

Transduodenal excision of ampullary tumours

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SUMMARY

The commonly recommended treatment for ampullary tumours – pancreaticoduodenectomy results in significant morbidity and mortality. This study is a retrospective evaluation of the procedure of transduodenal local excision of ampullary tumours. Demographics, symptoms, histological findings and outcomes were retrospectively analysed in 15 patients. Survival analysis was done by the method of Kaplan-Meier and log-rank test.

The median age was 68 years (range 54-78). Endoscopic biopsy was accurate in only 41% of cases. CT scan demonstrated a mass in 50% cases. Definitive histology reported 4 adenomas, 2 carcinomas-in-situ and 9 adenocarcinomas. Median hospital stay was 13 days. There was no operative mortality. Mean duration of follow-up was 31 months (range 7-70 months). The procedure appears curative for adenomas and in-situ carcinoma. Overall 3 year actuarial survival for ampullary tumours is 65% while that for moderately differentiated carcinomas is 50%.

Pre-operative investigations provide inadequate histological information. Wide local excision is a safe operation with low morbidity and good survival in carefully selected cases. However, the role of local excision for carcinoma appears to be palliative rather than curative.

INTRODUCTION

Ampullary tumours are uncommon tumours arising from the surface of the papilla of Vater or from the inner epithelial lining of the ampulla itself.¹ Carcinomas of the ampulla of Vater account for approximately 6% of all periampullary tumours.² Villous adenomas of the ampulla have a reported incidence of 0.04-0.12 per cent.³ The reported incidence of malignancy varies widely but seems to be around 25 per cent.^{4,5} It is difficult to get an accurate preoperative histological grading of the tumour.^{1,5} Villous adenomas of the ampulla are considered premalignant and there is controversy regarding optimum surgical management.^{1,4} There are two main surgical options – local, transduodenal excision of the tumour (ampullectomy) or pancreaticoduodenectomy. This study is an evaluation of 15 patients with ampullary tumours who underwent local excision.

PATIENTS AND METHODS

Between April, 1995 and June, 2000 fifteen patients with tumours of the ampulla of Vater

underwent transduodenal excision (TDE). The indications for TDE were either operative feasibility (i.e. tumour small enough macroscopically to allow confident complete local excision) or significant associated co-morbidity preventing a pancreaticoduodenectomy. Patients were identified from the hepatobiliary database and the records were reviewed for clinical presentation, preoperative investigations, surgery, immediate postoperative complications, pathological findings, hospital stay and follow-up.

The histology reports were reviewed with regards to tumour size, resection margins, pancreatic and lymphovascular invasion, the T stage (UICC) and tumour differentiation. Survival analysis was

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done by the method of Kaplan-Meier. Difference in survival between subsets was compared by the log-rank test.

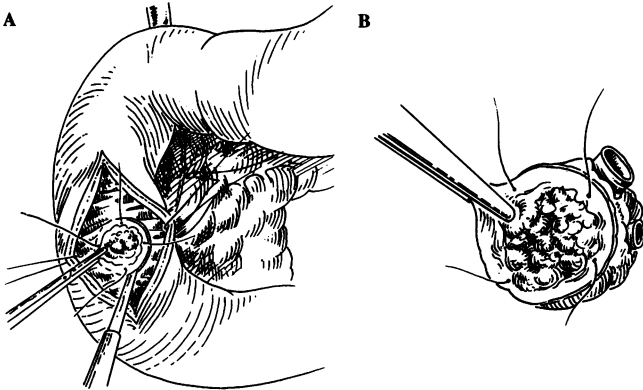


Fig 1. Stay sutures are inserted around the tumour as markers for wide diathermy excision (a) prior to excision of the papilla of Vater, encompassing part of biliary and pancreatic ducts and posterior duodenal wall (b).

Surgical procedure

The procedure involves a transduodenal approach via a longitudinal duodenotomy. Four stay sutures are inserted around the tumour as markers (figure 1a). A wide diathermy excision is performed around the stay sutures to ensure a clear margin. Excision involves a wide resection of the papilla of Vater, encompassing part of the biliary and pancreatic ducts and a part of the posterior duodenal wall (figure 1b). The bile duct and the pancreatic duct are sutured together to form a common septum and both ducts are then re-implanted (figures 2a and b). The duodenotomy is closed. Cholecystectomy is routinely performed to avoid cholecystitis secondary to duodenobiliary reflux. A feeding jejunostomy is routinely inserted to allow enteral nutrition in the immediate post-operative period.

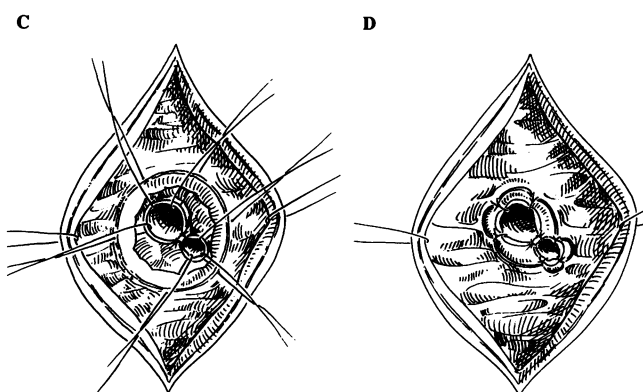


Fig 2. Bile duct and pancreatic duct sutured together to form a common Septum (c) prior to re-implantation in the duodenum (d).

RESULTS

Clinical Features

The clinical presentation, preoperative diagnosis, final pathological diagnosis, complications and outcome are summarized in Table 1. There were 12 males (80%) and 3 females (20%) with a median age of 68 years (range, 54 to 78 years). Ten patients (66%) had jaundice (of these 2 also had rigors). Seven patients (46%) complained of abdominal pain (of these 1 also had backache). In two patients the ampullary tumour was an incidental finding. The first of these (no. 2) was a 78 year old woman, found to have abnormal liver function tests during investigation of cardiac disease. The other was a 70 year old man (no. 13) who was initially admitted with fractured ribs and on examination was also found to have jaundice. One patient presented with haematemesis. One patient (no. 14) was operated on urgently as she was thought to have unresolving jaundice due to bile duct stones. Other presenting features were anorexia (n=4), weight loss (n=4), lethargy (n=3), nausea (n=3), anaemia (n=1) and steatorrhoea (n=1). The duration between onset of symptoms and surgery ranged from 3 to 56 weeks.

Investigations

CT Scan showed an ampullary mass in 6 (50%) of the 12 cases in which it was performed. Ultrasound Scan was performed in 9 patients and revealed a dilated biliary duct system in 8. Preoperative endoscopy was performed in 13 cases and biopsies were taken in 12 patients. Endoscopy was not done in 2 cases – 1 due to delay in surgery while waiting for ERCP and in 1 case jaundice was thought to be secondary to bile duct stones and the patient underwent intraoperative cholangiogram and duct exploration. Three patients were stented preoperatively at ERCP.

Complications and hospital stay

In the immediate post-operative period, one patient developed a subphrenic abscess which was drained percutaneously and one developed a wound infection. There was no postoperative hospital mortality. Median hospital stay was 13 days (range 7-49 days). In the long term, two patients developed incisional herniae and one developed a metastatic skin nodule with no evidence of recurrence intra-abdominally, 34 months after primary excision of ampullary carcinoma-in-situ (no. 6). This nodule was excised and the patient is alive and well at 41 months.

TABLE
Demography, Clinical features, Pathology and outcome

Patient No.	Age, y/sex	Clinical Features	Preoperative Diagnosis	Final Diagnosis T stage/ Differentiation	Complications	Follow-up in months/results
1	72/M	J, Rigors, Lethargy	Adenoma, Severe Dysp.	AdenoCa T2/Moderate	None	17 months, Disease free
2	78/M	Incidental	Adenoma, Severe Dysp	Adenoma, Severe Dysp.	None	70 months, Disease free
3	77/M	P, N, V, W Lethargy,	Adenoma	Adenoma, Severe Dysp.	None	15 months, Disease free
4	69/F	Anaemia	Adenoma, Severe Dysp.	AdenoCa T2/Poor	None	8 months, Disease free
5	65/M	J, P, W, N, V	Inadequate	AdenoCa T1/Poor	None	10 months, Died of local recurrence
6	68/F	J, N	Adenoma, Severe Dysp.	Ca-in-situ	None	41 months, Scar nodule
7	66/M	J	Adenoma	AdenoCa T2/Moderate	Sub-phrenic abscess	56 months Disease free
8	64/M	Haematemesis	Adenoma Mild Dysp.	Adenoma, Mild Dysp.	None	29 months, Disease free
9	54/M	P, J		AdenoCa T2/Moderate	Wound infection	43 months, Disease free
10	71/M	J, W, Steatorrhoea,	Normal	AdenoCa T2/Poor	None	10 months, Disease free
11	61/M	P, Rigor with temperature	Adenoma, Mild Dysp.	Adenoma, Moderate Dysp.	None	52 months, Disease free
12	62/M	J	Adenoca	AdenoCa T2/Moderate	None	30 months, Died of local recurrence, liver involved
13	70/M	Incidental, J	Adenoma	Ca-in-Situ	None	53 months, Disease free
14	70/F	J, P, N, V		AdenoCa T2/Poor	None	7 months, Died of local recurrence
15	66/M	J, P, W		AdenoCa T2/Moderate	None	30 months, Died of local recurrence

(J-jaundice, P-pain, N-nausea, V-vomiting, W-weight loss, Dysp.-Aysplasia, Ca.Carcinoma)

Histo-pathology

Preoperative endoscopic biopsy was accurate in only 5 patients (41%) of whom 4 had adenomas and 1 had an adenocarcinoma. Multiple biopsies were routinely undertaken at endoscopy. Amongst the remainder, preoperative biopsy revealed a villous adenoma with severe dysplasia in 5 patients of whom 2 eventually had carcinoma-in-situ, 2 had a moderately differentiated adenocarcinoma and 1 had a poorly differentiated adenocarcinoma. One preoperative biopsy was insufficient and 1 was normal. Both turned out to be poorly differentiated adenocarcinomas. In total, 4 patients had adenomas, 2 had carcinoma-in-situ and 9 had adenocarcinoma, of which 5 were moderately differentiated and 4 poorly differentiated. Of the 9 adenocarcinomas 1 was in stage T1 and 8 were T2. Frozen section biopsy performed in one patient (9) was reported as benign though definitive histology revealed moderately differentiated adenocarcinoma. Resection margins were clear in 14 patients. A re-laparotomy could not be undertaken in the one patient with involved resection margins due to significant associated co-morbidity. There was no pancreatic invasion, though lympho-vascular invasion was found in 3 cases. Mean tumour diameter was 2.5 cms (range, 1.5 to 4.2 cms). Mean duration of follow-up was 31.4 months (range, 7 to 70 months).

Outcome

The longest survival in this study was 70 months (no. 2) with a total of 4 patients alive after 50 months, 1 with a diagnosis of moderately differentiated adenocarcinoma, 1 with carcinoma-in-situ and 2 with dysplastic adenomas. Four patients (26 percent) died in this study. All the patients died of local recurrence. Two of these had T2, moderately differentiated tumours, and the other 2 had poorly differentiated tumours in stage T1 and T2. Survival was worst in the poorly differentiated group – 1 patient who also had involved resection margins surviving 7 months and another 10 months while both the patients with moderately differentiated carcinomas survived 30 months. Of the 3 patients with lymphovascular invasion 2 had poorly differentiated and 1 had a moderately differentiated carcinoma. The latter is alive at 43 months while of the patients with poorly differentiated carcinoma with lymphovascular invasion 1 is alive at 10 months and the other died at 7 months.

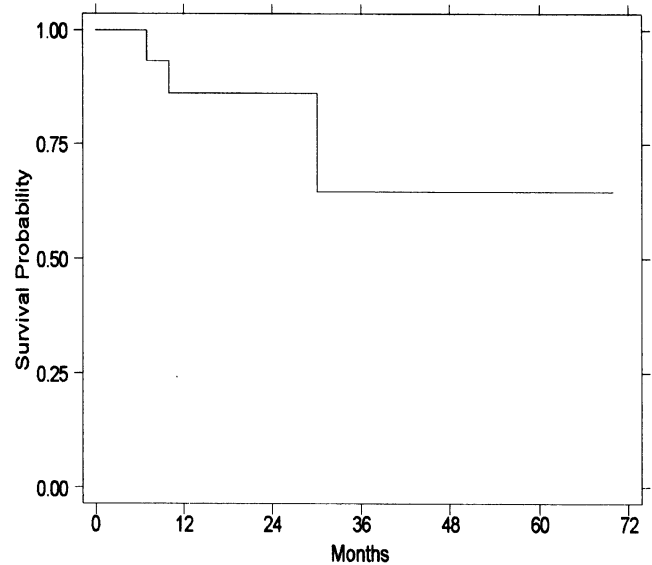


Fig 3. Overall actuarial survival (Kaplan Meier) – 1 year survival was 86% while 3 and 5 year survival was 65%.

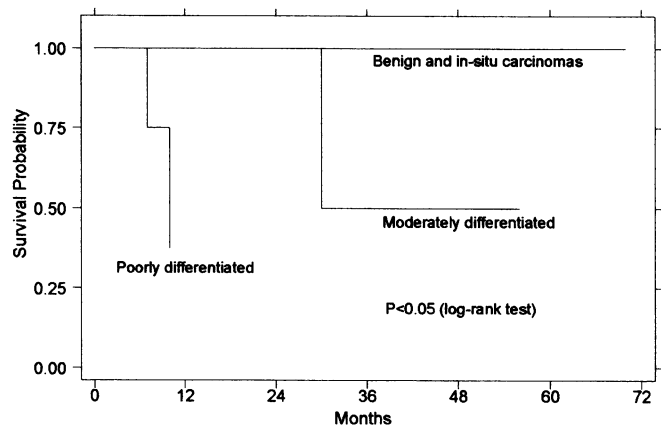


Fig 4. Survival by degree of differentiation.

The overall 1 year actuarial survival (Kaplan-Meier) for ampullary tumours (figure 3) was 86% (95% confidence interval 55-96%) while the 3 and 5 year survival was 65% (95% confidence interval 29-86%). Three year survival for moderately differentiated cancers (figure 4) was 50% (95% confidence interval 6-84%) while the longest survival for patients with poorly differentiated carcinoma was only 10 months in this study. Because of the relatively short follow-up and small series it is difficult to accurately interpret long-term survival at this point.

DISCUSSION

On the basis of autopsy investigations, the rate of neoplastic lesions of the ampulla ranges between 0.063-0.21%.⁵ Halsted first reported

transduodenal excision of an ampullary mass in 1899.⁶ In 1935 A. O. Whipple reported a 2-stage resection of ampullary carcinoma.⁷

Although the ampulla is easily accessible by endoscopy there is a high reported incidence of false negative results for biopsy of carcinoma, ranging from 25-60%.^{1, 5, 8, 9, 10, 11} The results in this study are similar, with a false negative rate of 59%. CT scan detection of a lesion is considered even less sensitive with a reported figure of around 20% in some studies.¹ Endoscopic ultrasonography aided diagnosis and staging has been widely recommended.^{1, 12, 13, 14} However, Cahen *et al* reported an accuracy of only 44 per cent with endoscopic ultrasonography assisted staging and a false positive outcome for metastatic lymph nodes in 31% of their cases.³ Endoscopic ultrasonography was not available for this study. Per-operative frozen sections are unreliable in excluding malignancy and can also give false positive results.^{5, 15} It seems nearly impossible to exclude, with certainty, the presence of carcinoma in an adenoma without complete excision.⁵

While TDE is now accepted as the procedure of choice for benign adenomas, pancreaticoduodenectomy is the commonly recommended surgery for ampullary cancer.¹⁰ There have been recommendations for radical surgery even for benign lesions with some authors citing problems like a high incidence of malignancy, difficulty in accurate pre-operative confirmation, tendency for tumours to recur and concerns regarding the oncological adequacy of local resection for ampullary cancers.^{8, 9, 16} A 3-year survival around 55 to 60 per cent and 5-year survival around 35 to 55 per cent has been reported after pancreaticoduodenectomy.¹⁷⁻¹⁹ Beger *et al* reported 3- and 5-year survival rates of 72% and 52% respectively with R0 resections after radical surgery, but R0 resection was possible in only 62% of the malignant cases in their study, with an intra-abdominal complication rate of 25%.⁵ The present study with overall actuarial 3 and 5 year survival projections of 65% would tend to favour the less radical approach.

Some reports also suggest that local resection is oncologically acceptable with comparable results and low morbidity in selective cases.^{3, 5, 10} Tarazi *et al* reported a 2 year survival of 55 per cent and a 5-year survival of 41 per cent following TDE for carcinomas.²⁰ Newman and Pittam reported a 5 year survival of 41 per cent and a surviving

patient 15 years after TDE for ampullary carcinoma.²⁰ Wise *et al* have reported a 3 year survival at 50 per cent and 5 year survival at 37.5 per cent.²² Knox and Kingston have reported a better 1, 2, 3 and 5 year survivals following TDE compared to radical procedures.²³ Robertson and Imrie reported a median survival of 57 months with 44% five-year actuarial survival, after TDE.²⁴ Fifty percent of their survivors developed recurrent disease while there was a 25% incidence of post-operative deaths. Talamini *et al* in a large study of 28 years experience from the John Hopkins Institution reported an overall mortality of 3.8% after radical resection with no deaths in the last 5 years in consecutive 45 patients.²⁵ Morbidity in the latter part of their study had reduced to 38%. Five-year survival was 38% and they believed avoidance of transfusion improved the prognosis. Various studies have proposed that TDE is justifiable when the ampullary tumour is pT1(UICC-staging) and graded G1 or G2 (highly or moderately differentiated) with no lymphatic infiltration and complete resection (R0).^{5, 26} The present study would tend to corroborate these suggestions. Unfortunately accurate TNM staging pre- or peroperatively is not feasible.

Howe *et al*, in a prospective study of the correlation between clinicopathological variables and survival of 123 patients presenting with ampullary carcinomas, found negative margins and negative nodes as independent predictors of improved survival.² Lymphatic drainage of tumours of the ampulla is distinct from pancreatic tumours in that, even in advanced cases, they seem to involve only a local group of lymph nodes near the ampulla, yielding a superior prognosis if the infiltration does not involve pancreatic tissue.^{5, 27} Pancreatic involvement is closely related to extensive nodal involvement and ampullary cancers invading the pancreatic parenchyma may act more like pancreatic cancers resulting in a poor prognosis.^{5, 27} In our study there was no pancreatic involvement in any of the cases and resection margins appeared clear in all but one case. Neither size nor duration of symptoms have been reported to accurately predict the presence of malignancy.¹⁰ Interestingly, in the present study all 10 patients with jaundice had carcinoma or carcinoma-in-situ while none of the patients with villous adenoma had jaundice. This would be in keeping with some reports which suggest that malignant lesions tend to present

with jaundice while benign lesions do not.^{1,9,10} It would be interesting to see from larger studies in the future if elevated bilirubin could be utilised as a guide to the general decision making regarding the appropriate procedure and also as a predictor of survival in tumours of the ampulla.

In conclusion, our study suggests that obtaining an exact preoperative diagnosis for ampullary tumours is very difficult. None of the existing investigative tools seem to be entirely confirmative about the true histological nature of the tumour and the extent of the disease. Transduodenal excision of ampullary tumours seems curative for benign tumours and for in-situ cancers. It is a low risk alternative for patients with carcinoma who are poor surgical risks due to age or co-morbidity. Oncologically, local excision of carcinoma appears to be a palliative rather than curative procedure.

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