

World Journal of *Clinical Cases*

World J Clin Cases 2022 November 26; 10(33): 12066-12461



MINIREVIEWS

- 12066** Review of risk factors, clinical manifestations, rapid diagnosis, and emergency treatment of neonatal perioperative pneumothorax
Zhang X, Zhang N, Ren YY

ORIGINAL ARTICLE**Clinical and Translational Research**

- 12077** Integrative analysis of platelet-related genes for the prognosis of esophageal cancer
Du QC, Wang XY, Hu CK, Zhou L, Fu Z, Liu S, Wang J, Ma YY, Liu MY, Yu H
- 12089** Comprehensive analysis of the relationship between cuproptosis-related genes and esophageal cancer prognosis
Xu H, Du QC, Wang XY, Zhou L, Wang J, Ma YY, Liu MY, Yu H
- 12104** Molecular mechanisms of Baihedihuang decoction as a treatment for breast cancer related anxiety: A network pharmacology and molecular docking study
Li ZH, Yang GH, Wang F
- 12116** Single-cell RNA-sequencing combined with bulk RNA-sequencing analysis of peripheral blood reveals the characteristics and key immune cell genes of ulcerative colitis
Dai YC, Qiao D, Fang CY, Chen QQ, Que RY, Xiao TG, Zheng L, Wang LJ, Zhang YL

Retrospective Study

- 12136** Diagnosis and treatment of tubal endometriosis in women undergoing laparoscopy: A case series from a single hospital
Jiao HN, Song W, Feng WW, Liu H
- 12146** Different positive end expiratory pressure and tidal volume controls on lung protection and inflammatory factors during surgical anesthesia
Wang Y, Yang Y, Wang DM, Li J, Bao QT, Wang BB, Zhu SJ, Zou L
- 12156** Transarterial chemoembolization combined with radiofrequency ablation in the treatment of large hepatocellular carcinoma with stage C
Sun SS, Li WD, Chen JL
- 12164** Coexistence of anaplastic lymphoma kinase rearrangement in lung adenocarcinoma harbouring epidermal growth factor receptor mutation: A single-center study
Zhong WX, Wei XF

Observational Study

- 12175** Prognostic values of optic nerve sheath diameter for comatose patients with acute stroke: An observational study
Zhu S, Cheng C, Wang LL, Zhao DJ, Zhao YL, Liu XZ
- 12184** Quality of care in patients with inflammatory bowel disease from a public health center in Brazil
Takamune DM, Cury GSA, Ferrás G, Herrerias GSP, Rivera A, Barros JR, Baima JP, Saad-Hossne R, Sasaki LY
- 12200** Comparison of the prevalence of sarcopenia in geriatric patients in Xining based on three different diagnostic criteria
Pan SQ, Li XF, Luo MQ, Li YM

Prospective Study

- 12208** Predictors of bowel damage in the long-term progression of Crohn's disease
Fernández-Clotet A, Panés J, Ricart E, Castro-Poceiro J, Masamunt MC, Rodríguez S, Caballol B, Ordás I, Rimola J

Randomized Controlled Trial

- 12221** Protective effect of recombinant human brain natriuretic peptide against contrast-induced nephropathy in elderly acute myocardial infarction patients: A randomized controlled trial
Zhang YJ, Yin L, Li J

META-ANALYSIS

- 12230** Prognostic role of pretreatment serum ferritin concentration in lung cancer patients: A meta-analysis
Gao Y, Ge JT

CASE REPORT

- 12240** Non-surgical management of dens invaginatus type IIIB in maxillary lateral incisor with three root canals and 6-year follow-up: A case report and review of literature
Arora S, Gill GS, Saquib SA, Saluja P, Baba SM, Khateeb SU, Abdulla AM, Bavabeedu SS, Ali ABM, Elagib MFA
- 12247** Unusual presentation of Loeys-Dietz syndrome: A case report of clinical findings and treatment challenges
Azrad-Daniel S, Cupa-Galvan C, Farca-Soffer S, Perez-Zincer F, Lopez-Acosta ME
- 12257** Peroral endoscopic myotomy assisted with an elastic ring for achalasia with obvious submucosal fibrosis: A case report
Wang BH, Li RY
- 12261** Subclavian brachial plexus metastasis from breast cancer: A case report
Zeng Z, Lin N, Sun LT, Chen CX
- 12268** Case mistaken for leukemia after mRNA COVID-19 vaccine administration: A case report
Lee SB, Park CY, Park SG, Lee HJ
- 12278** Orthodontic-surgical treatment of an Angle Class II malocclusion patient with mandibular hypoplasia and missing maxillary first molars: A case report
Li GF, Zhang CX, Wen J, Huang ZW, Li H

- 12289** Multiple cranial nerve palsies with small angle exotropia following COVID-19 mRNA vaccination in an adolescent: A case report
Lee H, Byun JC, Kim WJ, Chang MC, Kim S
- 12295** Surgical and nutritional interventions for endometrial receptivity: A case report and review of literature
Hernández-Melchor D, Palafox-Gómez C, Madrazo I, Ortiz G, Padilla-Viveros A, López-Bayghen E
- 12305** Conversion therapy for advanced penile cancer with tislelizumab combined with chemotherapy: A case report and review of literature
Long XY, Zhang S, Tang LS, Li X, Liu JY
- 12313** Endoscopic magnetic compression stricturoplasty for congenital esophageal stenosis: A case report
Liu SQ, Lv Y, Luo RX
- 12319** Novel *hydroxymethylbilane synthase* gene mutation identified and confirmed in a woman with acute intermittent porphyria: A case report
Zhou YQ, Wang XQ, Jiang J, Huang SL, Dai ZJ, Kong QQ
- 12328** Modified fixation for periprosthetic supracondylar femur fractures: Two case reports and review of the literature
Li QW, Wu B, Chen B
- 12337** Erbium-doped yttrium aluminum garnet laser and advanced platelet-rich fibrin+ in periodontal diseases: Two case reports and review of the literature
Tan KS
- 12345** Segmental artery injury during transforaminal percutaneous endoscopic lumbar discectomy: Two case reports
Cho WJ, Kim KW, Park HY, Kim BH, Lee JS
- 12352** Pacemaker electrode rupture causes recurrent syncope: A case report
Zhu XY, Tang XH, Huang WY
- 12358** Hybrid intercalated duct lesion of the parotid: A case report
Stankevicius D, Petroska D, Zaleckas L, Kutanovaite O
- 12365** Clinical features and prognosis of multiple myeloma and orbital extramedullary disease: Seven cases report and review of literature
Hu WL, Song JY, Li X, Pei XJ, Zhang JJ, Shen M, Tang R, Pan ZY, Huang ZX
- 12375** Colon mucosal injury caused by water jet malfunction during a screening colonoscopy: A case report
Patel P, Chen CH
- 12380** Primary malignant pericardial mesothelioma with difficult antemortem diagnosis: A case report
Oka N, Orita Y, Oshita C, Nakayama H, Teragawa H
- 12388** Typical imaging manifestation of neuronal intranuclear inclusion disease in a man with unsteady gait: A case report
Gao X, Shao ZD, Zhu L

- 12395** Multimodality imaging and treatment of paranasal sinuses nuclear protein in testis carcinoma: A case report
Huang WP, Gao G, Qiu YK, Yang Q, Song LL, Chen Z, Gao JB, Kang L
- 12404** T1 rectal mucinous adenocarcinoma with bilateral enlarged lateral lymph nodes and unilateral metastasis: A case report
Liu XW, Zhou B, Wu XY, Yu WB, Zhu RF
- 12410** Influence of enhancing dynamic scapular recognition on shoulder disability, and pain in diabetics with frozen shoulder: A case report
Mohamed AA
- 12416** Acute myocardial necrosis caused by aconitine poisoning: A case report
Liao YP, Shen LH, Cai LH, Chen J, Shao HQ
- 12422** Danggui Sini decoction treatment of refractory allergic cutaneous vasculitis: A case report
Chen XY, Wu ZM, Wang R, Cao YH, Tao YL
- 12430** Phlegmonous gastritis after biloma drainage: A case report and review of the literature
Yang KC, Kuo HY, Kang JW
- 12440** Novel *TINF2* gene mutation in dyskeratosis congenita with extremely short telomeres: A case report
Picos-Cárdenas VJ, Beltrán-Ontiveros SA, Cruz-Ramos JA, Contreras-Gutiérrez JA, Arámbula-Meraz E, Angulo-Rojo C, Guadrón-Llanos AM, Leal-León EA, Cedano-Prieto DM, Meza-Espinoza JP
- 12447** Synchronous early gastric and intestinal mucosa-associated lymphoid tissue lymphoma in a *Helicobacter pylori*-negative patient: A case report
Lu SN, Huang C, Li LL, Di LJ, Yao J, Tuo BG, Xie R

LETTER TO THE EDITOR

- 12455** Diagnostic value of metagenomics next-generation sequencing technology in disseminated strongyloidiasis
Song P, Li X
- 12458** Diagnostic value of imaging examination in autoimmune pancreatitis
Wang F, Peng Y, Xiao B

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Cornelia Bala, MD, PhD, Professor, Department of Diabetes and Nutrition Diseases, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca 400006, Romania. cbala@umfcluj.ro

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases (WJCC, World J Clin Cases)* is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for *WJCC* as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The *WJCC*'s CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

November 26, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Prognostic role of pretreatment serum ferritin concentration in lung cancer patients: A meta-analysis

Yang Gao, Jin-Tong Ge

Specialty type: Oncology

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Andriolo LG, Italy; Gupta P, United States; Yang X, China

Received: August 23, 2022

Peer-review started: August 23, 2022

First decision: October 17, 2022

Revised: October 19, 2022

Accepted: October 24, 2022

Article in press: October 24, 2022

Published online: November 26, 2022



Yang Gao, Jin-Tong Ge, Department of Cardiology Surgery, The Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University, Huaian 223001, Jiangsu Province, China

Corresponding author: Jin-Tong Ge, MD, Professor, Department of Cardiology Surgery, The Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University, No. 1 Yellow River West Road, Huaian 223001, Jiangsu Province, China. 15851861990@163.com

Abstract

BACKGROUND

The association between pretreatment serum ferritin concentration (SFC) and long-term survival in lung cancer remains unclear now.

AIM

To identify the prognostic value of pretreatment SFC in lung cancer patients based on current evidence.

METHODS

The PubMed, EMBASE and Web of Science databases were searched from inception to May 29, 2022 for relevant studies. The primary endpoint was overall survival (OS) and the hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) were combined to assess the predictive role of pretreatment SFC for long-term survival of lung cancer patients. The data were then extracted and assessed on the basis of the Reference Citation Analysis (<https://www.referencecitationanalysis.com/>).

RESULTS

Twelve retrospective studies involving 1654 patients were analyzed. The results manifested that increased pretreatment SFC was associated with worse OS (HR = 1.09, 95% CI: 1.03-1.15, $P = 0.004$). Subgroup analysis stratified by the country (China vs non-China) showed similar results. However, subgroup analysis stratified by tumor type revealed inconsistent results (lung cancer: HR = 1.39, $P = 0.008$; small cell lung cancer: HR = 1.99, $P = 0.175$; non-small cell lung cancer: HR = 1.03, $P = 0.281$).

CONCLUSION

Pretreatment SFC might serve as a promising prognostic indicator in lung cancer patients and elevated pretreatment SFC predicts worse prognosis. However, more high-quality studies with big sample sizes are still needed to further verify its prognostic value in lung cancer.

Key Words: Serum ferritin concentration; Prognosis; Lung cancer; Meta-analysis

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Our results manifested that increased pretreatment serum ferritin concentration (SFC) was significantly associated with worse overall survival ($P = 0.004$). Subgroup analysis based on the country (China vs non-China) showed similar results. However, subgroup analysis stratified by tumor type revealed inconsistent results (lung cancer: HR = 1.39, $P = 0.008$; small cell lung cancer: HR = 1.99, $P = 0.175$; non-small cell lung cancer: HR = 1.03, $P = 0.281$). Pretreatment SFC might serve as a promising prognostic indicator in lung cancer patients and elevated pretreatment SFC predicts worse prognosis. However, more high-quality studies with big sample sizes are still needed to further verify its prognostic value in lung cancer.

Citation: Gao Y, Ge JT. Prognostic role of pretreatment serum ferritin concentration in lung cancer patients: A meta-analysis. *World J Clin Cases* 2022; 10(33): 12230-12239

URL: <https://www.wjgnet.com/2307-8960/full/v10/i33/12230.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i33.12230>

INTRODUCTION

Lung cancer is the most common malignancy in China and remains the leading cause of cancer-related death[1]. Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) account for about 85% and 15% of all lung cancer cases, respectively[2,3]. Despite the great advances in the screening and therapy strategies of lung cancer, the overall prognosis of lung cancer patients is still not optimistic[1,4,5]. The tumor-node-metastasis (TNM) remains the most authoritative tool for prediction of long-term survival and formulation of treatment strategy. However, in some cases, TNM stage system is not enough for clinical guidance because of the significant heterogeneity between lung cancer patients with the same TNM stage. Thus, it is necessary to identify more valuable prognostic indicators in lung cancer.

Iron is an essential trace element for the human body. It is not only necessary for oxygen supply to all cells, but also participates in redox reactions and cell growth processes[6]. Besides, it also plays an important role in antioxidant defense reactions[6]. However, elevated serum iron levels would accelerate redox reactions and the production of reactive oxygen species like hydroxyl radicals. The hydroxyl radical is a highly active substance which can induce lipid peroxidation and DNA damage, leading to the occurrence and development of some cancers[7-10]. Compared with normal cells, tumor cells are highly dependent on iron, which is called iron addiction[11]. It is known that serum ferritin is a reliable indicator reflection the iron level. A number of studies have manifested that the serum ferritin concentration (SFC) is obviously increased and also associated with long-term survival in cancer patients[12-16]. Up to now, a number of studies explored the predictive role of pretreatment SFC for prognosis in lung cancer with inconsistent results[17-28].

Therefore, we aimed to further verify the prognosis value of pretreatment SFC in lung cancer.

MATERIALS AND METHODS

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA 2009) checklist[29].

Literature search

In this meta-analysis, the PubMed, EMBASE and Web of Science electronic databases were searched from inception to May 29, 2022 for studies exploring the prognostic value of pretreatment SFC in lung cancer. The following key words were used during the search process: Ferritin, lung, pulmonary, tumor, cancer, neoplasm, carcinoma, prognosis, prognostic and survival. The specific search strategy in the PubMed was as follows: (ferritin) AND (lung OR pulmonary) AND (tumor OR cancer OR neoplasm OR carcinoma) AND (prognosis OR prognostic OR survival). Furthermore, the references in the included studies were also reviewed for availability. Meanwhile, Reference Citation Analysis (<https://www.referencecitationanalysis.com/>) was used to supplement the search.

Inclusion criteria

The inclusion criteria were as follows: (1) Patients were pathologically diagnosed with primary lung cancer; (2) the SFC was calculated before anti-tumor treatment including the surgery, chemotherapy, radiotherapy and others; (3) the overall survival (OS) or other similar survival indexes of patients were compared between increased and decreased pretreatment SFC groups; and (4) the hazard ratios (HRs) with 95% confidence intervals (CIs) were reported in the articles or enough data were provided to calculate them.

Exclusion criteria

The exclusion criteria were as follows: (1) Reviews, meeting abstracts, editorials, letters or animal trials; (2) insufficient data for assessment of study quality; and (3) the HRs with corresponding 95% CIs were not available.

Data extraction

The following information was extracted from each included studies: the name of first author, publication year, country, sample size, tumor type, TNM stage, treatment (surgery *vs* non-surgery), cutoff value of SFC, endpoint, HR and 95% CI.

Quality assessment

The methodological quality of included studies was evaluated according to the Newcastle Ottawa Scale (NOS)[30]. The NOS consisted of three parameters of quality: Selection (representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure and outcome of interest), comparability (comparability of cohorts), and outcome (assessment of outcome, time of follow-up and adequacy of follow-up). Studies with a NOS score of 6 or higher were defined as high-quality studies[30].

Besides, the literature search, selection, data extraction and quality assessment were all conducted by two authors independently and any disagreement was resolved by team discussion.

Statistical analysis

All statistical analysis of this study were performed by STATA 15.0 software (College Station, TX, United States). The HRs with 95% CIs were combined to identify the association of pretreatment SFC with prognosis of lung cancer patients. The heterogeneity was evaluated by Cochran's Q test and Higgins I^2 statistic; $P < 0.10$ and/or $I^2 > 50\%$ was defined as significant heterogeneity among studies, and the random-effects model was used for the pooled effect estimates, otherwise the fixed-effects model was used[31]. Subgroup analyses stratified by the country (non-China *vs* China) and tumor type (SCLC *vs* lung cancer *vs* NSCLC) were conducted. Sensitivity analysis for OS was performed by removing individual study from the meta-analysis each time. Besides, the Begg's funnel plot and Egger's test were also conducted to detect the publication bias[32]. If publication bias was observed by presenting a $P < 0.05$, the nonparametric trim-and-fill method was applied to re-estimate a corrective effect size after publication bias was adjusted.

RESULTS**Literature search**

Initially, 978 records were found in databases and 181 duplicated records were removed. Then 763 irrelevant publications were excluded. Subsequently, the full texts of 18 publications were reviewed after removing 16 records due to the design nature. Eventually, only 12 publications were included [17-28]. The detailed selection process was presented in [Figure 1](#).

Basic characteristics of included studies

Among 12 retrospective included studies, 1654 patients were involved with the sample size ranged from 25 to 400. Most studies were from Asian countries. Five[19,23-26] and four[17,19,22,27] studies focused on NSCLC and SCLC, separately. The cutoff values of SFC ranged from 114.1 ng/dL to 400 ng/dL. All included studies were high-quality studies with a NOS score ≥ 6 . Detailed information was presented in [Table 1](#).

The association between pretreatment SFC and OS of lung cancer patients

The results demonstrated that increased pretreatment SFC was significantly associated with poorer OS in lung cancer (HR = 1.09, 95% CI: 1.03-1.15, $P = 0.004$; $I^2 = 86.5\%$, $P_{\text{heterogeneity}} < 0.001$) ([Figure 2](#)).

Subgroup analysis based on the country was performed and the results manifested that pretreatment SFC had high prognostic value in both non-Chinese (HR = 1.61, 95% CI: 1.27-2.03, $P < 0.001$) and Chinese patients (HR = 1.06, 95% CI: 1.00-1.12, $P = 0.042$) ([Table 2](#)). Besides, subgroup analysis stratified by the tumor type showed inconsistent results. Pretreatment SFC was related to the OS in lung cancer (HR =

Table 1 Basic characteristics of included studies

Ref.	Country	Sample size	Tumor type	TNM stage	Treatment	Cutoff value of ferritin (ng/dL)	NOS				Endpoint
							Selection	Comparability	Outcome	Overall	
Milman <i>et al</i> [17], 1991	Denmark	31	SCLC	Limited and advanced	Non-surgery	400	3	0	3	6	OS
Ferrigno <i>et al</i> [18], 1992	Italy	168	LC	I-IV	Mixed	236	4	0	2	6	OS
Milman <i>et al</i> [19], 2002	Denmark	90	NSCLC	I-IV	Mixed	300	4	0	3	7	OS
Milman <i>et al</i> [19], 2002	Denmark	25	SCLC	Limited and advanced	Mixed	300	3	0	3	6	OS
Erbaycu <i>et al</i> [20], 2008	Turkey	41	LC	I-IV	Mixed	220	3	0	3	6	OS
Zhao <i>et al</i> [21], 2014	China	69	LC	IV	Non-surgery	NR	4	0	3	7	OS
Xie <i>et al</i> [22], 2018	China	72	SCLC	Limited and advanced	NR	NR	4	0	3	7	OS
Lee <i>et al</i> [23], 2019	Republic of Korea	138	NSCLC	IIIB-IV	Non-surgery	200	4	0	3	7	OS
Ma <i>et al</i> [24], 2019	China	393	NSCLC	I-III	NR	382.65	4	0	3	7	OS
Sun[25], 2020	China	72	NSCLC	III-IV	Non-surgery	Male: 200, female: 150	3	0	3	6	OS
Ji <i>et al</i> [26], 2021	China	69	NSCLC	IIIB-IV	Non-surgery	311.1	3	0	3	6	OS
Xiao[27], 2021	China	86	SCLC	NR	NR	NR	3	0	3	6	OS
Zhu[28], 2021	China	400	LC	I-IV	NR	114.1	4	0	3	7	OS

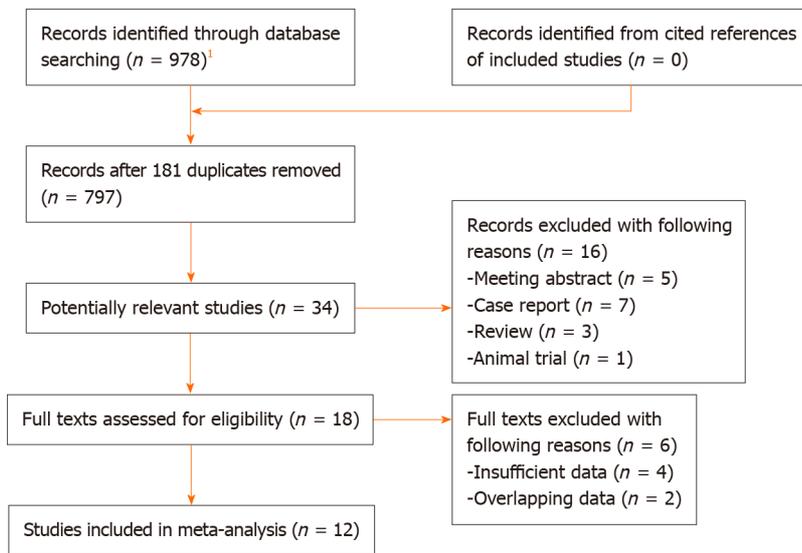
LC: Lung cancer; SCLC: Small cell lung cancer; NSCLC: Non-small cell lung cancer; NR: Not reported; OS: Overall survival; NOS: Newcastle Ottawa Scale.

Table 2 Results of meta-analysis

	No. of studies	HR	95%CI	P value	I ² (%)	P _{heterogeneity}
Overall survival	12 (17-28)	1.09	1.03-1.15	0.004	86.5	< 0.001
Country						
Non-China	5 (17-20, 23)	1.61	1.27-2.03	< 0.001	0.0	0.760
China	7 (21, 22, 24-28)	1.06	1.00-1.12	0.042	91.5	< 0.001
Tumor type						
SCLC	4 (17, 19, 22, 27)	1.99	0.74-5.35	0.175	90.7	< 0.001
LC	4 (18, 20, 21, 28)	1.39	1.09-1.77	0.008	0.0	0.666
NSCLC	5 (19, 23-26)	1.03	0.98-1.07	0.281	86.2	< 0.001

HR: Hazard ratio; CI: Confidence interval; SCLC: Small cell lung cancer; LC: Lung cancer; NSCLC: Non-small cell lung cancer.

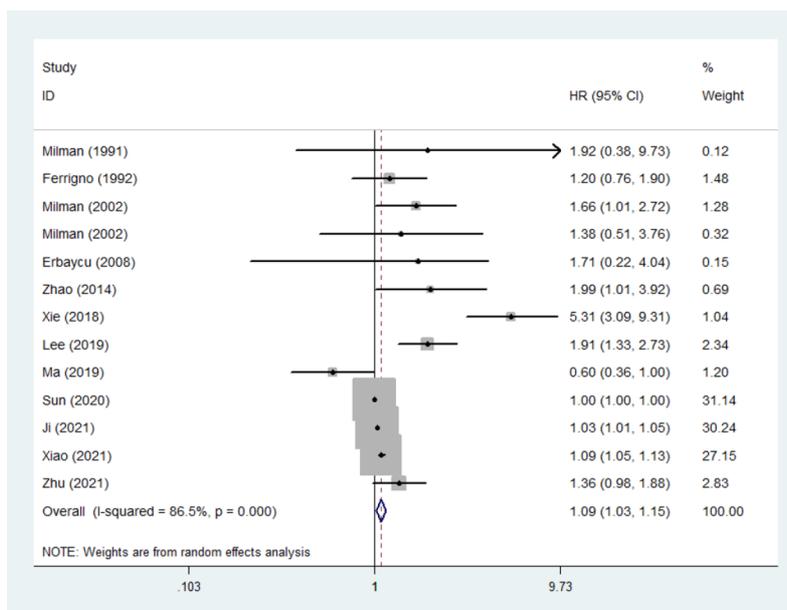
1.39, 95%CI: 1.09-1.77, $P = 0.008$), but no significant association between pretreatment SFC and OS in SCLC (HR = 1.99, 95%CI: 0.74-5.35, $P = 0.175$) and NSCLC (HR = 1.03, 95%CI: 0.98-1.07, $P = 0.281$) (Table 2).



¹PubMed (n = 154), EMBASE (n = 449), Web of Science (n = 287), CNKI (n = 69), VIP (n = 8) and WanFang (n = 11)

DOI: 10.12998/wjcc.v10.i33.12230 Copyright ©The Author(s) 2022.

Figure 1 The flow diagram of this meta-analysis.



DOI: 10.12998/wjcc.v10.i33.12230 Copyright ©The Author(s) 2022.

Figure 2 The association between pretreatment serum ferritin concentration and overall survival of lung cancer patients.

Sensitivity analysis and publication bias

The sensitivity analysis demonstrated that the results were stable and relatively reliable (Figure 3). However, the studies by Sun *et al*[25] and Ji *et al*[26] showed relatively obvious impacts on the overall results. Furthermore, due to the asymmetric Begg’s funnel plot (Figure 4) and $P = 0.009$ of Egger’s test, significant publication bias was observed. Then the trim-and-fill method was used and we detected five potentially unpublished studies (Figure 5). After combining these five studies, the new estimated HRs were 1.003 (95%CI: 1.000-1.006, $P = 0.031$) for fixed-effects model and 1.051 (95%CI: 0.984-1.123, $P = 0.139$) for random-effects model, separately. Thus, more prospective high-quality studies are still needed to further explore the prognostic value of pretreatment SFC in lung cancer patients.

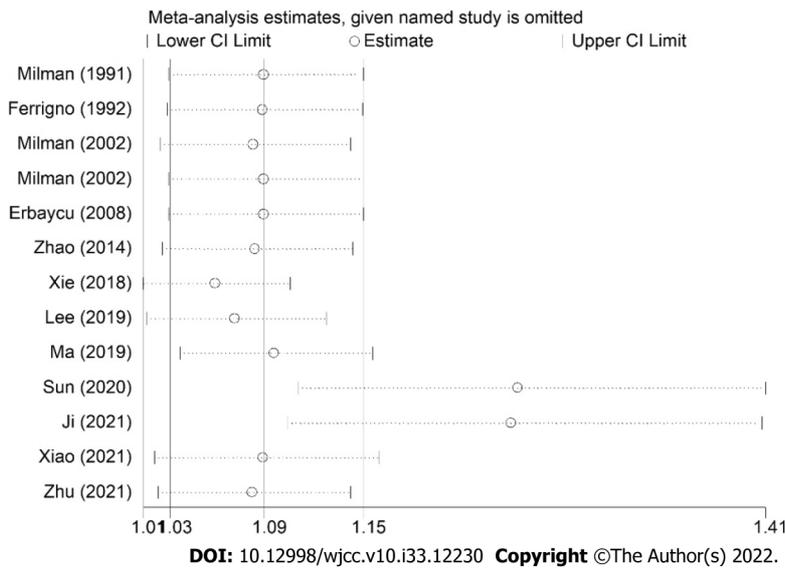


Figure 3 Sensitivity analysis about the association between pretreatment serum ferritin concentration and overall survival of lung cancer patients.

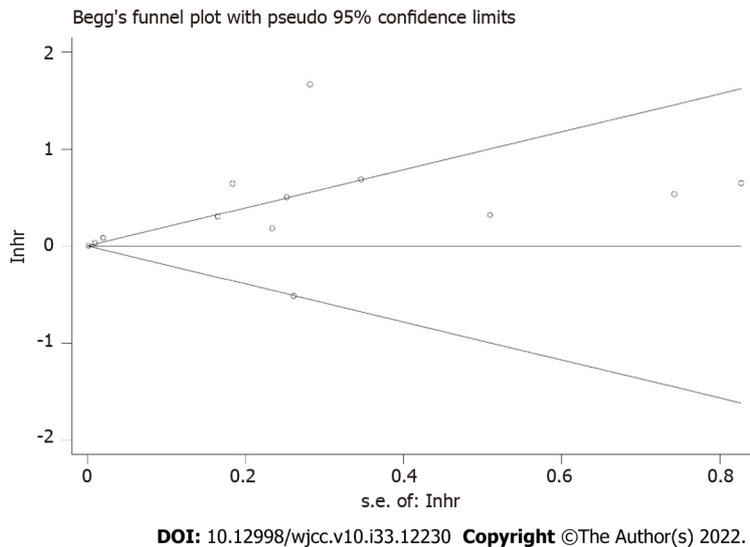


Figure 4 Begg's funnel plot.

DISCUSSION

In the current meta-analysis, 12 studies involving 1654 Lung cancer patients were included and the results demonstrated that elevated pretreatment SFC was a significant predictor for worse OS in lung cancer. Subgroup analysis based on the country (China *vs* non-China) showed similar results, but the subgroup analysis stratified by the tumor type (SCLC *vs* lung cancer *vs* NSCLC) showed inconsistent findings. Therefore, in overall, pretreatment SFC is believed to serve as a promising prognostic indicator in lung cancer. However, more prospective high-quality studies are still needed to further explore the prognostic role of pretreatment SFC in lung cancer.

Serum ferritin is the main indicator which reflects the amount of iron storage in the human body. The elevation of SFC is mainly caused by clearance barriers or increased sources of ferritin. In clinics, liver disease which results in the decreased liver function is a major cause of impaired clearance for ferritin [33]. On the other hand, tumor is the main cause of excess production of ferritin and it has been widely reported that cancer patients show obvious increased SFC compared with normal population[34,35]. Sukiennicki *et al*[36] conducted a case control study involving 200 Lung cancer patients and 200 matched healthy people, which indicated that lung cancer patients had significantly higher mean SFC ($P = 0.007$). The studies by Cobanoglu *et al*[37] and Zhu *et al*[28] manifested similar results. However, this phenomenon is different in male and female patients and positive association between increased SFC

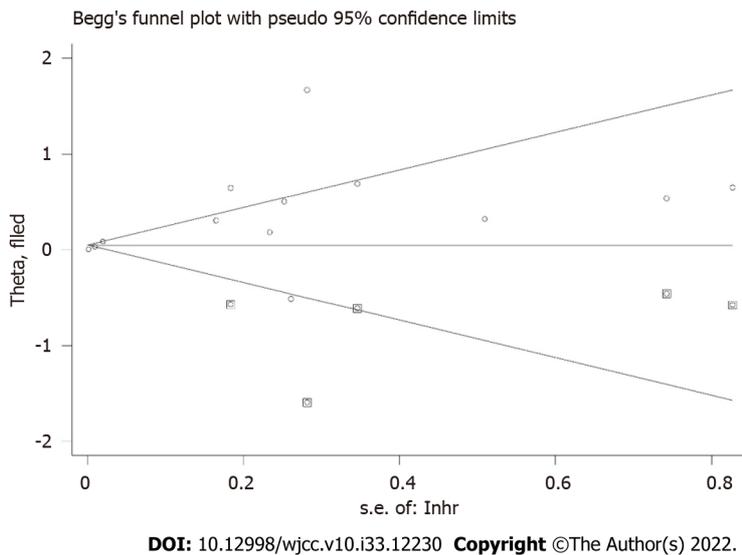


Figure 5 Filled funnel plot.

and incidence of lung cancer is only observed in male patients[36,37]. Meanwhile, in male lung cancer patients, smoking obviously contributes to the elevation of SFC ($P = 0.036$)[38,39]. However, for female lung cancer patients, menstruation is one of the important factors affecting SFC[40]. Besides, some other parameters may also affect the SFC like the tumor stage[40]. Thus, the baseline SFC varies in different populations and is regulated by many mechanisms.

Up to now, the prognostic value of pretreatment SFC in several types of cancers has been verified. Lin *et al*[41] included seven relevant studies involving 1244 patients and demonstrated that elevated pretreatment SFC was related to worse OS (HR = 1.60, $P < 0.001$) and RFS/progression-free survival (PFS)/time to recurrence (HR = 1.70, $P = 0.008$) in hepatobiliary and pancreas cancers. Besides, Demir *et al*[12] manifested that high SFC was associated with worse survival. Furthermore, Kim *et al*[42] manifested that elevated SFC was related to poor prognosis in patients with diffuse large B cell lymphoma.

Actually, there are still many fields worthy of further investigation about the SFC in lung cancer. First, the current meta-analysis only revealed that pretreatment SFC was related to prognosis of lung cancer. Thus, it is necessary to explore the association between the changes of SFC during the anti-tumor treatment and long-term survival. Second, as mentioned above, it is believed that the baseline SFC varies in different people. Therefore, the optimal cutoff value of SFC should be specific in different populations. Third, it is also needed to explore the clinical value of interfering with SFC.

There are several limitations in this meta-analysis. First, all included studies are retrospective and the overall sample size is relatively small, which may cause some bias. Second, we were unable to conduct more subgroup analyses based on other important parameters such as the TNM stage, age, sex and smoking history due to the unobtainable original data. Third, obvious heterogeneity existed in this meta-analysis. However, subgroup analysis did not find sources of heterogeneity. Four, in this type of meta-analysis, the optimal cutoff value of pretreatment SFC could not be determined. Five, the significant publication bias was observed in our meta-analysis, although the potentially unpublished studies did not have a significant impact on the pooled results.

CONCLUSION

In overall, pretreatment SFC might serve as a promising prognostic indicator in lung cancer patients and elevated pretreatment SFC predicts worse prognosis. However, more prospective high-quality studies with big sample sizes are still needed to further verify its prognostic value in lung cancer.

ARTICLE HIGHLIGHTS

Research background

The association between pretreatment serum ferritin concentration (SFC) and long-term survival in lung cancer remains unclear now.

Research motivation

Whether the pretreatment SFC could play a role in predicting long-term survival in lung cancer remains unclear.

Research objectives

To identify the prognostic value of pretreatment SFC in lung cancer patients based on current evidence.

Research methods

The PubMed, EMBASE and Web of Science databases were searched from inception to May 29, 2022 for relevant studies. The primary endpoint was overall survival (OS) and the hazard ratios (HRs) with 95% confidence intervals (CIs) were combined to assess the predictive role of pretreatment SFC for long-term survival of lung cancer patients. All statistical analysis was conducted by STATA 15.0.

Research results

A total of 12 retrospective studies involving 1654 patients were included. The pooled results manifested that increased pretreatment SFC was significantly associated with worse OS (HR = 1.09, 95%CI: 1.03-1.15, $P = 0.004$). Subgroup analysis based on the country (China *vs* non-China) showed similar results. However, subgroup analysis stratified by tumor type revealed inconsistent results (lung cancer: HR = 1.39, $P = 0.008$; small cell lung cancer: HR = 1.99, $P = 0.175$; non-small cell lung cancer: HR = 1.03, $P = 0.281$).

Research conclusions

Pretreatment SFC might serve as a promising prognostic indicator in lung cancer patients and elevated pretreatment SFC predicts worse prognosis.

Research perspectives

The pretreatment SFC might contribute to the clinical management and treatment of lung cancer patients.

FOOTNOTES

Author contributions: Ge JT made the substantial contributions to the conception and design of the work; Gao Y and Ge JT searched, selected materials and extracted data; Gao Y wrote this manuscript; Gao Y and Ge JT revised the paper carefully and also contributed to the statistical analysis; All authors have read and approved the final manuscript.

Conflict-of-interest statement: All the authors declare that there are no competing interests associated with this manuscript.

PRISMA 2009 Checklist statement: This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA 2009) checklist.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Yang Gao [0000-0002-7676-3261](https://orcid.org/0000-0002-7676-3261); Jin-Tong Ge [0000-0002-6470-9524](https://orcid.org/0000-0002-6470-9524).

S-Editor: Liu JH

L-Editor: A

P-Editor: Liu JH

REFERENCES

- 1 Li H, Guo J, Liang H, Zhang T, Zhang J, Wei L, Shi D, Wang Z. The Burden of Trachea, Bronchus, and Lung Cancer Attributable to Occupational Exposure From 1990 to 2019. *Front Public Health* 2022; **10**: 928937 [PMID: [35784215](https://pubmed.ncbi.nlm.nih.gov/35784215/) DOI: [10.3389/fpubh.2022.928937](https://doi.org/10.3389/fpubh.2022.928937)]
- 2 Thill PG, Goswami P, Berchem G, Doman B. Lung cancer statistics in Luxembourg from 1981 to 2008. *Bull Soc Sci Med*

- Grand Duche Luxemb* 2011; 43-55 [PMID: 22272445]
- 3 **Torre LA**, Siegel RL, Jemal A. Lung Cancer Statistics. *Adv Exp Med Biol* 2016; **893**: 1-19 [PMID: 26667336 DOI: 10.1007/978-3-319-24223-1_1]
 - 4 **Oncology Society of Chinese Medical Association**; Chinese Medical Association Publishing House. [Chinese Medical Association guideline for clinical diagnosis and treatment of lung cancer (2022 edition)]. *Zhonghua Zhong Liu Za Zhi* 2022; **44**: 457-490 [PMID: 35754224 DOI: 10.3760/cma.j.cn112152-20220413-00255]
 - 5 **Wang L**, Liu A, Wang Z, Xu N, Zhou D, Qu T, Liu G, Wang J, Yang F, Guo X, Chi W, Xue F. A Prognostic Model of Non-Small Cell Lung Cancer With a Radiomics Nomogram in an Eastern Chinese Population. *Front Oncol* 2022; **12**: 816766 [PMID: 35774128 DOI: 10.3389/fonc.2022.816766]
 - 6 **Toyokuni S**. Role of iron in carcinogenesis: cancer as a ferrotoxic disease. *Cancer Sci* 2009; **100**: 9-16 [PMID: 19018762 DOI: 10.1111/j.1349-7006.2008.01001.x]
 - 7 **Knekt P**, Reunanen A, Takkunen H, Aromaa A, Heliövaara M, Hakulinen T. Body iron stores and risk of cancer. *Int J Cancer* 1994; **56**: 379-382 [PMID: 8314326 DOI: 10.1002/ijc.2910560315]
 - 8 **Hino K**, Yanatori I, Hara Y, Nishina S. Iron and liver cancer: an inseparable connection. *FEBS J* 2021 [PMID: 34543507 DOI: 10.1111/febs.16208]
 - 9 **Schöttker B**, Gào X, Jansen EH, Brenner H. Associations of Human Colorectal Adenoma with Serum Biomarkers of Body Iron Stores, Inflammation and Antioxidant Protein Thiols. *Antioxidants (Basel)* 2021; **10** [PMID: 34439443 DOI: 10.3390/antiox10081195]
 - 10 **Yu YC**, Luu HN, Wang R, Thomas CE, Glynn NW, Youk AO, Behari J, Yuan JM. Serum Biomarkers of Iron Status and Risk of Hepatocellular Carcinoma Development in Patients with Nonalcoholic Fatty Liver Disease. *Cancer Epidemiol Biomarkers Prev* 2022; **31**: 230-235 [PMID: 34649958 DOI: 10.1158/1055-9965.EPI-21-0754]
 - 11 **Basuli D**, Tesfay L, Deng Z, Paul B, Yamamoto Y, Ning G, Xian W, McKeon F, Lynch M, Crum CP, Hegde P, Brewer M, Wang X, Miller LD, Dymnt N, Torti FM, Torti SV. Iron addiction: a novel therapeutic target in ovarian cancer. *Oncogene* 2017; **36**: 4089-4099 [PMID: 28319068 DOI: 10.1038/onc.2017.11]
 - 12 **Demir H**, Beypinar I, Urvay S, Davarcı SE, Baykara M. Prognostic role of pre-operative serum ferritin level in stage 2 colon cancer. *Eur Rev Med Pharmacol Sci* 2021; **25**: 6473-6479 [PMID: 34787851 DOI: 10.26355/eurrev_202111_27091]
 - 13 **Karakatsanis S**, Panitsas F, Arapaki M, Galopoulos D, Asimakopoulos JV, Liaskas A, Chatzidimitriou C, Belia M, Konstantinou E, Vassilopoulos I, Papadatos SS, Sachanas S, Efstathopoulou M, Yiakoumis X, Pardalis V, Iliakis T, Giannakopoulou N, Dimou M, Chatzidavid S, Boutsikas G, Petevi K, Kanellopoulos A, Gainaru G, Variamias E, Siakantaris MP, Kyrtsonis MC, Plata E, Tsafaridis P, Dimopoulou MN, Viniou NA, Syrigos KN, Pangalis GA, Panayiotidis P, Konstantopoulos K, Angelopoulou MK, Vassilakopoulos TP. Serum ferritin levels in previously untreated classical Hodgkin lymphoma: correlations and prognostic significance. *Leuk Lymphoma* 2022; **63**: 799-812 [PMID: 35188040 DOI: 10.1080/10428194.2021.2010054]
 - 14 **Park JM**, Mau CZ, Chen YC, Su YH, Chen HA, Huang SY, Chang JS, Chiu CF. A case-control study in Taiwanese cohort and meta-analysis of serum ferritin in pancreatic cancer. *Sci Rep* 2021; **11**: 21242 [PMID: 34711879 DOI: 10.1038/s41598-021-00650-7]
 - 15 **Ramirez-Carmona W**, Díaz-Fabregat B, Yuri Yoshigae A, Musa de Aquino A, Scarano WR, de Souza Castilho AC, Avansini Marsicano J, Leal do Prado R, Pessan JP, de Oliveira Mendes L. Are Serum Ferritin Levels a Reliable Cancer Biomarker? *Nutr Cancer* 2022; **74**: 1917-1926 [PMID: 34607491 DOI: 10.1080/01635581.2021.1982996]
 - 16 **Zhuge X**, Zhou H, Chen L, Chen H, Chen X, Guo C. The association between serum ferritin levels and malignant intraductal papillary mucinous neoplasms. *BMC Cancer* 2021; **21**: 1253 [PMID: 34800987 DOI: 10.1186/s12885-021-08986-z]
 - 17 **Milman N**, Sengeløv H, Dombernowsky P. Iron status markers in patients with small cell carcinoma of the lung. Relation to survival. *Br J Cancer* 1991; **64**: 895-898 [PMID: 1657106 DOI: 10.1038/bjc.1991.421]
 - 18 **Ferrigno D**, Buccheri G. A comprehensive evaluation of serum ferritin levels in lung cancer patients. *Lung Cancer* 1992; **8**: 85-94 [DOI: 10.1016/0169-5002(92)90090-7]
 - 19 **Milman N**, Pedersen LM. The serum ferritin concentration is a significant prognostic indicator of survival in primary lung cancer. *Oncol Rep* 2002; **9**: 193-198 [PMID: 11748482]
 - 20 **Erbaycu AE**, Ucar H, Uslu O, Tuksavul F, Kazanci MN, Batum O, Kalenci D, Guclu SZ. Prognostic significance of serum iron, iron-binding capacity, ferritin and bronchoalveolar lavage ferritin levels in primary lung cancer. *UHOD - Uluslararası Hematoloji-Onkoloji Dergisi* 2008; **18**: 217-225 Available from: http://www.uhod.org/summary_en.php?id=337
 - 21 **Zhao W**, Shi H, Wu C, Ji M. Association of serum ferritin expression and prognosis in patients with advanced lung carcinoma. *Jiangsu Med J* 2014; **40**: 2978-2980 [DOI: 10.19460/j.cnki.0253-3685.2014.24.007]
 - 22 **Xie J**, Ji H, Chen G, Wang Y, Shen Y. Relationship between serum ferritin, erythrocyte sedimentation rate, mean corpuscular indexes and prognosis in patients with small cell lung cancer. *J Int Oncol* 2018; **45**: 465-469 [DOI: 10.3760/cma.j.issn.1673-422X.2018.08.004]
 - 23 **Lee S**, Jeon H, Shim B. Prognostic Value of Ferritin-to-Hemoglobin Ratio in Patients with Advanced Non-Small-Cell Lung Cancer. *J Cancer* 2019; **10**: 1717-1725 [PMID: 31205527 DOI: 10.7150/jca.26853]
 - 24 **Ma C**, Zuo W. Preoperative serum bilirubin levels associated with stage and prognosis in patients with stages i-iii of non-small cell lung cancer in jiangxi province, china. *International Journal of Clinical and Experimental Medicine* 2019; **12**: 10433-10442 Available from: https://e-century.us/web/journal_toc.php?journal=ijcem&volume=12&number=8
 - 25 **Sun A**. Changes and clinical significance of serum CEA, Fer, A125 and CA199 in patients with NSCLC. *Contemporary Medicine* 2020; **26**: 39-42 Available from: https://jglobal.jst.go.jp/en/detail?JGLOBAL_ID=202002276860074699
 - 26 **Ji D**, Duan A, Li C. Predictive Value of Baseline Serum Ferritin Level for the Prognosis of NSCLC Patients Treated with EGFR-TKIs. *Zhongliu Yaoxue* 2021; **11** Available from: https://jglobal.jst.go.jp/en/detail?JGLOBAL_ID=202102229574263950
 - 27 **Xiao J**. Correlation between serum SF, ESR and average red blood cell index levels and the prognosis of patients with small cell lung cancer. *Qingdao Yiyao Weisheng* 2021; **53**: 105-107 Available from: https://jglobal.jst.go.jp/en/detail?JGLOBAL_ID=202102233347731725

- 28 **Zhu M.** The Correlation Study of Serum Ferritin in Patients with Lung Cancer. *Hangkong Hangtian Yixue Zazhi* 2021; **32**: 899-901 Available from: https://jglobal.jst.go.jp/en/detail?JGLOBAL_ID=202202246720602222
- 29 **Panic N, Leoncini E, de Belvis G, Ricciardi W, Boccia S.** Evaluation of the endorsement of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement on the quality of published systematic review and meta-analyses. *PLoS One* 2013; **8**: e83138 [PMID: 24386151 DOI: 10.1371/journal.pone.0083138]
- 30 **Stang A.** Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010; **25**: 603-605 [PMID: 20652370 DOI: 10.1007/s10654-010-9491-z]
- 31 **Higgins JP, Thompson SG, Deeks JJ, Altman DG.** Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557-560 [PMID: 12958120 DOI: 10.1136/bmj.327.7414.557]
- 32 **Begg CB, Mazumdar M.** Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994; **50**: 1088-1101 [PMID: 7786990]
- 33 **Cao P, Wu Y, Wu S, Wu T, Zhang Q, Zhang R, Wang Z, Zhang Y.** Elevated serum ferritin level effectively discriminates severity illness and liver injury of coronavirus disease 2019 pneumonia. *Biomarkers* 2021; **26**: 207-212 [PMID: 33284041 DOI: 10.1080/1354750X.2020.1861098]
- 34 **Shi HB, Li XD, Jiang JT, Zhao WQ, Ji M, Wu CP.** Serum ferritin is elevated in advanced non-small cell lung cancer patients and is associated with efficacy of platinum-based chemotherapy. *J Cancer Res Ther* 2014; **10**: 681-685 [PMID: 25313760 DOI: 10.4103/0973-1482.139156]
- 35 **Zhang XZ, Su AL, Hu MQ, Zhang XQ, Xu YL.** Elevated serum ferritin levels in patients with hematologic malignancies. *Asian Pac J Cancer Prev* 2014; **15**: 6099-6101 [PMID: 25124580 DOI: 10.7314/apjcp.2014.15.15.6099]
- 36 **Sukiennicki GM, Marciniak W, Muszyńska M, Baszuk P, Gupta S, Białkowska K, Jaworska-Bieniek K, Durda K, Lener M, Pietrzak S, Gromowski T, Prajzendanc K, Łukomska A, Waloszczyk P, Wójcik JZ, Scott R, Lubiński J, Jakubowska A.** Iron levels, genes involved in iron metabolism and antioxidative processes and lung cancer incidence. *PLoS One* 2019; **14**: e0208610 [PMID: 30640897 DOI: 10.1371/journal.pone.0208610]
- 37 **Cobanoglu U, Demir H, Sayir F, Duran M, Mergan D.** Some mineral, trace element and heavy metal concentrations in lung cancer. *Asian Pac J Cancer Prev* 2010; **11**: 1383-1388 [PMID: 21198297]
- 38 **Li S, Lin L, Mo Z, Qin X, Lv H, Gao Y, Tan A, Yang X, Huang S, Chen Z.** Reference values for serum ferritin in Chinese Han ethnic males: results from a Chinese male population survey. *Clin Biochem* 2011; **44**: 1325-1328 [PMID: 21907192 DOI: 10.1016/j.clinbiochem.2011.08.1137]
- 39 **Lapenna D, de Gioia S, Mezzetti A, Ciofani G, Consoli A, Marzio L, Cuccurullo F.** Cigarette smoke, ferritin, and lipid peroxidation. *Am J Respir Crit Care Med* 1995; **151**: 431-435 [PMID: 7842202 DOI: 10.1164/ajrccm.151.2.7842202]
- 40 **Kukulj S, Jaganjac M, Boranic M, Krizanac S, Santic Z, Poljak-Blazi M.** Altered iron metabolism, inflammation, transferrin receptors, and ferritin expression in non-small-cell lung cancer. *Med Oncol* 2010; **27**: 268-277 [PMID: 19308738 DOI: 10.1007/s12032-009-9203-2]
- 41 **Lin S, Fang Y, Lin Y, Mo Z, Hong X, Jian Z, Ji C.** Meta-analysis of the prognostic value of pretreatment serum ferritin in hepatobiliary and pancreas (HBP) cancers. *BMJ Open* 2021; **11**: e040801 [PMID: 34049899 DOI: 10.1136/bmjopen-2020-040801]
- 42 **Kim DJ, Kim T, Jeong JY, Jo JC, Lee WS, Shin HJ, Lee JH, Lee HS.** Poor prognostic impact of high serum ferritin levels in patients with a lower risk of diffuse large B cell lymphoma. *Int J Hematol* 2020; **111**: 559-566 [PMID: 31907736 DOI: 10.1007/s12185-019-02816-6]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

