

C-49

Tumor Size Correlates with Grading in Nonfunctioning Pancreatic Neuroendocrine Tumors and is Not Age-Dependent

Stefano Partelli¹; Francesca Muffatti¹; Valentina Andreasi¹; Gianpaolo Balzano¹; Paola Rancoita²; Renato Castoldi¹; Stefano Crippa¹; Domenico Tamburrino¹; Giuseppe Zamboni³; Corrado Rubini⁴; Claudio Doglioni⁵

¹Pancreatic Surgery Unit, Pancreas Translational & Clinical Research Center, San Raffaele Scientific Institute, “Vita-Salute” University, Milan, Italy; ²Center for Statistic, Pancreas Translational & Clinical Research Center, San Raffaele Scientific Institute, “Vita-Salute” University, Milan, Italy; ³Department of Pathology, Ospedale Sacro Cuore-Don Calabria, Negrar, Italy; ⁴Department of Pathology, Università Politecnica delle Marche, Ancona, Italy; ⁵Pathology Unit, Pancreas Translational & Clinical Research Center, San Raffaele Scientific Institute, “Vita-Salute” University, Milan, Italy

BACKGROUND: Adenoma-carcinoma sequence is strictly related with age in mucinous pancreatic neoplasms. Tumor growth and Ki67 value increase are both associated with aggressiveness in nonfunctioning pancreatic neuroendocrine tumors (NF-PanNET), but their natural history is largely unknown. In particular, it is unclear if the evolution of NF-PanNET is time-dependent or not. Aim of this study was to evaluate a possible correlation between age, tumor size and grading in patients with NF-PanNET and its impact on disease free survival (DFS).

METHODS: Patients who underwent surgery for sporadic NF-PanNET (excluding G3) were retrospectively analysed. Linear regression analysis was performed to evaluate possible correlation between continuous variables. Multiple logistic

regression and Cox's regression analysis was performed. Patients with R2 resection were excluded from survival analysis.

RESULTS: 235 patients were enrolled. Median age was 61 years. Tumors were PanNET G1 in 138 (59%) cases. Median radiological and histological diameter was 25 mm for both. Age was correlated neither with tumor size nor with Ki67 value. Conversely, tumor size was significantly associated with Ki67 value ($r: 0.273, P<0.0001$). On multivariate analysis, predictors of tumor grade were tumor size (OR: 3.72, $P=0.0001$) and microvascular invasion (OR: 6.94, $P<0.001$). A tumor size cut-off of 27 mm accurately predicted PanNET G2. At a median follow-up of 59 months, 192 patients were alive with no evidence of disease, 32 patients (14%) had recurrence and 9 patients (28%) eventually died of disease. On multivariable analysis, predictors of DFS were tumor size > 27 mm (HR: 3.400, $P<0.036$) and the presence of perineural invasion (HR: 5.27, $P<0.0001$).

CONCLUSION: Tumor size correlates with grade and it is a strong predictor of recurrence after surgery for NF-PanNET. Tumor size is not associated with increasing age suggesting that natural evolution of these neoplasms is not time-dependent, supporting the safety of a surveillance policy for small asymptomatic NF-PanNET.