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Histological Classification of Pancreatic Neuroendocrine Tumours: Optimizing the Ki67 Range for Grade of Tumours

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Background: Pancreatic neuroendocrine tumours are graded using the Ki67 antigen in accordance with the WHO 2010 classification. Despite the system's widespread use, a wide variety of tumour behaviours have been described leading to various proposed revisions. Specifically: a) the use of 5% rather than 2% as the boundary between Grades 1 and 2, b) the use of 55% rather than 20% as the boundary between Grades 2 and 3, c) the subdivision of Grade 3 using poorly vs well-differentiated appearances.

Methods: Of 223 patients who visited our institution between 2004 and 2013, Ki67 values were known for 168. Where data was available for the pancreas and liver metastases, the highest value was used. The significance of each system was investigated using Kaplan-Meier survival curves and specific Ki67 values searched for using ROC.

Results: a) G1 vs G2 prognostic significance was not improved using 5% instead of 2%. G3 vs G1/G2 remained significant ($p<0.001$). b) G2 vs G3 remained significant using 55% ($p<.001$). G1 vs G2 significance improved compared to 20% ($p=.019$ vs .193). ROC analysis showed that Ki67=55% has 100% specificity, but that Ki67 values between 10% and 20% offer the best specificity/sensitivity balance. c) Defining G3 using poor-differentiation rather than >20% improved G1 vs G2 ($p=.133$ vs .195).

Conclusions: 1) Prognostic relevance of Grades 2 and 3 may be improved by using either 55% or poor-differentiation as criteria. 2) There is no evidence to suggest that 5% offers increased prognostic relevance for Grade 1.