accepted the protocol of follow-up that surgery is the delayed option once the malignant tissue recurrent during the follow-up period. Among the 15 follow-up patients, only one patient was found to have local lymph node metastases, no distant metastasis was detected in any patient. None of the patients with stage T1a experienced recurrence. However, 75.0% patients with stage T1b had recurrence. Two patients with stage T2 both experienced recurrence after endoscopic papillectomy.

## Discussion

Traditional surgery, including pancreaticoduodenectomy (Whipple procedure) and local surgical resection, can treat the duodenal papillary tumor and reduce the risk of recurrence. However, increased postoperative mortality and morbidity, decreased quality of life, and longer hospitalization

**Table 8** Recurrence time and percentage of all recurrent patients occupied by recurrent patients

| Follow-up period | 1 year | ≤2 years | ≤3 years | ≤4 years | ≤5 years |
|---|---|---|---|---|---|
| Recurrence percentage (%) | 3/13 (23.1%) | 8/13 (61.5%) | 12/13 (92.3%) | 12/13 (92.3%) | 13/13 (100%) |

**Table 9** Statistical analysis of risk factors of recurrence

| Characteristics | Recurrence | | P |
|---|---|---|---|
| | No ($n=86$) | Yes ($n=13$) | |
| Gender (M: F) | 64:22 | 8:5 | 0.524 |
| Age, mean ± SD (year) | 59.2 ± 12.1 | 60.8 ± 14.1 | 0.660 |
| Tumor size, mean ± SD (mm) | 18.4 ± 9.2 | 19.1 ± 8.3 | 0.971 |
| Drinking | 14 (16.3%) | 2 (15.4%) | 1.000 |
| Smoking | 11 (12.8%) | 2 (15.4%) | 1.000 |
| Jaundice | 15 (17.4%) | 3 (23.1%) | 0.916 |
| Preprocedural HGIN | 21 (24.4%) | 7 (53.8%) | 0.062 |
| Resection | | | |
| En bloc | 68 (76%) | 9 (67%) | 0.662 |
| Piecemeal | 18 (24%) | 4 (33%) | |
| Complete resection | 81 (94.2%) | 7 (53.8%) | 0.001 |
| Final histology (%) | | | 0.001 |
| Benign | 79 (91.9%) | 6 (46.2%) | |
| Malignancy | 7 (8.1%) | 7 (53.8%) | |
| Bile duct dilatation | 9 (10.5%) | 3 (23.1%) | 0.399 |

*HGIN* high-grade intraepithelial neoplasia

are unacceptable for patients with early-stage papillary neoplasms. Endoscopic papillectomy for the treatment of duodenal papillary tumor, as a minimally invasive technique, has been reported to be a relatively safe procedure and has been accepted as an alternative approach to surgery [7, 8], and the primary success rate of 78.2% for endoscopic papillectomy for duodenal papillary tumors in this study. However, a major concern is that the indications for endoscopic papillectomy have not yet been uniformly established.

Endoscopic forceps biopsy diagnosis of adenoma with high-grade dysplasia has generally been regarded as an indication for surgery [16, 17]. In this present study, although patients with pre-procedural diagnoses of high-grade dysplasia accounts for 53.8% of patients had a recurrence during follow-up, the difference was not statistically significant. Rather, there was significant correlation between incomplete resection and recurrence and between the pathology diagnosis after endoscopic papillectomy and recurrence. Specifically, a final pathology diagnosis of ampullary carcinoma or incomplete resection should prompt more rigorous follow-up to promote immediate detection of recurrences. Interestingly, a total of seven patients with pathology diagnoses of adenoma combined with local carcinoma did not experience recurrence during the follow-up period, including five patients with stage T1a and two patients with stage T1b. Furthermore, none of the patients with stage T1a experienced recurrence in follow-up patients, which suggests that endoscopic papillectomy can be an option in T1a ampullary carcinoma without local lymphatic metastasis or distant metastasis. Indication for stage T1b still required further exploration and close follow-up was necessary. Surveillance during follow-up is also critically related to outcomes after endoscopic papillectomy. A post-endoscopic papillectomy surveillance period of at least 2 years has been proposed [18, 19]. However, we found that the recurrent patients at 2 years occupied 61.5% of all recurrent patients and there were 38.5% patients lost. In the present study, 92.3% of the recurrent patients could be found at 3 years. Therefore, we recommend that post-endoscopic papillectomy surveillance should continue for at least 3 years, and, when possible, we suggest surveillance for as long as 5 years.

Despite the therapeutic potential endoscopic papillectomy, procedure-related complications should also be taken into consideration. The unique physiology and intricate anatomy around the major papilla, which has a thin, highly vascular wall and is the site of the confluence of the pancreatic and biliary duct orifices, increases the risk of bleeding, pancreatitis, perforation, and other complications after endoscopic papillectomy, and operators must bear in mind the safety of endoscopic papillectomy. In our study, procedure-related complications occurred in 35.5% patients, and all complications but one (a duodenal perforation requiring surgical treatment) were controlled by conservative measures or endoscopic intervention. Delayed hemorrhage, which was the most common procedure-related complication, occurred in 20% of patients and was associated with intraoperative bleeding. This suggests that intraoperative bleeding should be treated more effectively and reliably. Furthermore, patients with intraoperative bleeding during endoscopic papillectomy should be closely monitored for signs of delayed hemorrhage after the procedure. The second most common complication was pancreatitis, and, contrary to previous research [20–22], in our study, stenting of the pancreatic duct did not decrease the risk of post-endoscopic papillectomy pancreatitis. This may be related to the fact that the pancreatic stent was not routinely implanted after the papillectomy at the beginning of the study. Later, we routinely implanted a stent in the pancreatic duct. Of note, we found that interventions for intraoperative bleeding were closely related to pancreatitis, which we have not seen in other reports. A possible reason for this result is that the pancreatic duct orifice may be affected by these interventions, which include endoscopic clip placement, injection therapy, and thermal therapy, resulting in poor circulation of pancreatic juice. Larger tumor size also increased the risk of pancreatitis. The greater the tumor, the higher the risk of surgery, and the greater the manipulation around the orifice of the pancreatic duct, thus affecting the pancreatic opening and pancreatic juice outflow. This is why we routinely implanted the stent in the pancreatic duct afterwards. Therefore, these patients should also be carefully monitored for pancreatitis after endoscopic papillectomy.

Accurate biopsy diagnosis is of paramount importance when considering tumor resection with endoscopic

papillectomy, and endoscopic papillectomy is also a useful method of diagnosis, particularly as accurate diagnosis by endoscopic forceps biopsy remains challenging. Tissue specimens obtained by routine endoscopic forceps biopsy may be inadequate and malignant cells may be missed. In this study, the rate of diagnostic coincidence between endoscopic forceps biopsy and the final specimen pathology after endoscopic papillectomy was 71.0%, similar to that reported previously (62–85%) [9–13]. There were 22 patients with initial biopsy findings of inflammation or adenoma who had final pathology diagnoses of ampullary carcinoma. Where deeper carcinomas cannot be diagnosed by routine endoscopic forceps biopsy, endoscopic papillectomy can be useful for obtaining sufficient tissue for complete histopathologic examination, thus overcoming the limitations of forceps biopsy [12] and promoting more accurate diagnosis and better treatment planning for duodenal papillary tumors. Thus, duodenal papillectomy is not only a therapeutic method, but also plays a diagnostic role. This is why we have expanded the indications for duodenal papillectomy, from 1 to 2 cm. The correlation between malignancy in the endoscopic papillectomy specimen and older age, jaundice, dilated bile duct, and tumor size $\geq$ 20 mm also suggest that these factors are strong indicators of malignancy and may contribute to the establishment of uniform clinical applications of endoscopic papillectomy. Furthermore, the diagnostic accuracy rate by endoscopic forceps biopsy before endoscopic papillectomy has a certain degree of improvement when combined with these factors. Finally, complete resection and recurrence were also related to endoscopic papillectomy diagnosis of malignancy.

In summary, endoscopic papillectomy can be regarded as a feasible and reasonable treatment option for suitable patients with tumors of the duodenal papilla. Endoscopic papillectomy is of paramount importance for treatment as well as for accurate diagnosis. Older age, jaundice, tumor size $\geq$ 2 cm, and dilation of the bile duct were associated with malignancy, and these characteristics must be evaluated carefully before endoscopic papillectomy. Furthermore, the safety of endoscopic papillectomy must be considered, because the rate of procedure-related complications is relatively high although most of them can be controlled under endoscopy. The complication rate was higher in patients who required intraoperative intervention for hemorrhage, and such patients should be closely monitored for post-endoscopic papillectomy pancreatitis and bleeding. Complete resection and pathology results of endoscopically resected specimens were strong predictors of endoscopic success. Long-term surveillance after endoscopic papillectomy is mandatory, and we recommend that surveillance should continue for at least 3 years if 5 years is difficult. Additional multicenter studies with larger numbers of patients will be needed to confirm our results.

**Author contributions** Wen Li and Shuling Li made contributions to the conception and design the study; the procedure was performed by Wen Li, Zikai Wang, Fengchun Cai, Enqiang Linghu, Gang Sun, Xiangdong Wang, Jiangyun Meng, Hong Du, Yunsheng Yang. Data were collected and analyzed by Shuling Li. The manuscript was drafted by Shuling Li, revised by Wen Li.

## Compliance with ethical standards

**Disclosures** Shuling li, Zikai Wang, Fengchun Cai, Enqiang Linghu, Gang Sun, Xiangdong Wang, Jiangyun Meng, Hong Du, Yunsheng Yang, Wen Li declare that they have no conflicts of interest or financial ties to disclose.

**Research involving human and animal participants** This article is a retrospective clinical study.

## References

1. Park SW, Song SY, Chung JB et al (2000) Endoscopic snare resection for tumors of the ampulla of Vater. Yonsei Med J 41(2):213–218
2. Jung MK, Cho CM, Park SY et al (2009) Endoscopic resection of ampullary neoplasms: a single-center experience. Surg Endosc 23(11):2568–2574
3. Stolte M, Pscherer C (1996) Adenoma-carcinoma sequence in the papilla of Vater. Scand J Gastroenterol 31(4):376–382
4. Di Giorgio A, Alfieri S, Rotondi F et al (2005) Pancreatoduodenectomy for tumors of Vater's ampulla: report on 94 consecutive patients. World J Surg 29(4):513–518
5. Yeo CJ, Cameron JL, Sohn TA et al (1997) Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg 226(3):248–257 (**discussion 257–260**)
6. Tran TC, Vitale GC (2004) Ampullary tumors: endoscopic versus operative management. Surg Innov 11(4):255–263
7. Dubois M, Labgaa I, Dorta G et al (2017) Endoscopic and surgical ampullectomy for non-invasive ampullary tumors: short-term outcomes. Biosci Trends 10(6):507–511
8. Ismail S, Marianne U, Heikki J et al (2014) Endoscopic papillectomy, single-centre experience. Surg Endosc 28(11):3234–3239
9. Bellizzi AM, Kahaleh M, Stelow EB (2009) The assessment of specimens procured by endoscopic ampullectomy. Am J Clin Pathol 132(4):506–513
10. Kimchi NA, Mindrul V, Broide E et al. (1998) The contribution of endoscopy and biopsy to the diagnosis of periampullary tumors. Endoscopy 30(6):538–543
11. Yamaguchi K, Enjoji M, Kitamura K (1990) Endoscopic biopsy has limited accuracy in diagnosis of ampullary tumors. Gastrointest Endosc 36(6):588–592
12. Elek G, Gyori S, Toth B et al (2003) Histological evaluation of preoperative biopsies from ampulla vateri. Pathol Oncol Res 9(1):32–41
13. Lee HS, Jang JS, Lee S et al (2015) Diagnostic accuracy of the initial endoscopy for ampullary tumors. Clin Endosc 48(3):239–246
14. Schlemper RJ, Riddell RH, Kato Y et al (2000) The Vienna classification of gastrointestinal epithelial neoplasia. Gut 47(2):251–255
15. Cotton PB, Lehman G, Vennes J et al (1991) Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc 37(3):383–393

16. Kim JH, Kim JH, Han JH et al (2009) Is endoscopic papillectomy safe for ampullary adenomas with high-grade dysplasia? Ann Surg Oncol 16(9):2547–2554
17. Beger HG, Treitschke F, Gansauge F et al (1999) Tumor of the ampulla of Vater: experience with local or radical resection in 171 consecutively treated patients. Arch Surg 134(5):526–532
18. Ahn DW, Ryu JK, Kim J et al (2013) Endoscopic papillectomy for benign ampullary neoplasms: how can treatment outcome be predicted? Gut Liver 7(2):239–245
19. Cheng CL, Sherman S, Fogel EL et al (2004) Endoscopic snare papillectomy for tumors of the duodenal papillae. Gastrointest Endosc 60(5):757–764
20. Napoleon B, Alvarez-Sanchez MV, Leclercq P et al (2013) Systematic pancreatic stenting after endoscopic snare papillectomy may reduce the risk of postinterventional pancreatitis. Surg Endosc 27(9):3377–3387
21. Yamao T, Isomoto H, Kohno S et al (2010) Endoscopic snare papillectomy with biliary and pancreatic stent placement for tumors of the major duodenal papilla. Surg Endosc 24(1):119–124
22. Harewood GC, Pochron NL, Gostout CJ (2005) Prospective, randomized, controlled trial of prophylactic pancreatic stent placement for endoscopic snare excision of the duodenal ampulla. Gastrointest Endosc 62(3):367–370