Pancreatic neuroendocrine tumor: correlation between contrast-enhanced CT findings and pathological grading in WHO classification

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Pancreatic neuroendocrine tumor (pNET) is a rare pancreatic neoplasm corresponding to an annual incidence of 2.2 in 1,000,000. However, pNET is clinically important because they have a high rate of malignancy. The updated World Health Organization (WHO) classification divides neuroendocrine tumor into NET G1, NET G2, and NEC according to pathological grade which is an independent prognostic factor for survival in pNET. Therefore, the prediction of pathological grade of pNET in WHO classification before treatment is very important in determining efficient treatment strategy. Contrast-enhanced CT is a widely accepted technique for detecting and staging pancreatic tumor. However, the research on the relationship between contrast enhanced CT findings and pathological grade of pNET has been limited.

The purpose of this study is to evaluate the effectiveness of CT findings in estimating pathological grade of pNET in recent WHO classification.
Methods and Materials

Patients:
The final diagnosis was confirmed by a pathologist at pathological evaluation following surgical resection. The pathologist, who was blinded to all clinical information and imaging findings, evaluated WHO classification by meaning the number of mitosis per 10 high-power field and Ki-67 index. By the WHO classification, 11 were classified as NET G1 and 16 as NET G2.

CT Imaging Technique:
CT was performed on 16- or 64-detector row CT scanners by using either of two CT units. Pancreatic parenchymal and portal venous phase scans were obtained by using a 23- and 50-second delay after the aortic enhancement exceeded 50-HU compared to baseline, respectively. Scan delay for the delayed phase was fixed at 180 seconds after intravenous injection of 2 mL/kg body weight of nonionic contrast material with an iodine concentration of 300 mgI/mL at a fixed duration of 30 seconds.

Imaging Analysis:
Two radiologists, who had no knowledge of clinical information, independently attempted to determine tumor size, delineation of tumor margin, tumor homogeneity, dilatation of upstream pancreatic duct, peripancreatic vascular involvement, and hepatic metastases. Attenuation values during each phase on CT of all pNETs were obtained by two radiologist. Circular or oval regions of interest (ROIs) were placed as large as possible within pNETs (mean size, 131.4 mm 2; range, 20-1100 mm 2). The contrast enhancement value on enhanced CT was calculated from the difference in CT values between the unenhanced and each of the enhanced images. We calculated the following diagnostic parameters:

\[
\text{wash-in pp} = \text{pancreatic parenchyma-phase attenuation - unenhanced attenuation}, \\
\text{wash-in pv} = \text{portal-venous-phase attenuation - unenhanced attenuation}, \\
\text{washout pp} = \text{pancreatic parenchyma-phase attenuation - delayed-phase attenuation}, \\
\text{washout pv} = \text{portal-venous-phase attenuation - delayed-phase attenuation}, \\
\text{percentage enhancement washout ratio (PEW) pp} = \left(\frac{\text{washout pp}}{\text{wash-in pp}}\right) \times 100, \\
\text{percentage enhancement washout ratio (PEW) pv} = \left(\frac{\text{washout pv}}{\text{wash-in pv}}\right) \times 100, \\
\text{relative percentage enhancement washout ratio (RPEW) pp} = \left(\frac{\text{washout pp}}{\text{pp attenuation}}\right) \times 100, \\
\text{relative percentage enhancement washout ratio (RPEW) pv} = \left(\frac{\text{washout pv}}{\text{pv attenuation}}\right) \times 100.
\]

Statistical Analysis:
The following tests were used for comparative analyses between NET G1 and NET G2; the Mann-Whitney U test for contrast enhancement of the tumor, tumor-to-pancreas contrast, wash-in and washout attenuations, PEW, RPEW, tumor size, chi square test for delineation of tumor margin, tumor homogeneity, dilatation of upstream pancreatic duct, peripancreatic vascular involvement, and hepatic metastases. All data were presented as mean ± SD with or without range. A p-value less than 0.05 was considered to indicate a statistical significance for all analyses. All statistical analyses were performed using SPSS version 14.0 (SPSS, Chicago, IL, USA).
Results

The mean of tumor size in NET G2 was larger than in NET G1. No significantly difference between NET G1 and NET G2 was obtained for delineation of tumor margin, tumor homogeneity, dilatation of upstream pancreatic duct or peripancreatic vascular involvement. Only 4 (25%) of 16 NET G2 showed hepatic metastases (Table 1.). During the pancreatic parenchymal and portal venous phases, mean contrast enhancement was significantly greater in NET G1 than in NET G2. Tumor-to-pancreas contrast was significantly greater in NET G1 than in NET G2 during the portal venous phase. The wash-in and washout attenuations were significantly greater in NET G1 than in NET G2 during pancreatic parenchymal and portal venous phases, respectively. PEW and RPEW during portal venous and delayed phases were significantly greater in NET G1 than in NET G2 (Table 2.).

<table>
<thead>
<tr>
<th>WHO classification</th>
<th>G1 (n=11)</th>
<th>G2 (n=16)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53.7±16.0</td>
<td>63.1±12.4</td>
<td>0.134</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>8:3</td>
<td>7:9</td>
<td>0.239</td>
</tr>
<tr>
<td>tumor size</td>
<td>16.7±12.3</td>
<td>26.6±19.4</td>
<td>0.030</td>
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<tr>
<td>clarity of tumor margin</td>
<td>8/11</td>
<td>9/16</td>
<td>0.448</td>
</tr>
<tr>
<td>tumor homogeneity</td>
<td>5/11</td>
<td>7/16</td>
<td>1.000</td>
</tr>
<tr>
<td>dilatation of upstream pancreatic duct</td>
<td>4/11</td>
<td>5/16</td>
<td>1.000</td>
</tr>
<tr>
<td>peripancreatic vascular involvement</td>
<td>1/11</td>
<td>2/16</td>
<td>1.000</td>
</tr>
<tr>
<td>hepatic metastases</td>
<td>0/11</td>
<td>4/16</td>
<td>0.123</td>
</tr>
</tbody>
</table>

Table 1: The mean of tumor size in NETG2 was larger than in NETG1. No significantly difference between NETG1 and NETG2 was obtained for delineation of tumor margin, tumor homogeneity, dilatation of upstream pancreatic duct or peripancreatic vascular involvement. Only 4 (25%) of 16 NETG2 showed hepatic metastases.

References: Radiology, Kagoshima University - Kogoshima/JP
Fig. 1: During the pancreatic parenchymal and portal venous phases, mean contrast enhancement was significantly greater in NETG1 than in NETG2.

References: Radiology, Kagoshima University - Kagoshima/JP
Fig. 2: Tumor-to-pancreas contrast was significantly greater in NETG1 than in NETG2 during the portal venous phase.  

References: Radiology, Kagoshima University - Kogoshima/JP

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<thead>
<tr>
<th>WHO classification</th>
<th>G1 (n=11)</th>
<th>G2 (n=16)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wash-in pp</td>
<td>166.34±60.1</td>
<td>120.7±48.2</td>
<td>0.034</td>
</tr>
<tr>
<td>Wash-in pv</td>
<td>115.2±25.8</td>
<td>78.5±23.2</td>
<td>&lt;0.001</td>
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<tr>
<td>Wash out pp</td>
<td>102.6±52.2</td>
<td>67.9±48.9</td>
<td>0.027</td>
</tr>
<tr>
<td>Wash out pv</td>
<td>49.9±19.8</td>
<td>22.3±8.9</td>
<td>0.001</td>
</tr>
<tr>
<td>PEW pp</td>
<td>58.6±21.3</td>
<td>48.4±20.2</td>
<td>0.109</td>
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<tr>
<td>PEW pv</td>
<td>42.7±13.6</td>
<td>28.4±9.8</td>
<td>0.003</td>
</tr>
<tr>
<td>RPEW pp</td>
<td>45.5±19.4</td>
<td>38.3±17.5</td>
<td>0.087</td>
</tr>
<tr>
<td>RPEW pv</td>
<td>31.3±10.7</td>
<td>19.2±6.4</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Table 2: The wash-in and washout attenuations were significantly greater in NETG1 than in NETG2 during pancreatic parenchymal and portal venous phases, respectively. PEW and RPEW during portal venous and delayed phases were significantly greater in NETG1 than in NETG2.

**References:** Radiology, Kagoshima University - Kogoshima/JP

**Fig. 3:** Pancreas neuroendocrine tumor (NET G1) shows early enhancement and delayed washout in the head of the pancreas (arrows) with dilatation of upstream pancreatic duct.

**References:** Radiology, Kagoshima University - Kogoshima/JP
Fig. 4: Pancreas neuroendocrine tumor (NET G2) shows poorly enhancement and washout pattern in the tail of the pancreas (arrows) with hepatic metastasis.

References: Radiology, Kagoshima University - Kogoshima/JP
Conclusion

Discussion:

Contrast-enhanced CT is also a feasible technique to assess tumor vascularity, which is an important element in the evaluation of the biological aggressiveness of a neoplasm\(^1\). A few studies have reported that pNETs with low microvascular density could be an unfavorable histoprognostic factor\(^2\)\(^{-4}\). Our results support these findings because the wash-in attenuations were significantly greater in NETG1 than in NETG2 during pancreatic parenchymal and portal venous phases, respectively.

Conclusion:

Enhancement pattern of the tumor in contrast-enhanced CT can be useful for estimation of pathological grading of pNET.
References


