SURGICAL OUTCOMES OF TRANSDUODENAL AMPULLECTOMY FOR EARLY CANCER OF THE AMPULLA OF VATER: A SINGLE-CENTER STUDY

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ABSTRACT

Background: Transduodenal ampullectomy (TDA) is performed for early cancer of the ampulla of Vater (AoV). This study aimed to analyze the short- and long-term outcomes of TDA.

Methods: Patients who underwent TDA performed for AoV malignancy with carcinoma in-situ (Tis) and T1 stage from August 2017 to February 2025 were reviewed.

Results: Twenty-eight patients with malignant tumors underwent TDA. The mean operation time was 118.6 ± 36.8 min. The median estimated blood loss was 60 (0-700)ml. The median length of hospital stays was 9 (6-22) days. The mean overall complication rate was 14.3 % with postoperative pancreatic fistula was 17.9%. Lymph node metastasis rates were 20%. The overall survival (OS) and disease-free survival (DFS) rate were 52.4 and 51.2 months, respectively.

Conclusion: TDA accompanied with lymph node dissection was advisable in Tis and T1 AoV cancers in view of superior perioperative outcomes and similar long-term survival rates.

Keywords: Transduodenal ampullectomy; ampulla of vater.

1. INTRODUCTION

Carcinoma of the ampulla of Vater (AoV) is the second most common periampullary malignancy after pancreatic cancer, yet it remains a rare disease, representing less than 1% of all gastrointestinal cancers [1]. The scarcity of this condition means that current clinical practices rely on retrospective data and lack standardized guidelines. For ampullary carcinoma, conventional pancreaticoduodenectomy (PD) or pylorus-preserving pancreaticoduodenectomy (PPPD) are the most frequently performed procedures, involving complete removal of the primary tumor and radical lymph node dissection (LND). However, PD is associated with significant complications, including postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), postoperative hemorrhage, and post-pancreatectomy diabetes mellitus [2]. As a result, a less invasive procedure, transduodenal ampullectomy (TDA), has been attempted for early-stage cancers confined to the AoV or sphincter of Oddi (carcinoma in situ or pT1).

The debate over TDA as an alternative to PD in early AoV cancer centers on the radicality of the procedure, which is influenced by the resection margin status and lymph node (LN) metastasis-key prognostic factors for recurrence and long-term survival [2], [3], [4]. Previous studies have

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examined histopathological factors related to LN metastasis [5] as well as patterns of lymphatic spread [4] and recurrence [3] to propose suitable indications for TDA. However, the role of TDA in early AoV cancers remains inconclusive. Despite this, the role of TDA in early AoV cancers remains uncertain. Some centers have performed TDA with LND and achieved oncologic outcomes comparable to PD in early AoV cancer [6]. These findings suggest that TDA with LND could be a viable surgical option for patients who are not candidates for PD. However, the appropriate extent of regional LND is still unclear. Studies on TDA in early AoV cancer have been limited by small sample sizes or short follow-up periods. This study aimed to review and summarize the experience of TDA in a single large-volume center, focusing on its viability as a surgical treatment for early AoV cancer with acceptable clinical and oncologic outcomes.

2. METHODS

2.1. Patient and data collection

In this retrospective study, we reviewed and analyzed a prospectively maintained database of patients with AoV cancer who underwent TDA at our hospital, between August 2017 and February 2025.

Clinical and pathological characteristics such as age, sex, tumor size, pathologic T stage, LN metastasis, and differentiation were retrieved, along with data on perioperative and long-term patient outcomes. The pathologic stage was defined according to the seventh edition of the American Joint Committee on Cancer (AJCC) staging system. Low-grade dysplasia was considered benign and high-grade dysplasia was regarded as Tis according to the current World Health Organization classification. Complications were graded using Clavien-Dindo (CD) classification [7]. CD grade C III was considered severe. Clinically relevant POPF (CR-POPF) and DGE were defined and graded according to the International Study Group of Pancreatic Surgery [8]. This retrospective study was approved by the Ethical Review board of our hospital.

2.2. Indication and procedure

Inclusion Criteria:

- Endoscopic papillectomy (EP) was contraindicated (e.g., bile duct and/ or pancreatic duct involvement).

- Failure of EP (incomplete tumor removal or recurrence).

- Patients unwilling to undergo PD for various reasons such as advanced age, uncontrolled hypertension, diabetes mellitus, bronchial asthma, cardiovascular conditions, etc.

- Preoperative diagnosis of adenocarcinoma of the Vater ampulla (cTis-1N0M0) according to the AJCC TNM staging system (2017), based on preoperative imaging modalities like computed tomography (CT), magnetic resonance imaging (MRI), or endoscopic ultrasonography.

Operative technique: (Figure 1).

- The patient was positioned supine under general anesthesia. Make a 20 cm midline incision. Observe the peritoneum to assess tumor invasion, suspected lymph nodes, and metastases.

- Cholecystectomy and Kocher maneuver to mobilize the duodenum and head of the pancreas from the retroperitoneum.

- Making an incision at the second part of duodenum (D2). Total excision of the ampulla of Vater included part of the pancreatic head, duodenum, and distal common biliary duct with electrocauterization. Frozen resection to determine resection border.

- Suture to anastomose the duct to the duodenum and close the duodenal excision with continuous absorbable 4/0 suture. Care was made when suturing far from the pancreatic duct to avoid belated stenosis.

- Lymph node dissection could be applied in case of suspected malignancy, including lymph nodes at stations 7, 8, 12, 13.

- A gastric tube was used to dilate and ensure no stenosis in the common bile duct. Another gastric tube was pushed down from the mouth to the duodenum for decompressive drainage to prevent post-operative duodenal fistula. Close the duodenal incision.

- Two subhepatic drains were placed. Hemostasis. Close the abdomen.

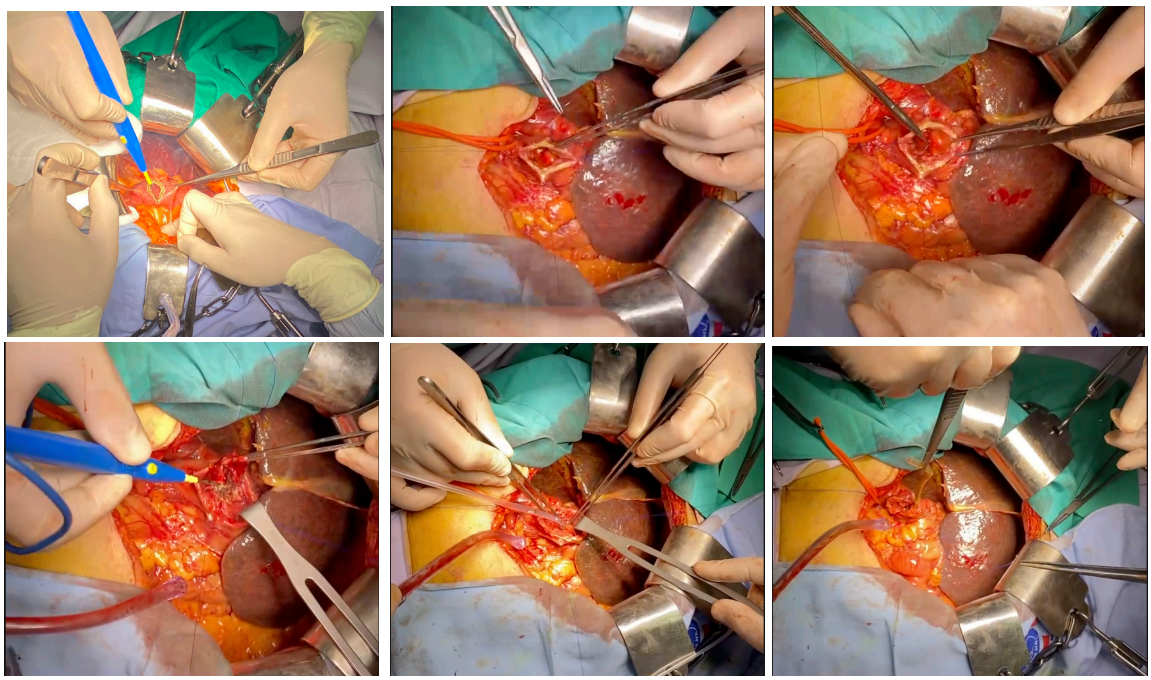

Fig. 1. *(1) After Kocher maneuver, make a transverse incision at D2 over the lesion. (2) Hang the duodenal wall for better exposure. (3) Suture to hang the ampullary lesion. (4) Cut the lesion, including part of the duodenum, distal common bile duct and pancreatic head. (5) Gastric tube for bile duct dilation to ensure no stenosis. (6) Decompressive nasal gastric tube to D2 duodenum. (7) Lymph node dissection.*

2.3. Statistical analyses

The Cox proportional hazards model was used to determine independent predictors of recurrence. Univariate analysis was performed for age, sex, tumor size, type of operation, intraoperative transfusion, T-stage, LN metastasis, lymphovascular invasion, perineural invasion, and adjuvant therapy. Variables with $p < 0.05$ were included for multivariate analysis. Disease-free survival (DFS) was defined as the time between the date of surgery and date of local or distal recurrence and censored at last follow-up or death irrelevant to cancer recurrence. Overall survival (OS) was calculated from the date of operation to the date of death. Patients not experiencing the relevant endpoint were censored at the last follow-up. Five-year OS was calculated using the Kaplan-Meier method, and differences were examined using the log-rank test. Data analyses were performed using SPSS 25.0

software (SPSS, Chicago, IL). A p-value of < 0.05 was considered statistically significant.

3. RESULTS

From August 2017 to February 2025, 28 patients at our hospital underwent TDA for ampullary cancer, excluding cases with other organ malignancies, history of TDA, M1 disease, preoperative chemotherapy, combined pancreatic malignancy, adenoma/low-grade dysplasia histology, T2-T4 stage, other pathology classifications.

Patient and tumor characteristics of the TDA cases for malignant AoV tumors

Table 1 shows the clinicopathological findings after TDA for malignant ampullary tumors (pTis, T1). LND was performed in 53.6% (15 of 28) of patients with 20% (3 cases) showing positive LN involvement. The rate of lymphovascular and perineural invasion were 17.9% and 7.1%, respectively.

Perioperative outcomes after TDA for malignant AoV tumors

According to Table 2, the TDA patients had significantly short surgery durations and hospital stays. Additionally, the TDA group experienced considerably less blood loss. Only one patient needed a blood transfusion during surgery. The overall complication rate was 14.3% while severe complications were 7.1%. There was no deaths within 90 days post-surgery.

Long-term outcomes after TDA for malignant AoV tumors

Over a median follow-up period of 23 months (ranging from 1 to 73 months), the recurrence rates was 17.9 %. The overall survival (OS) and disease-free survival (DFS) rate were 52.4 and 51.2 months, respectively (Fig. 2a,b). Based on the presence or absence of LND, showed that LND did not impact the 5-year DFS or OS (Fig. 2c, d).

Table 1. Clinicopathologic findings of the transduodenal ampullectomy (TDA) for malignant ampullary tumors (Tis/T1)

Characteristic	TDA (n = 28)	
Age (years), mean ± SD	62.8 ± 9.1	
Sex, n (%)		
Male	21	(75.0%)
Female	7	(25.0%)
ASA score, n (%)		
1	16	(57.1%)
2	12	(42.9%)
Preoperative endoscopic papillectomy, n (%)		
Yes	7	(25.0%)
No	21	(75.0%)
Preoperative tumor marker, median (range)		
CA 19-9 (U/ml)	173.8	(0.6-1200.0)
CEA (ng/ml)	4.8	(1.6-14.3)

Characteristic	TDA (n = 28)	
Tumor size (mm), mean ± SD	17.3 ± 4.6	
T stage (Seventh edition of AJCC)		
pTis	10	(35.7%)
pT1	18	(54.3%)
N stage (Seventh edition of AJCC)		
pN0	25	(89.3%)
pN1	3	(10.7%)
Stage (Seventh edition of AJCC)		
0	9	(32.1%)
I	10	(35.8%)
IB	9	(32.1%)
Differentiation		
Well	6	(21.4%)
Moderate	15	(53.6%)
Poor	3	(10.7%)
NA	4	(14.3%)
Lymphovascular invasion		
Yes	5	(17.9%)
No	13	(46.4%)
NA	10	(35.7%)
Perineural invasion		
Yes	2	(7.1%)
No	17	(60.7%)
NA	9	(32.1%)

SD, standard deviation; ASA, American Society of Anesthesiologists; Tis, carcinoma in situ; NA, not available.

Table 2. Surgical and oncologic outcomes after transduodenal ampullectomy (TDA) (pTis/T1)

Outcomes	TDA (n = 28)	
Operation time (min), mean ± SD	118.6 ± 36.8	
Estimated blood loss (ml), median (range)	60	(0-700)
Intraoperative transfusion, n (%)		

Outcomes	TDA (n = 28)	
Yes	1	(3.6%)
No	27	(96.4%)
Hospital stays (days), median (range)	9	(6-22)
Complications, n (%)		
Yes	4	(14.3%)
No	24	(85.7%)
Severe complications (CD grade ≥ IIIa), n (%)		
Yes	2	(7.1%)
No	26	(92.9%)
Clinically relevant POPF, n (%)	5	(17.9%)
Grade A	5	(17.9%)
Grade B	0	(0.0%)
DGE (grade ≥ B), n (%)	1	(3.6%)
Duodenal stricture, n (%)	0	(0.0%)
Complicated fluid collection, n (%)	2	(7.1%)
Bleeding, n (%)	2	(7.1%)
Readmission related with complications (<90 days)		
Yes	1	(3.6%)
No	27	(96.4%)
Surgical mortality, n (%)	0	(0.0%)
Recurrence, n (%)		
No	17	(60.7%)
Yes	5	(17.9%)
NA	6	(21.4%)
Local	1	(20.0%)
Systemic	4	(80.0%)
Both	0	(0.0%)
Adjuvant therapy		
No	1	(3.6%)
Yes	27	(96.4%)

SD, standard deviation; CD, Clavien-Dindo classification; POPF, postoperative pancreatic fistula; DGE, delayed gastric emptying.

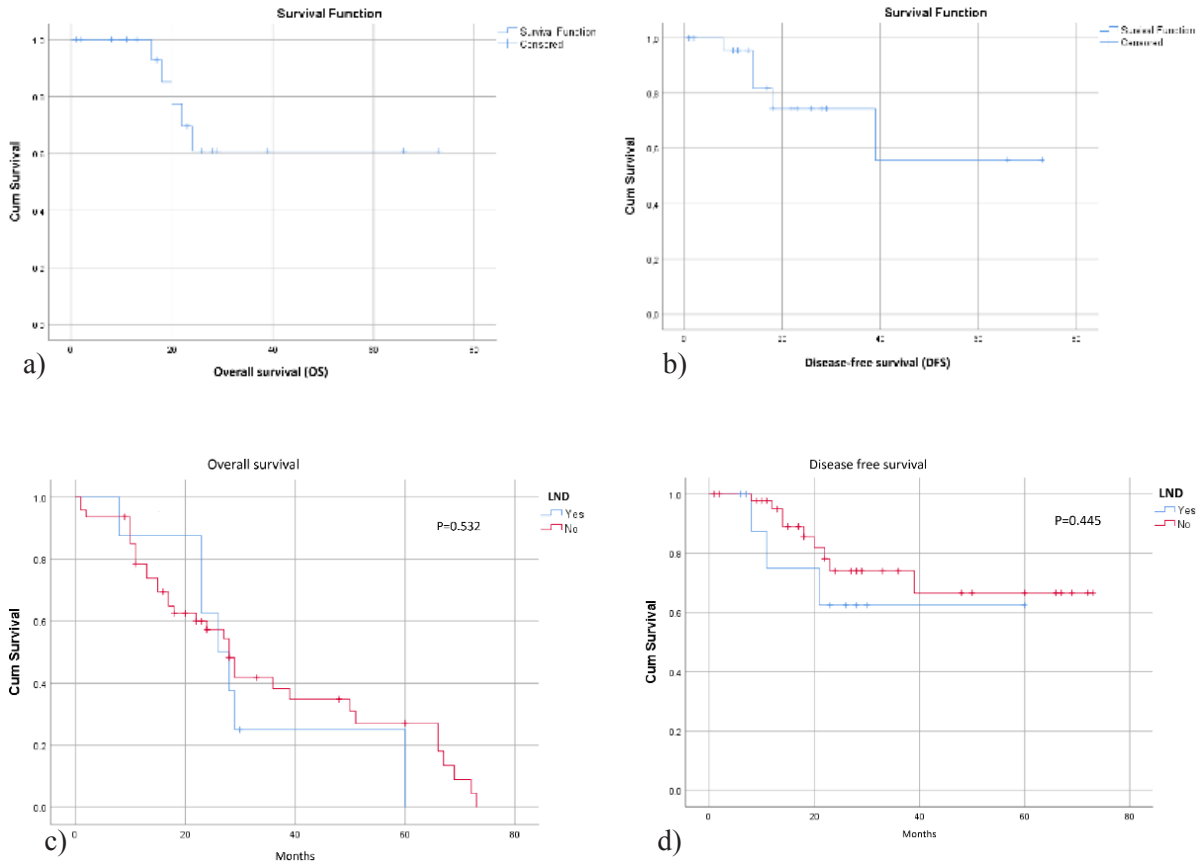

Fig 2. The survival outcomes of patients with malignant ampullary tumors after undergoing TDA. The overall survival (OS) (a) and the disease-free survival (DFS) rates (b) were showed. Additionally, based on whether lymph node dissection (LND) was performed, LND did not impact the 5-year DFS (c) or OS (d).

Risk factors affecting recurrence

Table 3 presents the uni- and multivariate analyses of risk factors influencing recurrence after TDA. Due to the limited patient sample and short follow-up duration, factors such as age, sex, tumor size, intraoperative transfusion, T classification, LN involvement, moderate/poor differentiation, lymphovascular invasion, perineural invasion, and adjuvant therapy were not linked to disease recurrence in the univariate analysis (all $p > 0.05$). In the multivariate analysis, perineural invasion emerged as an independent predictor of recurrence ($p=0.043$), while other factors like intraoperative transfusion, T classification, LN involvement, moderate/poor differentiation, lymphovascular invasion and adjuvant therapy did not show a significant association.

Table 3. Univariate and multivariate analysis of risk factors affecting recurrence in patients with malignant ampullary tumors (pTis/T1) undergoing transduodenal ampullectomy (TDA)

Variable	No	Univariate			Multivariate		
		HR	95% CI	p*	Exp(B)	95% CI	p*
Age, years							
≤ 60	25						
> 60	35	0.441	0.119-1.635	0.221			
Sex							
Male	29						
Female	28	1.226	0.395-3.811	0.724			
Tumor size							
< 18 mm	18						
≥ 18 mm	39	1.710	0.502-5.831	0.391			
Intraoperative transfusion							
No	53						
Yes	4	1.156	0.149-8.962	0.890			
T classification							
pTis	10						
pT1	15	0.408	0.051-3.265	0.398			
LN metastasis							
No	47						
Yes	10	1.656	0.445-6.161	0.452			
Differentiation							
Well	8						
Moderate/Poor	49	1.026	0.224-4.687	0.974			
Lymphovascular invasion							
No	21						
Yes	20	0.291	0.060-1.407	0.125			
Perineural invasion							
No	30						
Yes	14	2.044	0.456-9.162	0.350	0.096	0.010-0.931	0.043
Adjuvant therapy							
No	4						
Yes	40	0.040	0.000-606.610	0.512			

OR odds ratio; CI, confidence interval; Tis, carcinoma in situ; LN, lymph node. *p-values in multivariate analysis are from the Cox proportional hazard model.

4. DISCUSSION

The role of transduodenal ampullectomy (TDA) in the management of ampullary lesions has been a subject of debate, especially in comparison to pancreatoduodenectomy (PD) [9], [10]. TDA, first described by Halsted in 1899, represents a more localized surgical approach compared to the radical resection involved in PD, which was pioneered in its modern form by Whipple in 1940 [6], [9], [11].

Historically, PD became the standard surgical strategy for ampullary cancer [11]. However, PD is associated with a significant rate of postoperative complications, ranging from 33% to 52%. This has led to the application of TDA in patients who may not be suitable candidates for PD due to comorbidities [11].

Several studies, including a Korean multicenter study involving 486 patients, have compared the oncologic outcomes of TDA and PD for early ampulla of Vater (AoV) cancer (pTis-T2 stage) [11]. This study found that while the PPPD (pylorus-preserving pancreatoduodenectomy) group presented with more aggressive tumor behavior (larger size, higher T stage, poorer differentiation, lymphovascular invasion), the 5-year disease-free survival and overall survival did not differ significantly between the two groups when considering all T stages or only the Tis + T1 group. However, in T1 patients specifically, PPPD showed survival outcomes superior to those in the TDA group. Interestingly, lymph node dissection (LND) did not affect survival in the TDA group in this study. The authors concluded that PPPD should be the standard procedure for early AoV cancer.

Another study retrospectively reviewed 43 patients with early ampullary cancer who underwent either TDA or PD between 2001 and 2014 [6]. In this study, routine lymph node resection was performed during TDA. In our research, LND was performed in 53.6% of patients in the TDA group, with 20% showing positive LN involvement. In the PD group, the LN metastasis rate was 21.2%.

Some studies emphasized the role of intraoperative frozen pathological examination was used to confirm negative lymph node metastasis before proceeding with TDA [6]. If local resection criteria were not met, the operation was converted to the radical PD. That is also a limitation in our study due to the lack of equipment.

A systematic review and meta-analysis comparing endoscopic ampullectomy (EA), surgical ampullectomy (SA, which includes TDA), and PD for ampullary lesions found that SA and PD had significantly higher pooled R0 resection rates compared to EA [12]. The pooled R0 rate for SA was 96.4%, while for PD it was 98.9%, and for EA it was 76.6%. However, the rates of adverse events were 28.3% for SA, 44.7% for PD and 24.7% for EA. Recurrence rates were 9.4% for SA, 14.2% for PD, and 13.0% for EA, with no significant differences observed. This meta-analysis indicates that surgical interventions (SA and PD) achieve better complete resection but may be associated with a higher risk of complications, particularly PD. The authors noted significant heterogeneity and limitations in the included studies.

A single-institution study analyzing 60 patients with AoV neoplasms undergoing either TDA (n=23) or PD (n=37) between 2006 and 2020 aimed to compare surgical outcomes and survival [13]. This study found no significant differences in overall survival and recurrence-free survival between the two groups. However, similar to the Korean multicenter study, the PD group had more lymph node metastasis and perineural invasion. The authors suggested that TDA could be considered a feasible option for carefully selected early-stage

AoV cancers (pTis-T1N0M0), especially in patients with comorbidities. They also emphasized that TDA should be accompanied by lymph node dissection, and further research is needed to determine the appropriate extent of LND. In our study, recurrence rates and patterns were similar between the two groups. The 5-year disease-free survival (DFS) rates showed no significant difference between the TDA and PD groups, regardless of the inclusion of T2 cases (Fig. 2a, b).

The technical aspects of TDA involve a duodenotomy, identification and marking of the bile and pancreatic ducts, and circumferential dissection of the ampulla with a margin [9]. Reconstruction involves approximating the ducts to the duodenal wall [10]. Intraoperative frozen section analysis is crucial to ensure negative resection margins and to guide the decision to proceed with TDA or convert to PD if necessary [9].

In our study, over a median follow-up period of 23 months (ranging from 1 to 73 months), the recurrence rates was 17.9%. 3 patients were reoperated while 2 others experienced palliative care.

In conclusion, while PD remains the standard of care for resectable ampullary cancer due to its potentially superior outcomes in certain early-stage tumors and more comprehensive lymphadenectomy, TDA appears to be a viable option for carefully selected early-stage lesions and in patients with significant comorbidities that increase the risk associated with PD [11], [13]. Proper patient selection based on thorough pre-operative staging, including endoscopic ultrasound (EUS), and meticulous surgical technique with intraoperative margin assessment are essential for successful outcomes with TDA [9]. Further prospective, well-designed studies are needed to definitively define the indications for TDA in the modern management of ampullary lesions [10].

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DISCLOSURE

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