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**Comment on “Prognostic value of preoperative enhanced computed tomography as a quantitative imaging biomarker in pancreatic cancer”**

Yang J *et al*. Quantitative imaging predicts PC prognosis

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**Abstract**

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies because of its high invasiveness and metastatic potential. Computed tomography (CT) is often used as a preliminary diagnostic tool for pancreatic cancer, and it is increasingly used to predict treatment response and disease stage. Recently, a study published in *World Journal of Gastroenterology* reported that quantitative analysis of preoperative enhanced CT data can be used to predict postoperative overall survival in patients with PDAC. A tumor relative enhancement ratio of ≤ 0.7 indicates a higher tumor stage and poor prognosis.

**Key Words:** Pancreatic ductal adenocarcinoma; Computed tomography; Tumor relative enhancement ratio; Diagnostic imaging; Quantitative analysis; Prognosis

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**Core Tip:** Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal malignancies because of its high invasiveness and metastatic potential. The purpose of this letter is to highlight that a quantitative parameter based on enhanced computed tomography, namely the tumor relative enhancement ratio, can reveal the correlation between high malignant potential because of hypervascularity and poor prognosis in PDAC.

**TO THE EDITOR**

The stroma of pancreatic ductal adenocarcinoma (PDAC) is a fibroproliferative microenvironment mainly composed of fibroblasts, and its low vascular supply severely limits the tumor utilization of oxygen and nutrients[1,2]. In such a situation, invasion into fertile tissue becomes an acquired behavior of the tumor in response to severe metabolic stress[3,4]. We were extremely interested in a retrospective study by Gao *et al*[5] published in the June 2022 issue of *World Journal of Gastroenterology*. This was a moderate-quality observational study with a Newcastle-Ottawa Quality Assessment Scale score of 6 (3, 1, 2) that was assessed independently by two of our authors[6]. The importance of this study was that it revealed the ability to predict the overall survival of patients with resectable pancreatic cancer (PC) from an imaging perspective, providing assistance in developing early treatment plans and improving patient prognosis. Gao *et al*[5] initially found that enhanced computed tomography (CT) characterizing vascular perfusion could be used as a quantitative imaging biomarker (QIB) of the malignant potential of PC. Based on this innovative idea and combined with data analysis, the authors demonstrated the value of QIB for predicting the prognosis of patients with PC. In addition, the authors proposed some new concepts to calculate the difference between the region of the overall tumor of the portal venous (PV) phase and that of the non-enhancement phase as the tumor enhancement amplitude (TEA), and the difference between the pancreatic tissue outside the tumor of the PV phase and that of the non-enhancement phase was used as the pancreatic enhancement amplitude (PEA) outside the tumor[5]. The tumor relative enhancement ratio (TRER) was then derived as TEA/PEA. Based on a retrospective analysis of 67 patients with resectable PC, the conclusions drawn by the authors properly summarize the data in the study. Furthermore, this study provided the unique insight that preoperative enhanced CT is a simple and effective predictive tool for overall survival in patients with PDAC and highlighted the need for close monitoring of patients with a TRER ≤ 0.7 because their prognosis is likely to be poor. We would like to thank Gao *et al*[5] for this study, which helped to advance clinical diagnosis and treatment.

In recent years, QIB has become more widely used in clinical practice because the objective features obtained from *in vivo* images measured on a scale of proportions or intervals can serve as indicators of normal biological processes, pathogenic processes, or responses to therapeutic interventions[7]. We therefore use an open multidisciplinary citation analysis database based on artificial intelligence techniques termed *Reference Citation Analysis*. We used “quantitative imaging biomarker” and “pancreatic cancer” as search terms to find the most recent (last 5 years) and relevant cutting-edge research. Overall, the application of QIB is mainly combined with a clinical perspective, and it plays an important role in characterizing tissue, detecting disease, identifying phenotypes, defining longitudinal changes, or predicting outcomes[7]. As previously mentioned, the highly invasive and metastatic nature of PC makes the search for prognostic biomarkers with high accuracy challenging. Numerous studies developed different QIB models that, in addition to characterizing microvascular density[8], significantly compensate for the survival prediction rate of clinical models[9] and contribute to clinical decision making. Next, we provide a brief analysis of PC survival prediction based on the study by Gao *et al*[5] and in the context of the current state of research.

At present, radiomics research concerning the prediction of the prognosis of resectable PC mainly focuses on the analysis of tumor texture features based on CT images[10,11]. Low-attenuation radiomic features of tumors are associated with poorer survival[12,13]. In addition, current radiomics data suggest that first-order entropy is associated with overall survival in PDAC patients and can significantly improve prediction accuracy[14]. Gao *et al*[5] revealed that PDAC hypervascularity was positively associated with poorer survival based on a quantitative analysis of vascular perfusion imaging, which is consistent with the aforementioned low blood supply of highly invasive PDAC[1,2]. In addition, TRER is calculated using CT, which is simple and more easily accepted by clinicians and supports its strong practicability.

We are extremely concerned about the study of PDAC invasion and metastasis because high invasion and metastasis are the characteristics of PDAC itself[15]. Several current radiomics studies identified several predictors of survival following treatment in patients with unresectable or advanced PDAC, including the mean value of positive pixels and kurtosis[16], age and homogeneity on unenhanced CT[17], skewness[18], and cluster tendency with a square root filter[19]. Gao *et al*[5] cited several limitations, including the absence of patients with metastasis. We anticipate future research by Gao *et al*[5] on the use of TRER based on enhanced CT to predict the treatment response and survival of patients with metastatic PDAC after treatment, which will bring great benefits concerning the diagnosis and treatment of patients. In conclusion, quantitative analysis based on enhanced CT imaging (TRER) has good acceptability and utility for predicting the prognosis and survival of patients with PDAC.

**REFERENCES**

1 **Ryan DP**, Hong TS, Bardeesy N. Pancreatic adenocarcinoma. *N Engl J Med* 2014; **371**: 1039-1049 [PMID: 25207767 DOI: 10.1056/NEJMra1404198]

2 **Kleeff J**, Korc M, Apte M, La Vecchia C, Johnson CD, Biankin AV, Neale RE, Tempero M, Tuveson DA, Hruban RH, Neoptolemos JP. Pancreatic cancer. *Nat Rev Dis Primers* 2016; **2**: 16022 [PMID: 27158978 DOI: 10.1038/nrdp.2016.22]

3 **Keleg S**, Büchler P, Ludwig R, Büchler MW, Friess H. Invasion and metastasis in pancreatic cancer. *Mol Cancer* 2003; **2**: 14 [PMID: 12605717 DOI: 10.1186/1476-4598-2-14]

4 **Hanahan D**, Weinberg RA. The hallmarks of cancer. *Cell* 2000; **100**: 57-70 [PMID: 10647931 DOI: 10.1016/s0092-8674(00)81683-9]

5 **Gao JF**, Pan Y, Lin XC, Lu FC, Qiu DS, Liu JJ, Huang HG. Prognostic value of preoperative enhanced computed tomography as a quantitative imaging biomarker in pancreatic cancer. *World J Gastroenterol* 2022; **28**: 2468-2481 [PMID: 35979266 DOI: 10.3748/wjg.v28.i22.2468]

6 **Wells GA**, Shea B, O’Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. [cited 18 August 2022]. Available from: https://www.ohri.ca//programs/clinical\_epidemiology/oxford.asp

7 **Obuchowski NA**, Huang E, deSouza NM, Raunig D, Delfino J, Buckler A, Hatt C, Wang X, Moskowitz C, Guimaraes A, Giger M, Hall TJ, Kinahan P, Pennello G. A Framework for Evaluating the Technical Performance of Multiparameter Quantitative Imaging Biomarkers (mp-QIBs). *Acad Radiol* 2022 [PMID: 36180328 DOI: 10.1016/j.acra.2022.08.031]

8 **Mayer P**, Fritz F, Koell M, Skornitzke S, Bergmann F, Gaida MM, Hackert T, Maier-Hein K, Laun FB, Kauczor HU, Grenacher L, Klauß M, Stiller W. Assessment of tissue perfusion of pancreatic cancer as potential imaging biomarker by means of Intravoxel incoherent motion MRI and CT perfusion: correlation with histological microvessel density as ground truth. *Cancer Imaging* 2021; **21**: 13 [PMID: 33468259 DOI: 10.1186/s40644-021-00382-x]

9 **Gebauer L**, Moltz JH, Mühlberg A, Holch JW, Huber T, Enke J, Jäger N, Haas M, Kruger S, Boeck S, Sühling M, Katzmann A, Hahn H, Kunz WG, Heinemann V, Nörenberg D, Maurus S. Quantitative Imaging Biomarkers of the Whole Liver Tumor Burden Improve Survival Prediction in Metastatic Pancreatic Cancer. *Cancers (Basel)* 2021; **13** [PMID: 34830885 DOI: 10.3390/cancers13225732]

10 **Yun G**, Kim YH, Lee YJ, Kim B, Hwang JH, Choi DJ. Tumor heterogeneity of pancreas head cancer assessed by CT texture analysis: association with survival outcomes after curative resection. *Sci Rep* 2018; **8**: 7226 [PMID: 29740111 DOI: 10.1038/s41598-018-25627-x]

11 **Chakraborty J**, Langdon-Embry L, Cunanan KM, Escalon JG, Allen PJ, Lowery MA, O'Reilly EM, Gönen M, Do RG, Simpson AL. Preliminary study of tumor heterogeneity in imaging predicts two year survival in pancreatic cancer patients. *PLoS One* 2017; **12**: e0188022 [PMID: 29216209 DOI: 10.1371/journal.pone.0188022]

12 **Cassinotto C**, Chong J, Zogopoulos G, Reinhold C, Chiche L, Lafourcade JP, Cuggia A, Terrebonne E, Dohan A, Gallix B. Resectable pancreatic adenocarcinoma: Role of CT quantitative imaging biomarkers for predicting pathology and patient outcomes. *Eur J Radiol* 2017; **90**: 152-158 [PMID: 28583627 DOI: 10.1016/j.ejrad.2017.02.033]

13 **Attiyeh MA**, Chakraborty J, Doussot A, Langdon-Embry L, Mainarich S, Gönen M, Balachandran VP, D'Angelica MI, DeMatteo RP, Jarnagin WR, Kingham TP, Allen PJ, Simpson AL, Do RK. Survival Prediction in Pancreatic Ductal Adenocarcinoma by Quantitative Computed Tomography Image Analysis. *Ann Surg Oncol* 2018; **25**: 1034-1042 [PMID: 29380093 DOI: 10.1245/s10434-017-6323-3]

14 **Gao Y**, Cheng S, Zhu L, Wang Q, Deng W, Sun Z, Wang S, Xue H. A systematic review of prognosis predictive role of radiomics in pancreatic cancer: heterogeneity markers or statistical tricks? *Eur Radiol* 2022 [PMID: 35904618 DOI: 10.1007/s00330-022-08922-0]

15 **Rhim AD**, Mirek ET, Aiello NM, Maitra A, Bailey JM, McAllister F, Reichert M, Beatty GL, Rustgi AK, Vonderheide RH, Leach SD, Stanger BZ. EMT and dissemination precede pancreatic tumor formation. *Cell* 2012; **148**: 349-361 [PMID: 22265420 DOI: 10.1016/j.cell.2011.11.025]

16 **Sandrasegaran K**, Lin Y, Asare-Sawiri M, Taiyini T, Tann M. CT texture analysis of pancreatic cancer. *Eur Radiol* 2019; **29**: 1067-1073 [PMID: 30116961 DOI: 10.1007/s00330-018-5662-1]

17 **Cozzi L**, Comito T, Fogliata A, Franzese C, Franceschini D, Bonifacio C, Tozzi A, Di Brina L, Clerici E, Tomatis S, Reggiori G, Lobefalo F, Stravato A, Mancosu P, Zerbi A, Sollini M, Kirienko M, Chiti A, Scorsetti M. Computed tomography based radiomic signature as predictive of survival and local control after stereotactic body radiation therapy in pancreatic carcinoma. *PLoS One* 2019; **14**: e0210758 [PMID: 30657785 DOI: 10.1371/journal.pone.0210758]

18 **Cheng SH**, Cheng YJ, Jin ZY, Xue HD. Unresectable pancreatic ductal adenocarcinoma: Role of CT quantitative imaging biomarkers for predicting outcomes of patients treated with chemotherapy. *Eur J Radiol* 2019; **113**: 188-197 [PMID: 30927946 DOI: 10.1016/j.ejrad.2019.02.009]

19 **Salinas-Miranda E**, Khalvati F, Namdar K, Deniffel D, Dong X, Abbas E, Wilson JM, O'Kane GM, Knox J, Gallinger S, Haider MA. Validation of Prognostic Radiomic Features From Resectable Pancreatic Ductal Adenocarcinoma in Patients With Advanced Disease Undergoing Chemotherapy. *Can Assoc Radiol J* 2021; **72**: 605-613 [PMID: 33151087 DOI: 10.1177/0846537120968782]

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