Clin. Lab. 2020;66:XXX-XXX
©Copyright

ORIGINAL ARTICLE

Serum Procalcitonin, Smoking History Combined Age Established a New Prediction Model for Predicting Dynamic Changes of Chest CT Images in Adult Community-Acquired Pneumonia (CAP) Patients

Wen Q. Li, Yi Chen, Ai S. Fu, Li Q. Li, Yan L. Ge, Pei Min, Yang Lu, Yang Liu, Ye Sun, Lin L. Hou, Qin Jing, Hai F. Zhang, Jia B. Zhang

Department of Respiratory Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China

SUMMARY

Background: **Chest CT is widely used in clinical diagnosis and efficacy evaluation of CAP. While repeated chest CT examinations to evaluate dynamic changes in chest CT images in a short period of time is a common phenomenon, it causes a lot of waste of medical resources, and due to the large dose of CT radiation, it can cause some harm to the human body. The purpose of this study is to establish a new model to predict the dynamic chest CT image changes of CAP patients by analyzing the age, smoking history, and serum inflammatory markers.**
Methods: **This is a retrospective study. All patients had received chest CT scan and serum inflammatory indexes were measured, including procalcitonin (PCT), high-sensitivity C-reactive protein (hs-CRP), white blood cell (WBC) and erythrocyte sedimentation rate (ESR). The second chest CT examination was performed after a week of treatment. General information on the medical record was also recorded (including age, smoking history, drinking history, and others). Main outcome measures were the changes of chest CT images, including absorption and non-absorption (including patients with progressive inflammation). Single factor analysis and two-dimensional logistic regression analysis were used to explore the independent risk factors of the new CT image change prediction model for CAP patients. ROC was used to evaluate the sensitivity and specificity of the new model.**
Results: **Among 220 patients with CAP, 150 patients had absorption in chest CT after a week of treatment (150/220), the remaining 70 patients had no absorption or even progression (70/220). Age, PCT, and smoking history were independent risk factors for inflammatory absorption. The AUC of ROC curve was 0.89 (95% CI 0.83 - 0.94), the sensitivity was 88.70%, and the specificity was 80.00%.**
Conclusions: **A new prediction model consists of serum PCT, age, and smoking history has high specificity and sensitivity in predicting dynamic CT changes in adult CAP patients.**
(Clin. Lab. 2020;66:xx-xx. DOI: 10.7754/Clin.Lab.2020.200208)

Correspondence:
Yan L. Ge
Department of Respiratory Medicine
North China University of Science and Technology Affiliated Hospital
Jianshe Road 73
063000 Tangshan, Hebei
China
Email: geyanlei1983@qq.com

Manuscript accepted April 4, 2020

KEY WORDS

community acquired pneumonia, age, procalcitonin, smoking history, chest CT

INTRODUCTION

CAP continues to be a major cause of morbidity and mortality in adults. Among many causes, bacterial and viral agents are the main cause [1,2]. It has caused huge economic losses in both developed and developing countries, accounting for approximately 55,000 deaths,

1.2 million hospitalizations, and 1.7 million ED visits annually in the United States [3]. The diagnosis of pneumonia is based on clinical features plus radiological findings consistent with pulmonary infection [4]. The use of chest CT imaging to evaluate patients with acute respiratory symptoms has markedly increased during the past two decades as clinical practice has evolved to more commonly assess for noninfectious conditions, such as pulmonary embolism and aortic dissection, and to more thoroughly image the lungs for signs of pneumonia [5,6]. In addition, the importance of chest CT in the assessment of CAP-related complications, such as lung abscess and loculated pleural effusion, and in the investigation of reasons for the lack of clinical response to treatment has been emphasized [7,8]. Many studies have proven CT imaging is more sensitive than chest radiography for identifying radiological signs of pneumonia. CT enables detailed analysis of lung anatomy in a similar manner to gross pathology sections but is burdened by a higher radiation dose as compared to chest radiographs [9,10]. To reduce the damage to the body and the waste of resources, it is necessary to establish a new model to predict the dynamic chest CT image changes of CAP patients.

MATERIALS AND METHODS

Patients

We conducted a retrospective study. The study was conducted in a regional teaching hospital with 1,200 beds in China. Adult patients (over 18 years of age) who were mainly diagnosed with CAP from December 2018 to December 2019 were included. Those with history of hematological diseases, active pulmonary tuberculosis, pulmonary embolism, uremia, advanced lung cancer, refractory heart failure, rheumatic diseases, radiotherapy, immuno-suppressive agents, transplantation medical history, and incomplete history of auxiliary examination were excluded. General clinical data, image data, history of drinking and smoking, and laboratory inflammatory biomarkers tests were recorded.

Measurement of serum inflammatory marker biomarkers

According to our research design, WBC count, as part of routine testing, was measured by Beckmann Kurt LH750 blood analyzer. Serum CRP and PCT levels were measured by Rosi-Cobas 8000 automatic biochemical analyzer. Erythrocyte sedimentation rate was determined by hand. The image data is from Philips 256 slice spiral CT in the Netherlands and image results are determined by our senior imaging teacher.

Statistical analyses

SPSS 22.0 statistical software was used for data analysis. When the Kolmogorov Smirnov test does not satisfy the distribution, continuous variables are expressed as mean ± standard deviation (SD) or median and interquartile range (IQR). Single factor analysis and binary logistic regression analysis were used to explore the independent risk factors of chest CT image changes in CAP patients. ROC curve was used to evaluate the sensitivity and specificity of independent risk factors, and a new model was established to predict the changes of chest CT images in CAP patients. All the tests were double tailed, $p < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

A total of 220 eligible patients were included in this study, including 120 males and 100 females. Among them, 150 (68.18%) showed that inflammation was absorbed more than before when reexamining images, with a median age of 49 years (36 - 59 years). Of the patients, 40.45% suffered from one or more basic diseases. The general characteristics are showed (Table l).

Univariate analysis to implore the suspicious risk factors in predicting chest CT image changes in CAP patients.

The results showed that smoking history, age, and PCT were the suspected risk factors ($p < 0.05$), while gender, basic diseases, WBC, hs-CRP, body temperature, and ESR were not the suspected risk factors ($p > 0.05$) (Table 2).

Binary logistic regression analysis to implore the independent risk factors in predicting chest CT image changes in CAP patients

We found smoking history, age, and PCT were all independent risk factors for the chest CT image changes in CAP patients (Table 3).

The ROC curves for independent risk factors and the new model for evaluating chest CT image changes

The ROC curve with independent risk factors as continuous numerical variables was drawn and analyzed. A new model for predicting chest image changes in CAP patients was developed (Figure 1, 2). The AUC of independent risk factors (age, PCT) were 0.80 (95% CI 0.73 - 0.87), 0.82 (95% CI 0.76 - 0.88), respectively. The sensitivity was 72.90% and 84.30%, respectively. The specificity was 79.30 % and 67.30%, respectively (Table 4). The joint new prediction model was obtained, and ROC curve was drawn (Figure 2). The AUC of the new model was 0.89 (95% CI 0.83 - 0.94), the sensitivity was 88.70% and specificity was 80.00%, respectively (Table 4).

Table 1. Baseline characteristics of patients with community-acquired pneumonia.

Demographic data	
Chest CT indicates inflammatory absorption, n (%)	150 (68.18)
Age (year) *	49 (36 - 59)
Age ≥ 65 years, n (%)	73 (33.18)
Male gender, n (%)	120 (54.55)
Female gender, n (%)	100 (45.45)
Suffer from basic diseases, n (%)	89 (40.45)
Hypertension	61 (27.73)
Cerebrovascular disease	34 (15.45)
Diabetes mellitus	57 (25.91)
Chronic respiratory diseases	31 (14.09)
Chronic hepatitis	6 (0.03)
Chronic kidney disease	4 (0.02)
Heart disease	17 (0.08)
Smoking history, n (%)	93 (42.27)
Drinking history, n (%)	64 (29.09)

Note: * - Data presented as median (interquartile range).

Table 2. Single factor analysis results.

		Absorption of chest CT		Effective rate	Chi-square/Z	p
		Yes	No			
Gender	male	79	41	0.66	0.671	0.413
	female	71	29	0.71		
Basic disease	yes	56	33	0.63	1.907	0.167
	no	94	37	0.72		
Smoking history	yes	46	47	0.49	26.022	< 0.001 *
	no	104	23	0.82		
Age (year) #		49 (36 - 59)	72 (59 - 81)		-7.104	< 0.001 *
WBC (x 10^9) #		8.25 (6.40 - 11.93)	8.55 (6.58 - 13.85)		-0.564	0.573
Hs-CRP (mg/L) #		34.25 (16.18 - 64.00)	31.45 (14.98 - 69.43)		-0.157	0.875
PCT (mg/mL) #		0.22 (0.11 - 0.67)	2.29 (0.63 - 3.48)		-7.674	< 0.001 *
Temperature (℃) #		36.8 (36.5 - 37.9)	36.7 (36.5 - 37.48)		-0.992	0.321
ESR (mm/hour) #		23 (18 - 32)	26 (19 - 35)		-1.833	0.067

Note: * - indicates p < 0.05, # - indicates that SK normal test result is non normal distribution, and data is represented by median (quartile range).

Through single factor analysis, the following conclusions are drawn: Gender, basic diseases, leukocyte count, high-sensitivity C-reactive protein, body temperature, and erythrocyte sedimentation rate were not suspected risk factors: p = 0.413 > 0.05, p = 0.167 > 0.05, p = 0.573 > 0.05, p = 0.875 > 0.05, p = 0.321 > 0.05, p = 0.413 > 0.05, respectively.

Table 3. Results of multivariate analysis.

		B	S.E.	Wald	df	p	OR	95 % CI	
								lower limit	ceiling
Age (year)		-0.058	0.013	20.102	1	p < 0.001 *	0.944	0.920	0.968
PCT (mg/mL)		-0.754	0.167	20.292	1	p < 0.001 *	0.470	0.339	0.653
Smoking history	yes	1.545	0.400	14.928	1	p < 0.001 *	4.689	2.141	10.267
	no	0					1		
Constant		5.792	0.873	43.978	1	p < 0.001 *	327.507		

Note: * - indicates p < 0.05, multivariate analysis showed that age, procalcitonin, and smoking history were independent risk factors for image absorption.

Table 4. The ROC curve of independent risk factors and new models for evaluation of chest CT image changes.

Variable	The critical value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Younden's index	p-value
Age (year)	62	0.80 (0.73 - 0.87)	72.90	79.30	0.52	< 0.001 *
PCT (mg/mL)	0.35	0.82 (0.76 - 0.88)	84.30	67.30	0.52	< 0.001 *
New model	0.626	0.89 (0.83 - 0.94)	88.70	80.00	0.69	< 0.001 *

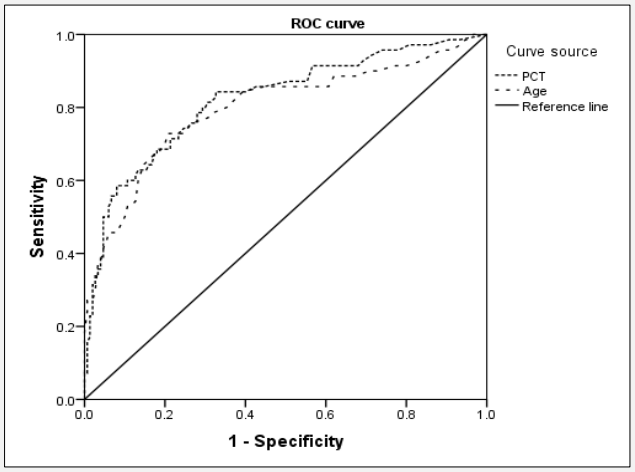

Figure 1. ROC curve of age and procalcitonin.

DISCUSSION

CAP is one of the most common infectious diseases and an important cause of death in children under 5 years old in developing countries and in adults over 65 in developed countries [11]. CAP diagnosis is based on the clustering of non-specific pulmonary and general symptoms, an increase in biomarkers reflecting systemic inflammatory response syndrome (SIRS), and the presence of new parenchymal infiltrates on chest CT [12-

14]. The pathogens of CAP include a wide variety of microbes, including not only ordinary bacteria but also mycobacteria, viruses, or fungi. Characteristic imaging findings of several pathogens are sometimes suggestive of the diagnosis of specific pneumonia. In addition, imaging examinations sometimes offer clues for the differentiation between infectious pneumonia and noninfectious diseases. Imaging examinations are indispensable for the management of CAP. The primary role of imaging examinations to confirm the diagnosis of pneumonia plays a complementary role for the evaluation of treatment effects of antibiotics, although treatment effects may be determined based solely on clinical findings [15,16]. The change of CT image actually reflects the development of pulmonary inflammation, but the damage caused by radiation to the body cannot be ignored, especially receiving multiple CT examinations in a short time. At present, there is almost no model to predict the changes of CT images. This paper establishes a new model to predict the changes of CT images of the chest, which will help to judge the development of pulmonary inflammation and reduce excessive imaging examination.

Many retrospective studies have proven that age, procalcitonin, and smoking history play an important role in judging the progress of pulmonary inflammation and evaluating the prognosis [17-18].

We found that PCT, smoking history, and age were independent risk factors of chest image changes in CAP patients. A new joint prediction model consisting of all independent risk factors is obtained. The new model has high sensitivity (88.70%) and specificity (80.00%). Therefore, it has a wide range of clinical application value. When using this model to predict that there is no change in the image of a patient, we cannot do the image examination temporarily. On the contrary, we need the image examination to confirm the pathological changes.

The main limitation of this study is that the sample size is small, and the possibility of selection bias cannot be avoided. The retrospective study was conducted in one hospital and lacked data analysis of other hospitals. The advantage of this study is to build a high sensitivity and high specificity prediction model, which has practical value.

CONCLUSION

Serum procalcitonin, smoking history combined with age established a new prediction model for predicting the dynamic changes of CT images in adult CAP patients, which has high sensitivity and specificity.

Acknowledgment:
Thank you for the criticism of other members of the Department of Respiratory Medicine, Affiliated Hospital of North China University of Technology.

Ethical Approval:
This study was approved by ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained from all individual participants included in this study.

Source of Support:
This work was supported by the Hebei Province Science Development Program [2020/246].

Declaration of Interest:
No conflicts of interest.

References:

1. Chen J, Li X, Wang W, Jia Y, Lin F, Xu J. The prevalence of respiratory pathogens in adults with community-acquired pneumonia in an outpatient cohort. Infect Drug Resist 2019;12:2335-41 (PMID: 31440068).
2. Self WH, Grijalva CG, Zhu Y, et al. Rates of emergency department visits due to pneumonia in the United States, July 2006-June 2009. Acad Emerg Med 2013;20:957-60 (PMID: 24033659).
3. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007; 2:S27-72 (PMID: 17278083).
4. Kocher KE, Meurer WJ, Fazel R, Scott PA, Krumholz HM, Nallamothu BK. National trends in use of computed tomography in the emergency department. Ann Emerg Med 2011;58:452-62 (PMID: 21835499).
5. Larson DB, Johnson LW, Schnell BM, Salisbury SR, Forman HP. National trends in CT use in the emergency department: 1995-2007. Radiology 2011;258:164-73 (PMID: 21115875).
6. Claessens YE, Debray MP, Tubach F, et al. Early Chest Computed Tomography Scan to Assist Diagnosis and Guide Treatment Decision for Suspected Community-acquired Pneumonia. Am J Respir Crit Care Med 2015;192:974-82 (PMID: 26168322).
7. Self WH, Courtney DM, McNaughton CD, Wunderink RG, Kline JA. High discordance of chest x-ray and computed tomography for detection of pulmonary opacities in ED patients: implications for diagnosing pneumonia. Am J Emerg Med 2013;31:401-5 (PMID: 23083885).
8. Prina E, Ranzani OT, Torres A. Community-acquired pneumonia. Lancet 2015;386:1097-108 (PMID: 26277247).
9. Tanaka N, Emoto T, Suda H, Matsumoto T, Matsunaga N. Community-acquired pneumonia: a correlative study between chest radiographic and HRCT findings. Jpn J Radiol 2015;33:317-28 (PMID: 25895159).
10. Savvateeva EN, Rubina AY, Gryadunov DA. Biomarkers of Community-Acquired Pneumonia: A Key to Disease Diagnosis and Management. Biomed Res Int 2019;2019:1701276 (PMID: 31183362).

11. Le Bel J, Hausfater P, Chenevier-Gobeaux C, et al. Diagnostic accuracy of C-reactive protein and procalcitonin in suspected community-acquired pneumonia adults visiting emergency department and having a systematic thoracic CT scan. Crit Care 2015;19:366 (PMID: 26472401).

12. Gennis P, Gallagher J, Falvo C, Baker S, Than W. Clinical criteria for the detection of pneumonia in adults: guidelines for ordering chest roentgenograms in the emergency department. J Emerg Med 1989;7:263-8 (PMID: 2745948).

13. Metlay JP, Fine MJ. Testing strategies in the initial management of patients with community-acquired pneumonia. Ann Intern Med 2003;138:109-18 (PMID: 12529093).

14. Nambu A, Ozawa K, Kobayashi N, Tago M. Imaging of community-acquired pneumonia: Roles of imaging examinations, imaging diagnosis of specific pathogens and discrimination from non-infectious diseases. World J Radiol 2014;6:779-93 (PMID: 25349 662).

15. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 Update by the Infectious Diseases Society of America. Clin Infect Dis 2011;52:427-31 (PMID: 21205 990).

16. Morimoto K, Suzuki M, Ishifuji T, et al. The burden and etiology of community-onset pneumonia in the aging Japanese population: a multicenter prospective study. PLoS One 2015;10:e0122247 (PMID: 25822890).

17. Torres A, Blasi F, Dartois N, Akova M. Which individuals are at increased risk of pneumococcal disease and why? Impact of COPD, asthma, smoking, diabetes, and/or chronic heart disease on community-acquired pneumonia and invasive pneumococcal disease. Thorax 2015;70:984-9 (PMID: 26219979).

18. Liu J, Zhang W, Wang Q, et al. The Early Diagnostic Value of Procalcitonin in Pneumonia After Off-Pump Coronary Artery Bypass Grafting Surgery. Med Sci Monit 2019;25:3077-89 (PMID: 31025657).