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Assessment of Microvascular Density in the Neuroendocrine Tumors of the Pancreas: a Correlation with Multidetector Computed Tomography (MCDT) Features and Tumor Grade

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Introduction/ Background

The biologic course of pancreatic neuroendocrine tumors (NET) can be accurately predicted on the basis of pathology parameters which, unfortunately, cannot be fully assessed until the entire tumor has been resected. When obvious landmarks of malignancy (metastases, vascular invasion) are lacking, tumour size is the only reliable preoperative parameter used to differentiate between presumably benign and malignant pancreatic NETs. It is generally accepted that pancreatic NETs exceeding 2 cm in their diameter may have borderline pathology or even malignancy. Anyway, up to 10% of tumors with diameter less than 2 cm are although malignant. That is why there is need in studies focusing on additional imaging characteristics, such as contrast-enhanced MDCT, useful for the aggressiveness assessment.

Aims

To determine whether it is possible to predict pancreatic NET Grade and microvascular density (MVD) according to contrast-enhanced MDCT findings.

Methods

A retrospective study was conducted and 70 patients with pancreatic NETs were retrieved from the institutional archives. Twenty eight of them had met the including criteria (a - patients underwent surgery in our Institution and b - patients underwent preoperative dynamic abdominal CT within 30 days prior surgery) and comprised the study population. Thus, research included 15 patients with functioning and non-functioning pancreatic NETs Grade 1 and 13 of patients with Grade 2 (according to the WHO classification of 2010). Radiology All preoperative CT examinations were performed by a 256-slice CT scanner. Dynamic CT images, including non-enhanced, arterial, portal venous and delay phase images, were obtained for all patients. For contrast-enhanced CT, 90–120 mL of high concentration contrast mediaiometrol 400 (Iomeron 400; Bracco Imaging SpA, Milan, Italy). CT images were reconstructed with a section thickness of 1-2 mm.

Pathology

For identification of vessels, regardless lymphatic or venous, immunohistochemistry with CD34 (clone QBEnd/10, CellMarque) was performed on formalin-fixed paraffin-embedded (FFPE) tumor blocks.

Image analysis

Density of vessels was defined on 3 fields at x 200 (~ 1,8 mm2). The choice of fields of vision was carried out among sites with visually greatest density of vessels ("hot spots"). Determined total number of the pixels belonging to vessels by the Color Threshold tool (ImageJ) and divided this number into total of pixels in the image.



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Results

The median of density of vessels at patients with NET Grade 1 made $8\% \pm 2\%$ whereas in group of patients with NET Grade 2 this indicator made $5 \pm 4\%$. The difference was statistically significant (p <0,05). Mean arterial enhancement ratio was 1.66(0.42) in Grade 1 and 1.04(0.39) in Grade 2 pancreatic NET (p<0.01); and correlated with intratumoral MVD (r=0.61, p<0.005) and tumor grade (p<0.01). Vascular invasion, metastases and pancreatic duct dilatation were observed in two cases, both in G2 tumors. Arterial enhancement ratio <1.1, size \geq 20 mm, ill-defined borders and tumor non-homogeneity showed 83%, 74%, 70% and 56% accuracy in diagnosing G2 tumor respectively, while the accuracy of two of these criteria used in combination was 91%. Contrast-enhanced MDCT-features of pancreatic NET correlate with MVD and can predict tumor grade during preoperative staging.