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ABOUT COVER

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ORIGINAL ARTICLE

Retrospective Study

Enhancement parameters of contrast-enhanced computed tomography for pancreatic ductal adenocarcinoma: Correlation with pathologic grading

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Abstract

BACKGROUND

Pancreatic ductal adenocarcinoma (PDA) is a malignancy with a high mortality rate and short survival time. The conventional computed tomography (CT) has been worldwide used as a modality for diagnosis of PDA, as CT enhancement pattern has been thought to be related to tumor angiogenesis and pathologic grade of PDA.

AIM

To evaluate the relationship between the pathologic grade of pancreatic ductal adenocarcinoma and the enhancement parameters of contrast-enhanced CT.

METHODS

In this retrospective study, 42 patients (Age, mean ± SD: 62.43 ± 11.42 years) with PDA who underwent surgery after preoperative CT were selected. Two radiologists evaluated the CT images and calculated the value of attenuation at the aorta in the arterial phase and the pancreatic phase ($VA_{arterial}$ and $VA_{pancreatic}$) and of the tumor ($VT_{arterial}$ and $VT_{pancreatic}$) by finding out four regions of interest. Ratio between the tumor and the aorta enhancement on the arterial phase and the pancreatic phase ($TAR_{arterial}$ and $TAR_{pancreatic}$) was figured out through dividing $VT_{arterial}$ by $VA_{arterial}$ and $VT_{pancreatic}$ by $VA_{pancreatic}$. Tumor-to-aortic enhancement fraction (TAF) was expressed as the ratio of the difference between attenuation of the tumor on arterial and parenchymal images to that between attenuation of the aorta on arterial and pancreatic images. The Kruskal-Wallis analysis of variance and Mann-Whitney *U* test for statistical analysis were used.

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RESULTS

Forty-two PDAs (23 men and 19 women) were divided into three groups: Well-differentiated (n = 13), moderately differentiated (n = 21), and poorly differentiated (n = 8). TAF differed significantly between the three groups (P = 0.034) but $TAR_{arterial}$ (P = 0.164) and $TAR_{pancreatic}$ (P = 0.339) did not. The median value of TAF for poorly differentiated PDAs (0.1011; 95%CI: 0.01100-0.1796) was significantly higher than that for well-differentiated PDAs (0.1941; 95%CI: 0.1463-0.3194).

CONCLUSION

Calculation of TAF might be useful in predicting the pathologic grade of PDA.

Key words: Computed tomography; Pancreatic ductal carcinoma; Diagnostic imaging; Clinical pathology; Neoplasm grading; Prognosis

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Core tip: The conventional computed tomography (CT) has been worldwide used as a modality for diagnosis of pancreatic ductal adenocarcinoma (PDA). In this study, the tumor-to-aortic enhancement fraction (TAF) values were statistically different among the well differentiated group, the moderately differentiated group and the poorly differentiated group ($P < 0.05$). It has been reported that $TAR_{arterial}$ and $TAR_{pancreatic}$ are related to histological finding of PDA, but in our study. there were no significant differences in $TAR_{arterial}$ and $TAR_{pancreatic}$ among the three groups. TAF can be obtained with conventional pancreatic CT, without additional radiation exposure and processing time, and this simple method could be useful for predicting prognosis of PDA.

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INTRODUCTION

Pancreatic ductal adenocarcinoma (PDA) is a malignancy with a high mortality rate and short survival time[1]. Several important prognostic factors including tumor size, lymph node status, pathological grading and differentiation of the tumor influence survival in patients with PDA[2]. The pathological grade of adenocarcinoma is associated with the intratumor microvessel density (MVD)[3]. The process of neoangiogenesis is mediated by tumor angiogenic factors. Adenocarcinomas that develop in various organs tend to have a characteristic neovascularization pattern[4-6].

Computed tomography (CT) is an imaging modality used for evaluating tumors. The degree of CT enhancement is thought to be dependent upon the increase or decrease of intratumor MVD[7]. Some reports have described the relationship between CT enhancement, tumor angiogenesis, and the pathological grade of PDA[8]. It was reported that the degree of CT enhancement was directly proportional to the pathological grade of lung cancer but inversely proportional to that of PDA[8,9]. However, to date, few quantitative studies have compared CT enhancement parameters and the pathologic grade of PDA[10,11]. Therefore, the aim of this study was to investigate the relationship between various CT enhancement parameters and the pathologic grade of PDA.

MATERIALS AND METHODS

Patients

This retrospective study was approved by the institutional review board and the requirement for informed consent was waived. We conducted a computerized search

of electronic medical records for patients with PDA. Forty-eight patients underwent surgery following CT examination from October 2012 to June 2017. We excluded 6 patients because they did not undergo arterial and pancreatic phase CT. A total of 42 patients were enrolled in our study. Forty-two patients with PDA (head and uncinate process: 30, body: 11, tail: 1) were treated using Whipple's procedure (n = 6), pylorus preserving pancreaticoduodenectomy (n = 28), and distal pancreatectomy (n = 8).

CT examination

All CT images were obtained with two 128-channel multi-detector scanners (Siemens SOMATOM Definition AS and Flash, Siemens Healthcare, Erlangen, Germany). The CT parameters were as follows: Slice thickness, 3-5 mm; field of view (FOV), 50 cm × 50 cm; matrix, 512 × 512; beam collimation, 128 mm × 0.625 mm; beam pitch, 0.7; gantry rotation time, 0.5 s; tube voltage, 100-120 kV; and automated dose modulation with a maximum allowable tube current set at 200 mA.

Each patient received 120-150 mL of iohexol 300 (300 mg iodine) (Bonorex 300; Central Medical Service, Seoul, South Korea). An automatic power injector operating at an injection rate of 3.5 mL/s was used. The arterial, pancreatic, and late phase images were obtained with delays of 40 s, 65 s, and 105 s, respectively, after the injection of the contrast agent.

Imaging analysis

Two radiologists, blinded to the clinical data, performed consensual analysis of the axial CT images on a picture archiving and communication system (PACS; G3, Infinitt Healthcare, Seoul, South Korea). The CT attenuation values [Hounsfield Unit (HU)] of the tumor were measured by drawing circular regions of interest (ROIs) on the arterial and pancreatic phases. The attenuation values of the tumor were analyzed in the arterial ($VT_{arterial}$) and pancreatic phases ($VT_{pancreatic}$) and expressed in HU; visible necrosis, adjacent pancreatic parenchyma, and large vessels were excluded[12]. The same ROIs were reproduced at the aorta of the corresponding images, which measured the ROI of the tumor, the attenuation value of the aorta in the arterial phase ($VA_{arterial}$), and the attenuation value of the aorta in the pancreatic phase ($VA_{pancreatic}$).

The enhancement parameters, *i.e.*, the tumor-to-aorta enhancement ratios of the arterial ($TAR_{arterial}$) and pancreatic phases ($TAR_{pancreatic}$) were the division of $VT_{arterial}$ to $VA_{arterial}$ and $VT_{pancreatic}$ to $VA_{pancreatic}$, respectively. $TAR_{arterial} = VT_{arterial}/VA_{arterial}$; $TAR_{pancreatic} = VT_{pancreatic}/VA_{pancreatic}$.

The tumor-to-aortic enhancement fraction (TAF) represents the ratio of difference between the attenuation of the tumor on arterial and parenchymal images to the difference between the attenuation of the aorta on arterial image and pancreatic images. The difference in tumor enhancement between the arterial and pancreatic phases (DT) was calculated by subtracting $VT_{arterial}$ from $VT_{pancreatic}$[13]. The difference in aortic washout between the arterial and pancreatic phases (DA) was calculated by subtracting $VA_{pancreatic}$ from $VA_{arterial}$ (Figure 1A and 1B). Thereafter, TAF was calculated by dividing DT by DA. Three equations can be summarized as follows: $DT = VT_{pancreatic} - VT_{arterial}$; $DA = VA_{arterial} - VA_{pancreatic}$; $TAF = DT/DA = (VT_{pancreatic} - VT_{arterial})/(VA_{arterial} - VA_{pancreatic})$.

Statistical analysis

Statistical analyses were performed with SPSS software (SPSS Statistics for Windows, version 20.0; IBM Corp, Armonk, NY, United States). The Kruskal-Wallis analysis of variance (ANOVA) and the Mann-Whitney U test were used to evaluate differences among the three groups, *i.e.*, poorly, moderately, and well-differentiated pancreatic tumors[14]. The patients' age, sex, tumor size, lesion location, $TAR_{arterial}$, $TAR_{pancreatic}$, and TAF were compared. Moreover, receiver operating characteristic (ROC) analysis was used to compare the diagnostic performance of $TAR_{arterial}$, $TAR_{pancreatic}$, and TAF for predicting the pathologic grade of PDA. $P < 0.05$ was considered statistically significant.

RESULTS

The study included 23 men and 19 women with a mean age of 62.43 years (SD: 11.42; range: 34–85 years). The 42 lesions investigated in our study were located in the pancreatic head and uncinate process (n = 30), body and neck (n = 11), and tail (n = 1).

A total of 42 PDAs were categorized into three groups: (1) The well-differentiated group (WD) (n = 13); (2) The moderately differentiated group (MD) (n = 21); and (3)

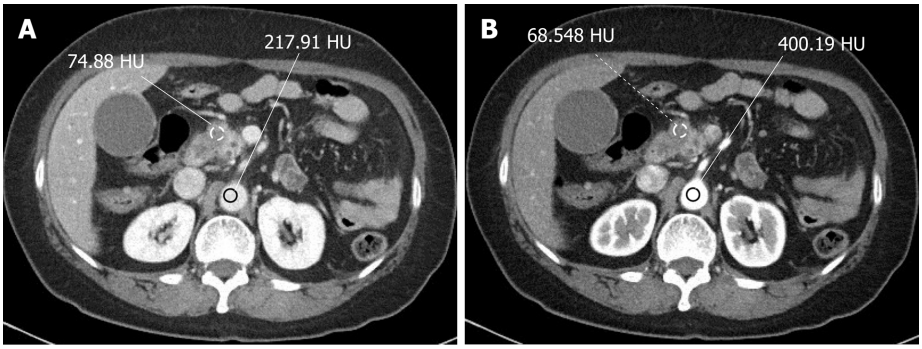

Figure 1 Axial computed tomography images on arterial phase (A) and pancreatic phase (B) of a 68-year-old woman, who was classified in the poorly differentiated group. A: Computed tomography (CT) attenuation values [Hounsfield Unit (HU)] of the tumor in the arterial phase ($VT_{arterial}$) and the aorta in the arterial phase ($VA_{arterial}$) were measured by drawing two separate circular regions of interest in the aorta and pancreas on arterial phase image; B: CT HU of the tumor in a pancreatic phase ($VT_{pancreatic}$) and the aorta in the pancreatic phase ($VA_{pancreatic}$) were measured in the aorta and pancreas on the pancreatic phase 65 s after the injection of the contrast agent.

The poorly differentiated group (PD) (n = 8). The size of the lesions ranged from 1.5 to 7 cm for WD lesions, 1.8 to 5.0 cm for MD lesions, and 2.2 to 13.0 cm for PD lesions, respectively. There were no significant differences in size and location of the lesion among the WD, MD, and PD groups ($P \leq 0.076$). Patient characteristics are summarized in Table 1.

There were no significant differences in values of $VT_{arterial}$, $VT_{pancreatic}$, $VA_{arterial}$, $VA_{pancreatic}$, DT, and DA among the three groups (Table 2). Moreover, there was no significant difference in the value of $TAR_{arterial}$ among the WD (mean: 0.26, 95%CI: 0.1903-0.3340), MD (mean: 0.27; 95%CI: 0.2284-0.3122), and PD groups (mean: 0.19; 95%CI: 0.1295-0.2465). There was no significant difference in the value of $TAR_{pancreatic}$ among the WD (mean: 0.45, 95%CI: 0.3493 to 0.5435), MD (mean: 0.48; 95%CI: 0.3988-0.5557), and PD groups (mean: 0.37; 95%CI: 0.2724-0.4759) ($P < 0.0001$) (Table 3).

The value of TAF was statistically different among the three groups; WD (median and mean, 0.19 and 0.28, respectively; 95%CI: 0.1370-0.4289), MD (median and mean, 0.17 and 0.19, respectively; 95%CI: 0.1377-0.2468), and PD (median and mean, 0.10 and 0.10, respectively; 95%CI: 0.02948-0.1675) ($P < 0.05$).

The diagnostic performances of $TAR_{arterial}$, $TAR_{pancreatic}$, and TAF for the prediction of the pathological grade of PDA are shown in Table 2. The diagnostic performance of TAF (Az = 0.692-0.757) was higher than that of $TAR_{arterial}$ (Az = 0.509-0.71) and $TAR_{pancreatic}$ (Az = 0.512-0.654) for predicting the pathological grade of PDA, although the difference was not statistically significant ($P > 0.093$).

DISCUSSION

The pathological tumor grade is an important prognostic factor of survival in patients with PDA[2]. PDA has unique characteristics and different CT enhancement patterns (such as lung and renal cancers)[8,9,12,15,16], based on the proportion of MVD, degree of fibrosis, and residual normal pancreatic tissue.

There were no significant differences in $VT_{arterial}$, and $VT_{pancreatic}$ among the three groups in our study. Several researchers[8,10] have studied the correlation between CT enhancement parameters and the histological findings of pancreatic adenocarcinomas. Wang *et al*[8] reported that the pathological grade showed a good correlation with $VT_{pancreatic}$ and MVD. In contrast, Hattori *et al*[10]'s study on pancreatic ductal cancer reported that $VT_{arterial}$ and $VT_{pancreatic}$ were negatively correlated with the degree of fibrosis. $VT_{arterial}$ showed a significant correlation with vascular endothelial growth factor and MVD but $VT_{pancreatic}$ was not correlated with MVD. Hattori *et al*[10] reported that $TAR_{arterial}$ was positively correlated with MVD and negatively correlated with the extent of fibrosis. However, our findings demonstrate that there were no significant differences in $TAR_{arterial}$ and $TAR_{pancreatic}$ among the three groups.

There were no significant differences in the values of DT and DA among the WD, MD, and PD groups. Aortic enhancement curves showed a decreased slope from the arterial to the pancreatic phases, after the arterial phase and tumor enhancement curves showed an increased slope. However, the degree of aortic enhancement is influenced by the dose of the contrast media, rate of injection, appropriate timing of

Table 1 Distribution of patient characteristics, lesion size and location

	WD group (*n* = 13)	MD group (*n* = 21)	PD group (*n* = 8)	*P* value
Age, mean ± SD	61.69 ± 10.13	64.85 ± 11.95	55.25 ± 10.17	0.051
Sex				0.542
Male	8	12	3	
Female	5	9	5	
Size, mean ± SD	2.75 ± 1.61	2.95 ± 0.91	4.23 ± 3.62	0.114
Location				0.076
Head and uncinate process	10	17	3	
Body and neck	3	4	4	
Tail	0	0	1	

Data are presented as mean ± SD. WD: Well-differentiated; MD: Moderately differentiated; PD: Poorly differentiated.

Table 2 Diagnostic performance of computed tomography parameters for the prediction of pathological grading

	WD-MD (*n* = 34) *vs* PD (*n* = 8)				WD (*n* = 13) *vs* MD-PD (*n* = 8)			
	Az	SD	*P* value	95%CI	Az	SD	*P* value	95%CI
$TAR_{arterial}$	0.71	0.101	0.467	0.549 - 0.839	0.509	0.107	0989	0.351 - 0.667
$TAR_{pancreatic}$	0.654	0.112	0.742	0.492 - 0.794	0.512	0.0993	0.196	0.353 - 0.669
TAF	0.757	0.102	0.428	0.601 - 0.876	0.692	0.0829	0.093	0.531 - 0.825

Data are presented as mean ± SD (median). CT: Computed tomography; WD: Well-differentiated; MD: Moderately differentiated; PD: Poorly differentiated group; $TAR_{arterial}$ and $TAR_{pancreatic}$: Tumor-to-aorta enhancement ratio in the arterial and pancreatic phases; TAF: Tumor-to-aortic enhancement fraction.

contrast-enhanced imaging, heart rate and cardiac output of the patient, weight, and age[17]. The renal cancer study divided tumor enhancement with aortic enhancement to correct these intrinsic factors[15].

Finally, the TAF values were statistically different among the WD (median and mean, 0.19 and 0.28, respectively; 95%CI: 0.1370-0.4289), MD (median and mean, 0.17 and 0.19, respectively; 95%CI: 0.1377-0.2468), and PD (median and mean, 0.10 and 0.10, respectively; 95%CI: 0.02948-0.1675) ($P < 0.05$). Perfusion imaging demonstrates blood flow in the target organ using single-photon emission computed tomography, CT, and magnetic resonance imaging. Perfusion CT can identify vascularity and fibrosis in the diseased pancreas[18,19]. Various perfusion CT parameters can be generated by postprocessing the CT data. Perfusion CT has a smaller FOV, requires additional radiation exposure, and processing time. However, TAF may be obtained with conventional pancreatic CT, without additional radiation exposure and processing time, and is more useful for practical staging than perfusion CT parameters.

There are several limitations to our study. First, we drew two similar ROIs at the aorta and tumor for minimizing intraobserver variation: Two radiologists consensually reviewed PDA lesions in the arterial and pancreatic phases. Therefore, we could not ascertain the inter or intraobserver variations. Second, this study had an inherent bias owing to its retrospective design. Third, our sample size was small, which made it difficult to obtain statistically significant data. Finally, there was no statistically significant difference, but the number of patients with MD PDAs was greater than patients with PD and WD PDAs. Therefore, prospective studies with large populations are needed in the future, to overcome these limitations.

Table 3 Differences in computed tomography parameters among the well-differentiated, moderately differentiated, and poorly differentiated group groups

	WD (*n* = 13)	MD (*n* = 21)	PD (*n* = 8)	*P* value
$VT_{arterial}$	69.01 ± 25.16 (64.22)	75.23 ± 19.69 (75.41)	59.80 ± 29.47 (56.30)	0.145
$VT_{pancreatic}$	85.34 ± 23.20 (76.08)	90.58 ± 21.99 (90.58)	73.19 ± 39.88 (69.01)	0.184
$VA_{arterial}$	280.71 ± 66.66 (262.74)	290.37 ± 61.12 (279.38)	320.04 ± 86.26 (311.20)	0.496
$VA_{pancreatic}$	201.73 ± 55.81 (200.00)	200.85 ± 43.82 (209.44)	188.28 ± 46.94 (195.43)	0.683
DT	16.32 ± 6.48 (13.65)	15.34 ± 8.06 (13.97)	13.39 ± 13.25 (10.16)	0.678
DA	78.98 ± 49.68 (61.54)	89.51 ± 34.84 (91.01)	131.76 ± 58.68 (120.79)	0.077
$TAR_{arterial}$	0.26 ± 0.12 (0.23)	0.27 ± 0.09 (0.25)	0.19 ± 0.07 (0.20)	0.164
$TAR_{pancreatic}$	0.45 ± 0.16 (0.36)	0.48 ± 0.17 (0.47)	0.37 ± 0.12 (0.38)	0.339
TAF	0.28 ± 0.24 (0.19)	0.19 ± 0.12 (0.17)	0.10 ± 0.08 (0.10)	0.034

Data are presented as mean ± SD (median). WD: Well-differentiated; MD: Moderately differentiated group; PD: Poorly differentiated group; $VT_{arterial}$ and $VT_{pancreatic}$: Attenuation value of the tumor in the arterial and pancreatic phases, respectively; $VA_{arterial}$ and $VA_{pancreatic}$: Attenuation value of the aorta in the arterial and pancreatic phases, respectively; DT and DA: Degree of tumor enhancement and aortic washout between the arterial and pancreatic phases, respectively; $TAR_{arterial}$ and $TAR_{pancreatic}$: Tumor-to-aorta enhancement ratio in arterial and pancreatic phases, respectively; TAF: Tumor-to-aortic enhancement fraction.

ARTICLE HIGHLIGHTS

Research background

Pancreatic ductal adenocarcinoma (PDA) is a malignancy with a high mortality rate and short survival time. The conventional computed tomography (CT) has been worldwide used as a modality for diagnosis of PDA. Also, it has been widely accepted that CT enhancement pattern is related to tumor angiogenesis and pathologic grade of PDA.

Research motivation

Although there is other modality, like perfusion CT that provide information about vascularity and fibrosis in the diseased pancreas, it has a smaller FOV, requires additional radiation exposure, and processing time. So, if there is any CT parameter that can predict pathologic grade of PDA, it would be useful for predicting prognosis of PDA using conventional CT.

Research objectives

In this study, we aimed to evaluate the relationship between the pathologic grade of pancreatic ductal adenocarcinoma and the enhancement parameters of contrast-enhanced CT.

Research methods

In this retrospective study, 42 patients with PDA who underwent surgery after preoperative CT were selected. Two radiologists evaluated the CT images and calculated the value of attenuation at the aorta in the arterial phase and the pancreatic phase ($VA_{arterial}$ and $VA_{pancreatic}$) and of the tumor ($VT_{arterial}$ and $VT_{pancreatic}$) by finding out four regions of interest. Ratio between the tumor and the aorta enhancement on the arterial phase and the pancreatic phase ($TAR_{arterial}$ and $TAR_{pancreatic}$) was figured out through dividing $VT_{arterial}$ by $VA_{arterial}$ and $VT_{pancreatic}$ by $VA_{pancreatic}$. Tumor-to-aortic enhancement fraction (TAF) was expressed as the ratio of the difference between attenuation of the tumor on arterial and parenchymal images to that between attenuation of the aorta on arterial and pancreatic images.

Research results

A total of 42 PDAs were categorized into three groups: Well-differentiated (n = 13), moderately differentiated (n = 21), and poorly differentiated (n = 8). TAF differed significantly between the three groups (P = 0.034) but $TAR_{arterial}$ (P = 0.164) and $TAR_{pancreatic}$ (P = 0.339) did not. The value of TAF was statistically different among the

three groups ($P < 0.05$).

Research conclusions

TAF was statistically different among the three pathologic grade groups. So, the TAF might be correlated with histological finding of PDA. Therefore, calculation of TAF using conventional CT might be useful in predicting the pathologic grade of PDA.

Research perspectives

The conventional CT has been useful modality for diagnosis of PDA. In our study, we suggest the CT enhancement parameter, TAF, could be used as a value for predicting pathologic grade of PDA. The pathologic grade is related to prognosis of PDA, then we can use conventional CT not only for diagnosis, but also for predicting pathologic grade and prognosis of PDA. Also, TAF may be obtained with conventional pancreatic CT, without additional radiation exposure and processing time, and is more useful for practical staging than perfusion CT parameters.

REFERENCES

1 **Rickes S**, Mönkemüller K, Malfertheiner P. Contrast-enhanced ultrasound in the diagnosis of pancreatic tumors. *JOP* 2006; **7**: 584-592 [PMID: 17095837 DOI: 10.1016/j.ejrad.2007.06.035]
2 **Lim JE**, Chien MW, Earle CC. Prognostic factors following curative resection for pancreatic adenocarcinoma: a population-based, linked database analysis of 396 patients. *Ann Surg* 2003; **237**: 74-85 [PMID: 12496533 DOI: 10.1097/00000658-200301000-00011]
3 **Numata K**, Ozawa Y, Kobayashi N, Kubota T, Shimada H, Nozawa A, Nakatani Y, Sugimori K, Matsuo K, Imada T, Tanaka K. Contrast-enhanced sonography of pancreatic carcinoma: correlations with pathological findings. *J Gastroenterol* 2005; **40**: 631-640 [PMID: 16007398 DOI: 10.1007/s00535-005-1598-8]
4 **Folkman J**. What is the evidence that tumors are angiogenesis dependent? *J Natl Cancer Inst* 1990; **82**: 4-6 [PMID: 1688381 DOI: 10.1093/jnci/82.1.4]
5 **Fontanini G**, Vignati S, Boldrini L, Chinè S, Silvestri V, Lucchi M, Mussi A, Angeletti CA, Bevilacqua G. Vascular endothelial growth factor is associated with neovascularization and influences progression of non-small cell lung carcinoma. *Clin Cancer Res* 1997; **3**: 861-865 [PMID: 9815760]
6 **Faviana P**, Boldrini L, Spisni R, Berti P, Galleri D, Biondi R, Camacci T, Materazzi G, Pingitore R, Miccoli P, Fontanini G. Neoangiogenesis in colon cancer: correlation between vascular density, vascular endothelial growth factor (VEGF) and p53 protein expression. *Oncol Rep* 2002; **9**: 617-620 [PMID: 11956638 DOI: 10.3892/or.9.3.617]
7 **Marin D**, Nelson RC, Barnhart H, Schindera ST, Ho LM, Jaffe TA, Yoshizumi TT, Youngblood R, Samei E. Detection of pancreatic tumors, image quality, and radiation dose during the pancreatic parenchymal phase: effect of a low-tube-voltage, high-tube-current CT technique--preliminary results. *Radiology* 2010; **256**: 450-459 [PMID: 20656835 DOI: 10.1148/radiol.10091819]
8 **Wang ZQ**, Li JS, Lu GM, Zhang XH, Chen ZQ, Meng K. Correlation of CT enhancement, tumor angiogenesis and pathologic grading of pancreatic carcinoma. *World J Gastroenterol* 2003; **9**: 2100-2104 [PMID: 12970915 DOI: 10.3748/wjg.v9.i9.2100]
9 **Tateishi U**, Nishihara H, Watanabe S, Morikawa T, Abe K, Miyasaka K. Tumor angiogenesis and dynamic CT in lung adenocarcinoma: radiologic-pathologic correlation. *J Comput Assist Tomogr* 2001; **25**: 23-27 [PMID: 11176288 DOI: 10.1097/00004728-200101000-00004]
10 **Hattori Y**, Gabata T, Matsui O, Mochizuki K, Kitagawa H, Kayahara M, Ohta T, Nakanuma Y. Enhancement patterns of pancreatic adenocarcinoma on conventional dynamic multi-detector row CT: correlation with angiogenesis and fibrosis. *World J Gastroenterol* 2009; **15**: 3114-3121 [PMID: 19575490 DOI: 10.3748/wjg.15.3114]
11 **Zhu L**, Shi X, Xue H, Wu H, Chen G, Sun H, He Y, Jin Z, Liang Z, Zhang Z. CT Imaging Biomarkers Predict Clinical Outcomes After Pancreatic Cancer Surgery. *Medicine (Baltimore)* 2016; **95**: e2664 [PMID: 26844495 DOI: 10.1097/MD.0000000000002664]
12 **Ouyang AM**, Wei ZL, Su XY, Li K, Zhao D, Yu DX, Ma XX. Relative Computed Tomography (CT) Enhancement Value for the Assessment of Microvascular Architecture in Renal Cell Carcinoma. *Med Sci Monit* 2017; **23**: 3706-3714 [PMID: 28757600 DOI: 10.12659/MSM.902957]
13 **Kim YC**, Kim MJ, Park YN, Kim KS, Ahn SH, Jung SE, Kim JK. Relationship between severity of liver dysfunction and the relative ratio of liver to aortic enhancement (RE) on MRI using hepatocyte-specific contrast. *J Magn Reson Imaging* 2014; **39**: 24-30 [PMID: 23553935 DOI: 10.1002/jmri.24100]
14 **Karayiannakis AJ**, Syrigos KN, Polychronidis A, Zbar A, Kouraklis G, Simopoulos C, Karatzas G. Circulating VEGF levels in the serum of gastric cancer patients: correlation with pathological variables, patient survival, and tumor surgery. *Ann Surg* 2002; **236**: 37-42 [PMID: 12131083 DOI: 10.1097/00000658-200207000-00007]
15 **Herts BR**, Coll DM, Novick AC, Obuchowski N, Linnell G, Wirth SL, Baker ME. Enhancement characteristics of papillary renal neoplasms revealed on triphasic helical CT of the kidneys. *AJR Am J Roentgenol* 2002; **178**: 367-372 [PMID: 11804895 DOI: 10.2214/ajr.178.2.1780367]
16 **Vikram R**, Ng CS, Tamboli P, Tannir NM, Jonasch E, Matin SF, Wood CG, Sandler CM. Papillary renal cell carcinoma: radiologic-pathologic correlation and spectrum of disease. *Radiographics* 2009; **29**: 741-54; discussion 755-7 [PMID: 19448113 DOI: 10.1148/rg.293085190]
17 **Moradi M**, Hashemi P, Momeni M. The influence of cardiac function on coronary arterial enhancement at coronary computed tomography angiography: A cross-sectional study. *J Res Med Sci* 2016; **21**: 132 [PMID:

28331518 DOI: 10.4103/1735-1995.196614]
18 **Almeida RR**, Lo GC, Patino M, Bizzo B, Canellas R, Sahani DV. Advances in Pancreatic CT Imaging. *AJR Am J Roentgenol* 2018; **211**: 52-66 [PMID: 29629796 DOI: 10.2214/AJR.17.18665]
19 **D'Onofrio M**, Gallotti A, Mantovani W, Crosara S, Manfrin E, Falconi M, Ventriglia A, Zamboni GA, Manfredi R, Pozzi Mucelli R. Perfusion CT can predict tumoral grading of pancreatic adenocarcinoma. *Eur J Radiol* 2013; **82**: 227-233 [PMID: 23127804 DOI: 10.1016/j.ejrad.2012.09.023]

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