77825_Auto_Edited.docx

WORD COUNT 3936
TIME SUBMITTED 01-AUG-2022 03:41PM
PAPER ID 89045730

Name of Journal: *World Journal of Clinical Cases*
Manuscript NO: 77825
Manuscript Type: ORIGINAL ARTICLE

Retrospective Study

Clinicopathological Characteristics and Prognosis of Gastric Signet Ring Cell Carcinoma

Characteristics and Prognosis of GSRC

Hua-kai Tian, zuo zhang, Zhi-Kun Ning, Jiang Liu, Zi-Tao Liu, haoyu huang, Zhen Zong, Hui Li

Abstract

BACKGROUND

The clinicopathological features and prognosis of gastric signet ring cell carcinoma (GSRC) remained controversial, particularly with regard to sensitivity to postoperative adjuvant therapy.

AIM

The aim of this study was to compare the pathological features of GSRC with those of gastric adenocarcinoma of different degrees of differentiation and the differences in survival prognosis between the different disease processes.

METHODS

Screening of gastric cancer patients from 2010 to 2015 in the database of Surveillance, Epidemiology and End Results (SEER), and collecting clinicopathological and prognostic data of gastric cancer patients who underwent surgery from January 2014 to December 2016 in the Second Affiliated Hospital of Nanchang University,we analyzed the general pathological characteristics of GSRC by chi-square test. Univariate and multivariate analysis were conducted to compare the factors affecting the survival and prognosis of early and advanced gastric adenocarcinoma. The Kaplan-Meier curves revealed the survival difference between early and advanced GSRC and different differentiated types of gastric adenocarcinoma. The prognosis model of advanced GSRC was established by R software, and the area under curve(AUC) and C-index indicated a high accuracy of the model.

RESULTS

Analysis of pathological features revealed that Signet Ring-cell Carcinoma (SRC) was more frequently seen in younger (<60 years), female, and white patients compared to non-SRC patients. SRC was less common in Early Gastric Cancer (EGC) (23.60% *vs* 39.10%), lower N0 (38.61% *vs* 61.03%) and larger tumour sizes >5cm (31.15% *vs* 27.10%)

compared to the differentiated type, while the opposite was true compared to the undifferentia ted type. Survival prognostic analysis found no significant difference in the prognosis of SRC patients among EGC patients. In contrast, among Advanced Gastric Cancer (AGC) patients, the prognosis of SRC patients was correlated with age, race, tumour size, AJCC stage, T-stage and post-operative adjuvant therapy. The predictive model showed 3-year AUC was 0.787, 5-year AUC was 0.806, and C-index was 0.766. Compared to non-SRC, patients with SRC had a better prognosis in EGC (HR 0.626,95%CI 0.427-0.919,P<0.05) and a worse prognosis in AGC (HR 1.139,95%CI 1.030-1.258,P<0.05). When non-SRC was divided into differentiated and undifferentiated types for comparison, it was found that in EGC, SRC had a better prognosis than differentiated and undifferentiated types, while differentiated and undifferentiated types were not significantly different. In AGC, there was no significant difference in prognosis between SRC and undifferentiated types, both of which were worse than differentiated types. A prognostic analysis of postoperative adjuvant therapy for SRC in patients with AGC also revealed that adjuvant postoperative radiotherapy or chemotherapy significantly improved patient survival (34.6% and 36.2% vs. 18.6%, P<0.05).

CONCLUSION

The prognosis of SRC was better than undifferentiated type, especially in EGC, and its prognosis was even higher than differentiated type. SRC patients can benefit from early detection, surgical resection, and aggressive adjuvant therapy.

Key Words: Gastric adenocarcinoma; Gastric signet ring cell carcinoma; Pathological features; Survival prognosis; Prognostic model; Adjuvant therapy

Tian HK, zhang Z, Ning ZK, Liu J, Liu ZT, huang H, Zong Z, Li H. Clinicopathological Characteristics and Prognosis of Gastric Signet Ring Cell Carcinoma. *World J Clin Cases* 2022; In press

Core Tip: This observational study analysed the clinicopathological features and prognosis of gastric signet ring cell carcinoma (GSRC). We compared GSRC with differentiated gastric adenocarcinoma and found that GSRC has unique clinicopathological features, is more common in younger female patients, and is more aggressive, showing higher lymph node metastasis and tumour size. However, the prognosis for early GSRC was relatively good, even higher than that of differentiated adenocarcinoma. The treatment of GSRC should be diagnosed early, and radical surgical resection with adjuvant radiotherapy and chemotherapy can significantly improve the survival rate of patients, though it still needs more clinical data to verify.

INTRODUCTION

Gastric cancer,a kind of extremely common malignancy, ranked fifth in morbidity and fourth in mortality worldwide[1, 2]. In accordance with the classification of the World Health Organization, gastric adenocarcinoma could be roughly divided into four histological types, mucinous adenocarcinoma, tubular adenocarcinoma, papillary adenocarcinoma, and signet ring cell carcinoma[3]. In addition, it is divided into undifferentiated,poorly-differentiated,moderately-differentiated and well-differentiated depending on the degree of differentiation[4]. Gastric Signet Ring cell Carcinoma (GSRC) is considered as a special type of gastric adenocarcinoma and characterized by the accumulation of mucin in the cytoplasm and the displacement of the nucleus to the periphery of the cells[5]. GSRC is divided into diffuse type in the light of Lauren classification[6], infiltrating type by Ming staging[7], and undifferentiated by type Nakamura staging [8].

GSRC is considered to be the histological type with the worst prognosis because of the low survival rate and high recurrence rate. However, with further research on GSRC, we found that it has unique clinicopathological characteristics and prognosis. It has been demonstrated that GSRC was highly aggressive, and once found, most of it had been in progressive stage with lymph node metastasis[9]. Other studies also showed

that the histological characteristics of GSRC were weak cohesion, and early tumor cells mainly spread in the mucosa or submucosa[10]. Moreover, the survival prognosis and treatment options for GSRC were controversial. Early western studies have shown that GSRC or diffuse gastric cancer had a poor prognosis[11]. However, scholars in Asian had expressed doubts and believed that research should be carried out according to the different processes of tumors. The results show that the prognosis of early signet ring cell carcinoma is good, while the prognosis in advanced stage is poor[9, 12]. Most recently, abundance evidence in the United States suggested that GSRC was not necessarily a risk factor affecting prognosis[13]. Combination of postoperative adjuvant radiotherapy, chemotherapy and targeted therapy had an excellent effect on improving the survival rate of gastric cancer patients.However,a number of studies and retrospective analysis had shown that GSRC was resistant to chemotherapy, and patients could not benefit from postoperative adjuvant treatment[14]. For this conclusion, we need more research to confirm.

In order to more accurately study the pathological features and survival prognosis of GSRC, the pathological features and prognosis of a large number of postoperative gastric cancer patients need to be analysed and compared with non-GSRC according to different tumour progression and different tumour differentiation types. Therefore, we explored the differences in pathological features and survival prognosis between GSRC and different differentiation types of gastric adenocarcinoma by analysing information related to pathological features and survival prognosis of surgically resected specimens from a large US National Registry database (Surveillance, Epidemiology and End Results SEER database) and the Second Affiliated Hospital of Nanchang University.

MATERIALS AND METHODS

Study Population

We applied the SEER database from the National Cancer Institute which recorded essential information of around 28% of US cases.Since the database is available to public, and we had achieved authorization from the database (account number: 12846-

Nov2019), there is no need to acquire patients` informed consent. Furthermore, the hospital ethics committee has approved the study to conduct. Several concerned information were obtained from the database, mainly including general characteristics, pathological characteristics and clinical tumor characteristics as well as treatment methods, survival and prognosis. Meanwhile, we collected clinical data of patients with gastric cancer who were implemented surgery from January 2014 to December 2017 in the Second Affiliated Hospital of Nanchang University. Inclusion criteria: 1. Postoperative diagnosis of gastric adenocarcinoma; 2. Complete survival information; 3. Gastric cancer as the first primary tumor. Exclusion criteria: 1. Suffering from multiple tumors in situ; 2. Incomplete tumor staging; 3. Distant metastasis 4. Not undergo surgical resection; 5. Incomplete information. Tumor histology, site, and grade were classified based on the International Classification of Diseases for Oncology, version 3. Stage of tumor was identified on the basis of the AJCC tumor–node–metastasis staging system, 7th edition[15]**.** The details of screening is displayed **in Figure 1.**

Data classification

Ages were divided into <40 years old, 40-60 years old, 60-80 years old, and > 80 years old. Race included black, white, Asian Pacific Islanders (API) and American Indians (AI). Size of tumor was classified into <2 cm, 2-5 cm, >5 cm and NA. The type of differentiation comprised Signet Ring-cell Carcinoma (SRC),differentiated type(highly differentiated and moderately differentiated) and undifferentiated(poorly differentiated and undifferentiated). T staging included T1a, T1b, T2, T3, T4a, T4b. N staging included N0, N1, N2, N3. AJCC staging included I, II, and III. Primary tumors could locate at different parts, divided into fundus, gastric body, pylorus, antrum, greater curvature, lesser curvature and overlapping/NOS. Tumor progression, could be sorted into Advanced Gastric Cancer(AGC) and Early Gastric Cancer (EGC).

Statistical methods

We applied the Fisher exact probability method or chi-square test to analyse categorical variables for descriptive statistics. Univariate factor and binary logistic regression were employed to conduct analysis of the risk factors of gastric cancer survival and

prognosis, after which the concequence was suggested as 95% confidence intervals(CIs) and odds ratios (ORs). The R software (version 4.0.5) was adopted to establish the survival prognostic model for the advanced GSRC. The AUC value and C-index indicated the accuracy of the model. The K-M curve was used to conduct comparative analysis about the difference in survival (Overall survival,OS)and the efficacy of adjuvant therapy, which contained early and advanced GSRC and gastric adenocarcinoma with different levels of differentiation, and validated by external data sets. We considered $p < 0.05$ as statistically significant.

RESULTS

General characteristics

Obeying the standard of inclusion and exclusion criteria, finally 5200 patients were chosen in the SEER database. The Second Affiliated Hospital of Nanchang University finally included 603 patients. Table 1 summarized the pathological and clinical variables of the two data sets.

Analysis of the clinical characteristics of GSRC

Compared with the differentiated type, GSRC was more common in young patients (<60years) (47.36% VS 16.39%, P<0.05), and the same results were obtained when compared with the undifferentiated type (47.36% VS 30.42%, P<0.05). In addition, GSRC was more frequent in female patients (52.87% VS 38.13% VS 41.95%, P<0.05). In the case of race, compared with the differentiated type, GSRC was more common in whites (61.74% VS 51.87%, P<0.05), while blacks and Asia-Pacific Islanders were less (Black: 14.19% VS 19.03%; API: 23.09% VS 28.07%, P<0.05); Compared with the undifferentiated type, GSRC was also more common in whites (61.74% VS 56.97%, P<0.05), and less in Asia-Pacific islanders (23.09% VS 27.11%, P<0.05).

At the initial diagnosis, 28.05% of GSRC patients were in stage I, while 47.10% of differentiated patients and 20.57% of undifferentiated patients were diagnosed as stage I (P<0.05). In terms of T stage and N stage, compared with differentiated type, the proportion of EGC (23.60% VS 39.10%, P<0.05) and N0 (38.61% VS 61.03%, P<0.05) in

GSRC patients were less; compared with the undifferentiated type, the proportion of EGC (23.60% VS 16.62%, P<0.05) and N0 (38.61% VS 33.35%, P<0.05) in GSRC patients is higher. As far as tumor size, compared with the differentiated type, GSRC patients had more tumors >5 cm (31.15% VS 27.10%, P<0.05), and showed the opposite result when compared to the undifferentiated type (31.15% VS 37.31%, P <0.05). (Table 2)

Survival and prognostic analysis of GSRC

As shown in the survival curve of Figure 2, no significant difference existed between the 5-year OS of SRC and non-SRC patients (44.6% VS 46.7%, P>0.05) (Figure 2A). Interestingly, when gastric cancer patients were divided into EGC and AGC, the 5-year OS of SRC patients was obviously higher than that of non-SRC in EGC (89.0% VS 71.4%, P<0.05) (Figure 2C), while the result indicated the opposite conclusion in AGC patients (30.6% VS 38.2%, P<0.05) (Figure 2E).

Afterwards, the comparison was conducted again when non-SRC was divided into differentiated type and undifferentiated type. We found that the 5-year OS of SRC was lower than that of differentiated patients (44.6% VS 55.3%, P<0.05), but higher than that of undifferentiated patients (44.6% VS 40.8%) (Figure 2B). Interestingly, different results were obtained when gastric cancer patients were divided into EGC and AGC. In EGC, the 5-year OS of SRC was better than that of differentiated and undifferentiated types (89.0% VS 71.2% and 71.9%, P<0.05), while there was no significant difference between differentiated and undifferentiated types (Figure 2D). And in the external data set, no obvious difference existed in survival rates between SRC and undifferentiated or differentiated types (Figure 3A). In AGC, the 5-year OS of SRC and undifferentiated type were worse than differentiated type (30.6% and 34.7% VS 45.3%, P<0.05). However, in pairwise comparison, no obvious difference existed in survival rate between SRC and undifferentiated type (Figure 2F). It was the same as the verification result of the external data set (Figure 3B).

At the same time our survival analysis of patients with advanced signet ring cell carcinoma after surgery and chemotherapy manifested that postoperative adjuvant chemotherapy or chemotherapy could significantly increase the 5-year OS of patients

(34.6% and 36.2% VS 18.6%, P<0.05) (Figure 4A). The external data set analysis showed that postoperative adjuvant chemotherapy had no effect on improving the survival rate of patients (P>0.05) (Figure 4B).

Prognosis prediction model of GSRC

In EGC, SRC was a favorable factor affecting patients` prognosis, and suggested a better prognosis when compared to the differentiated type (HR 0.636, 95%CI 0.426-0.950, P<0.05) and non-SRC (HR 0.626, 95%CI 0.427-0.919, P<0.05). In AGC, SRC was an unfavorable factor, and the results showed the prognosis was worse when compared to the differentiated type (HR 1.276, 95%CI 1.117-1.458, P<0.05) and non-SRC (HR 1.139, 95%CI 1.030-1.258, P<0.05), (Tables 3 and 4).

Among EGC, there was no obvious difference in SRC patients` prognosis. In AGC, the prognosis of GSRC was related to tumor size, age, race, AJCC stage, T stage, and postoperative adjuvant therapy (Tables 3 and 4). Finally, we established a prognostic prediction model for advanced GSRC, the model C-index =0.766, 3-year OS AUC=0.787, 5-year OS AUC=0.806(Figure 5 and 6). Table 5 showed the risk score of each factor.

DISCUSSION

The incidence of GSRC is 3.4%-39% in primary gastric cancer[16, 17]. In this study, GSRC patients in the SEER data set accounted for 25.5% of all patients undergoing gastrectomy. GSRC patients in the external validation set accounted for 13.9%. The clinical characteristics and prognosis of GSRC are still controversial. Eastern researchers believed that GSRC was not necessarily an unfavorable prognostic factor, while western researchers considered that the prognosis of GSRC was poor and the incidence rate continued to increase worldwide[9, 12, 18, 19]. However, most previous studies only included small heterogeneous patients, and did not distinguish distinct differentiation types. Comparing SRC and non-SRC together will inevitably cause a certain impact on the final results. Therefore, during our research, a large database was utilized to analyze, compare and verify the GSRC patients undergoing surgical resection in terms of different progression and differentiation degrees, so as to obtain

the pathological characteristics of GSRC and the survival differences between gastric adenocarcinoma with different differentiation degrees to provide more accurate guidance for clinical treatment.

Our research showed that GSRC, as a special pathological type of gastric adenocarcinoma, had different clinical characteristics from differentiated and undifferentiated adenocarcinoma. GSRC tended to occur in young and female patients, which was consistent with previous studies[9]. Although gastric cancer was considered to be the majority disease in men, a large number of studies had shown that the incidence of GSRC in women was higher[13]. At the same time, the age of onset of GSRC was significantly earlier than that of gastric adenocarcinoma. In terms of race, our research showed that GSRC was more frequent in whites, while there were fewer patients in Asia-Pacific Islanders. Part of the etiology of young patients may be attributed to genetic factors. Such patients should be diagnosed as hereditary diffuse gastric cancer (HDGC)[20]. The 2015 multidisciplinary symposium defined HDGC as "early-onset diffuse gastric cancer", where multiple generations of people in the family have a history of diffuse gastric cancer (DGC) or lobular breast cancer[21]. The performance of GSRC on gender differences may be related to the level of estrogen. Studies have shown that more frequent appearance of progesterone and estrogen receptors in the tissues of female patients suggests that they might be suspected of the appearance and progression of tumors[22]. The high-level CLDN18-ARHGAP26/6 fusion in GSRC results in genetic differences with other diffuse gastric cancer subtypes. These genetic types develop at a young age, have a high proportion of females, high tumor stages, poor survival outcomes, and chemoresistance[23].

The microscopic features of GSRC are scattered malignant cells containing intracytoplasmic mucin, accounting for more than 50% of tumors[16, 24]. GSRC is inert in the early stage and does not show strong invasiveness. When the tumor breaks through the submucosa, it shows strong aggression, rapidly invading the muscle layer, serosal layer and surrounding lymph nodes[25]. Large-scale data studies have found that GSRC showed a higher proportion of serosal layer invasion and distant metastasis in the

advanced stage, and it was prone to lymph node metastasis[25]. Our results found that compared to gastric adenocarcinoma, GSRC had a higher proportion of advanced stage, and showed larger tumor size and more lymph node metastasis. This is consistent with the results of most studies.

The prognosis of GSRC is unanimously controversial. Previous studies have suggested that GSRC had a poorer prognosis than non-GSRC. In this study, we divided non-GSRC into differentiated gastric adenocarcinoma and undifferentiated gastric adenocarcinoma, and compared EGC and AGC separately. The results showed that in EGC, the prognosis of differentiated and undifferentiated gastric adenocarcinoma was not significantly different, and were both worse than SRC. The external validation indicated that the difference in the prognosis between the early gastric adenocarcinoma and GSRC was not obvious. Interestingly, the prognosis of patients with early GSRC had nothing to do with age, gender, and tumor size factors. In AGC patients, SRC`s prognosis and undifferentiated patients did not have much difference, and were both worse than that of differentiated type. The external validation set also reached the same conclusion. Through data analysis, we could get that the prognosis of patients with advanced GSRC was related to tumor size, age, race, AJCC stage, T stage and postoperative adjuvant treatment. Undoubtedly, as the tumour progresses, the patient's prognosis deteriorates. Elderly patients had a poorer prognosis due to reduced immunity and poor tolerance. Interestingly, race was also an independent risk factor for the prognosis of GSRC patients, and AI patients had a poorer prognosis. Intrinsic molecular and biological differences between different ethnic groups and living environments may be responsible for the differences in survival among heterogeneous Western populations. Finally, we established a survival prognostic prediction model based on the prognostic risk factors of advanced GSRC. The 5-year OS (AUC=0.806) and 3-year OS (AUC=0.787) indicated that the model had accurate predictive ability. Unfortunately, the model cannot be externally validated due to the small amount of data in the external validation set.

Regarding the treatment of GSRC, surgical treatment methods are also controversial for different stages[26]. Endoscopic submucosal dissection (ESD) is an optional treatment for EGC. On the basis of the guidelines of the Japanese Gastric Cancer Association (JGCA), endoscopic therapy could be applied for the cases with well-differentiated and non-ulcerated carcinoma whose diameter is smaller than 2 cm, but the therapy might not be so feasible for ulcerated and undifferentiated submucosal carcinomas[27]. Research has demonstrated that tumor size and lymph node metastasis are are important factors that do not recommend endoscopic treatment in the early stage of GSRC[28]. According to the clinical characteristics of GSRC in our study, early GSRC showed a higher lymph node metastasis rate and larger tumor size, so endoscopic treatment of GSRC is also not recommended. For AGC, adjuvant radiotherapy and chemotherapy after surgical resection can significantly enhance the survival rate of patients. However, the specific treatment plan for GSRC is still uncertain. GSRC was resistant to chemical agents and many studies have confirmed it. However, it is still controversial about the efficiency of chemotherapy for GSRC. Voron T *et al* showed that postoperative chemotherapy has no significant effect on the survival rate of GSRC. In multivariate analysis, GSRC is an independent poor prognostic factor[29]. Another study also proved that GSRC patients cannot benefit from postoperative chemotherapy[30]. Shi *et al* indicated that postoperative chemotherapy could still be effective for the patients with stageIVGSRC [31].A recent large-scale data study based on SSER confirmed that surgical resection combined with adjuvant radiotherapy and chemotherapy provides a favorable prognosis for GSRC[32]. Our research showed that postoperative adjuvant radiotherapy and chemotherapy can improve the survival rate of advanced GSRC patients. However, the external validation set showed that postoperative adjuvant chemotherapy cannot benefit patients. This may be because our sample is small which makes it impossible to conduct accurate verification. Therefore, the effectiveness of adjuvant therapy after GSRC still needs a lot of clinical verification.

Certainly, our analysis was convincing, because we adopted a staged analysis method for GSRC and a large population-based study. Furthermore, we had conducted reasonable and effective verification through an external validation set. However, certain limitations still exist in our research. First of all, the SEER database lacks information related to postoperative adjuvant treatment, and information about adjuvant chemotherapy, duration, and neoadjuvant treatment is not available. Secondly, the analysis of SRC patients with metastasis are not included in the research. Therefore, another study of the particular population may need to be conducted. Finally, although we have established a prognostic prediction model for the advanced GSRC, the external validation set is insufficient and cannot be effectively externally verified.

CONCLUSION

In summary, our research analysis showed that GSRC was more common in young female patients, and the clinical characteristics of GSRC were significantly different from those of gastric adenocarcinoma. The early prognosis of GSRC is not worse, even better than that of differentiated gastric adenocarcinoma. The treatment of GSRC should be diagnosed early, and radical surgical resection with adjuvant radiotherapy and chemotherapy can significantly improve the survival rate of patients, though it still needs more clinical data to verify.

ARTICLE HIGHLIGHTS

Research background

The clinicopathological features and prognosis of gastric signet ring cell carcinoma (GSRC) remained controversial, particularly with regard to sensitivity to postoperative adjuvant therapy.

Research motivation

To our knowledge, this study is the first to analyse and compare the clinicopathological features and prognosis of GSRC with gastric adenocarcinoma of different degrees of differentiation and includes both Eastern and Western populations.

Research objectives

The aim of this study was to compare the pathological features of GSRC with those of gastric adenocarcinoma of different degrees of differentiation and the differences in survival prognosis between the different disease processes.

Research methods

This study was first conducted by analysing the differences in clinicopathological features between GSRC and gastric adenocarcinoma in Western populations and comparing the survival prognosis of the different processes. Finally, validation was performed using an Eastern population.

Research results

GSRC is more commonly seen in younger female patients and is more aggressive in the progressive stage, showing higher lymph node metastasis and tumour size. However, the prognosis for early GSRC cancer is relatively good, even higher than that of differentiated adenocarcinoma. The prognosis of advanced GSRC was not significantly different from that of undifferentiated gastric adenocarcinoma and was worse than that of differentiated gastric adenocarcinoma. Postoperative adjuvant radiotherapy can improve the survival rate of GPC.

Research conclusions

The prognosis of GSRC was better than undifferentiated type, especially in EGC, and its prognosis was even higher than differentiated type. GSRC patients can benefit from early detection, surgical resection, and aggressive adjuvant therapy.

Research perspectives

GSRC has unique clinicopathological features and prognosis, and early diagnosis and treatment can significantly improve survival rates. Patients may benefit from postoperative adjuvant radiotherapy, but further validation is needed.

77825_Auto_Edited.docx

ORIGINALITY REPORT

3%
SIMILARITY INDEX

PRIMARY SOURCES

1	academic.oup.com Internet	19 words — < 1%
2	Huakai Tian, Zuo Zhang, Zitao Liu, Cegui Hu, Jiang Liu, Tian Xu, Zhen Zong. "Early Gastric Cancer Lymph Node Metastasis Model and Prognostic Survival Prediction Model in Western Population", Research Square, 2020 Crossref Posted Content	18 words — < 1%
3	eprints.whiterose.ac.uk Internet	18 words — < 1%
4	www.zora.uzh.ch Internet	18 words — < 1%
5	Carol Byrd-Bredbenner, Michelle Johnson, Virginia M. Quick, Jennifer Walsh et al. "Sweet and salty. An assessment of the snacks and beverages sold in vending machines on US post-secondary institution campuses", Appetite, 2012 Crossref	13 words — < 1%
6	Lina Marcela Barranco-Garduño, Ivette Buendía-Roldan, Juan Jose Rodriguez, Rodrigo González-Ramírez et al. "Pharmacokinetic evaluation of two pirfenidone formulations in patients with idiopathic pulmonary fibrosis and chronic hypersensitivity pneumonitis", Heliyon, 2020	13 words — < 1%

Crossref

7	www.ncbi.nlm.nih.gov Internet	13 words — < 1%
8	www.omicsonline.org Internet	13 words — < 1%
9	www.ijpsonline.com Internet	12 words — < 1%

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 12 WORDS
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 12 WORDS