77205_Auto_EditedC.docx

25

Name of Journal: World Journal of Gastroenterology

Manuscript NO: 77205

Manuscript Type: ORIGINAL ARTICLE

Retrospective Study

Preoperative contrast-enhanced computed tomography-based radiomics model for overall survival prediction in hepatocellular carcinoma

Deng PZ et al. Radiomics model for HCC survival prediction

Peng-Zhan Deng, Bi-Geng Zhao, Xian-Hui Huang, Ting-Feng Xu, Zi-Jun Chen, Qiu-Feng Wei, Xiao-Yi Liu, Yu-Qi Guo, Sheng-Guang Yuan, Wei-Jia Liao

Abstract

BACKGROUND

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy with a rising incidence worldwide. The prognosis of HCC patients after radical resection remains poor. Radiomics is a novel machine learning method that extracts quantitative features from medical images and provides predictive information of cancer, which can assist with cancer diagnosis, therapeutic decision-making and prognosis improvement.

AIM

To develop and validate a contrast-enhanced computed tomography-based radiomics model for predicting the overall survival (OS) of HCC patients after radical hepatectomy.

METHODS

A total of 150 HCC patients 21ere randomly divided into a training cohort (n = 107) and a validation cohort (n = 43). Radiomics features were extracted from the entire tumour

lesion. The least absolute shrinkage and selection operator algorithm was applied for the selection of radiomics features and the construction of the radiomics signature.

Univariate and multivariate Cox regression analyses were used to identify the independent prognostic factors and develop the predictive nomogram, incorporating clinicopathological characteristics and the radiomics signature. The accuracy of the nomogram was assessed with the concordance index, receiver operating characteristic (ROC) curve and calibration curve. The clinical utility was evaluated by decision curve analysis (DCA). Kaplan–Meier methodology was used to compare the survival between the low- and high-risk subgroups.

RESULTS

In total, seven radiomics features were selected to construct the radiomics signature. According to the results of univariate and multivariate Cox regression analyses, alphafetoprotein (AFP), neutrophil-to-lymphocyte ratio (NLR) and radiomics signature were included to build the nomogram. The C-indices of the nomogram in the training and validation cohorts were 0.736 and 0.774, respectively. ROC curve analysis for predicting 1-, 3-, and 5-year OS confirmed satisfactory accuracy [training cohort, area under the curve (AUC) = 0.850, 0.791 and 0.823, respectively; validation cohort, AUC = 0.905, 0.884 and 0.911, respectively]. The calibration curve analysis indicated a good agreement between the nomogram-prediction and actual survival. DCA curves suggested that the nomogram had more benefit than traditional staging system models. Kaplan-Meier survival analysis indicated that patients in the low-risk group had longer OS and disease-free survival (all P < 0.0001).

CONCLUSION

The nomogram containing the radiomics signature, NLR and AFP is a reliable tool for predicting the OS of HCC patients.

Key Words: Hepatocellular carcinoma; Radiomics; Contrast-enhanced computed tomography; Survival prediction

Deng PZ, Zhao BG, Huang XH, Xu TF, Chen ZJ, Wei QF, Liu XY, Guo YQ, Yuan SG, Liao WJ. Preoperative contrast-enhanced computed tomography-based radiomics model for overall survival prediction in hepatocellular carcinoma. *World J Gastroenterol* 2022; In press

Core Tip: The prognosis of hepatocellular carcinoma (HCC) patients remains poor even after radical resection. Therefore, a precise and reliable tool to predict the prognosis of HCC patients is urgently needed. We established a predictive model incorporating radiomics features extracted from preoperative contrast-enhanced computed tomography images, alpha-fetoprotein and neutrophil-to-lymphocyte ratio to predict the overall survival of patients with HCC, and the model was visualized *via* a nomogram. The nomogram showed good accuracy for survival prediction.

INTRODUCTION

Primary liver cancer is the sixth most common malignancy and the third leading cause of cancer-related mortality in the world. Hepatocellular carcinoma (HCC) accounts for 75%-85% of primary liver cancers^[1]. Presently, the main therapies for HCC include surgical resection, local ablation, interventional embolization and liver transplantation. For HCC patients with early-stage disease, hepatectomy and liver transplantation are the mainstay curative treatments. Due to the insidious onset and lack of evident clinical symptoms in the early stage, patients with HCC are often diagnosed at an advanced stage. Even after surgical resection, the prognosis of HCC patients remains poor due to postoperative recurrence and metastasis. It has been reported that the recurrence rate within 5 years reaches 60%^[2].

Alpha-fetoprotein (AFP) has been widely applied as a biomarker of HCC for diagnosis, monitoring treatment response, assessing prognosis and detecting early recurrence. However, the specificity of AFP for diagnosing HCC is 99%-100%, but the sensitivity is only 20% to 45%^[3]. Moreover, nearly 31% of patients with HCC are AFP negative^[4]. Therefore, AFP still has limitations as a biomarker of HCC. It has been reported that the tumour microenvironment is closely related to the initiation and progression of HCC^[5]. Recent studies have shown that a high density of tumour-infiltrating lymphocytes is associated with favourable outcomes^[6]. The neutrophil-to-lymphocyte ratio (NLR) was reported to be an independent prognostic factor for patients with HCC^[7,8].

Radiomics is a new method of medical image analysis that uses a series of datamining algorithms or statistical analysis tools for the high-throughput extraction of quantitative metric features [9,10] to obtain prognostic and predictive information for clinical decision support. It has been recognized that intratumor heterogeneity is often associated with tumour subtyping and can significantly impact prognosis and response to treatment [11,12]. Traditional radiological analysis is mainly based on naked-eye observation, which primarily focuses on tumour size and anatomical location but ignores intratumor heterogeneity. Radiomics features are able to provide a

comprehensive overview of intratumor heterogeneity in a noninvasive manner^[13]. Several recent studies indicate that radiomics features may potentially be a useful diagnostic and prognostic biomarker in liver cancer and other tumour types^[14-16].

Due to the insufficiency of accurateness and objectiveness for prognostic markers in the prognostic evaluation of HCC patients, a precise and reliable tool to predict the prognosis of HCC patients is urgently needed. In the present study, we aimed to develop and validate a model based on contrast-enhanced computed tomography (CECT) images and clinical-pathologic characteristics to predict the overall survival (OS) of HCC patients.

MATERIALS AND METHODS

This study was composed of the following steps: (1) Patient recruitment and data collection; (2) CECT image acquisition, tumour segmentation, region of interest (ROI) selection, radiomics feature extraction and radiomics signature construction; (3) The radiomics signature and clinical-pathologic characteristics were combined to build a predictive model and visualized *via* a nomogram; and (4) Evaluation of the predictive model using receiver operating characteristic (ROC) curves, calibration curves, decision curve analysis (DCA) and Kaplan–Meier curves.

Patients

This retrospective study was approved by the research ethics committee of the Affiliated Hospital of Guilin Medical University and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients.

A total of 208 HCC patients who underwent radical resection at the Affiliated Hospital of Guilin Medical University with pathologically confirmed HCC were recruited from January 2014 to September 2017. Among them, 150 individuals fulfilled the inclusion and exclusion criteria (Figure 1). Radical resection was defined as a completed resection of the tumour mass with pathologically confirmed negative margins and no residual tumour or new lesion observed in two observations at an

interval of no less than 4 wk. All tumour tissue samples were diagnosed by at least two experienced pathologists independently. All patients underwent CECT scans and haematological examinations before surgery. The 150 enrolled HCC patients were randomly divided into a training cohort (n = 107) and a validation cohort (n = 43) at a ratio of 2.5:1. Demographic and clinical-pathologic data were collected from medical records, including age, sex, alanine aminotransferase, AFP, tumor, node and metastasis (TNM) stage, Barcelona clinic liver cancer (BCLC) stage, hepatitis B surface antigen (HBsAg) and NLR.

Each patient was followed up *via* outpatient review. Routine postoperative examinations, including routine blood tests, liver function tests, renal function tests, serum AFP levels and abdominal ultrasonography, were performed every 2 mo after surgery within 2 years and then every 6 mo thereafter. A CECT scan was recommended if the examination results were abnormal or tumour recurrence was suspected. For patients who did not attend the follow-up visit, follow-up information was obtained by phone. OS was defined as the time from surgery to death or the last follow-up date, while disease-free survival (DFS) was defined as the time from surgery to tumour first intrahepatic and/or extrahepatic recurrence, death, or the last follow-up date.

CECT scan protocols and image preprocessing

Abdominal CECT scans were performed with two scanners: a Lightspeed VCT XT (GE Healthcare, United States) and an Optima CT660 (GE Healthcare, United States). The scanner was operated in cine mode, and the parameters were as follows: tube voltage of 120 kV, automatic tube current modulation with noise index of 8, tube rotation speed of 600 ms, pitch of 0.985:1, collimator of 0.625 mm. Iopromide (Ultravist 300, Bayer-Schering Pharma, Germany) was given intravenously in a volume of 1.5 mL/kg at a rate of 4 mL/s *via* the antecubital vein. The slice thickness and interval of the arterial and portal venous phase images was 5 mm. All images were reconstructed into images with a 1.25 mm slice thickness and 1.25 mm interval. All data were transferred to an advanced workstation (AW 4.7).

All CECT images in this study met the criteria delineated by the American Association for the Study of Liver Disease guidelines^[17]. CECT images were exported in digital imaging and communication in medicine (DICOM) format from the picture archiving and communication system database. All DICOM images were converted to neuroimaging informatics technology initiative format by the SimpleITK package (version 1.2.0) of Python software (version 3.7).

Radiomics analysis and radiomics signature construction

Tumour segmentation was performed by 3D Slicer software (version 4.11.20210226). ROIs were drawn on each layer of the tumour in the horizontal plane from the upper boundary to the lower boundary. Tumour lesions were semiautomatically outlined on all arterial phase and portal venous phase images, and manual corrections were implemented whenever necessary. The images were reviewed independently by two blinded radiologists with 7 and 8 years of experience, and a third radiologist resolved any discrepancies. For patients with multiple tumours, only the largest tumour was selected.

CECT image normalization and radiomics feature extraction were conducted by the Pyradiomics package (version 3.0.3) of Python software. The radiomics features extracted from ROIs included first order features, shape features (2D and 3D), gray level co-occurrence matrix features, gray level size zone matrix features, gray level run length matrix features, gray level dependence matrix features and neighbouring gray tone difference matrix features. Due to the large number of features, dimensionality reduction was essential. The least absolute shrinkage and selection operator (LASSO) algorithm with a 10-fold cross-validation approach was used to reduce the data dimension in the training cohort. Afterwards, the radiomics score, which was defined as the radiomics signature, was generated by linearly combining the selected radiomics features and their weighted coefficients. The workflow of radiomics analysis and radiomics signature construction is shown in Figure 2A. Afterwards, the concordance

index (C-index) and ROC curve analysis were used to estimate the predictive value of the radiomics signature for 1-, 3- and 5-year OS.

Selection of the optimal cut-off value for NLR

According to our previous study^[18], the optimal cut-off value for NLR in predicting the prognosis of HCC patients after curative resection was 2.31, which had both maximum sensitivity and specificity [area under the curve (AUC) = 0.723, 95% CI: 0.664-0.777].

Statistical analysis

Normality of distributions was tested by the Shapiro-Wilk test. Clinical-pathologic characteristics were compared by Student's t test and are presented as the mean ± SD for continuous variables conforming to a normal distribution. Nonnormally distributed continuous variables were compared using the Wilcoxon signed rank test and are presented as the median with interquartile range. Categorical variables were compared using the Pearson c² test. Univariate and multivariate regression analyses were performed in the training cohort using the Cox proportional hazards model to identify the independent predictors for nomogram construction. The rms and regplot packages were used to establish a nomogram and calibration curve. The ROC curve analysis was performed using the timeROC package. The C-index, ROC curve and calibration curve were used to assess the accuracy of the nomogram. The Kaplan-Meier method and logrank test were conducted to compare the different survival rates between the low- and high-risk subgroups in different cohorts. We built two predictive models based on BCLC and TNM staging systems. Patients were categorized into stage 0, stage A, stage B and stage C according to BCLC staging system; grade I, grade II, grade III and grade IV according to TNM staging system. DCA was conducted to compare the abovementioned two traditional staging systems with the nomogram. All statistical analyses were performed using SPSS software (version 24.0) or R software (version **4.1.2**) and accepted as significant at P < 0.05.

RESULTS

Demographic and clinicopathological characteristics

A total of 150 HCC patients were enrolled in this study according to inclusion and exclusion criteria, with an average age of 49.9 years (range, 20-75 years), and 130 patients were male. A total of 136 patients were diagnosed with cirrhosis, while 137 patients were classified as Child-Pugh class A. A total of 124 patients were positive for HBsAg. Patients were randomly divided into a training cohort (n = 107) and a validation cohort (n = 43). The demographic and clinical-pathologic characteristics are summarized in Table 1. There were no significant differences in variables between the two cohorts.

Radiomics signature construction

In total, 1926 radiomics features were extracted from the ROIs. Based on the training cohort, radiomics features were reduced to 7 survival-related features by using the LASSO algorithm. The name of the selected features and the formula of the radiomics score are shown in Supplementary Table 1. The C-indices of the radiomics signature for predicting OS in the training and validation cohorts were 0.689 (95%CI: 0.626–0.751) and 0.746 (95%CI: 0.650–0.842), respectively. The ROC curves of the radiomics signature for predicting 1-, 3- and 5-year OS are shown in Figure 3 (AUC = 0.648, 0.753 and 0.807, respectively, in the training cohort; AUC = 0.921, 0.840 and 0.891, respectively, in the validation cohort).

Development and validation of the predictive nomogram

Based on the univariate regression analysis (Table 2), four variables with P < 0.05 were enrolled in the multivariate regression analysis. The results of multivariate regression analysis are displayed as forest plots (Figure 4). AFP [hazard ratio (HR), 1.8; 95%CI: 1.06–3.1, P = 0.03], NLR (HR, 2.5; 95%CI: 1.45–4.3, P < 0.001) and radiomics signature (HR, 3.7; 95%CI: 1.25–10.7, P = 0.018) were identified as independent predictors of OS. The abovementioned three variables were included to develop the predictive model

and visualized *via* a nomogram (Figure 2B). The C-indices of the nomogram in the training and validation cohorts were 0.736 (95%CI: 0.681–0.791) and 0.774 (95%CI: 0.697–0.851), respectively. The AUC values of 1-, 3-, and 5-year OS were 0.850, 0.791 and 0.823, respectively, in the training cohort (Figure 5A) and 0.905, 0.884 and 0.911, respectively, in the validation cohort (Figure 5B). The calibration curves of the nomogram demonstrated good agreement between the predicted and actual survival probabilities (Figure 5 C and D).

Evaluation of clinical practicality and risk stratification ability

DCA curves showed that the nomogram received more net benefit than the BCLC staging system model and TNM staging system model in predicting 3- and 5-year OS at reasonable threshold probability (Figure 6).

To further explore the risk stratification ability of the nomogram, we calculated the total points of the nomogram for each patient. The total points conformed to a normal distribution in the training and validation cohorts. Patients were categorized into lowand high-risk subgroups based on whether the total points of the patient were lower (training cohort ≤ 89.8 ; validation cohort ≤ 66.0) or higher (training cohort ≥ 89.8 ; validation cohort ≥ 66.0) than the median points of each cohort. Kaplan–Meier curves indicated that patients in the low-risk subgroup had significantly longer OS and DFS, with all P < 0.001 (Figure 7).

DISCUSSION

In this study, we developed a nomogram for predicting the survival of HCC patients after radical hepatectomy. Seven radiomics features were selected from 1926 radiomics features, and then integrated into a single radiomics signature to comprehensively estimate CECT images. We included AFP, NLR and radiomics signature to build the predictive nomogram. The C-indices of the nomogram in the training cohort and validation cohort were 0.736 and 0.774, respectively. The AUCs and the calibration curve indicated satisfactory accuracy in both the training and validation cohorts (AUC

of 1-, 3- and 5-year survival = 0.850, 0.791, 0.823 and 0.905, 0.884, 0.911, respectively). The high AUCs of the nomogram indicate a high accuracy in predicting OS. In DCA, comparing the traditional staging system with our nomogram with respect to predictive ability and clinical practicality, the predictive nomogram was superior to the traditional staging system (BCLC and TNM staging system) in predicting 3- and 5-year survival.

To our knowledge, our radiomics-based model that contains NLR and AFP to predict survival in patients with HCC is entirely novel. A few previous studies^[19,20] have investigated the capability of radiomics analysis in predicting the prognosis of HCC patients, and these studies analysed the largest cross-sectional area, whereas entire-tumour analysis was conducted in this study, which can provide more comprehensive information and more effective evaluation of the tumour. Thus, compared with previous studies, radiomics analysis in this study may achieve better performance. Various models combining radiomics features with clinical-pathologic factors to predict prognosis have been developed. Nevertheless, very few studies have enrolled radiomics features and NLR as variables to build a prognostic prediction model for HCC patients. Wang *et al*^[21] established an magnetic resonance imaging-based radiomics model incorporating a few clinical factors for predicting the 5-year survival of patients with HCC after radical surgery. The mean AUC in the validation cohort was 0.7578 (95% CI: 0.7056–0.8100).

As precision medicine has developed, accurate prediction of patient prognosis is the principal component of individualized therapy and improving patient prognosis. It has been reported that intratumor heterogeneity is common in a variety of tumours and correlated with clinical outcomes^[22]. However, information about intratumor heterogeneity obtained from routine clinical examinations is limited. Radiomics analysis refers to computer-aided data mining of quantitative high-throughput imaging features extracted from medical images^[9,10], and it has been reported that radiomics features have potential prognostic value in liver cancer^[14], lung cancer^[15] and breast cancer^[16]. Compared with the interpretation of traditional radiology, radiomics could provide comprehensive information regarding intratumor heterogeneity that may be

unable to be obtained by the naked eye of radiologists. To a certain extent, radiomics overcomes these limitations of traditional radiology. As a biomarker associated with HCC, AFP has been widely used for early diagnosis and monitoring of HCC. AFP was considered an independent risk factor for postoperative survival; moreover, patients with low serum AFP levels had longer OS after radical resection. However, AFP still has some limitations in the prognosis prediction of HCC. Prior studies have reported that AFP has no ability to predict prognosis in small HCC (diameter ≤ 3 cm)^[23]. Immune cells such as neutrophils, macrophages and lymphocytes within the tumour microenvironment have been confirmed to affect tumour development and progression^[24]. There is evidence suggesting that lymphocytes can inhibit tumour proliferation, invasion, and metastasis by enhancing immune surveillance^[25]. Moreover, tumour-infiltrating lymphocytes were associated with better outcomes in a variety of tumours, probably linked to tumour infiltration, antitumor activity, lymphocyte induction and inhibition of angiogenesis^[26]. One study indicated that neutrophils promote tumour invasion^[27]. Neutrophils can inhibit the proliferation of lymphocytes and induce lymphocyte apoptosis^[28]. Patients with an elevated NLR level have relative neutrophilia and lymphocytopenia. Therefore, a high NLR indicates a poor prognosis, and this has been confirmed in numerous cancers, including gastric cancer^[29], colorectal cancer^[30] and pancreatic cancer^[31]. To date, there is growing attention to the potential of NLR to be a prognostic biomarker in patients with HCC^[32,33]. The NLR is a modality of measuring systemic inflammation that is relatively inexpensive and conveniently obtained from routine preoperative blood tests. In our previous study, the optimal cutoff value of NLR was determined to be 2.31 for predicting the prognosis of patients with HCC, and this was confirmed by not only our previous retrospective trial but also other prospective clinical trials^[32]. In summary, NLR is a potential independent predictor for HCC.

As a standardized and noninvasive imaging modality, CECT is widely utilized for diagnosis, staging, clinical decision-making and treatment response monitoring across numerous cancer types. An advantage of radiomics analysis is that it was performed on existing CECT images as a routine preoperative examination for patients with malignant tumours. Moreover, the variables included in this nomogram were easily acquired from routine blood examinations.

All CECT images were reconstructed with a slice thickness of 1.25 mm, and a previous report showed that slice thickness does not considerably influence the stability of the parameters^[34].

The current study has several limitations. First, this study was a single-centre retrospective study. Insufficient data heterogeneity could be a major limitation of single-centre studies. Therefore, more patients from other centres are needed to further validate the reliability and clinical applicability of this prognostic model. Second, HCC is considered to be related to various aetiological factors, including alcohol, aflatoxin, hepatitis B virus and hepatitis C virus. Different aetiologies might result in different outcomes in HCC. Hepatitis B virus was the main aetiology of HCC in the present study. Thus, future studies are required to validate the efficacy and accuracy of this predictive model in HCC with different aetiologies. Third, the different contrast agents or the different injection speeds may affect the quantification of radiomic features[35] and thus affect the accuracy of the model. To overcome this limitation, multiinstitutional validation and cross-validation are required in the future. Fourth, regions of interest were outlined semiautomatically and corrected manually when necessary. Hence, a certain degree of selection bias of the ROIs might be created by the different observers. This is a challenging problem for radiomics analysis to eliminate or reduce biases. Fifth, the correlation between radiomics features and biological behaviour remains unknown. Recently, radio-genomics has become an emerging area that integrates radiomics and genomics. Radio-genomics is the discipline that studies the relationship between image phenotypes and genomics, which may contribute to precision medicine development^[36]. Further research is still required to determine the potential correlation between radiomics and genomics in HCC. In future studies, we will incorporate genomic characteristics associated with HCC prognosis to construct a more comprehensive radio-genomics predictive model.

CONCLUSION

In conclusion, the nomogram combining the radiomics signature, NLR and AFP may contribute to postoperative outcome prediction and clinical treatment decision-making for HCC patients.

ARTICLE HIGHLIGHTS

Research background

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy. The prognosis of HCC patients remains poor. Radiomics is an artificial intelligent-based method for obtaining prognostic and predictive information which may contribute to clinical outcomes improvement.

Research motivation

Currently, a few studies have analysed the largest cross-sectional area of HCC tumour. In this study, we have analysed the entire-tumour to build a more comprehensive prognostic prediction model with clinical characteristics. We aimed to develop a radiomics model for predicting the overall survival of HCC patients after hepatectomy.

Research objectives

In this study, we aimed to develop a radiomics model based on contrast-enhanced computed tomography (CECT) images for predicting the overall survival of HCC patients after radical hepatectomy.

Research methods

A total of 150 HCC patients were enrolled and randomly divided into a training cohort (n = 107) and a validation cohort (n = 43) at ratio 2.5:1. Radiomics features were extracted from the CECT images. In training cohort, the least absolute shrinkage and selection operator algorithm was applied for radiomics features selection and radiomics

signature construction. Univariate and multivariate Cox regression analyses were used to develop the predictive model. The accuracy of the model was assessed with the concordance index, receiver operating characteristic curve and calibration curve. The clinical practicality was evaluated by decision curve analysis. The survival between the low- and high-risk subgroups was compared using Kaplan–Meier methodology.

Research results

In total, seven radiomics features were selected to construct the radiomics signature. Alpha-fetoprotein, neutrophil-to-lymphocyte ratio and radiomics signature were identified as independent risk predictors to build the predictive model. The C-indices of the model in the training and validation cohorts were 0.736 and 0.774, respectively. In receiver operating characteristic curve for predicting 1-, 3-, and 5-year overall survival, area under the curve (AUC) = 0.850, 0.791 and 0.823, respectively in training cohort; AUC = 0.905, 0.884 and 0.911, respectively in validation cohort. The calibration curve analysis indicated a good agreement between the model-prediction and actual survival. Decision curve analysis suggested that the predictive model had more benefit than traditional staging system models. In Kaplan–Meier survival analysis, patients in the low-risk group had longer overall survival and disease-free survival.

Research conclusions

The predictive model is a reliable tool for predicting the overall survival of HCC patients after radical hepatectomy.

Research perspectives

More precise and reliable tool to predict the prognosis of HCC patients is urgently needed. Radiomics is a new method for obtaining prognostic and predictive information. In this study, we aimed to develop a predictive model based on CECT images and clinical-pathologic characteristics to predict the overall survival of HCC patients.

77205_Auto_EditedC.docx

\sim	ור	\sim	INI	ΛΙ	ıT	ΥF	٦г	~	–	т
() :	≺ι		ш	ΑI	11	YH	⟨⊢	Р١	ıк	

	7% ARITY INDEX							
PRIMA	PRIMARY SOURCES							
1	www.ncbi.nlm.nih.gov Internet	145 words — 3 %						
2	bmccancer.biomedcentral.com	118 words — 3%						
3	www.dovepress.com Internet	81 words — 2 %						
4	www.frontiersin.org	80 words — 2%						
5	www.mdpi.com Internet	41 words — 1%						
6	Chu-Yu Jing, Yi-Peng Fu, Su-Su Zheng, Yong Yi et al. "Prognostic nomogram for patients with hepatocellular carcinoma underwent adjuvant transchemoembolization following curative resection", N 2017 Crossref							
7	academic-accelerator.com Internet	40 words — 1 %						
8	Deling Song, Fei Yang, Yujiao Zhang, Yazhe Guo, Yingwu Qu, Xiaochen Zhang, Yuexiang Zhu, Shujun	35 words — 1 %						

Cui. "Dynamic contrast-enhanced MRI radiomics nomogram for

predicting axillary lymph node metastasis in breast cancer", Cancer Imaging, 2022

Crossref

- Kang Chen, Shaoming Zhu, Weimin Yu, Yuqi Xia, Ji
 Xing, Jie Geng, Fan Cheng. "Comprehensive Analysis of N6-Methylandenosine-Related Long Non-Coding RNAs
 Signature in Prognosis and Tumor Microenvironment of Bladder Cancer", Frontiers in Oncology
- Jing Ren, Yuan Li, Jun-Jun Yang, Jia Zhao et al. "MRIbased radiomics analysis improves preoperative diagnostic performance for the depth of stromal invasion in patients with early stage cervical cancer", Insights into Imaging, 2022

 Crossref
- onlinelibrary.wiley.com
 Internet

 28 words 1 %
- Xianli Li, Haoya Xu, Limei Yan, Jian Gao, Liancheng Zhu. "A Novel Clinical Nomogram for Predicting Cancer-Specific Survival in Adult Patients After Primary Surgery for Epithelial Ovarian Cancer: A Real-World Analysis Based on the Surveillance, Epidemiology, and End Results Database and External Validation in a Tertiary Center", Frontiers in Oncology, 2021

 Crossref
- link.springer.com 27 words 1 %
- Junmin Wang, Weirui Ren, Chuang Zhang, Xiaoya
 Wang. "A New Staging System Based on the
 Dynamic Prognostic Nomogram for Elderly Patients With

Primary Gastrointestinal Diffuse Large B-Cell Lymphoma", Frontiers in Medicine, 2022

Crossref

Crossref

- "ECR 2019: Book of Abstracts", Insights into Imaging, $_{23 \text{ words}} = 1\%$
- Xiangtian Zhao, Yukun Zhou, Yuan Zhang, Lujun Han, Li Mao, Yizhou Yu, Xiuli Li, Mengsu Zeng, Mingliang Wang, Zaiyi Liu. "Radiomics Based on Contrast-Enhanced MRI in Differentiation Between Fat-Poor Angiomyolipoma and Hepatocellular Carcinoma in Noncirrhotic Liver: A Multicenter Analysis", Frontiers in Oncology, 2021
- assets.researchsquare.com 22 words 1%
- "ECR Final Programme", European Radiology
 Supplements, 2004
 Crossref

 21 words < 1%
- bio-protocol.org
 Internet 21 words < 1 %
- Yongfu Xiong, Wenxian You, Min Hou, Linglong Peng, He Zhou, Zhongxue Fu. "Nomogram Integrating Genomics with Clinicopathologic Features Improves Prognosis Prediction for Colorectal Cancer", Molecular Cancer Research, 2018

21 Xin Jia, Yixuan Zhai, Dixiang Song, Yiming Wang, Shuxin Wei, Fengdong Yang, Xinting Wei. "A Multiparametric MRI-Based Radiomics Nomogram for Preoperative Prediction of Survival Stratification in

Glioblastoma Patients With Standard Treatment", Frontiers in Oncology

Internet

- Ling Xiao, Jiahua Lyu, Meihua Chen, Liu Wang, Jing 18 words <1% Huang, Yajun Wei, Tao Li. "The development of a nomogram and the prognostic prediction value of patients with esophageal squamous cell carcinoma undergoing radical radiotherapy", Future Science OA, 2022
- Kun Lv, Xin Cao, Peng Du, Jun-Yan Fu, Dao-Ying Geng, Jun Zhang. "Radiomics for the detection of microvascular invasion in hepatocellular carcinoma", World Journal of Gastroenterology, 2022

 Crossref
- e-sciencecentral.org \sim 17 words \sim 1 %
- f6publishing.blob.core.windows.net $\frac{16 \text{ words}}{16 \text{ words}} = \frac{1}{9}$
- www.pubfacts.com

 16 words < 1 %
- 27 Xueyao Zhang, Guangxiao Li, Yingxian Sun. "Nomogram Including Serum Ion Concentrations to Screen for New-Onset Hypertension in Rural Chinese Populations Over a Short-Term Follow-up", Circulation Journal, 2022 Crossref
- Yankun Gao, Xingwei Wang, Shihui Wang, Yingying Miao et al. "Differential Diagnosis of Type 1 and Type 2 Papillary Renal Cell Carcinoma Based on

Enhanced CT Radiomics Nomogram", Frontiers in Oncology, 2022

Crossref

Yusuke Nakayama, Naoto Gotohda, Hidehito Shibasaki, Shogo Nomura, Takahiro Kinoshita, Ryuichi Hayashi. "Usefulness of the neutrophil/lymphocyte ratio measured preoperatively as a predictor of peritoneal metastasis in patients with advanced gastric cancer", Surgery Today, 2014

Crossref

downloads.hindawi.com

15 words -<1%

- Dingkang Xu, Qingjie Wei, Zhe Li, Yan Hu et al. "Development and Validation of Predicting Nomograms for Craniopharyngioma: A Retrospective, Multiple-Center, Cohort Study", Frontiers in Oncology, 2021
- Wenhao Lin, Jun Dai, Jialing Xie, Jiacheng Liu, Fukang Sun, Xin Huang, Wei He, Chen Fang, Juping Zhao, Danfeng Xu. "S-GRAS score performs better than a model from SEER for patients with adrenocortical carcinoma", Endocrine Connections, 2022

 Crossref
- Xuerong Song, Haokun Liu, Dong Han, Junyan Jin, 13 words <1% Xiaoming Zhu, Yunxia Yang, Shouqi Xie. "Two Strains of Gibel Carp (Carassius gibelio) Exhibit Diverse Responses to Carbohydrates in a Low-Lipid Diet", Aquaculture Nutrition, 2022 Crossref
- hrjournal.net

36 www.wjgnet.com

13 words -<1%

- Cuiyu Jia, Guangxue Liu, Xinxin Wang, Dawei Zhao, Ruili Li, Hongjun Li. "Hepatic sclerosed hemangioma and sclerosing cavernous hemangioma: a radiological study", Japanese Journal of Radiology, 2021 Crossref
- Qi Zhang, Kangping Zhang, Xiangrui Li, Xi Zhang et al. "A novel model with nutrition-related parameters for predicting overall survival of cancer patients", Supportive Care in Cancer, 2021
- Yohei Oshima, Susumu Sato, Toyofumi F. Chen-Yoshikawa, Daisuke Nakajima, Manabu Nankaku, Hiroshi Date, Shuichi Matsuda. "Erector spinae muscle radiographic density is associated with survival after lung transplantation", The Journal of Thoracic and Cardiovascular Surgery, 2021
- academic.oup.com

 $_{12 \text{ words}}$ - < 1%

- Kai Zhu, Zhichao Lang, Yating Zhan, Qiqi Tao et al. 11 words < 1 % "Development and Validation of a Novel Prognostic Signature with 10 Ferroptosis-Related Genes in Acute Myeloid Leukemia", Research Square Platform LLC, 2021
- Meng Wan, Dan Zhao, Yan Sun, Weihu Wang. "A Novel Overall Survival Nomogram Prediction of 11 words < 1%

Secondary Primary Malignancies after Hypopharyngeal Cancer: A Population-Based Study", Journal of Oncology, 2022

Crossref

San-Yuan Dong, Wei Sun, Bin Xu, Wen-Tao Wang, 11 words — < 1 % Yu-Tao Yang, Xiao-Shan Chen, Meng-Su Zeng, Sheng-Xiang Rao. "Quantitative Image Features of Gadoxetic Acid–enhanced MRI for Predicting Glypican-3 Expression of Small Hepatocellular Carcinoma ≤ 3 cm", Research Square Platform LLC, 2022

Crossref Posted Content

- Xiaohong Zhong, Lei Wang, Lingdong Shao, Xueqing Zhang, Liang Hong, Gang Chen, Junxin Wu. "Prognostic Nomogram for Rectal Cancer Patients With Tumor Deposits", Frontiers in Oncology, 2022

 Crossref
- Xiuquan Shi, Lijun Xu, Bingwei Ma, Siben Wang. "Development and validation of a nomogram to predict the prognosis of patients with gastric cardia cancer", Scientific Reports, 2020 $_{\text{Crossref}}$
- Bing Xiao, Yanghua Fan, Zhe Zhang, Zilong Tan,
 Huan Yang, Wei Tu, Lei Wu, Xiaoli Shen, Hua Guo,
 Zhen Wu, Xingen Zhu. "Three-Dimensional Radiomics Features
 From Multi-Parameter MRI Combined With Clinical
 Characteristics Predict Postoperative Cerebral Edema
 Exacerbation in Patients With Meningioma", Frontiers in
 Oncology, 2021
 Crossref
- Chae Jung Park, Sooyon Kim, Kyunghwa Han, Sung Soo Ahn, Dain Kim, Yae Won Park, Jong Hee Chang, Se Hoon Kim, Seung-Koo Lee. "Diffusion- and Perfusion-

weighted MRI Radiomics for Survival Prediction in Patients with Lower-grade Gliomas", Research Square Platform LLC, 2022

Crossref Posted Content

- Shin Eun. "Glypican-3 and MAGE-1 are predictors of tumor invasiveness of hepatocellular carcinoma", Basic and Applied Pathology, 12/2008

 Crossref
- Yuduo Guo, Xiang Wang, Weihai Ning, Hongwei Zhang, Chunjiang Yu. "Identification of two core genes in glioblastomas with different isocitrate dehydrogenase mutation status", Molecular Biology Reports, 2020 Crossref
- Zhong-jie Zhou, Zhuang Zhang, Bo-wen Hu, Linnan Wang, Tao Li, Hui-liang Yang, Li-min Liu, Yueming Song. "Comparison of Long-term Clinical and Radiographical Outcomes Between the Anterior and Combined Anterior and Posterior Approaches for Treating Lumbosacral Tuberculosis", Research Square Platform LLC, 2022

EXCLUDE QUOTES OFF
EXCLUDE BIBLIOGRAPHY OFF

EXCLUDE SOURCES

< 9 WORDS

FXCLUDE MATCHES

< 10 WORDS