

A WORKING ALGORITHM FOR THE MANAGEMENT OF TUMOURS OF THE AMPULLA OF VATER.

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Aim: The aim of this study is to assess the integration of endoscopic and surgical resection in the definitive management of patients with tumours of the AoV based on tumour size through a prospective analytical study.

Patients and methods: A cohort of 15 consecutive patients with papillary neoplasms formed the study population. Patients with tumours ≤ 4 cm were offered endoscopic resection while patients with tumours > 4 cm were offered a pancreaticoduodenectomy after a short period of preoperative biliary stenting. Patients in the endoscopic and surgical groups underwent duodenoscopic or imaging surveillance, respectively, at their follow-up visits.

Results: The median age of the study population was 43 years (min - max: 30 - 80) with a male to female ratio of 3 : 2. Nine (60%) patients were found legible for endoscopic ampullectomy while the remaining six (40%) had a short period of preoperative biliary drainage followed by pancreaticoduodenectomy. In the endoscopy group, three patients required two sessions to obtain tumour free margins and one patient developed pancreatitis. In the surgery group, one patient suffered from an anastomotic biliary stricture requiring redo surgery. After a median of 15.3 (min - max: 4.67 - 39.5) months of follow-up all patients were living with no endoscopic or imaging evidence of tumour recurrence.

Conclusion: Pancreaticoduodenectomy remains the treatment of choice for large and malignant tumours while endoscopic resection with close follow-up for two years seems to be adequate for small size tumours.

Keywords: ampullectomy, endoscopic retrograde cholangiopancreatography, pancreaticoduodenectomy.

INTRODUCTION

Tumours of the ampulla of Vater (AoV) are frequently encountered during the diagnostic work-up of patients suffering from surgical jaundice. Adenomas are the most common pathology affecting the AoV accounting for 70% of all tumours followed by carcinoma in 25-30%.⁽¹⁾ However, adenomas of the AoV whether occurring spontaneous or part of the Familial Polyposis Syndrome are considered as premalignant lesions. The adenoma-carcinoma sequence is well-established⁽²⁾ as 30% of small size adenomas contain carcinomatous cell aggregations which reaches 60% in large villous adenomas.⁽³⁻⁵⁾

This fact stresses the importance of excision of tumours of the AoV in order to guard against malignant transformation. Furthermore, the accuracy of endoscopic biopsies, which is superficial in many times, in detecting carcinomatous changes in benign adenomas is at its best

variable ranging from 45% to 85%.^(4,5) In addition, false negative results prior to surgery range from 25% to 56%.⁽⁵⁻⁷⁾ Consequently, open surgery in the form of local resection or pancreaticoduodenectomy has been for long the only available modality of therapy.^(8,9) Such an approach although associated with low mortality is characterized by high morbidity and is often met with patient refusal leaving many of them with suboptimal treatment options.

Endoscopic excision of adenomas of the AoV, which sometimes are found later to harbour a carcinoma, has been reported to be feasible and safe.⁽¹⁰⁻¹²⁾ This approach spares many patients the hazards of major surgery and offers a radical form of therapy to patients who otherwise are considered of high surgical risk. The aim of this study is to assess the integration of endoscopic and surgical resection in the definitive management of patients with tumours of the AoV based on tumour size where patients harbouring tumours up to 4 cm are offered endoscopic

therapy while patients with larger tumors are offered surgical therapy through a prospective analytical study.

PATIENTS AND METHODS

Patient population: A cohort of consecutive patients with papillary neoplasms referred over a 4 year (2001-2004) period to the Endoscopy and Motility Unit, Department of Experimental and Clinical Surgery, Medical Research Institute, University of Alexandria for definitive management formed the study population which was then prospectively followed-up and analyzed.

Exclusion criteria: Patients were excluded from the study if they were not candidate for definitive treatment (excision) either through endoscopic ampullectomy or surgical resection (pancreaticoduodenectomy).

Clinical and diagnostic work-up: Patients were interviewed and data obtained by means of a preformed questionnaire. Non-invasive imaging of the pancreaticobiliary system was obtained either from an abdominal ultrasound or CT examination.

Laboratory investigations: Blood samples were withdrawn for routine haematological and liver function tests to be used for initial and follow-up assessment.

Initial endoscopic diagnosis and management: An ERCP was performed to all patients under light sedation and antibiotic coverage in order to confirm diagnosis, obtain tissue biopsy, and insert a biliary stent for preoperative biliary drainage in the subset of patients candidate for surgical management.

Inclusion criteria and technique for endoscopic ampullectomy: In this group of patients endoscopically accessible papillary lesions (4 cm at largest diameter) without lateral infiltration of the duodenal muscularis propria (mucosal elevation with submucosal injection of saline) were included. Patients suffering from lesions with direct biliary or pancreatic duct extension demonstrated at diagnostic ERCP were shifted to the surgical group. Endoscopic ampullectomy was performed using a standard polypectomy snare. After grasping the tumour by the snare at its base, resection was done using a blend current (Fig. 1). Lesions that were not possible to resect en bloc were excised in a piecemeal fashion. After each procedure, the resection site was checked and biopsied to exclude residual tumour. A cholangiogram was routinely performed after ampullectomy to ensure adequate biliary drainage and a stent inserted when drainage was found inadequate. No stents were inserted in the pancreatic duct.

Techniques of pancreaticoduodenectomy: Pancreaticoduodenectomy was performed in a standard manner⁽¹³⁾ after a short period of preoperative biliary stenting to ensure the return of serum bilirubin to near normal levels.

Outcome parameters and clinical follow-up: Endoscopic and surgical success were defined as complete excision; regardless to the number of sessions in the endoscopic group. Patients were clinical followed-up was every 6 months then yearly after the fourth follow-up visit. Patients in the endoscopic group underwent duodenoscopic surveillance at their follow-up visits in order to early detect any tumour recurrence.

Statistical analysis: Numerical data are expressed as median with minimum and maximum values in parenthesis.

RESULTS

Patient population: Patients' baseline data are shown in Table 1. A total number of 15 patients were found legible to enter the study; their median age in years was 43 (min-max: 30 - 80) while the male to female ratio was 3 : 2.

Clinical and imaging findings: All patients presented with painless jaundice with a subset of three (20%) patients who suffered from an initial period of intermittent jaundice. None of the patients at time of presentation suffered from weight loss or vomiting. There was also no history or signs of cholangitis in any of the patients. Clinical examination revealed a palpable gallbladder in three (20%) patients which was evident in the pre-intervention imaging in the form of a dilated gallbladder, furthermore, all patients had bile duct dilation down to its distal end on these images.

Liver function tests: The profile of liver function tests was that of an obstructive nature in all patients as shown in Table 1.

ERCP findings: Nine (60%) patients were found to be legible for endoscopic ampullectomy while the remaining six (40%) patients had a biliary stent inserted for preoperative drainage in preparation for surgical management in the form of a pancreaticoduodenectomy.

Management outcome: All patients in both groups had a successful resection of their tumours. In the endoscopy group, three patients required two sessions to obtain tumour free margins and one patient developed a self-limited mild pancreatitis. In the surgery group, one patient developed wound sepsis and during follow-up developed an anastomotic biliary stricture requiring redo surgery.

Final pathology: Two patients in the endoscopy group were found to harbour in their adenomas foci of invasive adenocarcinoma while one patient in the surgery group was found to suffer from carcinoma in-situ in the resected specimen although his preoperative endoscopic biopsy showed invasive adenocarcinoma.

Follow-up: After a median of 15.3 (min - max: 4.67 - 39.5) months of follow-up all patients were living with no endoscopic or imaging evidence of tumour recurrence.

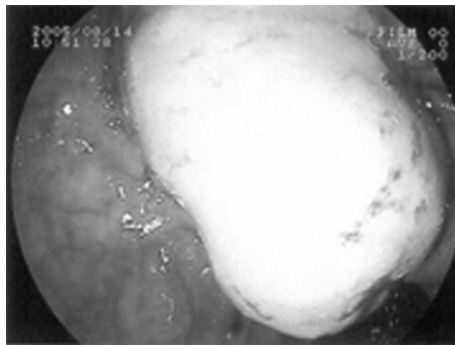
Table 1. Patient characteristics (15 patients).

Item	
Age in years	43 (30 - 80)
Male : Female	9 : 6
Presentation (%)	
Painless jaundice	15 (100)
Intermittent jaundice	3 (20)
Palpable gallbladder	3 (20)
Liver function tests	
Serum bilirubin	3.9 (2.9 - 21)
Alkaline phosphatase	1010 (15 - 1474)
SGOT	155 (140 - 171)
SGPT	95 (80 - 111)
Ultrasound and CT findings (%)	
Bile duct dilatation	15 (100)
Dilated gallbladder	3 (20)

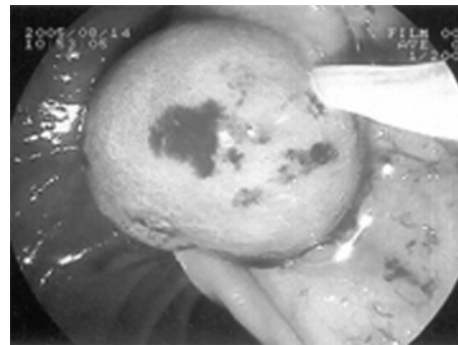
Table 2. Management outcome.

Item	
Modality of treatment	
Endoscopic ampullectomy	9
Surgical resection	6
Pathology	
Endoscopy group	
Adenoma	7
Adenoma with carcinoma	2
Surgery group	
Adenocarcinoma	5
Carcinoma in-situ*	1
Complications	
Endoscopy group	
Pancreatitis	1
Surgery group	
Anastomotic stricture	1
Wound sepsis	1
Disease-free follow-up in months	
Endoscopy group	5.9 (4.7 - 15.3)
Surgery group	34.1 (28.7 - 39.5)

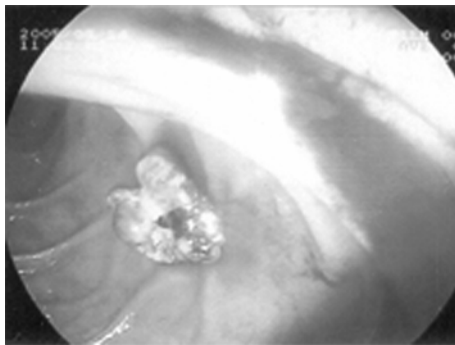
* Preoperative endoscopic biopsy: adenocarcinoma



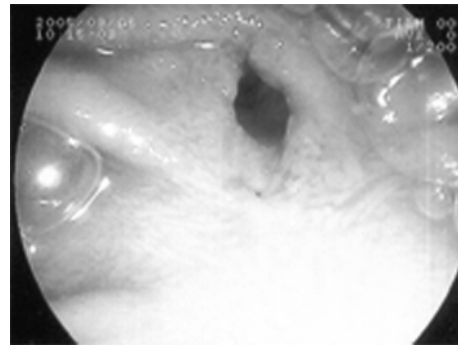
a



b



c



d

Fig 1. Endoscopic ampullectomy. A: papilla with tumour. B: tumour grasped with a snare. C: Resected tumour. D: Tumour free medial duodenal wall showing a wide bile duct orifice (b) and normal pancreatic duct orifice (p).

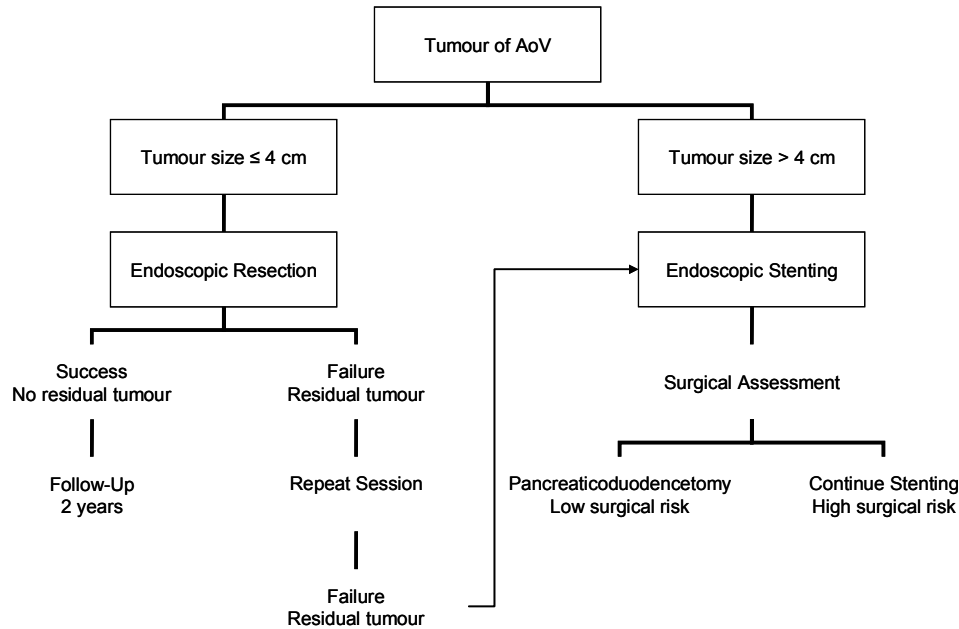


Fig 2. Management algorithm for tumours of the ampulla of Vater (AoV).

DISCUSSION

Treatment options for tumours of the AoV are numerous. On one end of the spectrum lies pancreaticoduodenectomy with its effective tumour control and considerable morbidity which reflects its complex nature. On the other end lies local surgical excision devised to minimize such morbidity.^(7,8) Although, associated with less tumour control it has been responsible for introducing the concept of endoscopic treatment of tumours of the AoV in the form of endoscopic snare resection, photodynamic therapy, or electrofulguration. The combination of the above mentioned techniques is associated with lower rates of tumour recurrence even in the presence of intramucosal carcinomas.⁽¹⁴⁾

An inherent problem with endoscopic resection of tumours of the AoV is early post-procedure pancreatitis. Reported incidence is around 15% which is in accordance with the 11% incidence found in this study.⁽¹⁵⁾ However, the degree of pancreatitis can sometimes be severe leading to a necrotizing pancreatitis and death.⁽¹⁶⁾ Some centres advocate the prophylactic placement of a pancreatic stent to ensure adequate pancreatic drainage thus minimize the risk of pancreatitis.⁽¹⁷⁾ Pancreaticoduodenectomy, on the other hand, is well known for its morbidity in the form of pancreatic or biliary leakage, abdominal sepsis and

collections, anastomotic strictures, etc.^(18,19) However, it should be emphasized that prompt and active management of these complications is the only key to minimize their impact on mortality.

Criteria for selection of appropriate treatment lie within the nature and physical characters of the tumour. Criteria such as soft consistency, regular margins, lack of ulcerations are at best descriptive and do not objectively guide towards the appropriate therapy. Furthermore, preoperative endoscopic ultrasonography has been shown not to be reliable in the differentiation of benign and malignant tumours of the AoV and therefore not useful in the selection of appropriate therapy.^(8,20,21) On the other hand, tumour size seems to be a more valid criterion for treatment selection. Tumours of a diameter of 4 cm and less can be successfully resected endoscopically and if found to harbour a carcinoma are usually early and limited to the mucosa or superficial submucosa. On the other hand, tumours larger than 4 cm are better managed surgically (pancreaticoduodenectomy) as they almost always harbour an invasive carcinoma.⁽¹⁰⁾ However, it should be mentioned that focal malignant change can be found in tumours of the AoV.⁽²²⁾ This sometimes causes inconsistency in the results of preoperative and postoperative tissue diagnosis as manifest in this series in one patient who had carcinoma in the preoperative tissue diagnosis but not in the resected specimen.

An ideal system of preoperative diagnosis would effectively separate patients with adenomas from those with carcinoma in order that patients with adenomas could be offered limited resection and those with carcinoma a more radical one. However, due to the well established adenoma-carcinoma sequence, such a situation will be difficult to establish and in many situations patients who will be offered a limited resection will be found to harbour a carcinoma. As long as there is no residual tumour such a situation seems at least in non-randomized trials not to affect outcome or long-term survival. Comparison between endoscopic and surgical therapy of carcinomas of the AoV have shown that long-term results of endoscopic therapy are not inferior to those obtained after radical surgery.^(23,24) Based on Kaplan-Meier analyses, median survival of surgically treated patients was 50% after 13 months and 7% after 5 years whereas 50% of endoscopically treated patients were alive at 9 months and 7% at 5 years. These differences were not found to be significant and may indicate a high impact of endoscopic therapy in the future management of patients with tumours of the AoV.

This study recommends the adoption of such a simple working algorithm for patients with tumours of the AoV based on tumour size as shown in (Fig. 2). This algorithm overcomes the problem of inaccurate preoperative differentiation between benign and malignant ampullary tumours. Pancreaticoduodenectomy remains the treatment of choice for large and malignant tumours while endoscopic resection with close follow-up for two years seems to be adequate for small size tumours.

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