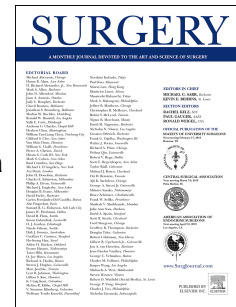


# Journal Pre-proof

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Jinpeng Li, Rongfen Gao, Gaosong Wu, Xiaolin Wu, Zeming Liu, Hongjing Wang, Yihui Huang, Zhenyu Pan, Jincao Chen, Xiaohui Wu



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## Clinical characteristics of emergency surgery patients-infected COVID-19

### pneumonia in Wuhan, China

Jinpeng Li<sup>1,2#</sup>, Rongfen Gao<sup>4#</sup>, Gaosong Wu<sup>2#</sup>, Xiaolin Wu<sup>1#</sup>, Zeming Liu<sup>5#</sup>,  
Hongjing Wang<sup>6</sup>, Yihui Huang<sup>5</sup>, Zhenyu Pan<sup>3\*</sup>, Jincao Chen<sup>1\*</sup>, Xiaohui Wu<sup>1\*</sup>

- 1) *Department of Neurosurgery, Zhongnan Hospital of Wuhan University, Wuhan, 430071, China*
- 2) *Department of Thyroid and Breast Surgery, Zhongnan Hospital of Wuhan University, Wuhan, 430071, China*
- 3) *Department of Orthopedic Surgery, Zhongnan Hospital of Wuhan University, Wuhan, 430071, China*
- 4) *Department of Rheumatology and Immunology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China*
- 5) *Department of Plastic Surgery, Zhongnan Hospital of Wuhan University, Wuhan, 430071, China*
- 6) *Department of Medical Affairs, Gansu Provincial Hospital, Lanzhou, Gansu, China*

#: equal contribution

\*: Co-corresponding authors

Address correspondence to:

Xiaohui Wu, MD, PhD

Email: wuxiaohui1971@sina.com

Department of Neurosurgery Zhongnan Hospital of Wuhan University, 169 Donghu Road, Wuhan, 430071, PR China

TEL: +8618971569409

Or

Jincao Chen, MD, PhD

Email: chenjincao@hotmail.com

Department of Neurosurgery Zhongnan Hospital of Wuhan University, 169 Donghu Road, Wuhan, 430071, PR China

TEL: +8613971091714

Or

Zhenyu Pan, MD, PhD

Email: soloistp@126.com

Department of Orthopedic Surgery Zhongnan Hospital of Wuhan University, 169 Donghu Road, Wuhan, 430071, PR China

TEL: +8615337200318

**Abstract**

**Objective:** We aimed to investigate clinical symptom and epidemiological features of ESP-infected COVID-19

**Summary Background Data:** Almost one million of 2019 novel coronavirus disease (COVID-19) patients were diagnosed in the world wide from December 2019 to now. Thousands of emergency operations were carried out in the interim. However no one focused on the clinical symptom of emergency surgery patients (ESP) with COVID-19 pneumonia.

**Methods:** Retrospective cohort study of 164 ESP with or without COVID-19 pneumonia in Zhongnan Hospital of Wuhan University in Wuhan, China, from January 1 to January 20, 2020. The final date of follow-up was February 5, 2020. The associated clinical, laboratory, epidemiological, demographic, radiological and outcome data were collected and analyzed.

**Results:** Of 164 ESP, the median age was 41 years old (interquartile range (IQR), 29-89) and 136 (82.9%) were women. Associated main clinical symptom including fever (93 [56.7%]), dry cough (56 [34.2%]), fatigue (86 [52.4%]), nausea (78 [47.6%]) and dizziness (77 [47%]). Of 54 ESP-infected COVID-19 patients, the median age was 46 (IQR: 25-89) and 45 (83.3%) were women. The pathological clinical symptoms including fever (54 [100%]), fatigue (48 [88.9%]), nausea (52 [96.3%]), dizziness (46 [85.2%]) and dry cough (44 [81.5%]) were investigated; the lymphopenia ( $0.37 \times 10^9/L$  [IQR: 0.23-0.65]) and increased C-reactive protein ( $24.7 \times 10^9/L$  [IQR: 13.57-38]) were observed. The preoperative fever and postoperative fever in ESP with or without COVID-19 pneumonia were analyzed in this study. Of 54 ESP with COVID-19 patients, 15 (27.8%) patients showed preoperative fever, 54 (100%) had the postoperative fever; Of 110 non-COVID-19 of ESP, 5 (4.5%) patients had preoperative fever, 31 (28.2%) patients had the postoperative fever. The fever in ESP with

COVID-19 lasted more than 7 days, markedly exceeded the non-COVID-19 patients (lasted about 3 days). Furthermore, 43 health care workers were infected from exposed to ESP with COVID-19 pneumonia.

**Conclusion:** In our study, the clinical symptoms of ESP-infected COVID-19 displayed marked differences from those reported common COVID-19 pneumonia cases. Additionally, the health care workers were confirmed to expose great risk in ESP with COVID-19 pneumonia. Management guidelines of ESP were described in our paper.

**Key words:** COVID-19, Emergency surgery patients, Clinical symptom, health care workers

## Introduction

2019 novel coronavirus disease (COVID-19), a cluster of acute respiratory illness, break out in Wuhan, Hubei Province, China in December 2019<sup>1-3</sup>. Almost one million of COVID-19 patients were diagnosed in the world wide from December 2019 to now. In this pandemic, not only China but also other country including Japan, Korea, Italy and Iran underwent the series outbreak<sup>4</sup>. A recent study reported that COVID-19 patients' clinical symptoms mainly include fever, dyspnea, nonproductive cough, fatigue, myalgia, normal or decreased leukocyte counts, and radiographic evidence of pneumonia<sup>4</sup>. Zhu et, al, analyzed the full-genome sequencing of COVID-19 that is a variant from the beta-coronaviruses associated with Middle East respiratory syndrome (MERS) and human Severe Acute Respiratory Syndrome (SARS)<sup>5</sup>. Furthermore, the proved hospital-related transmission in COVID-19 pneumonia has been reported. Of 138 hospitalized COVID-19 pneumonia patients, 26% of patients needed ICU care and the mortality was 4.3%<sup>6</sup>.

Deepali et al. reported one patient died in SARS after liver transplanting, that followed infection of several health-care workers and family<sup>7</sup>. The emergency surgery was thought to be extremely dangerous in Ebola epidemic in Africa<sup>8</sup>. Chen et al. reported the clinical characteristics of caesarean section with COVID-19 infection and denied the risk of vertical transmission<sup>9</sup>. In addition, stringent infection control procedure for operations in period of 2003 SARS was drawn out protecting the health care workers and control intrahospital transmission, and significantly decreased the intrahospital transmission of SARS in the operating room complex<sup>10,11</sup>. Although these reports investigated the risk for the healthcare workers and also made the stringent relative procedure, no one focused on the risk of emergency surgery patients (ESP) with COVID-19 pneumonia. The current study analyzed the clinical symptom of these patients including perioperative patients and postoperative patients. Furthermore the

relevant risk for healthcare workers in ESP was clearly described.

## **Methods**

### **Study design and patients**

All postoperative patients with COVID-19 pneumonia (PPCP) were collected from Zhongnan Hospital of Wuhan University from Jan 1, 2020 to 21. The final date of follow-up was February 5, 2020. All of ESP-infected COVID-19 were confirmed by World Health Organization interim guidance. This study obtained the Oral consent from patients, Zhongnan Hospital, Wuhan, Hubei Province, China. All 54 ESP-infected COVID-19 was proved by use of quantitative RT-PCR (qRT-PCR) on samples from the respiratory tract. In addition, this research was confirmed by institutional ethics Committee of Zhongnan Hospital of Wuhan University (approval number 2020068).

### **Data collection**

In this study, the clinical or epidemiological records, chest CT scans and laboratory findings were obtained from Information Center of Medical Service Zhongnan Hospital of Wuhan University. The data were reviewed by surgeon of Neurosurgery, Gynaecology and Obstetrics and Thyroid and Breast Surgery. All of patients in our case series had the surgical indication. The postoperative patients were transferred into their department. Then the patients, combined with COVID-19 pneumonia, were transferred into isolation ward. Collected throat swab samples were used to detect the COVID-19 pneumonia following Chinese Center for Disease Control and Prevention (CDC) recommended Kit (BioGerm, Shanghai, China), WHO guidelines for qRT-PCR<sup>9</sup>.

The throat swab samples from patients with COVID-19 pneumonia were collected and immediately extracting 2019-nCoV RNA. All infected patients were collected the samples from throat swab at least three times. The specific steps of

collection of sample based on Peng's reported<sup>9</sup>. The RT-PCR assay was performed using a 2019-nCoV nucleic acid detection kit according to the manufacturer's protocol (Shanghai bio-germ Medical Technology CoLtd). The process also according to Peng's reported<sup>9</sup>.

### Statistical analysis

The data for fevers (figure 1) analyzed by ANOVA followed by Tukey's analysis. One-way analysis of variance followed by Tukey's multiple comparison test was used to determine significance, which was defined as  $P < 0.05$ . The Mann-Whitney U test was used to analysis of median (IQR); categorical variables were expressed as number (%), median or IQR and compared by  $\chi^2$  test or Fisher's exact test between ESP with COVID-19 and non-COVID-19 groups.  $P < 0.05$  was considered as significance. Statistical analysis was performed by SPSS, version 25.0.

## Results

### Clinical characteristics of ESP-infected COVID-19 pneumonia

We collected 164 ESP in Zhongnan Hospital of Wuhan from January 1 to January 21. Of these patients, the median age was 41 years (IQR, 29-89), 136(82.9%) were women, 28(17.1%) were men (**Table 1**). Women outnumber men because of lots of cesarean section were analyzed in our study. All the ESP-infected COVID-19 pneumonia patients had a close history of epidemic contact (**Table 1**). Of the 164 ESP, The common clinical symptoms at onset of illness including fever (93 [56.7%]), fatigue (86 [52.4%]), nausea (78 [47.6%]), dizziness (77 [47%]), dry cough (56 [34.2%]), dyspnea (20 [12.2%]), vomiting (18 [11%]), headache (15 [9.1%]) and diarrhea (10 [6.1%]) (**Table 1**).

When compared with non-COVID-19 (n=110), the ESP-infected COVID-19 (n=54) showed more morbidity of fever (54 [100%]), dry cough (44 [81.5%]), fatigue (48 [88.9%]), nausea (52 [96.3%]) and dizziness (46 [85.2%]) (**Table 1**).

We analyzed the preoperative fever and postoperative fever in ESP with or without COVID-19 pneumonia (**Table 1**). Of 93 (56.7%) ESP with fever, 20 (12.2%) patients had the preoperative fever, 85 (51.8%) patients displayed postoperative fever; Of 54 ESP-infected COVID-19 pneumonia, 15 (27.8%) patients showed preoperative fever, 54 (100%) had the postoperative fever; Of 110 non-COVID-19 of ESP, 5 (4.5%) patients had preoperative fever, 31 (28.2%) patients had the postoperative fever. These data suggested that more ESP-infected COVID-19 displayed the clinical symptom of fever than non-COVID-19 patients. Furthermore, we analyzed the duration of fever between them, the results showed that the fever in ESP with COVID-19 lasted more than 7 days, markedly exceeded the non-COVID-19 patients (lasted about 3 days) (**Figure 1 A**). The level of fever in ESP with COVID-19 was also higher than non-COVID-19 patients (**Figure 1B**). Additionally, more clinical symptoms of dry cough, fatigue, nausea and dizziness in ESP-infected COVID-19 were observed when compared with non-COVID-19 patients. Interestingly, of 54 ESP-infected COVID-19, the incidence of dry cough, fatigue, nausea and dizziness in our study was higher than the reported common COVID-19 pneumonia cases<sup>6,12</sup>.

### **Imaging features of ESP-infected COVID-19 pneumonia**

The ESP main originated from gynaecology and obstetrics (72 [43.9]), neurosurgery (16 [9.8]), orthopaedic surgery (15 [9.2]), gastrointestinal surgery (20 [12.2]), cardio-thoracic surgery (8 [4.9]), urology surgery (9 [5.5]) and hepatobiliary surgery (24 [14.6]) in our research (**Table 2**). We first checked whether the COVID-19 pneumonia was excluded in ESP before operation through the chest CT scans and throat swab of nucleic acid detection. Only 20% patients were screened in the preoperative. 80% ESP with COVID-19 was confirmed in the postoperative. Of 54 ESP with COVID-19 patients, all of them



displayed bilateral involvement of chest CT scan (**Figure 2 A-C**).

### **Laboratory parameters in ESP-infected COVID-19 pneumonia**

The blood counts of patients from laboratory tests displayed the significant difference in the lymphocyte and C-reactive protein concentration between ESP-infected COVID-19 and non COVID-19 pneumonia, and no significant difference in neutrophil, monocyte, ALT, AST, BUN and ACR (**Table 3**). The ESP-infected COVID-19 patients showed lymphopenia (0.37[0.23-0.65]), increased C-reactive protein (24.7[13.57-38]). Of 110 ESP without COVID-19, almost all of the patients showed normal lymphocyte and C-reactive protein. These data is same as reported finding for COVID-19 pneumonia<sup>12</sup> (**Table 3**).

### **Hospital-Related Infection**

Of 164 ESP, 54 patients were assumed to be infected in hospital after the emergency surgery. In addition, 43 health care workers were infected by contacting the associated ESP-infected COVID-19 patients. Of the 54 hospitalized patients, 29 (53.7%) patients were from obstetrics and gynecology, 7 (13%) patients were from hepatobiliary surgery, 4 (7.4%) patients were from gastrointestinal surgery, 7 (13%) patients were neurosurgery, 2 (3.7%) patients were from orthopedic surgery, 3 (5.6%) patients were from urology surgery (**Table 2**). Of 43 infected health care workers, almost them were from operation room (anesthesiologist and nurses) and associated surgery departments. All of infected health care workers were directly contacted the ESP with COVID-19 patients, and infected in the January. The number of health care workers who infected in ESP-infected COVID-19 pneumonia significantly decreased after January.

## Discussion

In this research, we reported the potential risks of ESP-infected COVID-19 pneumonia for the clinician and other common patients. Almost the emergency patients could not be carried out systematically examination especially detection of COVID-19 pneumonia and chest CT scans. Here we summarized the clinical symptoms of emergence patients who infected COVID-19 pneumonia. 1) In 164 emergency patients, 54 patients were diagnosed as COVID-19 pneumonia after operation. Median age for 46 years (IQR, 25-89), 136 (82.9%) patients were women and 28 (17.1%) patients were men. 2) The fever in postoperative patients with COVID-19 pneumonia continued over 7 days, more than common postoperative patients. In addition, for ESP-infected COVID-19, 81.5% patients displayed cough, 88.9% patients showed fatigue, 96.3% had nausea, 85.2% showed dizziness. 3) All of ESP-infected COVID-19 had the bilateral or unilateral ground-glass opacities in lung CT. 4) Routine blood test displayed the lymphopenia and increased CRP. 5) Strong insidious and infectious risk for clinician.

Fever is the commonest postoperative complications, including physiological and pathological pyrexia, seen in medical and surgical settings<sup>13</sup>. Normally, the pathological fever originates in postoperative infection<sup>13</sup>. The physiological pyrexia is derived from digestion of necrosis material, characterized by short-term fever, slight fever and early stage<sup>14</sup>. As we all known, the slight fever is an important clinical symptom in the early stage of COVID-19 pneumonia. Chen et al. reported that 70% patients' body temperatures fluctuated within the range of 36.5 – 38.8°C, the average of all of the patients' body temperatures was 38.3°C. Such important phenomenon was also investigated by a recent research. Although many research showed the slight fever existence in COVID-19 pneumonia and postoperative patients, no one identified the difference between them. In our this study, we analyzed 54 ESP-infected COVID-19 pneumonia,

including 29 patients with cesarean section, 7 patients with neurosurgery, 4 patients with gastrointestinal surgery, 2 patients with orthopaedic trauma surgery, 2 patients with cardio-thoracic surgery, 3 patients with urology surgery, 7 patients with hepatobiliary surgery. All of ESP with COVID-19 patients displayed postoperative fever, the range of body temperature 37.1-39.6°C, the duration was 1-2 week. Of 110 ESP, 31 (28.2%) patients showed lighter fever (range of body temperature 36.3-38.0°C). The duration was less than 4 days. Based on our data, we found different both trend and duration in fever between ESP with or without COVID-19 pneumonia. It is an important phenomenon for us to identify the COVID-19 pneumonia in the postoperative patients. Also we think this point will be the early warning for ESP-infected COVID-19 on now and in the future.

Immunosuppressive state was thought to be a common phenomenon in postoperative patients<sup>15,16</sup>, and will be susceptible to infect severe pneumonia and respiratory pathogens. Jessica et al. reported that cataract surgery was safety in patients who detected negative of Ebola virus in ocular fluid specimens<sup>17</sup>. In Ebola epidemic in Africa, the emergency surgery was thought to be extremely dangerous<sup>8</sup>. In addition, during severe acute respiratory syndrome (SARS) in 2003, Deepali et al. reported one patient died in SARS after liver transplant, that followed infection of several health-care workers and family<sup>7</sup>. A resent research analyzed the clinical characteristics of caesarean section with COVID-19 infection and denied the risk of vertical transmission. Although lots of cases in the virus pandemic, there was no reports focused on the perioperative or postoperative patients especially during COVID-19 pneumonia. Our study not only investigated the clinical manifestation in ESP-infected COVID-19 including fever, cough, fatigue, nausea, dizziness and so on, but also described countermeasures and potential risks for the health care workers. Of 54 ESP-infected COVID-19, all of patients showed longer and higher postoperative

fever, also 81.5% patients with cough, 88.9% patients with fatigue, 96.3% patients with nausea and 85.2% patients with dizziness were observed. These associated clinical characteristic finding showed huge difference with reported cases for common COVID-19. The reason may be from the by-effects of surgery and anesthetics. In addition, all of them showed multiple patchy ground-glass shadows in lungs. Suggesting that we can make the preliminary clinical diagnose in the period of COVID-19 pneumonia even in the future for the ESP with COVID-19. From a recent research for COVID-19 pneumonia patients, of 1099 patients, only 43.8% of them had a fever<sup>18</sup>, less than our study for ESP-infected COVID-19 (100% with fever); 56.4% showed the ground-glass opacity in lung, less than our study (100%); 83.2% of them had lymphocytopenia which was also less than our investigation (100%). One reason for this phenomenon may be the immunosuppressive state or postoperative stress response in patients. Furthermore, 7 (13%) mortality in our report, obviously higher than those reported cases in China, also proves our hypothesis.

Another main focus of this research was to observe the huge risk of ESP-infected COVID-19 pneumonia for the health care workers. In the early stage of COVID-19 pneumonia, the research reported the characteristics of human transmission<sup>4,18</sup>. However, no one concentrated for the ESP in this meantime. In our study, we analyzed all of ESP (164 patients) from January 1 to January 21, 2020, the final date of follow-up was February 5, 2020 in our hospital. We found that these patients had a great threat for health care workers by the February 5. 43 of health care workers, including surgeon, anesthesiologist and associate nurse, were infected by ESP. Two of them were treated in intensive care unit (ICU) because of serious illness. One reason for this phenomenon is that incomplete preoperative examination especially lack of CT scans in lung and nucleic acid detection of COVID-19 pneumonia was

carried out in that time. In addition, lack of self-protection not only in gears (N-95 surgical mask and medical disposable chemical protective safety suit) but also in consciousness was a critical cause. In addition, lack of the relative knowledge of respiratory infectious diseases for surgeons is another reasons, conversely, no health care workers of respiratory, contagion section and ICU were infected in this epidemic situation, which proved our hypothesis. Our report aims to remind the health care workers especially take care of ESP to keep their eyes on the COVID-19 pneumonia even in the later stages of work.

Some limitations present in our study, first this study is limited by the short time of cases review (from January 1, 2020 to February 5, 2020). Second, the data statistics of health care workers-infected COVID-19 was incomplete. Third, we did not describe the management for ESP when they are accepted outpatient consultations. Here, we added the sketch of consultation for the ESP according to COVID-19 pneumonia guide of Hubei Provincial Health Council (**Figure 3**). In this process, all surgeon need to be three-level protection when they take care of emergency surgery (**Figure 3**).

In summary, ESP-infected COVID-19 pneumonia has a great threat for health care workers. This paper expounded the typical clinical symptom and laboratory examination, and provided directly evidence to identify the ESP-infected COVID-19. We believe that this study may give lots of assistance to health care workers in hospital.

### **Contributors**

JL performed most of the study and participated in writing the original manuscript. RG supervised the study and was involved in writing the results and discussion. GW, XW involved in collecting original data and discussion. HW participated in data analysis. XW proposed the original idea and design of the study, supervised the study, and edited the manuscript. JC provided intellectual input and involved

in discussion. ZP participated in original idea and discussion.

### COI/Disclosure:

We declare no competing interests.

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## Figure legends

**Figure 1. Dynamic Profile of postoperative fever for the ESP with or without COVID-19 pneumonia infection.** **A.** The duration of postoperative fever between them. **B.** The temperature of ESP with or without COVID-19 pneumonia infection. Emergency surgery patients were designated as ESP; 2019 novel coronavirus disease was designated as COVID-19 in the Figure. \*  $P<0.05$ , \*\*  $P<0.01$ .

**Figure 2. Transverse chest CT images. A-C.** Chest computed tomographic images of ESP-infected COVID-19, displayed marked ground glass opacity in both lungs. **D-F.** Transverse chest CT images of non COVID-19 infection of ESP. Emergency surgery patients was designated as ESP; 2019 novel coronavirus disease was designated as COVID-19 in the Figure. \*  $P<0.05$ , \*\*  $P<0.01$ .

**Figure 3. Administration guide for emergency surgery.** All the emergency surgery had to receive the COVID-19 investigation excepted critically ill patients (need to be rescued first). All the positive or suspected positive or critically ill patients were operated in negative pressure operating room. Additionally, the surgeons were performed to three-level protection. All of the patients were required to re-check the COVID-19 pneumonia after operation.



**Table 1** Clinical Characteristics of ESP with or without COVID-19 Pneumonia

Clinical Characteristics	NO.(%)			P Value
	Total (N=164)	COVID-19 (N=54)	Non-COVID-19 (N=110)	
<b>Age, median, (IQR), y</b>	41(29-89)	46(25-89)	39(29-87)	0.023
<b>Sex</b>				
<b>Male</b>	28(17.1)	9(16.7)	19(17.2)	0.744
<b>Female</b>	136(82.9)	45(83.3)	91(82.7)	
<b>Epidemiological history</b>		yes		
<b>Fever</b>	93(56.7)	54(100)	39(35.5)	<0.0001
<b>Preoperative fever</b>	20(12.2)	15(27.8)	5( 4.5)	0.0233
<b>Postoperative fever</b>	85(51.8)	54(100)	31(28.2)	<0.0001
<b>Dry cough</b>	56(34.2)	44(81.5)	12(11)	<0.0001
<b>Fatigue</b>	86(52.4)	48(88.9)	38(34.5)	0.82
<b>Nausea</b>	78(47.6)	52(96.3)	26(23.6)	<0.0001
<b>Dizziness</b>	77(47.0)	46(85.2)	31(28.2)	<0.0001
<b>Dyspnea</b>	20(12.2)	11(20.4)	9( 8.2)	0.0342
<b>Vomiting</b>	18(11.0)	6(11.1)	12(10.9)	0.899
<b>Headache</b>	15( 9.1)	4( 7.4)	11(10.0)	0.639
<b>Diarrhea</b>	10( 6.1)	4( 7.4)	6( 5.5)	0.771
<b>Death</b>	10	8	4	<0.0001

**Abbreviations:** ESP, emergency surgery patients; COVID-19, 2019 novel coronavirus disease; IQR, interquartile range. P values indicate differences between ESP-infected COVID-19 and non-COVID-19 of ESP. P < .05 was considered statistically significant.

**Table 2** Surgical Intervention Departments in ESP with or without COVID-19

Department	No.(%)	
	Total (N=164)	COVID-19 (N=54)
Gynaecology and Obstetrics	72(43.9)	29(53.7)
Neurosurgery	16(9.8)	7(13)
Orthopaedic Surgery	15(9.2)	2(3.7)
Gastrointestinal Surgery	20(12.2)	4(7.4)
Cardio-Thoracic Surgery	8(4.9)	2(3.7)
Urology Surgery	9(5.5)	3(5.6)
Hepatobiliary Surgery	24(14.6)	7(13)

Abbreviations: COVID-19, 2019 novel coronavirus disease.

**Table 3** Laboratory Findings of ESP with or without COVID-19 Pneumonia

Item	Median(IQR)			
	Normal Range	COVID-19	Non-COVID-19	P value
White blood cell count ( $\times 10^9$ cells/L)	3.5-9.5	7.4(5.95-8.96)	9.13(6.9-11.4)	0.026
Red blood cell count ( $\times 10^{12}$ cells/L)	3.5-5.5	3.7(3.2-4.2)	3.8(3.5-4.2)	0.612
Neutrophil count ( $\times 10^9$ cells/L)	1.8-6.3	6.24(4.94-8.38)	6.8(5.18-8.96)	0.677
Lymphocyte count ( $\times 10^9$ cells/L)	1.1-3.2	0.37(0.23-0.65)	1.4(0.98-1.72)	<.0001
Monocyte count ( $\times 10^9$ cells/L)	0.1-0.6	0.44(0.28-0.57)	0.52(0.43-0.65)	0.0102
C-reactive protein (mg/L)	0-8	24.7(13.57-38)	7.85(3.15-56)	0.0314
ALT (U/L)	0-40	34(12-71)	13(9-20)	<.0001
AST (U/L)	0-40	29(22-64)	20(16-26)	<.0001
BUN (mmol/L)	2.9-7.5	5.53(3.37-7.36)	3.7(2.9-5.3)	0.085
CREA (umol/L)	30-110	62.9(48.2-71.9)	55.6(47.8-71.7)	0.483

**Abbreviations:** ESP, emergency surgery patients; COVID-19, 2019 novel coronavirus disease; IQR, interquartile range; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CREA, creatinine. P values indicate differences between ESP-infected COVID-19 and non-COVID-19 of ESP. P < .05 was considered statistically significant.

Fig. 1

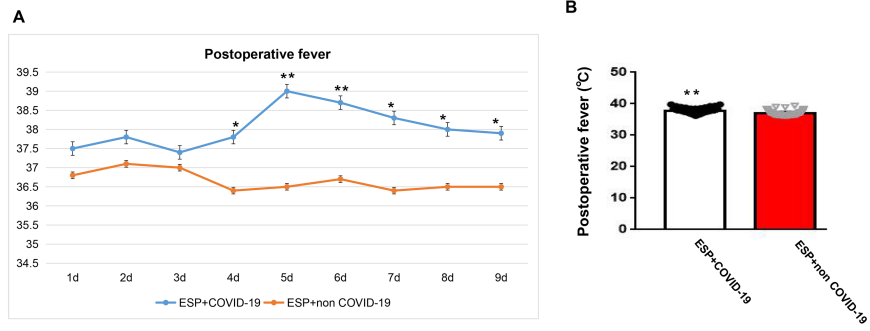


Fig. 2

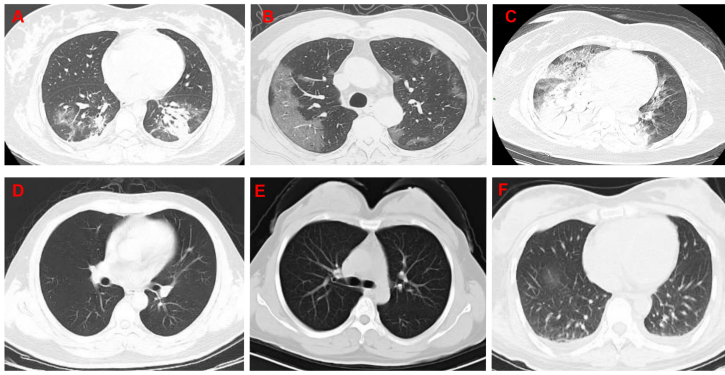
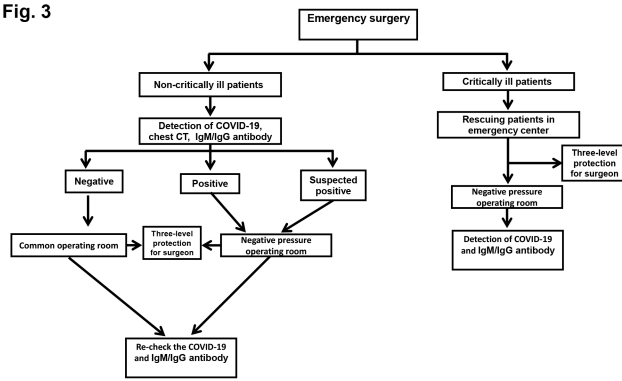


Fig. 3



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In our study, the clinical symptoms of ESP-infected COVID-19 displayed marked differences from those reported common COVID-19 pneumonia cases and the health care workers were confirmed to expose great risk in ESP with COVID-19 pneumonia. The importance of this findings is these will provide early warning for health care workers who take care of the ESP-infected COVID-19 patients on now and in the future.