

**Introduction:**

Ampullary tumours are increasingly identified and resection often advised but it is unknown which factors are associated with higher grade histological changes. We reviewed practice in UK pancreaticobiliary units to identify risk factors for high grade histology.

**Methods:**

Patients who underwent endoscopic ampullectomy between 2010 and 2023 across 10 tertiary units in the United Kingdom were included. Data were collected retrospectively for demographics, lesion characteristics, procedural details, pre-ampullectomy histology and histology following ampullectomy. Univariate and multivariable analysis was performed to identify independent risk factors for high grade dysplasia or cancer on histology. Cohen's Kappa was used to assess agreement between pre- and post-ampullectomy histology.

**Results:**

82 patients (median age 67 years, 47 females) had complete data with a mean lesion size of 22.9mm. 73.6% of lesions underwent endoscopic ultrasound prior to resection, 16.7% had evidence of intraductal extension and 33.3% had evidence of a lateral spreading component. Enbloc resection was achieved in 38/82 (46.3%) lesions. Lesions removed piecemeal were significantly larger than enbloc (25.0 vs 17.5mm,  $p < 0.0001$ ). Pre-ampullectomy histology showed low grade dysplasia in 60, high grade dysplasia in 11 and cancer in 1 but following ampullectomy only 54 had low grade dysplasia, 13 had high grade dysplasia and 5 contained cancer: 49 samples gave the same grade, 15 were upgraded and 8 were downgraded. The Kappa value for histological agreement was 0.24 (standard error 0.12) indicating only fair agreement. Multivariable analysis adjusted for age and lesion size revealed that intraductal extension (adj OR 3.76, 0.98 – 14.49,  $p = 0.055$ ) and enbloc resection (adj OR 0.28, 0.08 – 0.98,  $p = 0.047$ ) were independently associated with high grade dysplasia or cancer on final histology.

**Conclusions:**

Pre-ampullectomy histology does not correlate well with degree of dysplasia on the final specimen. Most inconsistencies are underestimation but some do overestimate degree of dysplasia. The main predictor of higher grades of dysplasia is intraductal extension whereas enbloc resection appears protective.