

# World Journal of *Clinical Cases*

*World J Clin Cases* 2021 July 16; 9(20): 5352-5753



## Contents

Thrice Monthly Volume 9 Number 20 July 16, 2021

### EDITORIAL

- 5352** COVID-19: Considerations about immune suppression and biologicals at the time of SARS-CoV-2 pandemic

*Costanzo G, Cordeddu W, Chessa L, Del Giacco S, Firinu D*

### REVIEW

- 5358** Obesity in people with diabetes in COVID-19 times: Important considerations and precautions to be taken

*Alberti A, Schuelter-Trevisol F, Iser Betine PM, Traebert E, Freiburger V, Ventura L, Rezin GT, da Silva BB, Meneghetti Dallacosta F, Grigollo L, Dias P, Fin G, De Jesus JA, Pertille F, Rossoni C, Hur Soares B, Nodari Junior RJ, Comim CM*

- 5372** Revisiting delayed appendectomy in patients with acute appendicitis

*Li J*

### MINIREVIEWS

- 5391** Detection of short stature homeobox 2 and RAS-associated domain family 1 subtype A DNA methylation in interventional pulmonology

*Wu J, Li P*

- 5398** Borderline resectable pancreatic cancer and vascular resections in the era of neoadjuvant therapy

*Mikulic D, Mrzljak A*

- 5408** Esophageal manifestation in patients with scleroderma

*Voulgaris TA, Karamanolis GP*

- 5420** Exploration of transmission chain and prevention of the recurrence of coronavirus disease 2019 in Heilongjiang Province due to in-hospital transmission

*Chen Q, Gao Y, Wang CS, Kang K, Yu H, Zhao MY, Yu KJ*

- 5427** Role of gastrointestinal system on transmission and pathogenesis of SARS-CoV-2

*Simsek C, Erul E, Balaban HY*

### ORIGINAL ARTICLE

#### Case Control Study

- 5435** Effects of nursing care in fast-track surgery on postoperative pain, psychological state, and patient satisfaction with nursing for glioma

*Deng YH, Yang YM, Ruan J, Mu L, Wang SQ*

#### Retrospective Study

- 5442** Risk factors related to postoperative recurrence of dermatofibrosarcoma protuberans: A retrospective study and literature review

*Xiong JX, Cai T, Hu L, Chen XL, Huang K, Chen AJ, Wang P*

- 5453** Prediction of presence and severity of coronary artery disease using prediction for atherosclerotic cardiovascular disease risk in China scoring system

*Hong XL, Chen H, Li Y, Teeroovengadum HD, Fu GS, Zhang WB*

- 5462** Effects of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors on COVID-19

*Li XL, Li T, Du QC, Yang L, He KL*

- 5470** Prognostic factors and its predictive value in patients with metastatic spinal cancer

*Gao QP, Yang DZ, Yuan ZB, Guo YX*

### Clinical Trials Study

- 5479** Prospective, randomized comparison of two supplemental oxygen methods during gastro-scopy with propofol mono-sedation in obese patients

*Shao LJZ, Hong FX, Liu FK, Wan L, Xue FS*

### SYSTEMATIC REVIEWS

- 5490** Herb-induced liver injury: Systematic review and meta-analysis

*Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldera J*

### META-ANALYSIS

- 5514** Type 2 diabetes mellitus increases liver transplant-free mortality in patients with cirrhosis: A systematic review and meta-analysis

*Liu ZJ, Yan YJ, Weng HL, Ding HG*

### CASE REPORT

- 5526** Duplication of 19q (13.2-13.31) associated with comitant esotropia: A case report

*Feng YL, Li ND*

- 5535** Multiple left ventricular myxomas combined with severe rheumatic valvular lesions: A case report

*Liu SZ, Hong Y, Huang KL, Li XP*

- 5540** Complete pathological response in locally advanced non-small-cell lung cancer patient: A case report

*Parisi E, Arpa D, Ghigi G, Micheletti S, Neri E, Tontini L, Pieri M, Romeo A*

- 5547** Successful reversal of ostomy 13 years after Hartmann procedure in a patient with colon cancer: A case report

*Huang W, Chen ZZ, Wei ZQ*

- 5556** Delayed papillary muscle rupture after radiofrequency catheter ablation: A case report

*Sun ZW, Wu BF, Ying X, Zhang BQ, Yao L, Zheng LR*

- 5562** Temporary coronary sinus pacing to improve ventricular dyssynchrony with cardiogenic shock: A case report

*Ju TR, Tseng H, Lin HT, Wang AL, Lee CC, Lai YC*

- 5568** Hemoglobin Fukuoka caused unexpected hemoglobin A<sub>1c</sub> results: A case report  
*Lin XP, Yuan QR, Niu SQ, Jiang X, Wu ZK, Luo ZF*
- 5575** Giant androgen-producing adrenocortical carcinoma with atrial flutter: A case report and review of the literature  
*Costache MF, Arhirii RE, Mogos SJ, Lupascu-Ursulescu C, Litcanu CI, Ciunanghel AI, Cucu C, Ghiciuc CM, Petris AO, Danila N*
- 5588** Can kissing cause paraquat poisoning: A case report and review of literature  
*Ly B, Han DF, Chen J, Zhao HB, Liu XL*
- 5594** Spinal dural arteriovenous fistula 8 years after lumbar discectomy surgery: A case report and review of literature  
*Ouyang Y, Qu Y, Dong RP, Kang MY, Yu T, Cheng XL, Zhao JW*
- 5605** Perianal superficial CD34-positive fibroblastic tumor: A case report  
*Long CY, Wang TL*
- 5611** Low-dose clozapine-related seizure: A case report and literature review  
*Le DS, Su H, Liao ZL, Yu EY*
- 5621** Rapid diagnosis of disseminated *Mycobacterium mucogenicum* infection in formalin-fixed, paraffin-embedded specimen using next-generation sequencing: A case report  
*Liu J, Lei ZY, Pang YH, Huang YX, Xu LJ, Zhu JY, Zheng JX, Yang XH, Lin BL, Gao ZL, Zhuo C*
- 5631** Cytomegalovirus colitis induced segmental colonic hypoganglionosis in an immunocompetent patient: A case report  
*Kim BS, Park SY, Kim DH, Kim NI, Yoon JH, Ju JK, Park CH, Kim HS, Choi SK*
- 5637** Primary extra-pancreatic pancreatic-type acinar cell carcinoma in the right perinephric space: A case report and review of literature  
*Wei YY, Li Y, Shi YJ, Li XT, Sun YS*
- 5647** Muscular atrophy and weakness in the lower extremities in Behçet's disease: A case report and review of literature  
*Kim KW, Cho JH*
- 5655** Novel technique of extracorporeal intrauterine morcellation after total laparoscopic hysterectomy: Three emblematic case reports  
*Macciò A, Sanna E, Lavra F, Calò P, Madeddu C*
- 5661** Rare isolated extra-hepatic bile duct injury: A case report  
*Zhao J, Dang YL, Lin JM, Hu CH, Yu ZY*
- 5668** Gelfoam embolization for distal, medium vessel injury during mechanical thrombectomy in acute stroke: A case report  
*Kang JY, Yi KS, Cha SH, Choi CH, Kim Y, Lee J, Cho BS*



- 5675** Oncocytic adrenocortical tumor with uncertain malignant potential in pediatric population: A case report and review of literature  
*Chen XC, Tang YM, Mao Y, Qin DR*
- 5683** Submucosal hematoma with a wide range of lesions, severe condition and atypical clinical symptoms: A case report  
*Liu L, Shen XJ, Xue LJ, Yao SK, Zhu JY*
- 5689** Chorioamnionitis caused by *Serratia marcescens* in a healthcare worker: A case report  
*Park SY, Kim MJ, Park S, Kim NI, Oh HH, Kim J*
- 5695** Endoscopic management of biliary ascariasis: A case report  
*Wang X, Lv YL, Cui SN, Zhu CH, Li Y, Pan YZ*
- 5701** Role of ranulas in early diagnosis of Sjögren's syndrome: A case report  
*Chen N, Zeng DS, Su YT*
- 5709** Sacral chondroblastoma — a rare location, a rare pathology: A case report and review of literature  
*Zheng BW, Niu HQ, Wang XB, Li J*
- 5717** Primary liver actinomycosis in a pediatric patient: A case report and literature review  
*Liang ZJ, Liang JK, Chen YP, Chen Z, Wang Y*
- 5724** Splenosis masquerading as gastric stromal tumor: A case report  
*Zheng HD, Xu JH, Sun YF*
- 5730** Hemorrhagic transformation of ischemic cerebral proliferative angiopathy: A case report  
*Xia Y, Yu XF, Ma ZJ, Sun ZW*
- 5737** Multidisciplinary team therapy for left giant adrenocortical carcinoma: A case report  
*Zhou Z, Luo HM, Tang J, Xu WJ, Wang BH, Peng XH, Tan H, Liu L, Long XY, Hong YD, Wu XB, Wang JP, Wang BQ, Xie HH, Fang Y, Luo Y, Li R, Wang Y*
- 5744** Histopathology and immunophenotyping of late onset cutaneous manifestations of COVID-19 in elderly patients: Three case reports  
*Mazzitelli M, Dastoli S, Mignogna C, Bennardo L, Lio E, Pelle MC, Trecarichi EM, Pereira BI, Nisticò SP, Torti C*

**CORRECTION**

- 5752** Corrigendum to "Probiotic mixture VSL#3: An overview of basic and clinical studies in chronic diseases"  
*Sang LX*

**ABOUT COVER**

Editorial Board Member of *World Journal of Clinical Cases*, Fan-Zheng Meng, MD, PhD, Director, Professor, Department of Pediatrics, The First hospital of Jilin University, Changchun 130021, Jilin Province, China. mengfanzheng1972@163.com

**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 indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJCC as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Jia-Hui Li; Production Department Director: Yu-Jie Ma; 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**

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

**EDITORIAL BOARD MEMBERS**

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

**PUBLICATION DATE**

July 16, 2021

**COPYRIGHT**

© 2021 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>

## Retrospective Study

## Effects of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors on COVID-19

Xiao-Long Li, Tao Li, Qi-Cong Du, Li Yang, Kun-Lun He

**ORCID number:** Xiao-Long Li 0000-0002-3911-0448; Tao Li 0000-0001-6689-2951; Qi-Cong Du 0000-0002-1239-9659; Li Yang 0000-0001-8373-8198; Kun-Lun He 0000-0002-3335-5700.

**Author contributions:** Li XL, Li T and Du QC contribute equally to this article and should be considered as co-first authors; Li XL and Du QC performed the operation; Li XL and He KL designed this retrospective study; Du QC and Yang L wrote this paper; Li T was responsible for sorting the data.

**Institutional review board**

**statement:** The study was reviewed and approved by the Institutional Review Board of Huoshenshan Hospital, Wuhan, China (Approval No. HSSL019).

**Informed consent statement:**

Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

**Conflict-of-interest statement:** The authors declare that they have no competing interests.

**Data sharing statement:** No additional data are available.

**Xiao-Long Li**, Department of Diagnostic Radiology, PLA General Hospital, Beijing 100853, China

**Tao Li, Li Yang**, Department of Radiology, The First Medical Center of PLA General Hospital, Beijing 100853, China

**Qi-Cong Du**, Department of Diagnostic Radiology, The First Medical Center of PLA General Hospital, Beijing 100853, China

**Kun-Lun He**, Translational Medical Research Center, Key Laboratory of Ministry of Industry and Information Technology of Biomedical Engineering and Translational Medicine, Medical Innovation Research Division of Chinese PLA General Hospital, Beijing 100853, China

**Corresponding author:** Kun-Lun He, MD, Chief Physician, Translational Medical Research Center, Key Laboratory of Ministry of Industry and Information Technology of Biomedical Engineering and Translational Medicine, Medical Innovation Research Division of Chinese PLA General Hospital, No. 28 Fuxing Road, Haidian District, Beijing 100853, China.

[kunlunhe@plagh.org](mailto:kunlunhe@plagh.org)

## Abstract

## BACKGROUND

The World Health Organization reported that 28637952 people worldwide had been infected with severe acute respiratory syndrome coronavirus 2, the causative agent of coronavirus disease 2019 (COVID-19), by September 13.

## AIM

The aim was to investigate whether long-term use of renin-angiotensin-aldosterone system (RAAS) inhibitors for the treatment of hypertension aggravates the performance of COVID-19 patients with hypertension.

## METHODS

This was a retrospective analysis of lung computed tomography (CT) data and laboratory values of COVID-19 patients with hypertension who were admitted to Huoshenshan Hospital, Wuhan, Hubei Province, between February 18 and March 31, 2020. Patients were divided into two groups. Group A included 19 people who were long-term users of RAAS inhibitors for hypertension; and group B included 28 people who were randomly selected from the database and matched with group A by age, sex, basic diseases, and long-term use of other antihypertensive

**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: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Unsolicited manuscript

**Specialty type:** Cardiac and cardiovascular systems

**Country/Territory of origin:** China

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): B, B  
Grade C (Good): 0  
Grade D (Fair): 0  
Grade E (Poor): 0

**Received:** April 6, 2021

**Peer-review started:** April 6, 2021

**First decision:** April 28, 2021

**Revised:** April 30, 2021

**Accepted:** May 24, 2021

**Article in press:** May 24, 2021

**Published online:** July 16, 2021

**P-Reviewer:** Hirooka Y, Lipsitch M

**S-Editor:** Yan JP

**L-Editor:** Filipodia

**P-Editor:** Li JH



drugs. All patients underwent a series of CT and laboratory tests. We compared the most severe CT images of the two groups and the laboratory examination results within 2 d of the corresponding CT images.

## RESULTS

The time until the most severe CT images from the onset of COVID-19 was  $30.37 \pm 14.25$  d group A and  $26.50 \pm 11.97$  d in group B. The difference between the two groups was not significant ( $t = 1.01$ ,  $P = 0.32$ ). There were no significant differences in blood laboratory values, C-reactive protein, markers of cardiac injury, liver function, or kidney function between the two groups. There was no significant difference in the appearance of the CT images between the two groups. The semiquantitative scores of each involved lobe were  $11.84 \pm 5.88$  in group A and  $10.36 \pm 6.04$  group B. The difference was not significantly different ( $t = 0.84$ ,  $P = 0.41$ ).

## CONCLUSION

Chest CT is an important imaging tool to monitor the characteristics of COVID-19 and the degree of lung injury. Chronic use of RAAS inhibitors is not related to the severity of COVID-19, and it does not worsen the clinical process.

**Key Words:** COVID-19 infection; Hypertensive patients; Angiotensin-converting enzyme inhibitors; Angiotensin receptor blockers

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** We investigated whether the use of renin-angiotensin-aldosterone system inhibitors by coronavirus disease 2019 patients with hypertension aggravated the severity of pneumonia by comparing the differences in computed tomography images.

**Citation:** Li XL, Li T, Du QC, Yang L, He KL. Effects of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors on COVID-19. *World J Clin Cases* 2021; 9(20): 5462-5469

**URL:** <https://www.wjgnet.com/2307-8960/full/v9/i20/5462.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v9.i20.5462>

## INTRODUCTION

The World Health Organization reported that 28,637,952 people worldwide had been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), by September 13. Animal experiments have shown that angiotensin-converting enzyme 2 (ACE2) is abundantly expressed in lung, heart and other tissues, and coronaviruses use it as a functional receptor to invade human cells[1-3]. Inhibitors of the renin-angiotensin-aldosterone system (RAAS), namely angiotensin receptor blockers (ARBs) and ACE inhibitors, are first-line drugs for the treatment of hypertension. Some scholars believe that the use of RAAS inhibitors by COVID-19 patients with hypertension will aggravate COVID-19[4-6]. Some investigators also believe that ARBs and ACE inhibitors can inhibit both the activity of the RAAS and the progression of respiratory injury, thus playing a protective role in COVID-19 patients[7-9]. However, those assumptions are mainly based on animal experiments and lack clinical evidence. This study aimed to investigate whether the use of RAAS inhibitors by COVID-19 patients with hypertension aggravated the severity of pneumonia.

## MATERIALS AND METHODS

### Case data

COVID-19 patients with hypertension who were hospitalized in Huoshenshan



Hospital in Wuhan, Hubei Province, between February 18 and March 31, 2020 were analyzed retrospectively. COVID-19's diagnostic criteria refer to the National Health Commission's "diagnosis and treatment plan of pneumonia infected by corona virus disease 2019" (trial version 7)[10]. All patients were positive for 2019 novel coronavirus by a laboratory nucleic acid assay (real-time fluorescence polymerase chain reaction, RT-PCR) of pharyngeal swab samples. The standard of cure and discharge required a return of body temperature to normal for more than 3 d, improved respiratory symptoms, significant improvement of the exudative lesions on chest CT, and negative RT-PCR assays of throat swabs with intervals of more than 24 h. COVID-19 patients with hypertension were divided into two groups. Group A included COVID-19 patients with long-term use of ACE inhibitors or/and ARBs recorded in their medical records. Group B included COVID-19 patients with long-term use of other antihypertensive drugs (calcium channel blockers, diuretics,  $\beta$ -adrenoceptor blockers). Group A and group B were matched by age, sex, and underlying diseases, and were randomly selected from the database with a ratio of 1:1.5.

The clinical histories, laboratory test results, and epidemiological histories of the patients were collected. The patients were stratified by mild, normal, severe, and critical disease following the "diagnosis and treatment of pneumonia infected by corona virus disease 2019 (trial version 7)" criteria[10]. All patients underwent a series of CT and laboratory examinations. The most severe CT findings and laboratory results obtained in the two groups within 2 d of the CT examination were compared. Laboratory tests included routine blood counts, C-reactive protein, liver function, renal function, and myocardial injury markers, myoglobin, hypersensitive troponin I and creatine kinase (CK), and the heart failure marker B-type natriuretic peptide. The difference in severity of COVID-19 in patients with hypertension in group A and group B was determined by comparing the chest CT findings.

### Image analysis

Chest CT images were read independently by two chest radiology specialists without knowing the clinical laboratory results and patient grouping, and resolved by discussion when there were differences. COVID-19 CT signs included ground glass density (GGD), consolidation, paving stone sign (thickening of the interlobular septum and intralobular septum on the GGD background), fibrous band, air bronchus sign, thickening of small blood vessels, and pleural exudation[11]. We used a semiquantitative scoring system to evaluate the degree of lung involvement based on the number of lobes involved[12], that is, five lobes on both sides. According to the lung parenchyma volume ratio of pneumonia to lobe, the score was 0-5 points in each lobe. The score was 0 if there were no lesions. The subsequent scores, defined as percentages of the lobe volume, were one point if the lesion volume was < 5%, two points if the lesion volume was 5%-25%, three points if the lesion volume was 26%-49%, four points if the lesion volume was 50%-75%, and five points if the lesion volume was > 75%. The total score was the sum of the cumulative scores of each lung lobe. Theoretically, the pulmonary lesions scores could be between 0 and 25 points.

### Statistical analysis

Comparison of the characteristics of COVID-19 patients in the two groups who were treated with different antihypertensive drugs included age, sex, laboratory results, time from chest CT examination to onset, and chest CT score. The Kolmogorov-Smirnov test was used to determine whether the laboratory results and CT scores of the two groups were normally distributed. The values of normally distributed data were reported as means  $\pm$  SD. Between-group differences were compared by *t*-tests. Measurement data that were not normally distributed were reported as medians (M) and quartiles (Q1, Q3), and between-group differences were compared by the Wilcoxon signed-rank test. Categorical variables were reported as frequencies and percentage and between-group comparisons were performed by  $\chi^2$  or Fisher exact tests. A two-tailed *P* value of < 0.05 was statistically significant. SPSS 21.0 (SPSS Inc., Chicago, IL, United States) was used for the statistical analysis.

## RESULTS

### Clinical features

Forty-seven COVID-19 patients with hypertension were evaluated and compared, 19 in group A and 28 in group B. The clinical data are shown in Table 1. There were no significant differences in age and sex between the two groups. Initial clinical

**Table 1 Comparison of the clinical data of coronavirus disease 2019 patients treated with antihypertensive drugs**

	Group A (n = 19)	Group B (n = 28)	t- or $\chi^2$ value	P value
Age, yr	64.68 $\pm$ 8.48	63.46 $\pm$ 6.53	0.56	0.58
Gender	12 (63.2%)	18 (64.3%)	0.006	0.937
Mean Hospitalization stay, d	11.56 $\pm$ 4.82	12.83 $\pm$ 5.35	-0.80	0.429
Mechanical ventilation, n	1	2	-	1.0
Intensive care unit, n	1	2	-	1.0
Death, n	1	2	-	1.0

Data are n (%) or mean  $\pm$  SD.

symptoms included fever, cough, chest tightness, shortness of breath, fatigue, and diarrhea. The average hospital stay was 11.56  $\pm$  4.82 d in group A and 12.83  $\pm$  5.35 d in group B. The difference was not significant. In addition, there were no significant differences in the number of patients needing mechanical ventilation, the number admitted to the intensive care unit, or the number of deaths in the two groups.

### Laboratory examination

The laboratory results of the two groups are shown in Table 2. There were no significant differences in the routine blood count, C-reactive protein, myoglobin, hypersensitive troponin I, CK, B-type natriuretic peptide, liver function, and renal function between the two groups.

### CT performance

The time between the onset of disease and the CT images were 30.37  $\pm$  14.25 d in group A and 26.50  $\pm$  11.97 d in group B. The difference was not significant ( $t = 1.01$ ,  $P = 0.32$ ). The peak of the course of disease was characterized in both groups by large GGD shadow, paving stone-like changes, and consolidation accompanied by thickening of small blood vessels, and air bronchial signs. The GGD shadow, paving stone sign, and consolidation gradually decreased and the fibrous band gradually increased (Figure 1) with recovery from the disease. There were no significant between-group differences in the GGD shadow, paving stone change, consolidation, and fibrous band formation. The total cumulative lung scores (Table 3) were 11.84  $\pm$  5.88 in group A and 10.36  $\pm$  6.04 in group B. The difference was not significant ( $t = 0.84$ ,  $P = 0.41$ ).

## DISCUSSION

The results showed that in COVID-19 patients with hypertension, chronic use of ACE inhibitors and/or ARBs did not worsen the clinical process compared with taking other antihypertensive drugs. In addition, there were no significant differences in the clinical characteristics or the results of routine blood, myocardial enzyme, liver function, renal function testing, or chest CT pneumonia findings.

SARS-CoV-2 enters the cell by binding to a protein called ACE2 followed by virus replication and cell death[13]. The ACE2 protein is widely distributed in the vascular endothelial cells of many tissues of the kidneys, heart, intestine, and liver. Animal experiments show that intravenous administration of ACE inhibitors and/or ARBs upregulates ACE2, thus worsening the clinical process of COVID-19[14]. However, clinical studies have shown that ACE inhibitors and ARBs may play a protective role against pneumonia[15]. This study showed that there were no significant differences in routine blood values, C-reactive protein, myocardial enzyme activity, liver function, renal function, chest CT pneumonia characteristics, or lung CT scores between COVID-19 patients treated with ACE inhibitors and ARBs and COVID-19 patients treated with other antihypertensive drugs. The results are consistent with recent studies showing that the use of ACE inhibitors and ARBs had nothing to do with the severity of COVID-19[16,17].

As a noninvasive and rapid imaging diagnostic tool, chest CT is an important means of diagnosing COVID-19. The sensitivity of chest CT to detect COVID-19 pneumonia is 98%[18]. The main imaging findings of COVID-19 include ground glass opacity,

**Table 2 Comparison of laboratory examination results of coronavirus disease 2019 patients currently using different antihypertensive drugs**

	Group A, n = 19	Group B, n = 28	t- or U-value	P value
White blood cells	6.64 ± 3.65	6.55 ± 1.82	0.095	0.925
Neutrophils	4.47 ± 3.24	4.20 ± 1.61	0.329	0.744
Lymphocytes	1.54 ± 0.64	1.65 ± 0.40	-0.649	0.522
Neutrophil percentage	64.16 ± 10.59	62.15 ± 8.09	0.677	0.503
Lymphocyte percentage	25.64 ± 9.08	26.06 ± 6.30	-0.168	0.868
C-reactive protein	1.67 (0.97, 9.11)	2.00 (1.00, 2.00)	187	0.316
Markers of myocardial infarction	-	-	-	-
Myoglobin	13.13 ± 15.40	9.16 ± 5.96	0.657	0.532
Hypersensitive troponin	0.16 ± 0.37	0.01 ± 0.001	1.107	0.311
Creatine kinase	10.88 ± 6.64	12.71 ± 7.86	-0.742	0.463
NT-proBNP	9.67 ± 13.30	20.33 ± 23.29	-0.958	0.352
Glutamic pyruvic transaminase	34.18 ± 21.89	30.36 ± 23.85	0.493	0.625
Albumin	38.01 ± 3.97	37.12 ± 2.87	0.759	0.453
γ-glutamyl transpeptidase	65.01 ± 38.64	58.23 ± 51.38	0.421	0.677
Total bilirubin	12.63 ± 7.23	11.92 ± 4.71	0.34	0.736
Creatinine	73.86 ± 28.85	69.95 ± 15.50	0.504	0.618
Urea nitrogen	4.83 ± 2.41	4.75 ± 1.32	0.127	0.900
Glutamic oxaloacetic transaminase	24.04 ± 11.63	25.21 ± 13.46	-0.279	0.782
Procalcitonin	0.078 ± 0.081	0.047 ± 0.025	1.4	0.174

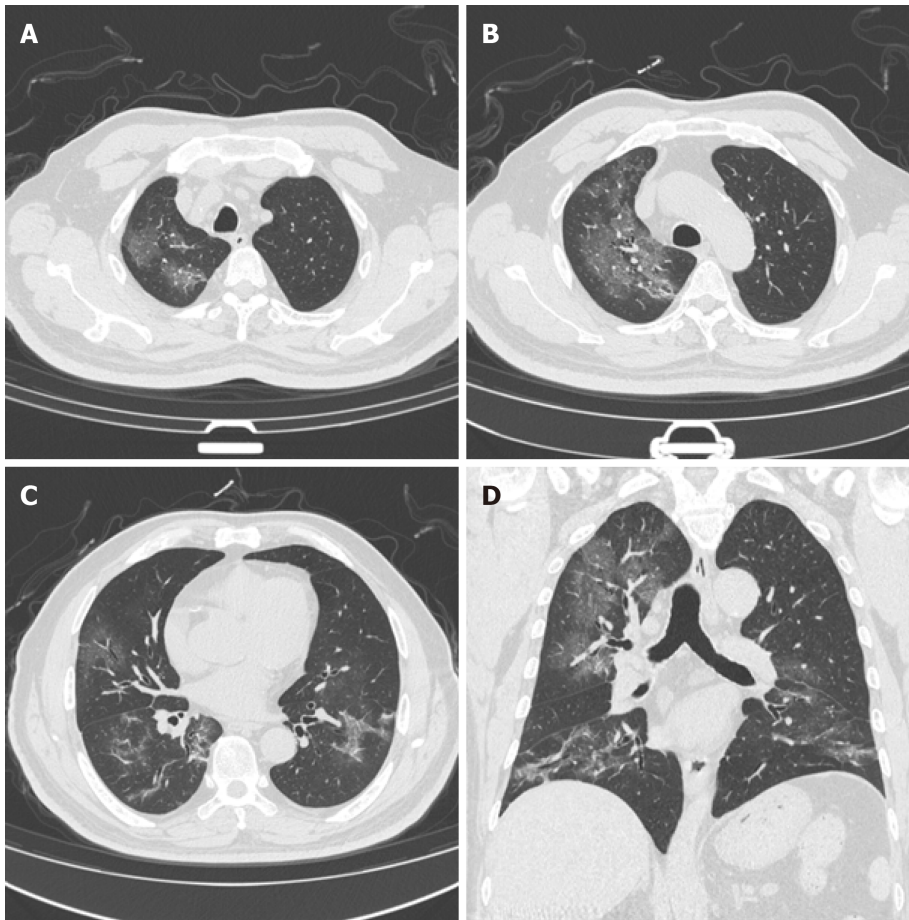
Data are mean ± SD. NT-proBNP: N-terminal-pro-brain natriuretic peptide.

**Table 3 Comparison of the computed tomography characteristics of coronavirus disease 2019 patients currently using various antihypertensive drugs, n (%)**

	Group A, n = 19	Group B, n = 28	t or $\chi^2$ value	P value
Time between CT to onset of disease in d	30.37 ± 14.25	26.50 ± 11.97	1.01	0.32
Ground glass density	13 (68.4)	21 (75)	0.25	0.62
Solid change	9 (47.4)	14 (50)	0.03	0.86
Paving stone sign	16 (84.2)	19 (67.9)	0.85	0.36
Fibrous band	17 (89.5)	17 (60.7)	3.35	0.07
CT score	11.84 ± 5.88	10.36 ± 6.04	0.84	0.41

CT: Computed tomography.

compaction, and paving stone-like changes[19]. Chest CTs can also monitor the progress and prognosis of the disease. Zhang *et al*[20] divided the course of COVID-19 into early, progressive, peak, and recovery stages. Ground glass opacity was mainly seen in the early stage and progressed to consolidation and paving stone-like changes as the disease evolved. In addition, the ground glass opacity can have a mixed form in the peak stage, and the fibrous band lesions can significantly increase in the recovery stage. Consolidation, paving stone-like lesions, and ground glass lesions decreased gradually, so the stages were not completely separated. This study showed that the most serious chest CT signs and chest CT lung-involvement scores were not significantly different between COVID-19 patients with hypertension treated with ACE inhibitors and ARBs and COVID-19 patients treated with other antihypertensive



**Figure 1** CT images from a 61-year-old male patient with a total lung score of 16 obtained 14 d after the onset of disease. A: A large ground glass density shadow of the right upper lobe; B: A large ground glass density of the right upper lobe with a small amount of flaky consolidation; C: A ground glass density shadow of the middle lobe of the right lung, paving-stone lesions of the lower lobe of the left lung, and a striped shadow in the lower lobe of both lungs; D: Coronal reconstruction images show a ground glass density shadow in the right upper lung. Both lower lungs are dominated by fibrous strips.

drugs.

This study had the following shortcomings: (1) The sample size was small and may be biased; and (2) It was a short-term retrospective study. We performed few preliminary exploratory evaluations. In addition, some patients had residual lung lesions when they met the discharge criteria. Long-term follow-up of large patient samples is still needed to monitor the outcome of pulmonary lesions.

## CONCLUSION

Overall, this study shows that the clinical process of chronic treatment of hypertensive COVID-19 patients with ACE inhibitors and ARBs did not worsen their pneumonia. Chest CT is an important imaging method to monitor the characteristics of COVID-19 and the degree of lung involvement.

## ARTICLE HIGHLIGHTS

### Research background

The World Health Organization reported that 28637952 people worldwide had been infected with severe acute respiratory syndrome coronavirus 2, the causative agent of coronavirus disease 2019 (COVID-19), by September 13.

### Research motivation

Some investigators believe that the use of RAAS inhibitors by COVID-19 patients with hypertension aggravates COVID-19. Some also believe that angiotensin receptor

blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors can inhibit the activity of the RAAS and as well as the progression of respiratory injury, thus playing a protective role in COVID-19 patients. However, those assumptions are based on animal experiments and lack clinical evidence. This study intended to resolve whether the use of RAAS inhibitors by COVID-19 patients with hypertension aggravated their degree of pneumonia.

### Research objectives

The objective was to investigate whether long-term treatment with RAAS inhibitors aggravated the performance of COVID-19 patients with hypertension.

### Research methods

This was a retrospective analysis of lung computed tomography (CT) data and laboratory values of COVID-19 patients with hypertension who were admitted to Huoshenshan Hospital, Wuhan, Hubei Province, between February 18 and March 31, 2020. Patients were divided into two groups. Group A included 19 people who were long-term users of RAAS inhibitors for hypertension and group B included 28 people who were randomly selected from the patient database and matched with group A by age, sex, other diseases, and long-term use of other antihypertensive drugs. All patients underwent a series of CT and laboratory tests. We compared the most severe CT images of the two groups and the laboratory examination results within 2 d of obtaining the corresponding CT images.

### Research results

Chest CT is an important imaging tool to monitor the characteristics of COVID-19 and the degree of lung injury. Chronic use of RAAS inhibitors was not related to the severity of COVID-19, and they did not worsen the clinical course.

### Research conclusions

The clinical responses to the long-term treatment of hypertensive COVID-19 patients with ACE inhibitors and ARBs did not worsen their pneumonia. Chest CT is an important imaging method to monitor the characteristics of COVID-19 and the degree of lung involvement. This study showed that the most serious chest CT signs and chest CT scores of lung involvement were not significantly different between COVID-19 patients with hypertension treated with ACE inhibitors and ARBs and COVID-19 patients treated with other antihypertensive drugs. Animal experiments show that intravenous administration of ACE inhibitors and/or ARBs upregulates ACE2, thus worsening the clinical course of COVID-19. Clinical studies have shown that ACE inhibitors and ARBs may play a protective role against pneumonia. This study showed that there were no significant differences in routine blood values, C-reactive protein, myocardial enzyme activity, liver function, renal function, chest CT pneumonia characteristics, or lung CT scores between COVID-19 patients treated with ACE inhibitors and ARBs and COVID-19 patients treated with other antihypertensive drugs. The results are consistent with recent studies finding that the use of ACE inhibitors and ARBs had nothing to do with the severity of COVID-19.

### Research perspectives

This study has two shortcomings: (1) The sample size was small and may be biased; and (2) It was a short-term retrospective study. We performed few preliminary exploratory evaluations. In addition, some patients had residual lung lesions when they met the discharge criteria. The best perspective for future research is to conduct that long-term follow-up of large samples to monitor the outcome of pulmonary lesions.

## REFERENCES

- 1 **Zhou P**, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD, Chen J, Luo Y, Guo H, Jiang RD, Liu MQ, Chen Y, Shen XR, Wang X, Zheng XS, Zhao K, Chen QJ, Deng F, Liu LL, Yan B, Zhan FX, Wang YY, Xiao GF, Shi ZL. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; **579**: 270-273 [PMID: [32015507](#) DOI: [10.1038/s41586-020-2012-7](#)]
- 2 **Chen L**, Liu W, Zhang Q, Xu K, Ye G, Wu W, Sun Z, Liu F, Wu K, Zhong B, Mei Y, Zhang W, Chen Y, Li Y, Shi M, Lan K, Liu Y. RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. *Emerg Microbes Infect*



- 2020; **9**: 313-319 [PMID: [32020836](#) DOI: [10.1080/22221751.2020.1725399](#)]
- 3 **Yan Y**, Shin WI, Pang YX, Meng Y, Lai J, You C, Zhao H, Lester E, Wu T, Pang CH. The First 75 Days of Novel Coronavirus (SARS-CoV-2) Outbreak: Recent Advances, Prevention, and Treatment. *Int J Environ Res Public Health* 2020; **17** [PMID: [32235575](#) DOI: [10.3390/ijerph17072323](#)]
  - 4 **Fang L**, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med* 2020; **8**: e21 [PMID: [32171062](#) DOI: [10.1016/S2213-2600\(20\)30116-8](#)]
  - 5 **Pizzolo F**, Rigoni AM, De Marchi S, Friso S, Tinazzi E, Sartori G, Stefanoni F, Nalin F, Montagnana M, Pilotto S, Milella M, Azzini AM, Tacconelli E, Marchi G, Girelli D, Olivieri O, Martinelli N. Deep vein thrombosis in SARS-CoV-2 pneumonia-affected patients within standard care units: Exploring a submerged portion of the iceberg. *Thromb Res* 2020; **194**: 216-219 [PMID: [33074107](#) DOI: [10.1016/j.thromres.2020.08.008](#)]
  - 6 **Ahamed Mim M**, Naznin Rakhi N, Saha O, Rahaman MM. Recommendation of fecal specimen for routine molecular detection of SARS-CoV-2 and for COVID-19 discharge criteria. *Pathog Glob Health* 2020; **114**: 168-169 [PMID: [32407189](#) DOI: [10.1080/20477724.2020.1765651](#)]
  - 7 **Kuba K**, Imai Y, Rao S, Gao H, Guo F, Guan B, Huan Y, Yang P, Zhang Y, Deng W, Bao L, Zhang B, Liu G, Wang Z, Chappell M, Liu Y, Zheng D, Leibbrandt A, Wada T, Slutsky AS, Liu D, Qin C, Jiang C, Penninger JM. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. *Nat Med* 2005; **11**: 875-879 [PMID: [16007097](#) DOI: [10.1038/nm1267](#)]
  - 8 **Alsufyani HA**, Alrefaie Z. Renin-Angiotensin System Implications to COVID-19 Comorbidities. *J Microsc Ultrastruct* 2020; **8**: 148-151 [PMID: [33623738](#) DOI: [10.4103/jmau.jmau\\_105\\_20](#)]
  - 9 **Guo YR**, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, Tan KS, Wang DY, Yan Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. *Mil Med Res* 2020; **7**: 11 [PMID: [32169119](#) DOI: [10.1186/s40779-020-00240-0](#)]
  - 10 **National Health Commission of the People's Republic of China**. Notice on the issuance of New Coronavirus pneumonia diagnosis and treatment plan (trial 7th ed). March 3, 2020. [cited 1 April 2021]. Available from: <http://www.nhc.gov.cn/xcs/zhengcwj/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml>
  - 11 **Salehi S**, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19) imaging reporting and data system (COVID-RADS) and common lexicon: a proposal based on the imaging data of 37 studies. *Eur Radiol* 2020; **30**: 4930-4942 [PMID: [32346790](#) DOI: [10.1007/s00330-020-06863-0](#)]
  - 12 **Pan F**, Ye T, Sun P, Gui S, Liang B, Li L, Zheng D, Wang J, Hesketh RL, Yang L, Zheng C. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). *Radiology* 2020; **295**: 715-721 [PMID: [32053470](#) DOI: [10.1148/radiol.2020200370](#)]
  - 13 **Hoffmann M**, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* 2020; **181**: 271-280. e8 [PMID: [32142651](#) DOI: [10.1016/j.cell.2020.02.052](#)]
  - 14 **Wan Y**, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J Virol* 2020; **94** [PMID: [31996437](#) DOI: [10.1128/JVI.00127-20](#)]
  - 15 **Tan WSD**, Liao W, Zhou S, Mei D, Wong WF. Targeting the renin-angiotensin system as novel therapeutic strategy for pulmonary diseases. *Curr Opin Pharmacol* 2018; **40**: 9-17 [PMID: [29288933](#) DOI: [10.1016/j.coph.2017.12.002](#)]
  - 16 **Mehra MR**, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. *N Engl J Med* 2020; **382**: e102 [PMID: [32356626](#) DOI: [10.1056/NEJMoa2007621](#)]
  - 17 **Mehta N**, Kalra A, Nowacki AS, Anjewierden S, Han Z, Bhat P, Carmona-Rubio AE, Jacob M, Procop GW, Harrington S, Milinovich A, Svensson LG, Jehi L, Young JB, Chung MK. Association of Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Testing Positive for Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol* 2020; **5**: 1020-1026 [PMID: [32936273](#) DOI: [10.1001/jamacardio.2020.1855](#)]
  - 18 **Fang Y**, Zhang H, Xie J, Lin M, Ying L, Pang P, Ji W. Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. *Radiology* 2020; **296**: E115-E117 [PMID: [32073353](#) DOI: [10.1148/radiol.2020200432](#)]
  - 19 **Chung M**, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, Cui J, Xu W, Yang Y, Fayad ZA, Jacobi A, Li K, Li S, Shan H. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). *Radiology* 2020; **295**: 202-207 [PMID: [32017661](#) DOI: [10.1148/radiol.2020200230](#)]
  - 20 **Zhang H**, Liu X, Yu P, Cheng M, Wang W, Sun Y, Zeng B, Fan B. Dynamic CT assessment of disease change and prognosis of patients with moderate COVID-19 pneumonia. *J Xray Sci Technol* 2020; **28**: 851-861 [PMID: [32741802](#) DOI: [10.3233/XST-200711](#)]



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](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

